CLINICAL STUDY REPORT

Final Clinical Study Report: Study CO40016, (IPATunity130). A Double-Blind, Placebo-Controlled, Randomized Phase III Study of Ipatasertib in Combination with Paclitaxel as a Treatment for Patients with *PIK3CA/AKT1/PTEN*-Altered, Locally Advanced or Metastatic, Triple-Negative Breast Cancer or Hormone Receptor-Positive, HER2-Negative Breast Cancer. Report No. 1120396. August, 2023.

Study Sponsors	F. Hoffmann-La Roche Ltd.
Principal Investigator and Affiliation: Nicholas Turner, MA, MRCP, PhD Breast Unit, The Royal Marsden NHS Foundation Trust London, UK. Breast Cancer Now Research Centre The Institute of Cancer Research London, UK. Rebecca Dent, MSc, MD, FRCP National Cancer Centre; Medical Oncology, 11 Hospital Drive, 0, Singapore, Singapore	**Study Dates:** First Patient Enrolled: 06-Jan-2018 Data cutoff Efficacy analysis: 30-Oct-2021 Safety analysis: 21-Mar-2023 Last Patient Last Visit: 04-Jan-2023
Trial Phase: Phase III	**Indications:** • Triple Negative Breast Cancer • Hormone Receptor Positive, HER2-Negative Breast Cancer

Clinical Study Report Approval Date: See electronic signature on the last page of this document

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GCP Compliance: This study was conducted in accordance with the principles of GCP.

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Description
ADA	Anti-drug antibody
AE	Adverse event
AESI	Adverse event of special interest
Akt	Protein kinase B
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ATP	Adenosine triphosphate
BAR	Bioanalytical report
$C_{1\text{-}3hr}$	Plasma concentration at 1–3 hours post ipatasertib dose
$C_{2–4hr,ss}$	Plasma concentration at 2–4 hours post ipatasertib dose at steady state
$C_{min,ss}$	Trough concentration at steady state
CBR	Clinical benefit rate
CCOD	Clinical cutoff date
COVID-19	Coronavirus disease 2019
CR	Complete response
CRF	Case Report Form
CSR	Clinical study report
DOR	Duration of response
ECG	Electrocardiogram
ECOG PS	Eastern Cooperative Oncology Group Performance Status
eCRF	Electronic Case Report Form
EORTC QLQ-C30	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30
GCP	Good Clinical Practice
geoCV%	Geometric mean coefficient of variations
GHS	Global health status
HER2–	Human epidermal growth factor receptor 2-negative
HR	Hazard ratio
HRQoL	Health-related quality of life
HR+	Hormone receptor-positive
ICF	Informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
iDMC	Independent Data Monitoring Committee

iEC	Independent ethics committee
IMP	Investigational medicinal product
Ipat	Ipatasertib
IRB	Institutional Review Board
ITT	Intent-to-treat
KM	Kaplan-Meier
LPLV	Last patient last visit
MedDRA	Medical Dictionary for Regulatory Activities
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
ORR	Objective response rate
OS	Overall survival
Pac	Paclitaxel
Pbo	Placebo
PFS	Progression-free survival
PI3K	Phosphoinositide 3-kinase
PI3KCA	Phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit, alpha
PK	Pharmacokinetic
PR	Partial response
PT	Preferred Term
PRO	Patient-reported outcome
PTEN	Phosphatase and tensin homolog
QoL	Quality of life
QTL	Quality tolerance limit
RECIST	Response Evaluation Criteria in Solid Tumors
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SGOT	Serum glutamic-oxaloacetic transaminase
SGPT	Serum glutamic-pyruvic transaminase
SOC	System Organ Class
TNBC	Triple-negative breast cancer
ULN	Upper limit of normal

ETHICS

INDEPENDENT ETHICS COMMITTEE AND/OR INSTITUTIONAL REVIEW BOARD

- The protocol, protocol amendments, informed consent form (ICF), Investigator Brochure, and other relevant documents (e.g., advertisements) were submitted to an Institutional Review Board (IRB)/Independent Ethics Committee (IEC) by the investigator and reviewed and approved by the IRB/IEC before the study was initiated.
- Any amendments to the protocol required IRB/IEC approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study patients.

ETHICAL CONDUCT OF THE STUDY

This study was conducted in accordance with the protocol and with the following:

- Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines
- Applicable International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines
- Applicable laws and regulations

PATIENT INFORMATION AND CONSENT

- The investigator or his/her representative explained the nature of the study to the patient or his/her legally authorized representative and answered all questions regarding the study.
- Patients were informed that their participation was voluntary. Patients or their legally authorized representative were required to sign a statement of informed consent that met the requirements of 21 Code of Federal Regulations 50, local regulations, ICH guidelines, Health Insurance Portability and Accountability Act requirements, where applicable, and the IRB/IEC or study center.
- The medical record included a statement that written informed consent was obtained before the patient was enrolled in the study and the date the written consent was obtained. The authorized person obtaining the informed consent also signed the ICF.
- Patients were re-consented to the most current version of the ICF(s) during their participation in the study.
- A copy of the ICF(s) was provided to the patient or the patient's legally authorized representative.

Institutional Review Boards (IRBs) and/or Independent Ethics Committee (IECs) approval	Protocol v11, Section 8.3. A list of IRBs and IECs is provided. See note below.
Compliance with laws and regulations	Protocol v11, Section 8.1.
Informed Consent procedures	Protocol v11, Section 8.2.

1. INTRODUCTION

Globally, breast cancer is the second most common invasive malignancy and the most common cause of cancer-related mortality in women, with a 5-year survival rate following metastatic diagnosis of approximately 15% (Jemal et al. 2011; Ferlay et al. 2015).

Triple-negative breast cancer (TNBC) accounts for approximately 20% of all breast cancers and patients with metastatic TNBC exhibit a particularly poor clinical outcome, generally with rapid progression and a median overall survival (OS) rate of approximately 16 months (Rodler et al. 2010; Miles et al. 2013). At the time that Study CO40016 was initiated, there were no approved first-line regimens or targeted therapies for patients with this specific subtype of breast cancer. Paclitaxel was considered an appropriate first-line regimen, with a median progression-free survival (PFS) of approximately 6 months in patients with TNBC (Miles et al. 2013; Miles et al. 2017).

Hormone receptor–positive, human epidermal growth factor receptor 2-negative breast cancer (hereinafter referred to as HR+/HER2– breast cancer) accounts for over 70% of all breast cancers. Chemotherapy is indicated in patients with symptomatic visceral disease (visceral crisis) or with disease progression after demonstration of endocrine resistance (Cardoso et al. 2017; [NCCN] National Comprehensive Cancer Network 2017). Patients with HR+/HER2– breast cancer receiving first-line chemotherapy with paclitaxel had a median PFS of approximately 7–8 months in recent studies (RIBBON-1, Robert et al. 2011; PEGGY, Vuylsteke et al. 2016). As with TNBC, at the time that Study CO40016 was initiated, there was no clear standard or defined treatment regimen for patients with metastatic HR+/HER2– breast cancer who have progressed after endocrine therapy; in particular, effective treatment is needed for patients when continued endocrine therapy is not indicated.

Ipatasertib is a potent, highly selective small-molecule inhibitor of all three isoforms of the serine/threonine kinase Akt. Ipatasertib binds to the activated conformation of Akt and is adenosine trisphosphate competitive. Ipatasertib binding inhibits the kinase activity of Akt and suppresses the phosphorylation of its direct substrates, including PRAS40, and additional downstream targets, such as S6 ribosomal protein, resulting in G_1 arrest and/or apoptosis in human cancer cells (Lin et al. 2012).

Based on the scientific rationale that phosphoinositide 3-kinase/protein kinase B (PI3K/Akt) blockade attenuates survival signals associated with mitotic stress from treatment with microtubule inhibitors and the high prevalence of PI3K/Akt pathway activation signatures in TNBC and in HR+/HER2– tumors (Cancer Genome Atlas Network 2012), clinical trials evaluating the preliminary safety and efficacy of the combination of ipatasertib and paclitaxel in patients with breast cancer have been conducted and have shown the benefit of ipatasertib in patients with phosphatidylinositol-4, 5–bisphosphate 3-kinase, catalytic subunit α/AKT1/phosphatase

and tensin homolog (PIK3CA/AKT1/PTEN)-altered tumors (Interim Clinical Study Report 2017; Final Clinical Study Report 2020).

Study CO40016 was a Phase III, double−blind, placebo−controlled study designed to assess ipatasertib in combination with paclitaxel as a treatment for patients with locally advanced unresectable or metastatic TNBC or HR+/HER2− breast cancer.

Study CO40016 had three cohorts:

- Cohort A was designed to evaluate first-line treatment with ipatasertib plus paclitaxel (Ipat+Pac) in patients with locally advanced unresectable or metastatic TNBC with *PIK3CA/AKT1/PTEN*-altered tumors.
- Cohort B was designed to evaluate Ipat+Pac in patients with HR+/HER2− breast cancer with *PIK3CA/AKT1/PTEN*-altered tumors and no prior chemotherapy in the advanced disease setting, and who were suitable for chemotherapy (as defined in the protocol).
- Cohort C was an open-label, non-randomized cohort for patients with locally advanced unresectable or metastatic TNBC which lacks *PIK3CA/AKT1/PTEN* alteration to evaluate ipatasertib in combination with atezolizumab and paclitaxel (Ipat+Atezo+Pac).

Summary of Primary Analysis Results for Cohort A and Cohort B

The primary analyses were performed for Study CO40016 Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941) based on the clinical cutoff dates (CCOD) of 7 May 2020 and 17 January 2020, respectively. Overall, both cohorts did not meet their primary efficacy endpoint (investigator-assessed PFS). For Cohorts A and B, a similar proportion of patients in both arms had progressed or died in the intent-to-treat (ITT) population (Cohort A, Ipat+Pac: 54.8% vs. Pbo+Pac: 55.2%; Cohort B, Ipat+Pac: 68.5% vs. Pbo+Pac: 69.7%).

For both Cohorts A and B, data for the interim analysis of the key secondary efficacy endpoint of OS was immature at the primary analysis CCOD. For Cohort A, a similar proportion of deaths had occurred in the Ipat+Pac arm and Pbo+Pac arm and the stratified hazard ratio (HR) was 0.99 (95% CI: 0.54, 1.80). The Kaplan-Meier (KM) estimated median OS was not reached in the Ipat+Pac arm and was 21.9 months (95% CI: 16.0, NE) in the Pbo+Pac arm. For Cohort B, more deaths were reported in the Pbo+Pac arm compared with the Ipat+Pac arm, and the stratified HR was 0.72 (95% CI: 0.42, 1.24). The KM-estimated median OS was not reached in the Ipat+Pac arm and was 20.9 months (95% CI: 17.3, NE) in the Pbo+Pac arm.

In both cohorts, results of other secondary efficacy endpoints (e.g., investigator-assessed objective response rate [ORR], duration of response [DOR], and clinical benefit rate [CBR]) were consistent with those of the primary endpoint of PFS, with no clinically meaningful benefit observed for ipatasertib in combination with paclitaxel over paclitaxel alone.

Overall, ipatasertib in combination with paclitaxel was well tolerated, and the safety profile of the combination treatment regimen was consistent with the known risks of each individual study treatment component. No new safety signal was identified.

On 15 September 2021, a memo was released to investigators that the decision was made to reduce the burden of study assessments for patients and sites, with 30 October 2021 defined as the final CCOD for the efficacy analyses; no efficacy data were analyzed after this date. Last Patient Last Visit (LPLV) for this study took place on 4 January 2023. For the purposes of this final Clinical Study Report (CSR), a snapshot date of 21 March 2023 was utilized for safety analyses (also used for other analyses such as study population, etc.). It is provided in an abbreviated format because ipatasertib in combination with either paclitaxel alone (i.e., Cohorts A and B) or with atezolizumab and paclitaxel (i.e., Cohort C) is no longer being pursued for use in patients with *PIK3CA/AKT1/PTEN*-altered, locally advanced or metastatic TNBC or HR+/HER2- breast cancer.

In consideration of the coronavirus disease 19 (COVID-19) pandemic, details of the Sponsor's assessment of the impact of COVID-19 on data collection, reporting and analysis for all cohorts are provided in the Covid19 Annex. Overall, the COVID-19 pandemic had minor impact on the study conduct, data collection and analyses.

2. OBJECTIVES AND ENDPOINTS

Sections 2–3 of this final CSR have been populated using Study CO40016 Protocol Version 11 (v11), and as such they contain information that is pertinent to all three cohorts. The objectives and corresponding endpoints for Cohort A and B were presented in the primary CSRs for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941).

The objectives and corresponding endpoints for Cohort C are presented in Table 1. Since ipatasertib in combination with paclitaxel or with atezolizumab and paclitaxel in patients with *PIK3CA/AKT1/PTEN*-altered, locally advanced or metastatic TNBC or HR+/HER2– breast cancer is no longer being pursued, the exploratory objectives and results from these analyses are not presented in the CSR.

The complete list of objectives and corresponding endpoints are provided in study Protocol v11, Section 2.

Table 1 Objectives and Corresponding Endpoints (Cohort C)

Objectives	Corresponding Endpoints
Primary Efficacy Objective	
• To evaluate the efficacy of ipatasertib + paclitaxel + atezolizumab	• PFS, defined as the time from enrollment to the first occurrence of disease progression, as determined locally by the investigator through the use of RECIST v1.1, or death from any cause, whichever occurs first
Secondary Efficacy Objectives	
• To evaluate the efficacy of ipatasertib + paclitaxel + atezolizumab	• Objective response rate, defined as a CR or PR on two consecutive occasions ≥ 4 weeks apart, as determined locally by the investigator through the use of RECIST v1.1 • Duration of response, defined as the time from the first occurrence of a documented objective response to disease progression, as determined locally by the investigator through use of RECIST v1.1, or death from any cause, whichever occurs first • Clinical benefit rate, defined as an objective response (CR or PR), or stable disease for at least 24 weeks, as determined locally by the investigator through the use of RECIST v1.1 • OS, defined as the time from enrollment to death from any cause • 1-year PFS, defined as progression-free survival probabilities at 1 year • 1-year OS, defined as overall survival probabilities at 1 year
• To evaluate PROs of GHS/QoL associated with ipatasertib + paclitaxel + atezolizumab	• Mean and mean changes from baseline GHS/QoL score as measured by the GHS/QoL scale (Questions 29 and 30) of the EORTC QLQ-C30, by cycle

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Safety Objective	
• To evaluate the safety of ipatasertib + paclitaxel + atezolizumab	• Incidence of adverse events as assessed by the investigator, with severity determined through the use of NCI CTCAE v4.0 • Incidence of prespecified adverse events • Change from baseline in targeted vital signs • Change from baseline in targeted clinical laboratory test results
Pharmacokinetic Objective	
• To characterize the pharmacokinetics of atezolizumab, ipatasertib and its metabolite (G-037720) when administered in combination with paclitaxel	• Plasma concentration of ipatasertib and its metabolite, G-037720 at specified timepoints for analysis using population PK methodology • Serum concentration of atezolizumab at specified timepoints
Immunogenicity Objective	
• To evaluate the immune response to atezolizumab	• Incidence of ADAs to atezolizumab during the study relative to the prevalence of ADAs at baseline

ADA = anti-drug antibody; CR = complete response; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; GHS = global health status; NCI CTCAE v4.0 = National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0; OS = overall survival; PK = pharmacokinetics; PFS = progression-free survival; PR = partial response; PRO = patient-reported outcome; QoL = Quality of life; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors, Version 1.1.

3. INVESTIGATIONAL PLAN

3.1 OVERVIEW OF STUDY DESIGN

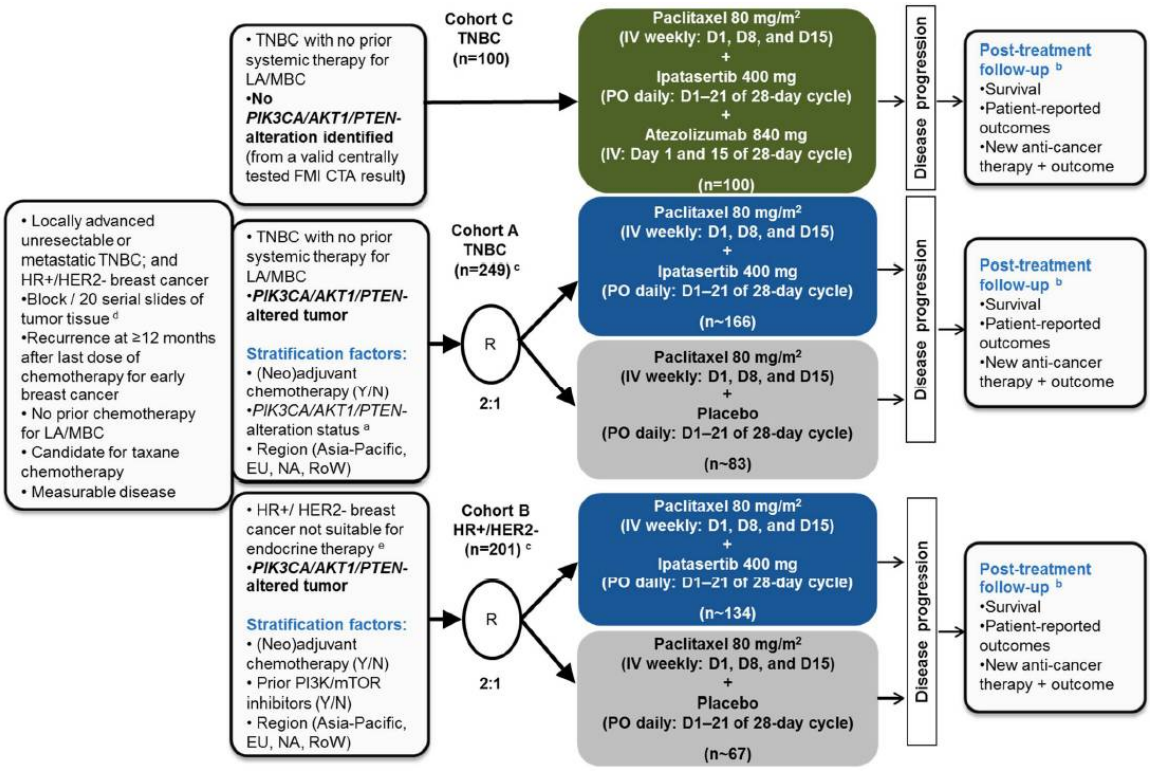
An overview of the study design, including information on the patient screening, allocation, and stratification process, treatment regimens and follow-up assessments, determination of tumor *PIK3CA/AKT1/PTEN*-altered and hormone receptor status, tumor assessments and measurements for disease evaluation, as well as efficacy, safety, and pharmacokinetic (PK) evaluation, data analysis methodology, and schedules of study assessments is provided in the Protocol v11, Section 3.1.1. The study design is depicted in Figure 1.

End of Study and Length of Study

The end of this study was defined as the date when the LPLV occurred or the date at which the last data point required for statistical analysis or safety follow-up was received from the last patient, whichever occurred later. In addition, the Sponsor could have

decided to terminate a cohort or the study at any time. The total length of the study, from screening of the first patient to the end of the study, was approximately 62 months.

Figure 1 Study Design



BC = breast cancer; CTA = clinical trial assay; D = day; EU = Europe; FMI = Foundation Medicine Inc.; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor; IV = intravenous; LA = locally advanced unresectable; MBC = metastatic breast cancer; n = number of patients; NA = North America; PIK3CA = phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; PO = by mouth; PTEN = phosphatase and tensin homolog; R = randomization; RoW = Rest of the World; TNBC = triple-negative breast cancer; Y/N = yes or no.

Note: If allowed locally, prophylaxis loperamide was mandated in Cycle 1, dose adjustment was as necessary, and continuation was per investigator judgment.

[a] *PIK3CA/AKT1* mutant versus *PTEN*-altered (and non-*PIK3CA/AKT1* mutant).

[b] If applicable, patients returned to the clinic every 8–12 weeks for tumor assessments (disease follow-up visit) until disease progression, elective withdrawal from study, or study completion or termination. As of Protocol CO40016 Version 11 (Cohort C), follow-up tumor assessments were no longer required.

[c] As needed to potentially support a regulatory submission in China, additional Chinese patients may be subsequently enrolled at CFDA-recognized sites in an extended enrollment phase (China extension phase), for up to a total of 90 Chinese patients with TNBC with *PIK3CA/AKT1/PTEN*-altered tumors and up to 120 Chinese patients with HR+/HER2– breast cancer with *PIK3CA/AKT1/PTEN*-altered tumors, constituting the analysis population of the China subgroup (including Chinese patients enrolled in the global enrollment phase).

[d] A lower number of slides may have been required if FoundationONE CDx™ was commercially already run and used for biomarker qualification.

[e] Patients with HR+/HER2– breast cancer who were not suitable candidates for endocrine therapy (as defined by Sponsor; see eligibility criteria) and who met one of the following criteria: the patient had recurrent disease (locoregional or metastatic) during adjuvant endocrine therapy

(i.e., ≤5 years of being on therapy), or if the patient had de novo metastatic disease, patient had progressive disease within 6 months of being on first-line endocrine treatment of metastatic disease.

3.1.1 Discussion of Study Design

The scientific rationale for features of the study design, including chosen control group(s), dose(s), and endpoint(s), as applicable, are discussed in the Scientific Rationale for Study Design section of the Protocol v11, Section 3.3.

3.1.2 Changes in Study Conduct

Key updates for each protocol amendment from v2 to v7 (including Germany specific amendments) for Cohorts A and B and from v7 to v9 for Cohort C were summarized in the primary CSR for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941).

Key updates (details for all updates are provided in the relevant appendix) for each protocol amendment since then are summarized below.

Version 8 of the protocol (dated February 2021), Version 9 (Germany; dated February 2021) and Version 10 (Cohort C Countries; dated February 2021)

- Language has been amended to indicate that images for tumor assessments will no longer be collected for blinded independent central review.
- Changes that were specific to Cohort C were:
  - Definitions of secondary efficacy endpoints have been updated to clarify that these are based on PFS or OS at 1 year after enrollment for Cohort C.
  - Language has been updated to allow follow-up tumor assessments in Cohort C to be performed every 8–12 weeks (in alignment with Cohorts A and B).

An end-of-trial notification for Germany occurred under Protocol v9 (Germany).

Version 9 of the protocol (dated February 2022) and Version 11 (Cohort C Countries, dated February 2022)

- Language added to allow Tumor Assessments to be performed per standard of care to reduce burden on patients.
- Language added to remove the requirement for assessments in long-term follow-up.

3.2 INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

An independent Data Monitoring Committee (iDMC) periodically evaluated the safety of ipatasertib or placebo combined with paclitaxel (Cohorts A and B). The analysis supporting iDMC review was conducted by an independent Data Coordinating Center and provided to the iDMC. Interactions between the iDMC and Sponsor were carried out as specified in the iDMC Charter, which has been unchanged since the primary CSRs

for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941). Safety monitoring was performed by the Sponsor for Cohort C.

3.3 SELECTION OF STUDY POPULATION

3.3.1 Inclusion/Exclusion Criteria

In Study CO40016, Cohort A and B included patients with histologically confirmed locally advanced unresectable or metastatic TNBC or HR+/HER2− adenocarcinoma of the breast, respectively, with *PIK3CA/AKT1/PTEN* alteration and no prior systemic chemotherapy in the advanced disease setting and who were candidates for taxane monotherapy. Cohort C included patients with histologically confirmed locally advanced unresectable or metastatic TNBC without *PIK3CA/AKT1/PTEN*-altered tumors and no prior systemic chemotherapy in the advanced disease setting.

Detailed inclusion and exclusion criteria are provided in the Protocol v11, Section 4.1.1 and 4.1.2, respectively.

3.3.2 Removal of Patients from Treatment or Study

The specific criteria and procedures for early discontinuation from study treatment(s) or withdrawal from the study are described in the Protocol v11, Sections 4.6.

3.4 STUDY TREATMENTS

3.4.1 Study Treatment(s) Administered

The investigational medicinal products (IMPs) for this study were ipatasertib (all Cohorts), matching placebo (Cohorts A and B), atezolizumab (Cohort C), and, dependent on local regulations, paclitaxel. Paclitaxel is an approved treatment for breast cancer and is considered standard of care in some countries. Loperamide (racecadotril as used in Europe) was a non-IMP in the study.

The treatment regimens are summarized in the Protocol v11, Section 3.1. The sequence of drug administration was ipatasertib/placebo, then atezolizumab (only for patients in Cohort C), and then paclitaxel. On non-atezolizumab administration days (Cohort C), the sequence of drug administration was ipatasertib and then paclitaxel.

Any dose modification had to be noted on the Study Drug Administration electronic Case Report Form (eCRF). Cases of overdose, medication error, drug abuse, or drug misuse, along with any associated adverse events (AEs), had to be reported as described in the Protocol v11, Section 5.3.5.12.

Guidelines for dosage modification and treatment interruption or discontinuation for patients who experience AEs are provided in the Protocol v11, Section 5.1.5.

Details regarding continued access to ipatasertib and atezolizumab have been presented in the Protocol v11, Section 4.3.5.

The manufacturing lot numbers for the study treatment(s) available to be dispensed in this study are provided in Appendix 16.1.6.

3.4.1.1 Dosage and Administration

Details on the study treatment dosage and administration for ipatasertib/placebo, atezolizumab, and paclitaxel are provided in Protocol v11, Section 4.3.2.

3.4.1.2 Formulation and Packaging

Details on the study treatment formulation and packaging for ipatasertib/placebo, atezolizumab, and paclitaxel are provided in Protocol v11, Section 4.3.1.

3.4.2 Measures to Minimize Bias

Method of Treatment Assignment and Blinding

There were three cohorts in this study (Figure 1). The first two cohorts, A and B, were randomized, double-blind, placebo-controlled cohorts in biomarker-positive populations designed to estimate the effect on PFS of the addition of ipatasertib to paclitaxel compared with placebo plus paclitaxel. The third cohort, Cohort C, had a single-arm open-label design to test safety and efficacy of the combination of ipatasertib plus atezolizumab plus paclitaxel in a biomarker-negative population.

The methods used to assign/allocate patients to treatment(s) groups, including any stratification factors, if applicable, and for blinding/masking for Cohorts A and B are described in Protocol v11, Section 4.2.

3.4.3 Study Treatment Accountability and Compliance

The methods used to assess study treatment compliance are described in the study treatment compliance section of the Protocol v11, Section 4.3.2.

Details on investigational medicinal product accountability are provided in Protocol v11, Section 4.3.4.

3.4.4 Prior and Concomitant Therapy

Concomitant therapy consisted of any medication (e.g., prescription drugs, over-the-counter drugs, vaccines, herbal or homeopathic remedies, nutritional supplements) used by a patient in addition to protocol-mandated treatment from 14 days prior to initiation of study drug to the study drug discontinuation visit. All such medications had to be reported to the investigator and recorded on the Concomitant Medications eCRF.

The details regarding permitted therapy, cautionary therapy, prohibited therapy, prohibited food, and additional restrictions have been presented in the Protocol v11, Section 4.4. Details on other treatments relevant to the study design (e.g., premedication and prophylactic treatment) are provided in the Protocol v11, Section 4.3.3.

3.4.5 Criteria for Dose Modification

General guidelines and details for dose modification and treatment interruption or discontinuation are provided in Protocol v11, Section 5.1.5.

Any dose modification was to be noted on the corresponding Study Drug Administration eCRF. Cases of accidental overdose or medication error, along with any associated AEs, were to be reported as described in Protocol v11, Section 5.3.5.12.

3.5 STUDY ASSESSMENTS AND PROCEDURES

The schedule of activities performed for all cohorts during the study is provided in Protocol v11, Appendix 1 (Schedule of Activities: Cohorts A and B), Appendix 2 (Schedule of Activities: Cohort C), Appendix 3 (Schedule of Pharmacokinetic and Immunogenicity Samples: Cohorts A and B), and Appendix 4 (Schedule of Pharmacokinetic and Immunogenicity Samples: Cohort C).

Patients were closely monitored for safety and tolerability throughout the study. Patients were assessed for toxicity prior to each dose; dosing occurred only if the clinical assessment and local laboratory test values were acceptable.

3.5.1 Planned Measurements and Timing of Assessments

Full details on the specific efficacy, safety, PK, immunogenicity, and biomarker assessments, their schedule and measurement/collection methods for all cohorts are provided in the Schedule of Assessments and described in Protocol v11, Section 4.5. The collection and assessment of safety information during the study (evaluation, definitions, recording, and reporting of AEs, serious adverse events [SAEs] and other reportable safety events) is detailed in the AE reporting section of the Protocol v11, Section 5.

3.6 DATA QUALITY ASSURANCE

Data Quality Assurance and Data Collection and Management	Protocol v11, Section 7. The blank eCRF is provided.
Audits and Good Clinical Practice (GCP) compliance	See statements of GCP compliance under Ethics and the audit certificate
Roche Clinical Quality Assurance	See the detailed audit summary.

No new audits were conducted for this study since the last Audit Certificate and Audit Summary issued in April 2020 and reported in the primary CSRs for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941).

A Quality Tolerance Limit (QTL) Plan was implemented retrospectively for Cohort A of this study. A summary of QTL deviations and remedial actions for Cohort A only can be found in the Appendix 16.1.13 (Quality Tolerance Limit Deviations and Remedial Actions). Overall, there was no impact to the conduct of the study.

3.7 DATA ANALYSIS PLAN

The Statistical Analysis Plan (SAP) v1 was approved on 6 February 2020 and SAP v2 was approved on 12 March 2020.

All details of the statistical analyses and determination of sample size for Study CO40016 Cohorts A and B are described in the final version of the SAP v2 and supersede those specified in the study protocol, where applicable. Cohort C was an open-label single-arm cohort, therefore the analysis plan for Cohort C is provided in Protocol v11, Section 6.

The three cohorts, Cohort A (TNBC biomarker-positive), Cohort B (HR+/HER2– biomarker-positive breast cancer), and Cohort C (TNBC biomarker-negative) were three independent cohorts and were analyzed separately for the following reasons:

- The three patient populations were distinct patient populations and were expected to have different prevalence and PFS and OS expectations, and thus different enrollment and analysis timelines.
- The readout from one cohort was independent of the readout of the other cohorts.
- This study was essentially three independent trials running under one protocol for operational efficiency.

Further details on statistical considerations and analysis plan for all cohorts are provided in Protocol v11, Section 6.

3.7.1 Statistical Hypothesis and Planned Sample Size

3.7.1.1 Statistical Hypothesis

For details on the statistical hypothesis and analysis plan for Cohort A and B, please refer to the primary CSR for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941), respectively, the SAP v2, Section 4, and Protocol v11, Section 6. Cohort C was a single-arm cohort with no statistical hypothesis testing and the results are descriptive only.

3.7.1.2 Planned Sample Size

For Cohort A, approximately 249 patients with TNBC with *PIK3CA/AKT1/PTEN*-altered tumors were to be enrolled and randomized in a 2:1 ratio to the experimental arm (ipatasertib 400 mg + paclitaxel) and control arm (placebo + paclitaxel). The sample size of 249 patients was determined on the basis of the power calculation for the PFS and OS endpoints.

For Cohort B, approximately 201 HR+/HER2– patients with *PIK3CA/AKT1/PTEN*-altered tumors were to be enrolled and randomized in a 2:1 ratio to the experimental arm (ipatasertib 400 mg + paclitaxel) and control arm (placebo + paclitaxel). The sample size of 201 patients was determined on the basis of the power calculation for the primary endpoint, PFS.

For Cohort C, approximately 100 patients with TNBC lacking *PIK3CA/AKT1/PTEN*-altered tumors were to be enrolled and assigned to a single arm of ipatasertib plus atezolizumab plus paclitaxel. The sample size of 100 patients was determined on the basis of having a sufficient number of patients for efficacy signal seeking, as well as adding to current knowledge on the safety profile of this combination, and not delaying the enrollment of patients with TNBC for Cohorts A and C.

Further details on the determination of sample size for all cohorts in Study CO40016 are provided in Protocol v11, Section 6.1.

3.7.2 Analysis Populations

Randomized/ITT Population

The randomized population, which was also referred as the ITT population, was defined as all randomized patients in Cohorts A and B regardless of whether the patient received the assigned treatment. For Cohort C, the ITT population consisted of all enrolled patients in Cohort C. All efficacy analyses were performed in the ITT population, unless otherwise specified.

Safety Population

The safety population was defined as patients who received any amount of study treatment. All safety analyses were performed in the safety population, unless otherwise specified. Patients were analyzed according to the treatment group associated with the actual regimen received. Patients who were randomized (Cohorts A and B) or enrolled (Cohort C) into the study but who did not receive any study drug were not included in the safety population.

PRO Evaluable Population

The patient-reported outcome (PRO)-evaluable population included all randomized (Cohorts A and B) or enrolled (Cohort C) patients who had a baseline and at least 1 postbaseline PRO assessment. The PRO-evaluable patients were analyzed according to the treatment arm assigned at randomization by interactive voice/web response system (Cohorts A and B) and to the treatment received (Cohort C).

Analyses for PRO efficacy endpoints were performed in the PRO evaluable population, unless otherwise specified.

3.7.3 Efficacy Analysis

All efficacy analyses were based on the ITT population (see Analysis Populations) according to the treatment arm to which patients were allocated and DOR analysis included all patients with an objective response.

All primary and secondary endpoints based on tumor burden were based on radiological (or photographical, if applicable) assessments by the local radiologist or investigator.

3.7.3.1 Primary Efficacy Analysis

The primary efficacy endpoint was investigator-assessed PFS, defined as the time from randomization (Cohorts A and B) or enrollment (Cohort C) to the first occurrence of disease progression, as determined by the investigator using Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v1.1), or death from any cause, whichever occurred first. Data for patients who did not experience disease progression or death were censored at the last date of evaluable tumor assessment. For patients who did not have an evaluable tumor assessment after randomization/enrollment, the data were censored at the date of randomization plus 1 day.

For further details, refer to SAP v2, Section 4.4.1 and Protocol v11, Section 6.4.1.

3.7.3.2 Key Secondary Efficacy Analysis

Overall survival was a key secondary efficacy endpoint and was tested only if the primary analysis of respective PFS in the corresponding cohort reached statistical significance at the level of 5%.

Overall survival was defined as the time from randomization (Cohorts A and B) or enrollment (Cohort C) to death from any cause. Data for patients who were not reported as having died at the time of analysis were censored at the date when they were last known to be alive. Data for patients who did not have postbaseline information were censored at the randomization (Cohorts A and B) or enrollment (Cohort C) date plus 1 day.

For further details, refer to SAP v2, Section 4.4.2 and Protocol v11, Section 6.4.2.3.

3.7.3.3 Other Secondary Efficacy Analysis

For all cohorts, secondary efficacy endpoints included ORR with DOR and CBR. The data analysis plan for these secondary efficacy endpoints for Cohorts A and B were previously described in the SAP v2, Section 4.4.3 and the primary CSR for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941). The data analysis plan presented below is applicable to Cohort C.

Objective response rate was defined as the proportion of patients who had an objective response. For each cohort, an estimate of ORR was calculated for each treatment arm, and its 95% CI was calculated using the Blyth-Still-Casella method.

Duration of response was defined as the time from the first occurrence of a documented objective response to disease progression, as determined by the investigator through the use of RECIST v1.1, or death from any cause, whichever occurred first. The censoring method for DOR was the same as that for PFS. For each cohort, the KM approach was used to estimate the median DOR and the corresponding 95% CIs. Analysis of DOR included only patients with objective responses. Because of the

non-randomized nature of this analysis population, the analysis of DOR was considered descriptive.

Clinical benefit rate was defined as the proportion of patients who had an objective response (complete response [CR] or partial response [PR]), or stable disease for at least 24 weeks, as determined by the investigator through the use of RECIST v1.1. For each cohort, CBR was analyzed using methods similar to those used for ORR.

Additional secondary efficacy endpoints specific to Cohort C included 1-year PFS and 1-year OS rate. They were estimated using the KM method and their 95% CIs were provided using Greenwood's formula.

For further details, refer to SAP v2, Section 4.4.3 and the Protocol v11, Section 6.4.2.1 (ORR with DOR), Section 6.4.2.2 (CBR), and Section 6.4.2.4 (1-Year PFS and 1-Year OS Rate [Cohort C only]).

Patient-Reported Outcome Analyses

The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) (version 3) data were scored according to the EORTC scoring manual (Fayers et al. 2001). Missing data were assessed and reported by cycle. In the event of incomplete data, if the scale had more than 50% of the constituent items completed, a pro-rated score was computed consistent with the scoring manual and validation papers of the measure. For subscales with less than 50% of the items completed, the subscale was considered missing.

Completion rates of the EORTC QLQ-C30 in the ITT population of Cohort C were summarized by number and proportion of patients among those expected to complete the QLQ-C30 at each time point. Reasons for non-completion were summarized at each time point for Cohort C.

Secondary Patient-Reported Outcome Endpoint: Patient-Reported Outcomes of Global Health Status/Quality of Life – EORTC Data

Details on the PRO analysis plan for Cohorts A and B were provided in the primary CSR for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941). Details on the PRO analysis plan for Cohort C is provided below.

A secondary patient-reported endpoint was mean and mean changes from baseline score of global health status/quality of life (GHS/QoL). Summary statistics (number of patients, mean, standard deviation [SD], 95% CIs, median, and range) of linearly transformed absolute scores and mean changes from baseline were calculated for the GHS/QoL (Q29 and Q30) scale of the EORTC QLQ-C30 at each assessment time point within Cohort C, in the PRO-evaluable population. Line charts depicting the mean changes (and 95% confidence intervals) from the baseline assessment of GHS/QoL

over time were also provided. A 10-point change was used to identify clinically meaningful change from baseline on the GHS/QoL scale (Osoba et al. 1998).

3.7.4 Safety Analysis

All safety analyses were based on the safety evaluable population for each cohort (see Analysis Populations) according to the treatment received.

Safety analyses were conducted by treatment arms for Cohorts A and B, and by treatment received in Cohort C, and included frequency, nature, and severity of treatment-emergent AEs, including AEs leading to death, SAEs, and AEs of special interest (AESI). All deaths were summarized. In addition, AEs leading to study drug discontinuation and dose modification were summarized. Laboratory measurements outside of the normal range were identified. Selected laboratory data were summarized by treatment arm and grade compared with baseline. Relevant vital signs were presented using summary statistics by treatment arm and visit. Drug exposure was summarized as well, including duration of treatment, cumulative dose, and dose intensity.

After initiation of study drug, SAEs and AESIs were reported until 28 days after the final dose of study treatment or until initiation of new systemic anti-cancer therapy, whichever occurred first (Cohorts A and B), or for patients in Cohort C, all AEs were reported until 30 days after the final dose of study treatment or until initiation of new systemic anti-cancer therapy, whichever occurred first, and SAEs and AESIs continued to be reported until 90 days after the final dose of study treatment or until initiation of new systemic anti-cancer therapy, whichever occurred first (Protocol v11, Section 5.4.2.2).

Treatment-emergent AEs were defined as AEs that occur after the first dose of study treatment. AEs were summarized by mapped Medical Dictionary for Regulatory Activities (MedDRA) v25.1 preferred terms (PTs) and appropriate MedDRA hierarchy. AE severity was graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v4.0. Multiple occurrences of the same event were counted once at the maximum severity.

For classification purposes, lower level terms were assigned by the Sponsor to the original terms entered on the Case Report Form (CRF), using the most up-to-date version of the MedDRA v25.1 terminology for AEs and diseases and the World Health Organization Drug Global Dictionary (B3, 1 September 2022) for treatments. Glossaries of AEs (Cohort A: l_ae_gloss_A_SE; Cohort B: l_ae_gloss_B_SE; Cohort C: l_ae_gloss_C_SE), selected AEs (Cohort A: l_aesi_gloss_A_SE; Cohort B: l_aesi_gloss_B_SE; Cohort C: l_aesi_gloss_C_SE), medical history (Cohort A: l_mh_gloss_A_IT; Cohort B: l_mh_gloss_B_IT; Cohort C: l_mh_gloss_C_IT), concomitant medications (Cohort A: l_cm_gloss_A_IT; Cohort B: l_cm_gloss_B_IT; Cohort C: l_cm_gloss_C_IT), and death coded terms (Cohort A: l_dd_gloss_A_SE; Cohort B: l_dd_gloss_B_SE; Cohort C: l_dd_gloss_C_SE) are provided.

Patient narratives are provided for the following categories of events:

- Deaths Due to AEs
- Deaths Due to Disease Progression
- SAEs
- AE Leading to Study Treatment Discontinuation
- Pregnancy
- The following AEs (which includes ipatasertib AESIs [See Protocol v11, Section 5.2.3])
    - Grade ≥ 3 Hyperglycemia
    - Grade ≥ 3 Diarrhea
    - Grade ≥ 2 Colitis/ Enterocolitis
    - Grade ≥ 3 Rash
    - Grade ≥ 2 Pneumonitis
    - Grade ≥ 3 Hepatotoxicity
    - Cases of potential drug-induced liver injury that include an elevated alanine aminotransferase (ALT) or aspartate aminotransferase (AST) in combination with either an elevated bilirubin or clinical jaundice, as defined by Hy's Law
    - Suspected transmission of an infectious agent by the study drug
- COVID -19 SAEs

Laboratory data were classified according to NCI CTCAE and summarized descriptively over time, including change from baseline. The highest NCI CTCAE grades after baseline are also reported in addition to shift tables (from baseline to worst value after baseline). Normal ranges for laboratory values are provided.

Laboratory data are summarized descriptively over time, including change from baseline. Values outside the normal ranges and marked abnormalities are summarized separately. Handling of laboratory data and the Roche standard reference range, the marked reference range, and the criteria for potentially clinically relevant changes from baseline for each laboratory parameter are provided (Handling and Reporting of Laboratory Data).

3.7.5 Pharmacokinetic Data Analysis

Pharmacokinetic analyses for Cohort A and B are described in the primary CSRs (Cohort A Report No. 1101889; Cohort B Report No. 1100941). Ipatasertib and its M1 metabolite (G-037720) levels for Cohort C were measured on Day 1 of Cycle 1 (1–3 hours post-ipatasertib/placebo), Day 15 of Cycle 1 (predose and 1–3 hours post ipatasertib/placebo) and Day 15 of Cycle 3 (predose and 2–4 hours post ipatasertib/placebo). Atezolizumab levels were measured on Day 1 of Cycle 1 (prior to

start of infusion and 30 minutes after end of infusion), Day 15 of Cycle 1 (prior to start of infusion), and Day 1 of Cycle(s) 2, 3, 4, 8, 12 and 16 (prior to start of infusion). Pharmacokinetic concentrations of ipatasertib and atezolizumab were tabulated and summarized (mean, standard deviation, coefficient of variation, median, range, geometric mean, and geometric mean coefficient of variation) by cycle, as appropriate.

Bioanalytical reports (BAR; CO40016 PK Covance Final BAR and CO40016 PK ICON 188355 Final BAR) are provided.

3.7.6 Immunogenicity Analysis (Cohort C Only)

Serum samples were used to characterize the immunogenicity of atezolizumab. For the schedule of immunogenicity samples for Cohort C, refer to Protocol v11, Appendix 4.

Please refer to the bioanalytical report (CO40016 ADA ICON 188357 Final BAR) for the detailed methodology for the anti-drug antibody (ADA) analysis.

3.7.7 Changes in Planned Analyses

No changes to the planned analyses occurred since the SAP v2 was finalized. The statistical considerations and analysis plan are also provided in Protocol v11, Section 6 and are pertinent for all three cohorts. All details of statistical analyses for Study CO40016 Cohort A and B are described in the SAP v2 and supersede those specified in the study protocol where applicable.

4. STUDY POPULATION

4.1 DISPOSITION OF PATIENTS

At the time of the final efficacy cutoff date (30 October 2021), long-term follow-up was discontinued and patients in long-term follow-up were discontinued from the study. In addition, patients who were still on study treatment at this time were moved onto a post-trial access program where required. Discontinuations from the study due to this were captured as either “Other” or “Physician Decision”, and account for most of the discontinuations captured under these reasons.

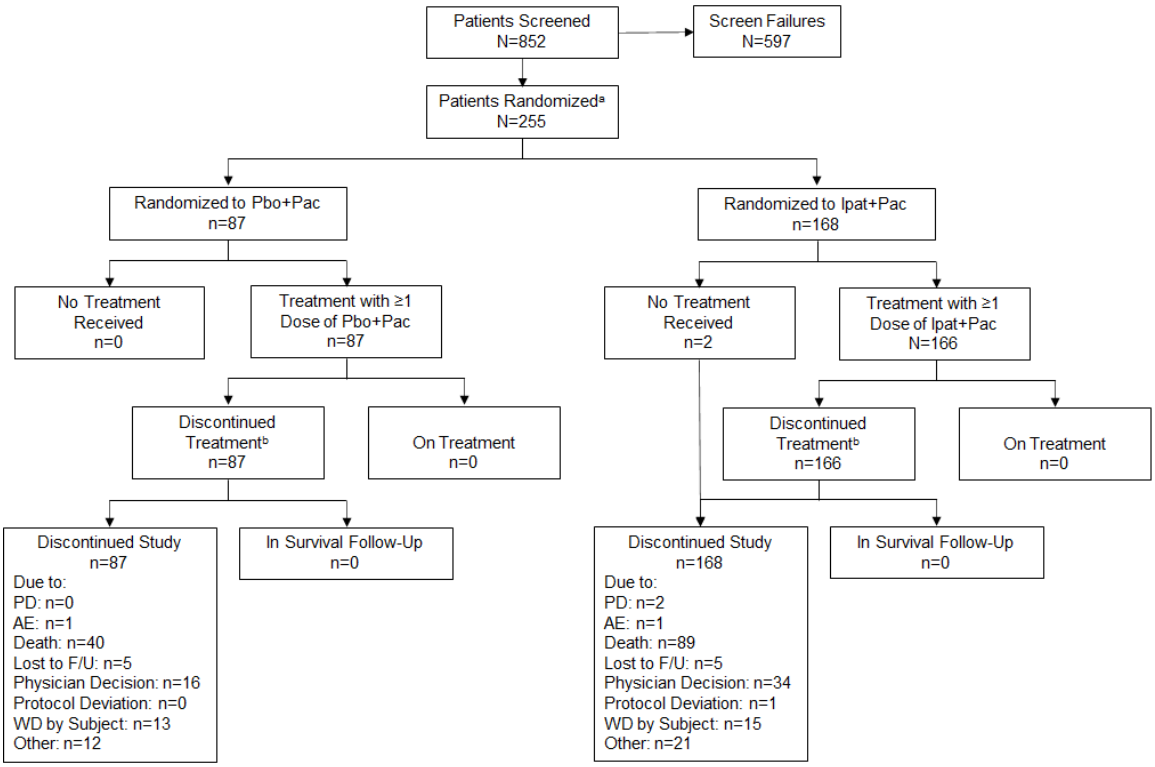
Cohort A

Data for screen failures and randomization assignments for Cohort A were reported in the primary CSR (Report No. 1101889).

Of the 255 randomized patients (ITT population), 253 patients received treatment; 166 (65.1%) and 87 (34.1%) in the Ipat+Pac arm and Pbo+Pac arm, respectively (Figure 2). At the time of CCOD, all patients had discontinued from study (t_ds_cut_A_IT).

The patient disposition for Cohort A is illustrated in Figure 2, and a list of investigators (List and Description of Investigators and Sites) for Cohort A is appended.

Figure 2 Patient Disposition (Cohort A, ITT Population)



AE = adverse event; F/U = follow-up; Ipat = ipatasertib; Pac = paclitaxel; Pbo = placebo; PD = progressive disease; WD = withdrawal.

[a] Patients were randomized 2:1 to the Ipat+Pac and Pac+Pbo arms.

[b] Discontinued treatment = Ipat/Pbo and Pac.

Cohort B

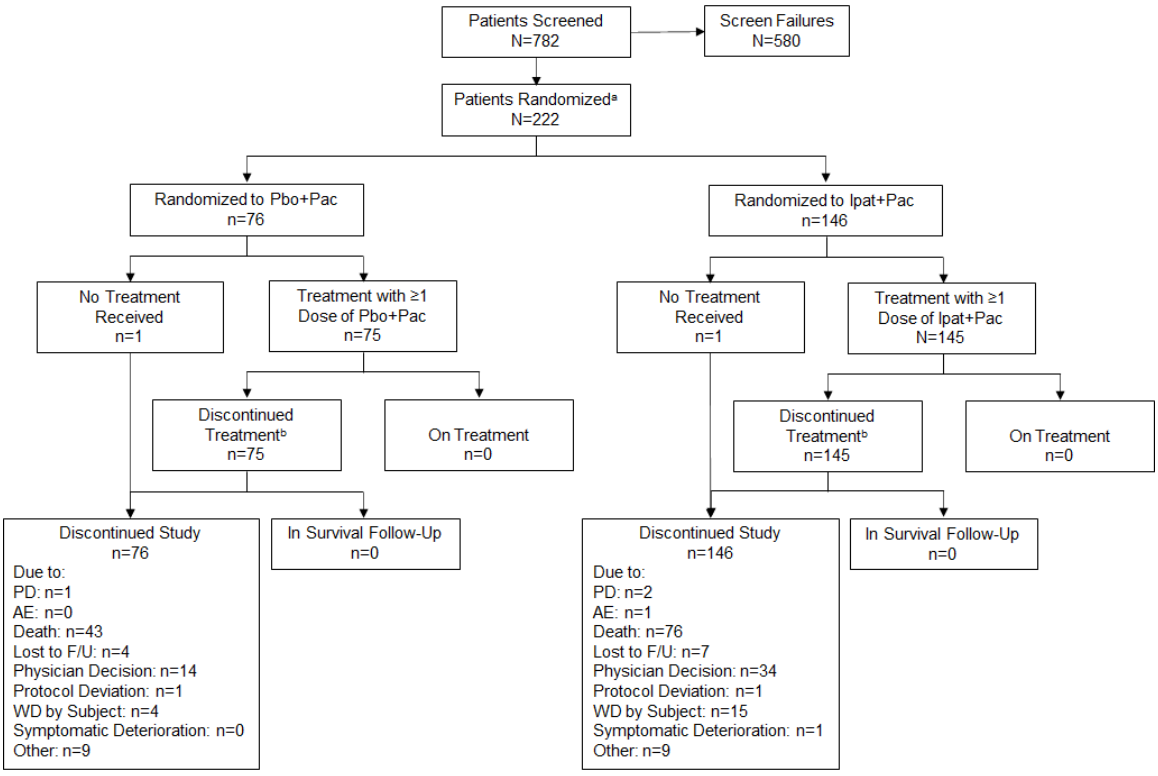
Data for screen failures and randomization assignments for Cohort B were reported in the primary CSR (Report No. 1100941).

A list of investigators (List and Description of Investigators and Sites) for Cohort B is appended.

Of the 222 randomized patients (ITT population), 220 patients overall received treatment; 145 (65.3%) and 75 (33.7%) in the Ipat+Pac arm and Pbo+Pac arm, respectively (Figure 3). At the time of CCOD, all patients had discontinued from study (t_ds_cut_B_IT).

The patient disposition for Cohort B is illustrated in Figure 3.

Figure 3 Patient Disposition (Cohort B, ITT Population)



AE = adverse event; F/U = follow-up; Ipat = ipatasertib; Pac = paclitaxel; Pbo = placebo; PD = progressive disease; WD = withdrawal.

[a] Patients were randomized 2:1 to the Ipat+Pac and Pac+Pbo arms.

[b] Discontinued treatment = Ipat/Pbo and Pac.

Cohort C

Patients who did not meet the biomarker eligibility for Cohort A were allowed to participate in Cohort C open-label treatment, provided they met all other eligibility criteria per protocol.

A total of 102 patients screened and all were enrolled. The first patient was enrolled on 25 March 2019 and the LPLV was on 4 January 2023.

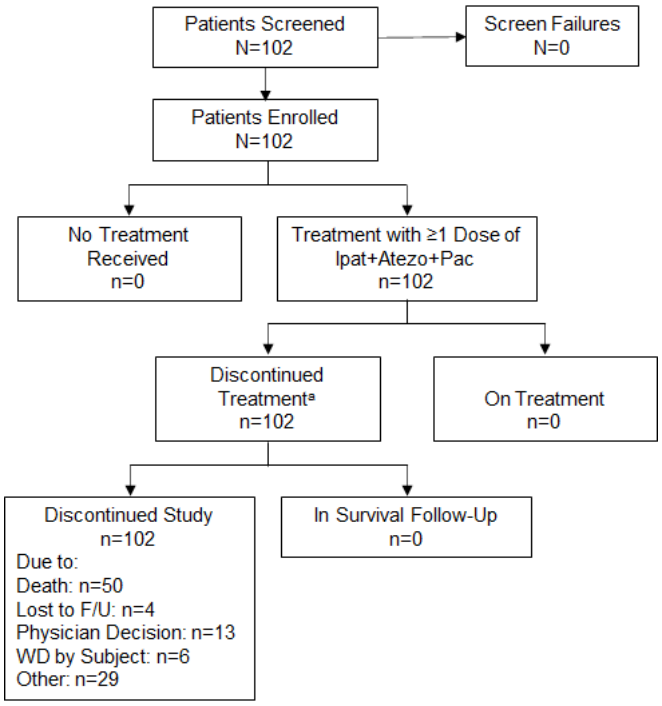
Study CO40016 (Cohort C) was conducted across 102 centers in the following 11 countries: Australia (3 centers), Republic of Korea (6), Singapore (1), Taiwan (3), France (6), United Kingdom (8), Poland (10), Ukraine (14), United States (13), Brazil (27), and Peru (11) (t_enroll_C_IT).

A list of investigators (List and Description of Investigators and Sites) for Cohort C is appended.

All 102 enrolled patients (ITT population) received treatment (Figure 4). At the time of CCOD, all patients had discontinued from study (t_ds_cut_C_IT).

The patient disposition for Cohort C is illustrated in Figure 4.

Figure 4 Patient Disposition (Cohort C, ITT Population)



Atezo = atezolizumab; F/U = follow-up; Ipat = ipatasertib; Pac = paclitaxel; WD = withdrawal.

[a] Discontinued treatment = Ipat, Atezo, and Pac.

4.2 PATIENTS WITHDRAWN PREMATURELY FROM TREATMENT OR STUDY

4.2.1 Discontinuation from Treatment

4.2.1.1 Discontinuation from Ipatasertib/Placebo

Cohort A

In the safety evaluable population, all patients in the Ipat+Pac arm and in the Pbo+Pac arm had discontinued ipatasertib/placebo. The most common reason for discontinuation in both treatment arms was progressive disease, which occurred in 65.7% and 72.4% of patients in the Ipat+Pac and Pbo+Pac arms, respectively. The second most common reason for discontinuation in the Ipat+Pac arm was AE (9.0%), and in the Pbo+Pac arm it was AE, withdrawal by subject, and “other” in the Pbo+Pac arm (each 6.9%) (Table 2).

Table 2 Discontinuation from Ipatasertib/Placebo (Cohort A, Safety Evaluable Population)

Patients Withdrawn from Ipatasertib/Placebo, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)	All Patients (N=253)
Reason for Treatment Discontinuation			
n	87	166	253
Adverse event	6 (6.9%)	15 (9.0%)	21 (8.3%)
Death	0	2 (1.2%)	2 (0.8%)
Lost to follow-up	0	1 (0.6%)	1 (0.4%)
Other	6 (6.9%)	7 (4.2%)	13 (5.1%)
Physician decision	3 (3.4%)	11 (6.6%)	14 (5.5%)
Progressive disease	63 (72.4%)	109 (65.7%)	172 (68.0%)
Symptomatic deterioration	3 (3.4%)	10 (6.0%)	13 (5.1%)
Withdrawal by subject	6 (6.9%)	11 (6.6%)	17 (6.7%)

Percentages are based on N in the column heading.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_ipat.sas
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Cohort B

In the safety evaluable population, all patients in the Ipat+Pac arm and in the Pbo+Pac arm had discontinued ipatasertib/placebo. The most common reason for discontinuation in both treatment arms was progressive disease, which occurred in 67.6% and 72.0% of patients in the Ipat+Pac and Pbo+Pac arms, respectively. The second most common reason for discontinuation in the Ipat+Pac arm was AE (11.0%) and in the Pbo+Pac arm, it was physician decision and “other” (each 8.0%) (Table 3).

Table 3 Discontinuation from Ipatasertib/Placebo (Cohort B, Safety Evaluable Population)

Patients Withdrawn from Ipatasertib/Placebo, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)	All Patients (N=220)
Reason for Treatment Discontinuation			
n	75	145	220
Adverse event	3 (4.0%)	16 (11.0%)	19 (8.6%)
Death	0	1 (0.7%)	1 (0.5%)
Non-compliance with study drug	0	1 (0.7%)	1 (0.5%)
Other	6 (8.0%)	2 (1.4%)	8 (3.6%)
Physician decision	6 (8.0%)	8 (5.5%)	14 (6.4%)
Progressive disease	54 (72.0%)	98 (67.6%)	152 (69.1%)
Protocol deviation	1 (1.3%)	1 (0.7%)	2 (0.9%)
Symptomatic deterioration	4 (5.3%)	7 (4.8%)	11 (5.0%)
Withdrawal by subject	1 (1.3%)	11 (7.6%)	12 (5.5%)

Percentages are based on N in the column heading.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_ipat.sas
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Cohort C

In the safety evaluable population, all patients had discontinued ipatasertib. The most common reason for discontinuation was progressive disease, which occurred in 61.8% of patients, followed by “other” (11.8%) and AE (10.8%) (Table 4).

Table 4 Discontinuation from Ipatasertib (Cohort C, Safety Evaluable Population)

Patients Withdrawn from Ipatasertib, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Reason for Treatment Discontinuation	
n	102
Adverse event	11 (10.8%)
Death	1 (1.0%)
Non-compliance with study drug	1 (1.0%)
Other	12 (11.8%)
Physician decision	7 (6.9%)
Progressive disease	63 (61.8%)
Symptomatic deterioration	3 (2.9%)
Withdrawal by subject	4 (3.9%)

Percentages are based on N in the column heading.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_ipat.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ds_ipat_C_SE.out
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4.2.1.2 Discontinuation from Paclitaxel

Cohort A

In the safety evaluable population, 99.4% of patients in the Ipat+Pac arm and all patients in the Pbo+Pac arm had discontinued paclitaxel. Of note, all patients in the Ipat+Pac arm had discontinued paclitaxel, however, a study drug discontinuation eCRF for paclitaxel was inadvertently not completed for 1 patient. The most common reason for discontinuation in both treatment arms was progressive disease, which occurred in 61.4% and 69.0% of patients in the Ipat+Pac and Pbo+Pac arms, respectively. The second most common reason for discontinuing paclitaxel was AE in both arms (14.5% in the Ipat+Pac arm and 16.1% in the Pbo+Pac arm) (Table 5).

Table 5 Discontinuation from Paclitaxel (Cohort A, Safety Evaluable Population)

Patients Withdrawn from Paclitaxel, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)	All Patients (N=253)
Reason for Treatment Discontinuation			
n	87	165	252
Adverse event	14 (16.1%)	24 (14.5%)	38 (15.0%)
Death	0	2 (1.2%)	2 (0.8%)
Lost to follow-up	0	1 (0.6%)	1 (0.4%)
Other	1 (1.1%)	5 (3.0%)	6 (2.4%)
Physician decision	3 (3.4%)	10 (6.0%)	13 (5.1%)
Progressive disease	60 (69.0%)	102 (61.4%)	162 (64.0%)
Symptomatic deterioration	2 (2.3%)	10 (6.0%)	12 (4.7%)
Withdrawal by subject	7 (8.0%)	11 (6.6%)	18 (7.1%)

Percentages are based on N in the column heading.
Data Cutoff Date - 21MAR2023 ; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ds_pac_A_SE.out
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Cohort B

In the safety evaluable population, all patients in the Ipat+Pac arm and in the Pbo+Pac arm had discontinued paclitaxel. The most common reason for discontinuation in both treatment arms was progressive disease, which occurred in 51.7% and 62.7% of patients in the Ipat+Pac and Pbo+Pac arms, respectively. The second most common reason for discontinuing paclitaxel was AE in both arms (28.3% in the Ipat+Pac arm and 16.0% in the Pbo+Pac arm) (Table 6).

Table 6 Discontinuation from Paclitaxel (Cohort B, Safety Evaluable Population)

Patients Withdrawn from Paclitaxel, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)	All Patients (N=220)
Reason for Treatment Discontinuation			
n	75	145	220
Adverse event	12 (16.0%)	41 (28.3%)	53 (24.1%)
Death	0	1 (0.7%)	1 (0.5%)
Non-compliance with study drug	0	1 (0.7%)	1 (0.5%)
Other	7 (9.3%)	3 (2.1%)	10 (4.5%)
Physician decision	4 (5.3%)	6 (4.1%)	10 (4.5%)
Progressive disease	47 (62.7%)	75 (51.7%)	122 (55.5%)
Protocol deviation	0	1 (0.7%)	1 (0.5%)
Symptomatic deterioration	4 (5.3%)	4 (2.8%)	8 (3.6%)
Withdrawal by subject	1 (1.3%)	13 (9.0%)	14 (6.4%)

Percentages are based on N in the column heading.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_pac.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ds_pac_B_SE.out
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Cohort C

In the safety evaluable population, all patients had discontinued paclitaxel. The most common reason for discontinuation was progressive disease, which occurred in 54.9% of patients. The second most common reason for discontinuing paclitaxel was AE (21.6%) (Table 7).

Table 7 Discontinuation from Paclitaxel (Cohort C, Safety Evaluable Population)

Patients Withdrawn from Paclitaxel, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Reason for Treatment Discontinuation	
n	102
Adverse event	22 (21.6%)
Other	9 (8.8%)
Physician decision	8 (7.8%)
Progressive disease	56 (54.9%)
Symptomatic deterioration	3 (2.9%)
Withdrawal by subject	4 (3.9%)

Percentages are based on N in the column heading.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_pac.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ds_pac_C_SE.out
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4.2.1.3 Discontinuation from Atezolizumab (Cohort C Only)

In the safety evaluable population, all patients had discontinued atezolizumab. The most common reason for discontinuation was progressive disease, which occurred in 61.8% of patients. The second most common reason for discontinuing atezolizumab was AE (12.7%) (Table 8).

Table 8 Discontinuation from Atezolizumab (Cohort C, Safety Evaluable Population)

Patients Withdrawn from Atezolizumab, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Reason for Treatment Discontinuation	
n	102
Adverse event	13 (12.7%)
Death	1 (1.0%)
Other	12 (11.8%)
Physician decision	6 (5.9%)
Progressive disease	63 (61.8%)
Symptomatic deterioration	3 (2.9%)
Withdrawal by subject	4 (3.9%)

Percentages are based on N in the column heading.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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4.2.2 Discontinuation from Study

Cohort A

Overall, in the ITT population, all patients in the Ipat+Pac arm and in the Pbo+Pac arm had discontinued from the study (Table 9). The most common reason for study discontinuation was death, which occurred in 53.0% and 46.0% of patients in the Ipat+Pac arm and the Pbo+Pac arm, respectively. The second most common reason for study discontinuation was physician decision in both arms (20.2% in the Ipat+Pac arm and 18.4% in the Pbo+Pac arm [see Disposition of Patients]).

A listing of patients who had discontinued from study (l_ds_A_IT) by discontinuation reason is provided.

Table 9 Patient Discontinuation from Study (Cohort A, ITT Population)

Patient Disposition (Study Discontinuation), Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
Received any treatment	87 (100%)	166 (98.8%)	253 (99.2%)
Did not receive any treatment	0	2 (1.2%)	2 (0.8%)
Reason for Study Discontinuation			
n	87	168	255
Progressive Disease	0	2 (1.2%)	2 (0.8%)
Adverse event	1 (1.1%)	1 (0.6%)	2 (0.8%)
Death	40 (46.0%)	89 (53.0%)	129 (50.6%)
Lost to follow-up	5 (5.7%)	5 (3.0%)	10 (3.9%)
Physician decision	16 (18.4%)	34 (20.2%)	50 (19.6%)
Protocol deviation	0	1 (0.6%)	1 (0.4%)
Withdrawal by subject	13 (14.9%)	15 (8.9%)	28 (11.0%)
Other	12 (13.8%)	21 (12.5%)	33 (12.9%)

Percentages are based on N in the column headings.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds.sas
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Cohort B

Overall, in the ITT population, all patients in the Ipat+Pac arm and in the Pbo+Pac arm had discontinued from the study (Table 10). The most common reason for study discontinuation was death, which occurred in 52.1% and 56.6% of patients in the Ipat+Pac arm and the Pbo+Pac arm, respectively. The second most common reason for study discontinuation was physician decision in both arms (23.3% in the Ipat+Pac arm and 18.4% in the Pbo+Pac arm [see Disposition of Patients]).

A listing of patients who had discontinued from study (l_ds_B_IT) by discontinuation reason is provided.

Table 10 Patient Discontinuation from Study (Cohort B, ITT Population)

Patient Disposition (Study Discontinuation), Cohort B: HR+/HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
Received any treatment	75 (98.7%)	145 (99.3%)	220 (99.1%)
Did not receive any treatment	1 (1.3%)	1 (0.7%)	2 (0.9%)
Reason for Study Discontinuation			
n	76	146	222
Progressive Disease	1 (1.3%)	2 (1.4%)	3 (1.4%)
Adverse event	0	1 (0.7%)	1 (0.5%)
Death	43 (56.6%)	76 (52.1%)	119 (53.6%)
Lost to follow-up	4 (5.3%)	7 (4.8%)	11 (5.0%)
Physician decision	14 (18.4%)	34 (23.3%)	48 (21.6%)
Protocol deviation	1 (1.3%)	1 (0.7%)	2 (0.9%)
Withdrawal by subject	4 (5.3%)	15 (10.3%)	19 (8.6%)
Symptomatic deterioration	0	1 (0.7%)	1 (0.5%)
Other	9 (11.8%)	9 (6.2%)	18 (8.1%)

Percentages are based on N in the column headings.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds.sas
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Cohort C

Overall, in the ITT population, all patients had discontinued from the study (Table 11). The most common reason for study discontinuation was death, which occurred in 49.0% of patients. The second most common reason for study discontinuation was “other” (28.4% [see Disposition of Patients]).

A listing of patients who had discontinued from study (l_ds_C_IT) by discontinuation reason is provided.

Table 11 Patient Discontinuation from Study (Cohort C, ITT Population)

Patient Disposition (Study Discontinuation), Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Received any treatment	102 (100%)
Reason for Study Discontinuation	
n	102
Death	50 (49.0%)
Lost to follow-up	4 (3.9%)
Physician decision	13 (12.7%)
Withdrawal by subject	6 (5.9%)
Other	29 (28.4%)

Percentages are based on N in the column headings.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds.sas
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4.3 PROTOCOL DEVIATIONS AND QUALITY TOLERANCE LIMITS

4.3.1 Protocol Deviations

Major protocol deviations were defined as those that had the potential to significantly impact patient safety, the efficacy of the treatment regimen, or the study analysis (i.e., the validity/reliability of the data).

The major protocol deviations were grouped into four categories: procedural, medication, inclusion criteria, and exclusion criteria. All patients with protocol deviations were included in the efficacy analyses presented in this CSR.

Cohort A

As of the CCOD, 32.2% of the ITT population had at least one major protocol deviation (Table 12). The proportion of patients with protocol deviations was slightly higher in the Ipat+Pac arm (33.9%) as compared with the Pbo+Pac arm (28.7%). There were no notable differences between the two treatment arms with respect to the type of major deviations. The most frequent protocol deviations were procedural (20.0%), followed by inclusion criteria (10.2%), medications (5.9%), and exclusion criteria (3.5%).

A listing of patients with major protocol deviations is appended (l_dv_A_IT).

Table 12 Major Protocol Deviations (Cohort A, ITT Population)

Major Protocol Deviations, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

Category Description	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
Total number of patients with at least one major protocol deviation	25 (28.7%)	57 (33.9%)	82 (32.2%)
Total number of major protocol deviations	28	73	101
EXCLUSION CRITERIA			
Total	4 (4.6%)	5 (3.0%)	9 (3.5%)
Chemo <12 months prior to recurrence/chemo in ABC	2 (2.3%)	3 (1.8%)	5 (2.0%)
Medical hx/current diagnosis of excluded condition	1 (1.1%)	0	1 (0.4%)
Prior systemic therapy (chemo, checkpoint inhibitors, targeted agent) for LA or metastatic TNBC	0	1 (0.6%)	1 (0.4%)
Uncontrolled Type1 or TypeII Diabetes requiring insulin	1 (1.1%)	1 (0.6%)	2 (0.8%)
INCLUSION CRITERIA			
Total	5 (5.7%)	21 (12.5%)	26 (10.2%)
Adequate hematologic/organ function within 14days prior to first study treatment	3 (3.4%)	9 (5.4%)	12 (4.7%)
Key screening assessments outside relevant window	2 (2.3%)	7 (4.2%)	9 (3.5%)
Measurable disease per RESIST v1.1	0	1 (0.6%)	1 (0.4%)
Signed Informed Consent	0	4 (2.4%)	4 (1.6%)
MEDICATION			
Total	2 (2.3%)	13 (7.7%)	15 (5.9%)
Dosage - study drugs not adjusted despite toxicity	0	2 (1.2%)	2 (0.8%)
Dosage - underdosage, ipatasertib/placebo	0	2 (1.2%)	2 (0.8%)
Dosage - underdosage, paclitaxel	0	1 (0.6%)	1 (0.4%)
Patient received incorrect treatment/ damaged drug	0	3 (1.8%)	3 (1.2%)
Prohibited concomitant medication or food	2 (2.3%)	1 (0.6%)	3 (1.2%)
Study treatment not discontinued per guidelines	0	4 (2.4%)	4 (1.6%)
PROCEDURAL			
Total	17 (19.5%)	34 (20.2%)	51 (20.0%)
Delay of 2 or more cycles to complete an updated ICF	1 (1.1%)	3 (1.8%)	4 (1.6%)
Dose not modified following specific toxicity	0	1 (0.6%)	1 (0.4%)
Failure to report a SAE per protocol	1 (1.1%)	0	1 (0.4%)
Improper Stratification Criteria Selection	3 (3.4%)	8 (4.8%)	11 (4.3%)
Incorrect Cohort Assignment or Incorrect Randomization	1 (1.1%)	2 (1.2%)	3 (1.2%)
Missed 2 or more efficacy assessments	0	3 (1.8%)	3 (1.2%)
Non-compliance with impact to patient safety or study integrity	10 (11.5%)	17 (10.1%)	27 (10.6%)
Unblinding without appropriate reason	1 (1.1%)	0	1 (0.4%)

Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Cohort B

As of the CCOD, 46.8% of the ITT population had at least one major protocol deviation (Table 13). The proportion of patients with protocol deviations was similar between treatment arms (Ipat+Pac: 45.2% vs. Pbo+Pac: 50.0%). There were no notable differences between the two treatment arms with respect to the type of major deviations. The most frequent protocol deviations were procedural (41.4%), followed by inclusion criteria (10.4%), exclusion criteria (9.0%), and medication (8.1%).

A listing of patients with major protocol deviations is appended (l_dv_B_IT).

Table 13 Major Protocol Deviations (Cohort B, ITT Population)

Major Protocol Deviations, Cohort B: HR+/HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

Category Description	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
Total number of patients with at least one major protocol deviation	38 (50.0%)	66 (45.2%)	104 (46.8%)
Total number of major protocol deviations	51	102	153
EXCLUSION CRITERIA			
Total	5 (6.6%)	15 (10.3%)	20 (9.0%)
Active infection requiring systemic antibiotics, anti-fungals or antivirals	0	1 (0.7%)	1 (0.5%)
Anti-cancer agent within 14 days prior to C1D1	0	3 (2.1%)	3 (1.4%)
Chemo <12 months prior to recurrence/chemo in ABC	0	1 (0.7%)	1 (0.5%)
Clinically significant history of liver disease consistent with Child-Pugh B or C	0	2 (1.4%)	2 (0.9%)
Endocrine therapy appropriate (HR+/HER2- only) or not meeting current protocol requirements	4 (5.3%)	5 (3.4%)	9 (4.1%)
Grade>=2 uncontrolled hypercholesterolemia/ hypertriglyceridemia	1 (1.3%)	2 (1.4%)	3 (1.4%)
Major surgery/trauma within 28 days of C1D1	0	1 (0.7%)	1 (0.5%)
INCLUSION CRITERIA			
Total	6 (7.9%)	17 (11.6%)	23 (10.4%)
Adequate hematologic/organ function within 14days prior to first study treatment	3 (3.9%)	3 (2.1%)	6 (2.7%)
Key screening assessments outside relevant window	1 (1.3%)	10 (6.8%)	11 (5.0%)
PIK3CA/AKT1/PTEN requirements not met	0	1 (0.7%)	1 (0.5%)
Signed Informed Consent	2 (2.6%)	3 (2.1%)	5 (2.3%)
MEDICATION			
Total	6 (7.9%)	12 (8.2%)	18 (8.1%)
Dosage - overdosage, ipatasertib/placebo	1 (1.3%)	2 (1.4%)	3 (1.4%)
Dosage - study drugs not adjusted despite toxicity	1 (1.3%)	4 (2.7%)	5 (2.3%)
Dosage - underdosage, ipatasertib/placebo	2 (2.6%)	0	2 (0.9%)
Patient received incorrect treatment/ damaged drug	0	3 (2.1%)	3 (1.4%)
Prohibited concomitant medication or food	1 (1.3%)	1 (0.7%)	2 (0.9%)
Study treatment not discontinued per guidelines	1 (1.3%)	2 (1.4%)	3 (1.4%)
PROCEDURAL			
Total	34 (44.7%)	58 (39.7%)	92 (41.4%)
>1 consecutive tumor assessments missing	1 (1.3%)	0	1 (0.5%)
Delay of 2 or more cycles to complete an updated ICF	5 (6.6%)	9 (6.2%)	14 (6.3%)
Failure to report a SAE per protocol	2 (2.6%)	6 (4.1%)	8 (3.6%)
Improper Stratification Criteria Selection	13 (17.1%)	22 (15.1%)	35 (15.8%)
Incorrect Cohort Assignment or Incorrect Randomization	0	2 (1.4%)	2 (0.9%)
Non-compliance with impact to patient safety or study integrity	12 (15.8%)	19 (13.0%)	31 (14.0%)
Unblinding without appropriate reason	1 (1.3%)	0	1 (0.5%)

Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Cohort C

As of the CCOD, 39.2% of the ITT population had at least one major protocol deviation (Table 14). The most frequent protocol deviations were procedural (28.4%), followed by medication (12.7%), inclusion criteria (8.8%), and exclusion criteria (2.9%).

A listing of patients with major protocol deviations is appended (l_dv_C_IT).

Table 14 Major Protocol Deviations (Cohort C, ITT Population)

Major Protocol Deviations, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Category Description	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one major protocol deviation	40 (39.2%)
Total number of major protocol deviations	54
EXCLUSION CRITERIA	
Total	3 (2.9%)
Grade>=2 uncontrolled hypercholesterolemia/ hypertriglyceridemia	1 (1.0%)
History / Presence of brain metastases	1 (1.0%)
Unable to comply with study procedures	1 (1.0%)
INCLUSION CRITERIA	
Total	9 (8.8%)
Adequate hematologic/organ function within 14days prior to first study treatment	1 (1.0%)
Histologically documented TNBC or HR+/HER2-locally advanced or mBC, and not curative resectable	1 (1.0%)
Key screening assessments outside relevant window	6 (5.9%)
Signed Informed Consent	1 (1.0%)
MEDICATION	
Total	13 (12.7%)
Dosage - overdosage, ipatasertib/placebo	1 (1.0%)
Dosage - study drugs not adjusted despite toxicity	2 (2.0%)
Patient received incorrect treatment/ damaged drug	4 (3.9%)
Prohibited concomitant medication or food	1 (1.0%)
Study treatment not discontinued per guidelines	5 (4.9%)
PROCEDURAL	
Total	29 (28.4%)
>1 consecutive tumor assessments missing	1 (1.0%)
Delay of 2 or more cycles to complete an updated ICF	1 (1.0%)
Failure to report a SAE per protocol	4 (3.9%)
Non-compliance with impact to patient safety or study integrity	23 (22.5%)

Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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4.3.2 Quality Tolerance Limits

A risk-based quality management approach was used in this study to manage quality throughout all stages and focused on essential activities to ensure human subject protection and the reliability of study results. The QTL plan documents risks and controls that were retrospectively applied to Cohort A of the study after first patient in. QTLs were implemented as per the QTL plan for Cohort A only. Descriptions of important deviations from the defined QTLs and remedial actions taken are provided in Quality Tolerance Limit Deviations and Remedial Actions.

4.4 POPULATIONS ANALYZED

The overviews of analysis populations for Cohorts A and B were presented in the primary CSR for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941).

An overview of the analysis populations for Cohort C is presented below. Analysis populations are defined in Analysis Populations.

For Cohort C, the number of patients included in each analysis population is shown in Table 15. One patient was excluded from the PRO evaluable population, due to missing baseline assessments.

A listing of patients excluded from analysis populations is appended (l_pop_C_IT).

Table 15 Overview of Analysis Populations (Cohort C, ITT Population)

Analysis Populations, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel
Randomized Patients (ITT)	102
Safety Evaluable Patients (by actual treatment)	102
PRO Evaluable Patients (by planned treatment)	101

PRO: Patient reported outcome.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_pop.sas
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4.5 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

4.5.1 Demographics and Baseline Characteristics

Demographics and baseline characteristics for Cohorts A and B were presented in the primary CSR for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941). Demographics and baseline characteristics for Cohort C are presented below.

Cohort C

In the ITT population, all patients were women, and the majority were White (53.9%), followed by Unknown (14.7%), or Asian (11.8%). The median age was 55 years (range: 22–83 years). In accordance with the protocol inclusion criteria, all patients had a high baseline functional status (i.e., Eastern Cooperative Oncology Group Performance Status [ECOG PS] 0: 59.8% or 1: 40.2%). The majority of patients (74.5%) had metastatic disease at baseline. Prior breast cancer radiotherapy, prior anthracycline therapy, or prior taxane therapy were reported in 35.3%, 35.3%, and 37.3% of patients, respectively (Table 16).

The proportion of patients with a disease-free interval and chemotherapy-free interval of >3 years were 5.9% and 3.9%, respectively.

Table 16 Demographics and Baseline Characteristics (Cohort C, ITT Population)

Demographics and Baseline Characteristics, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Age (Years)	
n	102
Mean (SD)	54.6 (11.7)
Median	55.0
Min - Max	22 - 83
Age group (Years)	
n	102
18 - 40	13 (12.7%)
41 - 64	68 (66.7%)
>=65	21 (20.6%)
Sex	
n	102
Female	102 (100%)
Race	
n	102
American Indian or Alaska Native	5 (4.9%)
Asian	12 (11.8%)
Black or African American	9 (8.8%)
Native Hawaiian or other Pacific Islander	1 (1.0%)
White	55 (53.9%)
Multiple	5 (4.9%)
Unknown	15 (14.7%)
ECOG performance status	
n	102
0	61 (59.8%)
1	41 (40.2%)
Region (eCRF)	
n	102
Asia-Pacific	13 (12.7%)
Europe	38 (37.3%)
North America	13 (12.7%)
Rest of World	38 (37.3%)
Prior breast cancer radiotherapy	
n	102
Yes	36 (35.3%)
No	66 (64.7%)
Prior anthracycline therapy	
n	102
Yes	36 (35.3%)
No	66 (64.7%)
Prior taxane therapy	
n	102
Yes	38 (37.3%)
No	64 (62.7%)
Baseline disease status	
n	102
Locally Advanced Unresectable	26 (25.5%)
Metastatic	76 (74.5%)
Disease-free interval (Years)	
n	102
< 1	4 (3.9%)
1 - 3	30 (29.4%)
> 3	6 (5.9%)
No Prior Curative Breast Surgery	58 (56.9%)
Not Available	4 (3.9%)
Chemotherapy-free interval (Years)	
n	102
1 - 3	35 (34.3%)
> 3	4 (3.9%)
No Prior Chemotherapy	60 (58.8%)
Not Available	3 (2.9%)

Visceral disease in patients with mBC	
n	102
Yes	58 (56.9%)
No	18 (17.6%)
Not Applicable	26 (25.5%)
Number of sites of disease in patients with mBC	
n	102
1 - 2	34 (33.3%)
>= 3	42 (41.2%)
Not Applicable	26 (25.5%)
BRCA1/2 mutation status*	
n	102
Positive	17 (16.7%)
Negative	85 (83.3%)
PD-L1 status	
n	102
PD-L1 Positive	40 (39.2%)
PD-L1 Negative	25 (24.5%)
PD-L1 Unknown	37 (36.3%)

The percentages are based on n. Disease Free Interval is defined as time from the final curative-intent breast surgery to the initial diagnosis of LABC/MBC. Chemotherapy Free Interval is defined as time from the last date of neoadjuvant/adjuvant chemotherapy administered to the start date of study treatment. DFI and CFI are "Not Available" for subjects having a Partial Date or Missing Date. Visceral disease is displayed as Yes or No for patients with metastatic disease, and displayed as Not Applicable for patients without metastatic disease. All recorded sites of disease except for the following are counted as visceral sites: bone, bone marrow, breast, chest, head, lymph node, neck, skin, soft tissue. Number of sites of disease in patients with mBC is displayed as Not Applicable for patients without metastatic disease. *BRCA1/2 mutation is by molecular testing and cannot distinguish between germline and somatic.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_dm.sas
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Adapted from: t_dm_C_IT

4.5.2 Baseline Disease Characteristics

Baseline disease characteristics for Cohorts A and B were presented in the primary CSR for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941). Baseline disease characteristics for Cohort C is presented below.

Overall, in the Cohort C ITT population, the most common diagnosed histopathological subtype was ductal (73.3%). Most patients were initially diagnosed with poorly differentiated Grade 3 breast cancer (60.8%). The most common stage at initial diagnosis was Stage IV (36.3%) followed by Stage III (30.4%) and Stage II (22.5%) (t_mh_bchist_C_IT).

4.5.3 Prior and Concurrent Diseases

Prior diseases (defined as diseases resolved at baseline) and concurrent diseases (defined as ongoing diseases at baseline) for Cohorts A and B were presented in the primary CSR for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941). Concurrent diseases for Cohort C are presented below.

In the ITT population, 75.5% of patients had at least one active medical condition at baseline (t_mh_CNCR_C_IT). The most common concurrent disease by System Organ Class (SOC; ≥30% of patients) was Vascular disorders (32.4%).

4.6 PRIOR AND CONCOMITANT THERAPY

Prior medications for Cohorts A and B were presented in the primary CSR for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941). Concomitant medications for all cohorts are presented below.

Concomitant medications were coded using WHODRUG GLOBAL dictionary (B3, 1 September 2022), using this coding system, a single concomitant medication may code to more than one class (e.g., use of corticosteroids as premedication for paclitaxel is counted towards the following categories: corticosteroids for systemic use, ophthalmological, nasal preparations, stomatological preparations, etc.).

In accordance with the protocol (Protocol v11, Section 4.3.3), if allowed locally, prophylactic loperamide for diarrhea management was mandated in the first cycle, dose adjusted as necessary, and continued as per investigator judgment.

Cohort A

Almost all patients received at least one concomitant medication that temporally overlapped with study drug administration (Ipat+Pac 98.8% vs. Pbo+Pac 100%) (t_cm_CNCM_NFC_A_IT). The most commonly used concomitant medications were as expected for this patient population and generally similar between the treatment arms. The most commonly used classes of drugs (≥ 80%) were premedications administered for paclitaxel (i.e., steroids, antihistamines and histamine H_2-receptor antagonists).

Cohort B

Almost all patients received at least one concomitant medication that temporally overlapped with study drug administration (Ipat+Pac 98.6% vs. Pbo+Pac 98.7%) (t_cm_CNCM_NFC_B_IT). The most commonly used concomitant medications were as expected for this patient population and generally similar between the treatment arms. The most commonly used classes of drugs (≥80%) were premedications administered for paclitaxel (i.e., steroids, antihistamines and histamine H_2-receptor antagonists).

Cohort C

All patients received at least one concomitant medication that temporally overlapped with study drug administration (t_cm_CNCM_NFC_C_IT). The most commonly used concomitant medications were as expected for this patient population. The most commonly used classes of drugs (≥ 80%) were premedications administered for paclitaxel and atezolizumab (i.e., steroids, antihistamines, histamine H_2-receptor antagonists, anti-emetics and anti-nauseants).

4.7 EXPOSURE

4.7.1 Exposure to Study Treatment

4.7.1.1 Ipatasertib/Placebo

Cohort A

At the time of the CCOD, the median duration of ipatasertib/placebo treatment was 5.3 months (range: 0–46) in the Ipat+Pac arm and 5.7 months (range: 0–44) in the Pbo+Pac arm (Table 17). Patients in the Ipat+Pac arm received a median number of 115.5 doses with a mean dose intensity (with respect to total number of doses) of 96.3%. The mean dose intensity (with respect to total dose) was 90.7% in the Ipat+Pac arm. Patients in the Pbo+Pac arm received a median number of 126 doses with a mean dose intensity (with respect to total number of doses) of 97.9%.

A higher proportion of patients had dose modifications in the Ipat+Pac arm (33.7%) compared with the Pbo+Pac arm (16.1%). The most common reason for ipatasertib/placebo dose modification in both treatment arms was AEs (Ipat+Pac: 91.1% vs. Pbo+Pac: 57.1%).

A summary of treatment discontinuation of ipatasertib/placebo in the safety evaluable population is appended (t_ds_ipat_A_SE).

Table 17 Ipatasertib/Placebo Exposure (Cohort A, Safety Evaluable Population)

Ipatasertib/Placebo Exposure, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Treatment duration (MONTHS)		
n	87	166
Mean (SD)	7.3 (6.5)	8.0 (7.7)
Median	5.7	5.3
Min - Max	0 - 44	0 - 46
Number of doses		
n	87	166
Mean (SD)	171.0 (168.1)	181.9 (182.3)
Median	126.0	115.5
Min - Max	1 - 1280	6 - 1356
Total cumulative dose(mg)		
n	87	166
Mean (SD)	0.0 (0.0)	66618.7 (60562.0)
Median	0.0	43750.0
Min - Max	0 - 0	2400 - 410200
Dose intensity (%) (with respect to total number of doses)		
n	87	166
Mean (SD)	97.90 (7.58)	96.33 (7.41)
Median	100.00	99.75
Min - Max	53.8 - 127.7	61.8 - 129.1
Dose intensity (%) (with respect to total dose)		
n	87	166
Mean (SD)	0.00 (0.00)	90.74 (13.16)
Median	0.00	97.64
Min - Max	0.0 - 0.0	50.0 - 102.4
Subjects with any dose modification		
n	87	166
Yes	14 (16.1%)	56 (33.7%)
No	73 (83.9%)	110 (66.3%)
Reason for Dose Modification		
n	14	56
Adverse Event	8 (57.1%)	51 (91.1%)
Medication Error	2 (14.3%)	3 (5.4%)
Other Reason	4 (28.6%)	4 (7.1%)

Treatment duration is the date of the last dose of Ipatasertib/Placebo minus the date of the first dose plus one day.
Dose intensity with respect to total number of doses is defined as the total number of doses taken divided by the total number of planned doses. Dose intensity with respect to total dose is defined as the total doses taken divided by the total planned doses.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ex.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ex_IPAT_A_SE.out
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Cohort B

At the time of the CCOD, the median duration of ipatasertib/placebo treatment was 8 months (range: 0–48) in the Ipat+Pac arm and 9.1 months (range: 0–48) in the Pbo+Pac arm (Table 18). Patients in the Ipat+Pac arm received a median number of 188 doses with a mean dose intensity (with respect to total number of doses) of 95.58%. The mean dose intensity (with respect to total dose) was 87.87% in the Ipat+Pac arm. Patients in the Pbo+Pac arm received a median number of 210 doses with a mean dose intensity (with respect to total number of doses) of 98.97%.

A higher proportion of patients had dose modifications in the Ipat+Pac arm (36.6%) compared with the Pbo+Pac arm (13.3%). The most common reason for ipatasertib/placebo dose modification in both treatment arms was AEs (Ipat+Pac: 94.3% vs. Pbo+Pac: 60.0%).

A summary of treatment discontinuation of ipatasertib/placebo in the safety evaluable population is appended (t_ds_ipat_B_SE).

Table 18 Ipatasertib/Placebo Exposure (Cohort B, Safety Evaluable Population)

Ipatasertib/Placebo Exposure, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Treatment duration (MONTHS)		
n	75	145
Mean (SD)	11.8 (10.9)	10.7 (10.1)
Median	9.1	8.0
Min - Max	0 - 48	0 - 48
Number of doses		
n	75	145
Mean (SD)	272.3 (266.2)	241.0 (229.0)
Median	210.0	188.0
Min - Max	6 - 1525	1 - 1099
Total cumulative dose(mg)		
n	75	145
Mean (SD)	0.0 (0.0)	88477.2 (87529.0)
Median	0.0	66800.0
Min - Max	0 - 0	400 - 439600
Dose intensity (%) (with respect to total number of doses)		
n	75	145
Mean (SD)	98.97 (5.63)	95.58 (9.99)
Median	100.00	98.89
Min - Max	82.6 - 137.1	13.3 - 104.3
Dose intensity (%) (with respect to total dose)		
n	75	145
Mean (SD)	0.00 (0.00)	87.87 (16.19)
Median	0.00	96.63
Min - Max	0.0 - 0.0	13.3 - 104.3
Subjects with any dose modification		
n	75	145
Yes	10 (13.3%)	53 (36.6%)
No	65 (86.7%)	92 (63.4%)
Reason for Dose Modification		
n	10	53
Adverse Event	6 (60.0%)	50 (94.3%)
Medication Error	2 (20.0%)	2 (3.8%)
Other Reason	2 (20.0%)	1 (1.9%)

Treatment duration is the date of the last dose of Ipatasertib/Placebo minus the date of the first dose plus one day.
Dose intensity with respect to total number of doses is defined as the total number of doses taken divided by the total number of planned doses. Dose intensity with respect to total dose is defined as the total doses taken divided by the total planned doses.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ex.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ex_IPAT_B_SE.out
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Cohort C

At the time of the CCOD, the median duration of ipatasertib treatment was 6.2 months (range: 0–43) (Table 19). Patients received a median number of 138.5 doses with a mean dose intensity (with respect to total number of doses) of 93.99%. The mean dose intensity (with respect to total dose) was 87.08%.

The proportion of patients with ipatasertib dose modifications was 41.2%. The most common reason for ipatasertib dose modification was AEs (90.5%).

A summary of treatment discontinuation of ipatasertib in the safety evaluable population is appended (t_ds_ipat_C_SE).

Table 19 Ipatasertib Exposure (Cohort C, Safety Evaluable Population)

Ipatasertib Exposure, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Treatment duration (MONTHS)	
n	102
Mean (SD)	8.8 (8.5)
Median	6.2
Min - Max	0 - 43
Number of doses	
n	102
Mean (SD)	197.6 (199.7)
Median	138.5
Min - Max	14 - 1269
Total cumulative dose(mg)	
n	102
Mean (SD)	71870.6 (75510.3)
Median	50400.0
Min - Max	5600 - 507600
Dose intensity (%) (with respect to total number of doses)	
n	102
Mean (SD)	93.99 (10.49)
Median	97.77
Min - Max	54.9 - 130.2
Dose intensity (%) (with respect to total dose)	
n	102
Mean (SD)	87.08 (17.08)
Median	94.86
Min - Max	45.1 - 130.2
Subjects with any dose modification	
n	102
Yes	42 (41.2%)
No	60 (58.8%)
Reason for Dose Modification	
n	42
Adverse Event	38 (90.5%)
Medication Error	3 (7.1%)
Other Reason	4 (9.5%)

Treatment duration is the date of the last dose of Ipatasertib minus the date of the first dose plus one day.
Dose intensity with respect to total number of doses is defined as the total number of doses taken divided by the total number of planned doses. Dose intensity with respect to total dose is defined as the total doses taken divided by the total planned doses.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ex.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ex_IPAT_C_SE.out
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4.7.1.2 Paclitaxel

Cohort A

At the time of the CCOD, the median duration of paclitaxel treatment in the Ipat+Pac arm was 5.1 months (range: 0– 38) and 5.3 months (range: 0– 39) in the Pbo+Pac arm (Table 20). Patients in the Ipat+Pac arm received a median number of 16 doses with a mean dose intensity (with respect to total number of doses) of 97.45%. Patients in the Pbo+Pac arm received a median number of 18 doses with a mean dose intensity (with respect to total number of doses) of 97.45%. The mean dose intensity (with respect to total dose) was 95.29% in the Ipat+Pac arm and 96.16% in the Pbo+Pac arm.

The proportion of patients with dose modifications was higher in the Ipat+Pac arm (24.1%) and the Pbo+Pac arm (18.4%). The most common reason for paclitaxel dose modification in both treatment arms was AEs (Ipat+Pac: 95.0% vs. Pbo+Pac: 87.5%).

A summary of treatment discontinuation of paclitaxel in the safety evaluable population is appended (t_ds_pac_A_SE).

Table 20 Paclitaxel Exposure (Cohort A, Safety Evaluable Population)

Paclitaxel Exposure, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Treatment duration (MONTHS)		
n	87	166
Mean (SD)	6.7 (5.9)	7.2 (6.6)
Median	5.3	5.1
Min - Max	0 - 39	0 - 38
Number of doses		
n	87	166
Mean (SD)	22.0 (19.0)	23.5 (20.2)
Median	18.0	16.0
Min - Max	1 - 124	1 - 121
Total cumulative dose(mg)		
n	87	164
Mean (SD)	2946.4 (2381.4)	3131.2 (2529.3)
Median	2385.4	2167.8
Min - Max	133 - 14317	138 - 13554
Dose intensity (%) (with respect to total number of doses)		
n	87	166
Mean (SD)	97.45 (6.56)	97.45 (14.12)
Median	100.00	100.00
Min - Max	75.0 - 120.0	40.0 - 200.0
Dose intensity (%) (with respect to total dose)		
n	87	164
Mean (SD)	96.16 (7.87)	95.29 (15.33)
Median	100.00	100.00
Min - Max	64.5 - 120.0	40.0 - 200.0
Subjects with any dose modification		
n	87	166
Yes	16 (18.4%)	40 (24.1%)
No	71 (81.6%)	126 (75.9%)
Reason for Dose Modification		
n	16	40
Adverse Event	14 (87.5%)	38 (95.0%)
Other Reason	2 (12.5%)	3 (7.5%)

Treatment duration is the date of the last dose of Paclitaxel minus the date of the first dose plus one day.
Dose intensity with respect to total number of doses is defined as the total number of doses taken divided by the total number of planned doses. Dose intensity with respect to total dose is defined as the total doses taken divided by the total planned doses.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ex.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ex_PAC_A_SE.out
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Cohort B

At the time of the CCOD, the median duration of paclitaxel treatment in the Ipat+Pac arm was 6.9 months (range: 0– 48) and 8.8 months (range: 0– 47) in the Pbo+Pac arm

(Table 21). Patients in the Ipat+Pac arm received a median number of 23.5 doses with a mean dose intensity (with respect to total number of doses) of 97.37%. Patients in the Pbo+Pac arm received a median number of 29 doses with a mean dose intensity (with respect to total number of doses) of 97.64%. The mean dose intensity (with respect to total dose) was 94.39% in the Ipat+Pac arm and 94.53% in the Pbo+Pac arm.

The proportion of patients with dose modifications was similar between the Ipat+Pac arm (34%) and the Pbo+Pac arm (32%). The most common reason for paclitaxel dose modification in both treatment arms was AEs (Ipat+Pac: 93.9% vs. Pbo+Pac: 79.2%).

A summary of treatment discontinuation of paclitaxel in the safety evaluable population is appended (t_ds_pac_B_SE).

Table 21 Paclitaxel Exposure (Cohort B, Safety Evaluable Population)

Paclitaxel Exposure, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Treatment duration (MONTHS)		
n	75	144
Mean (SD)	10.9 (10.1)	9.2 (8.7)
Median	8.8	6.9
Min - Max	0 - 47	0 - 48
Number of doses		
n	75	144
Mean (SD)	35.4 (31.0)	29.9 (27.2)
Median	29.0	23.5
Min - Max	1 - 141	1 - 158
Total cumulative dose(mg)		
n	74	144
Mean (SD)	4613.4 (3758.0)	3852.2 (3312.4)
Median	3816.2	3144.0
Min - Max	171 - 19062	110 - 18862
Dose intensity (%) (with respect to total number of doses)		
n	75	144
Mean (SD)	97.64 (6.36)	97.37 (12.07)
Median	100.00	100.00
Min - Max	65.0 - 120.0	40.0 - 200.0
Dose intensity (%) (with respect to total dose)		
n	74	144
Mean (SD)	94.53 (9.12)	94.39 (13.52)
Median	98.52	97.94
Min - Max	65.0 - 120.0	36.3 - 200.0
Subjects with any dose modification		
n	75	144
Yes	24 (32.0%)	49 (34.0%)
No	51 (68.0%)	95 (66.0%)
Reason for Dose Modification		
n	24	49
Adverse Event	19 (79.2%)	46 (93.9%)
Medication Error	1 (4.2%)	2 (4.1%)
Other Reason	6 (25.0%)	3 (6.1%)

Treatment duration is the date of the last dose of Paclitaxel minus the date of the first dose plus one day.
Dose intensity with respect to total number of doses is defined as the total number of doses taken divided by the total number of planned doses. Dose intensity with respect to total dose is defined as the total doses taken divided by the total planned doses.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ex.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ex_PAC_B_SE.out
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Cohort C

At the time of the CCOD, the median duration of paclitaxel treatment was 6.1 months (range: 0– 29) (Table 22). Patients received a median number of 18.5 doses with a mean dose intensity (with respect to total number of doses) of 95.56%. The mean dose intensity (with respect to total dose) was 93.08%.

The proportion of patients with dose modifications was 36.3%. The most common reason for paclitaxel dose modification was AEs (78.4%).

A summary of treatment discontinuation of paclitaxel in the safety evaluable population is appended (t_ds_pac_C_SE).

Table 22 Paclitaxel Exposure (Cohort C, Safety Evaluable Population)

Paclitaxel Exposure, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Treatment duration (MONTHS)	
n	102
Mean (SD)	7.2 (5.8)
Median	6.1
Min - Max	0 - 29
Number of doses	
n	102
Mean (SD)	23.2 (17.5)
Median	18.5
Min - Max	2 - 90
Total cumulative dose(mg)	
n	101
Mean (SD)	3119.2 (2358.8)
Median	2519.0
Min - Max	369 - 11174
Dose intensity (%) (with respect to total number of doses)	
n	102
Mean (SD)	95.56 (8.02)
Median	100.00
Min - Max	61.9 - 112.5
Dose intensity (%) (with respect to total dose)	
n	101
Mean (SD)	93.08 (9.59)
Median	96.34
Min - Max	61.9 - 112.5
Subjects with any dose modification	
n	102
Yes	37 (36.3%)
No	65 (63.7%)
Reason for Dose Modification	
n	37
Adverse Event	29 (78.4%)
Other Reason	10 (27.0%)

Treatment duration is the date of the last dose of Paclitaxel minus the date of the first dose plus one day.
Dose intensity with respect to total number of doses is defined as the total number of doses taken divided by the total number of planned doses. Dose intensity with respect to total dose is defined as the total doses taken divided by the total planned doses.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ex.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ex_PAC_C_SE.out
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4.7.1.3 Atezolizumab (Cohort C Only)

At the time of the CCOD, the median duration of atezolizumab treatment was 5.7 months (range: 0– 41) (Table 23). Patients received a median number of 12 doses with a mean dose intensity (with respect to total number of doses) of 94.74%. The mean dose intensity (with respect to total dose) was 94.74%.

As per protocol, no dose modification for atezolizumab was allowed.

A summary of treatment discontinuation of atezolizumab in the safety evaluable population is appended (t_ds_atezo_C_SE).

Table 23 Atezolizumab Exposure (Cohort C, Safety Evaluable Population)

Atezolizumab Exposure, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Treatment duration (MONTHS)	
n	102
Mean (SD)	8.2 (8.0)
Median	5.7
Min - Max	0 - 41
Number of doses	
n	102
Mean (SD)	17.5 (16.6)
Median	12.0
Min - Max	1 - 86
Total cumulative dose(mg)	
n	102
Mean (SD)	14708.2 (13974.0)
Median	10080.0
Min - Max	840 - 72240
Dose intensity (%) (with respect to total number of doses)	
n	102
Mean (SD)	94.74 (10.98)
Median	100.00
Min - Max	50.0 - 125.0
Dose intensity (%) (with respect to total dose)	
n	102
Mean (SD)	94.74 (10.98)
Median	100.00
Min - Max	50.0 - 125.0

Treatment duration is the date of the last dose of Atezolizumab minus the date of the first dose plus one day.
Dose intensity with respect to total number of doses is defined as the total number of doses taken divided by the total number of planned doses. Dose intensity with respect to total dose is defined as the total doses taken divided by the total planned doses.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ex.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ex_ATEZO_C_SE.out
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4.8 EFFICACY OBSERVATION TIME

The overall median duration of survival follow-up for Cohorts A, B, and C were 17.9 months (min. 0 months; max. 43.5 months) (t_ef_fudur_A_IT_30OCT2021_40016), 22.42 months (min. 0 months; max. 44.6 months) (t_ef_fudur_B_IT_30OCT2021_40016), and 18.02 months (min. 1.8 months; max. 28.4 months) (t_ef_fudur_C_IT_30OCT2021_40016), respectively.

5. EVALUATION OF RESPONSE TO STUDY TREATMENT

5.1 EFFICACY

The efficacy results presented throughout Section 5.1 of the final CSR for Study CO40016 are based on a CCOD of 30 October 2021.

5.1.1 Efficacy Summary

As described in the primary CSRs for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941), these did not meet its primary efficacy endpoint, with no clinically meaningful benefit observed for ipatasertib in combination with paclitaxel over paclitaxel alone. For both Cohorts A and B, data for the interim analysis of the key secondary endpoint of OS was immature at the CCOD for primary analysis. Results of other secondary endpoints were consistent with those of the primary endpoint, PFS.

This CSR describes the final efficacy data for all cohorts, specifically, final OS for Cohort A and Cohort B (Table 24), and PFS, OS, and other secondary efficacy endpoints for Cohort C (Table 25). While efficacy results for Cohort C were descriptive in nature, the median duration of PFS and OS were consistent with the Ipat+Pac arm in Cohort A.

Table 24 Final Overall Survival for Cohort A and Cohort B (CCOD: 30 October 2021)

Key Secondary Efficacy Endpoint				
Overall Survival (Final Analysis)				
	Cohort A		**Cohort B**	
	Pbo + Pac	**Ipat + Pac**	**Pbo + Pac**	**Ipat + Pac**
ITT Population	**n=87**	**n=168**	**n=76**	**n=146**
Patients with event (%)	39 (44.8%)	87 (51.8%)	43 (56.6%)	77 (52.7%)
Median duration of survival – months (95% CI)	24.9 (16.9, 40.4)	24.2 (19.2, 29.4)	28.4 (20.6, 37.3)	29.0 (22.4, 34.8)
Stratified Hazard Ratio (95% CI)	1.08 (0.73, 1.58)		0.94 (0.65, 1.37)	
Unstratified Hazard Ratio (95% CI)	1.05 (0.72, 1.54)		0.92 (0.64, 1.34)	

CCOD = clinical cutoff date; Ipat = ipatasertib; ITT = intent-to-treat; n = number of patients; Pac = paclitaxel; Pbo = placebo.

Source: t_ef_tte_OS_A_IT_30OCT2021_40016; t_ef_tte_OS_B_IT_30OCT2021_40016.

Table 25 Summary of Efficacy for Cohort C (CCOD: 30 October 2021)

Primary Efficacy Endpoint	
Progression-Free Survival: INV-Assessed per RECIST v1.1	
ITT Population	**Ipat + Atezo + Pac (n = 102)**
Patients with event (%)	78 (76.5%)
Median duration of PFS – months (95% CI)	7.1 (5.5, 9.1)
1-year event-free rate - % (95% CI)	31.17 (21.59, 40.76)
Key Secondary Efficacy Endpoints	
Overall Survival	
ITT Population	**Ipat + Atezo + Pac (n = 102)**
Patients with event (%)	49 (48.0%)
Median duration of survival – months (95% CI)	22.8 (17.8, NE)
1-year event-free rate - % (95% CI)	79.38 (71.31, 87.44)
Other Secondary Efficacy Endpoints	
Objective Response Rate: INV-Assessed per RECIST v1.1	
Patients with Measurable Disease at Baseline	**Ipat + Atezo + Pac (n = 102)**
Responders 95% CI	54 (52.9%) (42.80, 62.90)
Complete Response (CR) 95% CI	7 (6.9%) (2.80, 13.63)
Partial Response (PR) 95% CI	47 (46.1%) (36.16, 56.23)
Duration of Response: INV-Assessed per RECIST v1.1	
Patients with Objective Response	**Ipat + Atezo + Pac (n = 54)**
Patients with event (%)	32 (59.3%)
Patients without event (%)	22 (40.7%)
Median duration of response – months 95% CI	8.7 (5.7,12.7)

Table continued from previous page

Clinical Benefit Rate: INV-Assessed per RECIST v1.1	
Patients with Measurable Disease at Baseline	**Ipat + Atezo + Pac (n = 102)**
Patients with clinical benefit 95% CI	56 (54.9%) (44.74, 64.78)
Patient-Reported Outcomes – GHS/QoL – EORTC QLQ-C30	
PRO Evaluable Population	N = 101
Please refer to Patient-Reported Outcomes for an overview of the PRO results.	

Atezo = atezolizumab; CCOD = clinical cutoff date; CR = complete response; EORTC QLQ C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; GHS = global health status; INV = investigator; Ipat = ipatasertib; ITT = intent-to-treat; n = number of patients; Pac = paclitaxel; PFS = progression-free survival; PR = partial response; PRO = patient-reported outcome; QoL = Quality of life; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors, Version 1.1.

Source: t_ef_tte_PFSINV_C_IT_30OCT2021_40016; t_ef_tte_OS_C_IT_30OCT2021_40016; t_ef_bor_BORINV_C_MDBI_IT_30OCT2021_40016; t_ef_dor_DORINV_C_MDBI_IT_30OCT2021_40016; t_ef_ccb_CCBINV_C_MDBI_IT_30OCT2021_40016.

5.1.2 Primary Efficacy Endpoint: Progression-Free Survival (Investigator)

The primary efficacy endpoint results for Cohort A and B were reported in the primary CSR for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941), respectively.

For Cohort C, at the time of CCOD, 78 (76.5%) patients had progressed or died in the ITT population. The one-year event-free rate was 31.17% (95% CI: 21.59, 40.76). The KM-estimated median duration of PFS was 7.1 months (95% CI: 5.5, 9.1) (Table 25, Table 26, g_ef_km_PFSINV_C_IT_30OCT2021_40016).

Table 26 Time to Event Summary for Investigator-Assessed Progression-Free Survival (ITT Population)

Time to Event Summary for Progression-Free Survival (Investigator), Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Earliest Contributing Event to Progression Free Survival by Investigator

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Patients with event (%)	78 (76.5%)
Earliest contributing event	
Death	6
Disease Progression	72
Patients without event (%)	24 (23.5%)
Time to Event (Months)	
Median	7.1
95% CI	(5.5, 9.1)
25% and 75%-ile	3.7 - 13.9
Range	1 - 28*
One year duration	
Patients remaining at risk	24
Event Free Rate (%)	31.17
95% CI	(21.59, 40.76)

* Censored value. ^ Censored and event.
Summaries of Progression-Free Survival (median, percentiles) are Kaplan-Meier estimates.
95% CI for median was computed using the method of Brookmeyer and Crowley.
Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/program/t_ef_tte.sas
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5.1.3 Key Secondary Efficacy Endpoints

5.1.3.1 Overall Survival

As the primary endpoint of PFS was not met, the OS analysis results for all cohorts were considered descriptive.

Cohort A

At the time of CCOD, deaths had occurred in 51.8% and 44.8% of patients in the Ipat+Pac arm and Pbo+Pac arm, respectively, and the stratified HR was 1.08 (95% CI: 0.73, 1.58) (Table 27). The KM-estimated median OS was 24.2 months in the Ipat+Pac arm (95% CI: 19.2, 29.4) and 24.9 months in the Pbo+Pac arm (95% CI: 16.9, 40.4), with no clinically meaningful separation between the OS curves of the two treatment arms (Figure 5).

Table 27 Time to Event Summary for Overall Survival, Cohort A (ITT Population)

Time to Event Summary for Overall Survival, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

Overall Survival

	Placebo + Paclitaxel (N=87)		Ipatasertib + Paclitaxel (N=168)
Patients with event (%)	39 (44.8%)		87 (51.8%)
Patients without event (%)	48 (55.2%)		81 (48.2%)
Time to Event (Months)			
Median	24.9		24.2
95% CI	(16.9, 40.4)		(19.2, 29.4)
25% and 75%-ile	12.1 - 40.4		12.7 - NE
Range	0* - 41*		0* - 44*
Stratified Analysis			
p-value (log-rank)		0.7068	
Hazard Ratio		1.08	
95% CI		(0.73, 1.58)	
Unstratified Analysis			
p-value (log-rank)		0.7855	
Hazard Ratio		1.05	
95% CI		(0.72, 1.54)	
One year duration			
Patients remaining at risk	56		114
Event Free Rate (%)	76.28		75.24
95% CI	(66.93, 85.63)		(68.40, 82.08)
Difference in Event Free Rate		-1.04	
95% CI		(-12.63, 10.54)	
p-value (Z-test)		0.8597	
Two year duration			
Patients remaining at risk	22		53
Event Free Rate (%)	52.30		50.60
95% CI	(40.48, 64.12)		(42.39, 58.81)
Difference in Event Free Rate		-1.70	
95% CI		(-16.09, 12.69)	
p-value (Z-test)		0.8168	

* Censored value. ^ Censored and event.
Summaries of OS (median, percentiles) are Kaplan-Meier estimates. 95% CI for median was computed using the method of Brookmeyer and Crowley. Stratification variables are: prior adjuvant/neoadjuvant chemotherapy (yes vs. no), tumor PIK3CA/AKT1/PTEN-alteration status (PIK3CA/AKT1-activating mutations vs. PTEN alterations with no PIK3CA/AKT1-activating mutations). Hazard ratios were estimated by Cox regression.
Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

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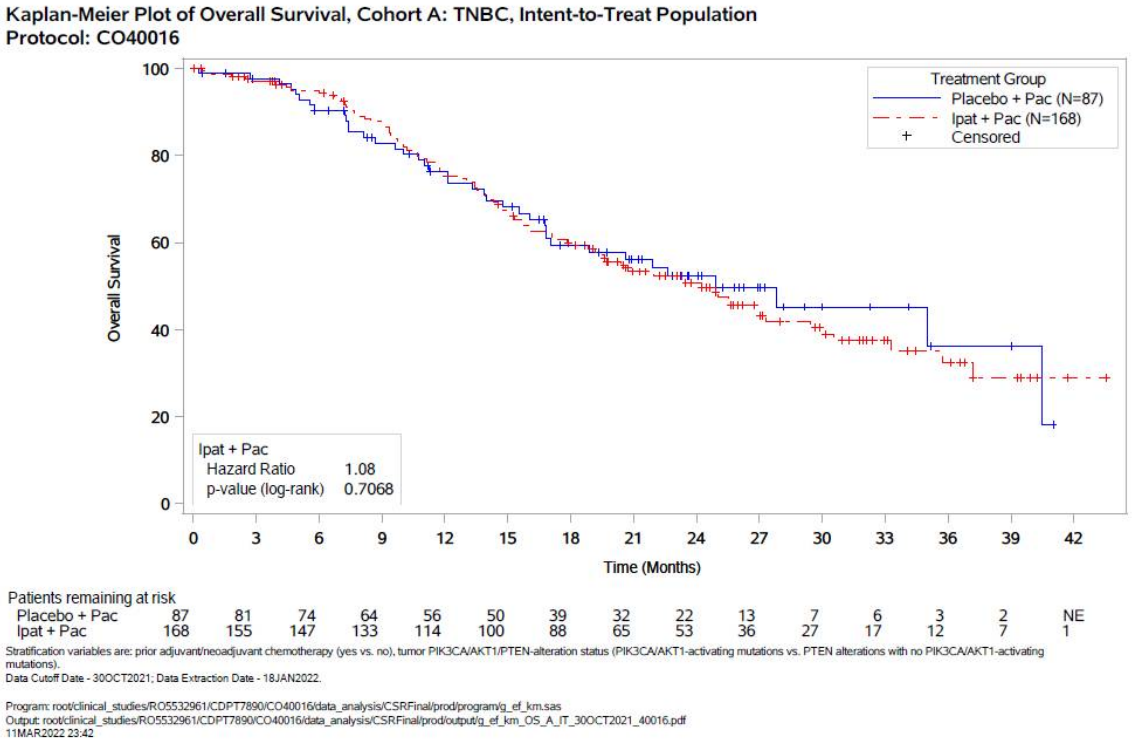
11MAR2022 23:44 Page 1 of 1

Figure 5 Kaplan-Meier Plot of Overall Survival, Cohort A (ITT Population)



Cohort B

At the time of CCOD, a similar proportion of deaths had occurred in the Ipat+Pac arm (52.7%%) and the Pbo+Pac arm (56.6%) and the stratified HR was 0.94 (95% CI: 0.65, 1.37) (Table 28). The KM-estimated median OS was 29.0 months in the Ipat+Pac arm (95% CI: 22.4, 34.8) and 28.4 months in the Pbo+Pac arm (95% CI: 20.6, 37.3), with no clinically meaningful separation between the OS curves of the two treatment arms (Figure 6).

Table 28 Time to Event Summary for Overall Survival, Cohort B (ITT Population)

Time to Event Summary for Overall Survival, Cohort B: HR+/HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

Overall Survival

	Placebo + Paclitaxel (N=76)		Ipatasertib + Paclitaxel (N=146)
Patients with event (%)	43 (56.6%)		77 (52.7%)
Patients without event (%)	33 (43.4%)		69 (47.3%)
Time to Event (Months)			
Median	28.4		29.0
95% CI	(20.6, 37.3)		(22.4, 34.8)
25% and 75%-ile	14.3 - NE		14.9 - NE
Range	0* - 44*		0* - 45*
Stratified Analysis			
p-value (log-rank)		0.7562	
Hazard Ratio		0.94	
95% CI		(0.65, 1.37)	
Unstratified Analysis			
p-value (log-rank)		0.6798	
Hazard Ratio		0.92	
95% CI		(0.64, 1.34)	
One year duration			
Patients remaining at risk	54		110
Event Free Rate (%)	78.75		83.38
95% CI	(69.18, 88.31)		(77.17, 89.59)
Difference in Event Free Rate		4.63	
95% CI		(-6.77, 16.04)	
p-value (Z-test)		0.4257	
Two year duration			
Patients remaining at risk	38		68
Event Free Rate (%)	56.50		55.45
95% CI	(44.75, 68.25)		(46.92, 63.98)
Difference in Event Free Rate		-1.05	
95% CI		(-15.57, 13.47)	
p-value (Z-test)		0.8872	

* Censored value. ^ Censored and event.
Summaries of OS (median, percentiles) are Kaplan-Meier estimates. 95% CI for median was computed using the method of Brookmeyer and Crowley. Stratification variables are: prior adjuvant/neoadjuvant chemotherapy (yes vs. no), prior therapy with a phosphoinositide 3-kinase (PI3K) or mTOR inhibitor (yes vs. no). Hazard ratios were estimated by Cox regression.
Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

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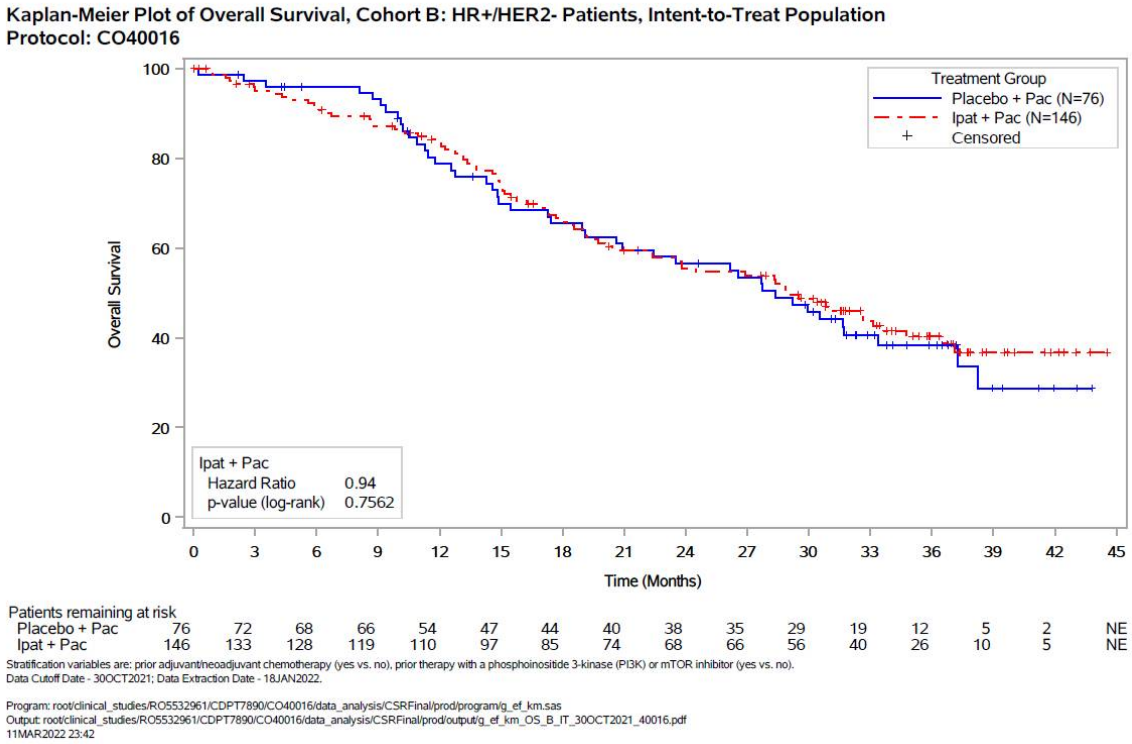
Figure 6 Kaplan-Meier Plot of Overall Survival, Cohort B (ITT Population)



Cohort C

At the time of CCOD, death was reported in 48.0% of patients (Table 29). The one-year event-free rate was 79.38% (95% CI: 71.31, 87.44). The KM-estimated median OS was 22.8 months (95% CI: 17.8, NE) (g_ef_km_OS_C_IT_30OCT2021_40016).

Table 29 Time to Event Summary for Overall Survival, Cohort C (ITT Population)

Time to Event Summary for Overall Survival, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Overall Survival

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Patients with event (%)	49 (48.0%)
Patients without event (%)	53 (52.0%)
Time to Event (Months)	
Median	22.8
95% CI	(17.8, NE)
25% and 75%-ile	12.9 - NE
Range	2* - 28*
One year duration	
Patients remaining at risk	74
Event Free Rate (%)	79.38
95% CI	(71.31, 87.44)
Two year duration	
Patients remaining at risk	17
Event Free Rate (%)	46.58
95% CI	(35.45, 57.70)

* Censored value. ^ Censored and event.
Summaries of OS (median, percentiles) are Kaplan-Meier estimates. 95% CI for median was computed using the method of Brookmeyer and Crowley.
Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/output/t_ef_tte_OS_C_IT_30OCT2021_40016.out
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5.1.4 Other Secondary Efficacy Endpoints (Cohort C Only)

The results for other secondary efficacy endpoints (investigator-assessed ORR, DOR, and CBR) for Cohorts A and B were reported in the primary CSR for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941), respectively. The results for these secondary efficacy endpoints for Cohort C are presented below.

5.1.4.1 Objective Response Rate (Investigator)

Among patients with measurable disease, 52.9% were responders, with 7 patients having a CR and 47 patients having a PR (Table 25, t_ef_bor_BORINV_C_MDBI_IT_30OCT2021_40016).

5.1.4.2 Duration of Objective Response (Investigator)

Among responders, 40.7% of patients (n=22) had ongoing response by the CCOD. The KM-estimated median DOR was 8.7 months (95% CI: 5.7, 12.,7) (Table 25, t_ef_dor_DORINV_C_MDBI_IT_30OCT2021_40016).

5.1.4.3 Clinical Benefit Rate (Investigator)

The investigator-assessed CBR was 54.9% (95% CI: 44.74, 64.78) (Table 25, t_ef_ccb_CCBINV_C_MDBI_IT_30OCT2021_40016).

5.1.4.4 Patient-Reported Outcomes

The results for PROs for Cohorts A and B were reported in the primary CSR for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941), respectively. The results for PROs for Cohort C are presented below and are based on a snapshot of 21 March 2023.

5.1.4.4.1 Questionnaire Completion Rates: EORTC QLQ-C30

The completion rate of the EORTC QLQ-C30 at baseline (Cycle 1, Day 1) was high at 100% (at least one question completed). Completion rates remained ≥85.7% for all cycles, except for Cycle 31 (75%). Completion rates during long-term follow-up visits ranged from a high of 67.4% at 12 months to a low of 25% (n=2/8) at 21 months. PRO completion rates and reasons for missing data for the EORTC QLQ-C30 by timepoint are appended (t_qs_comp_C30INST_C_IT).

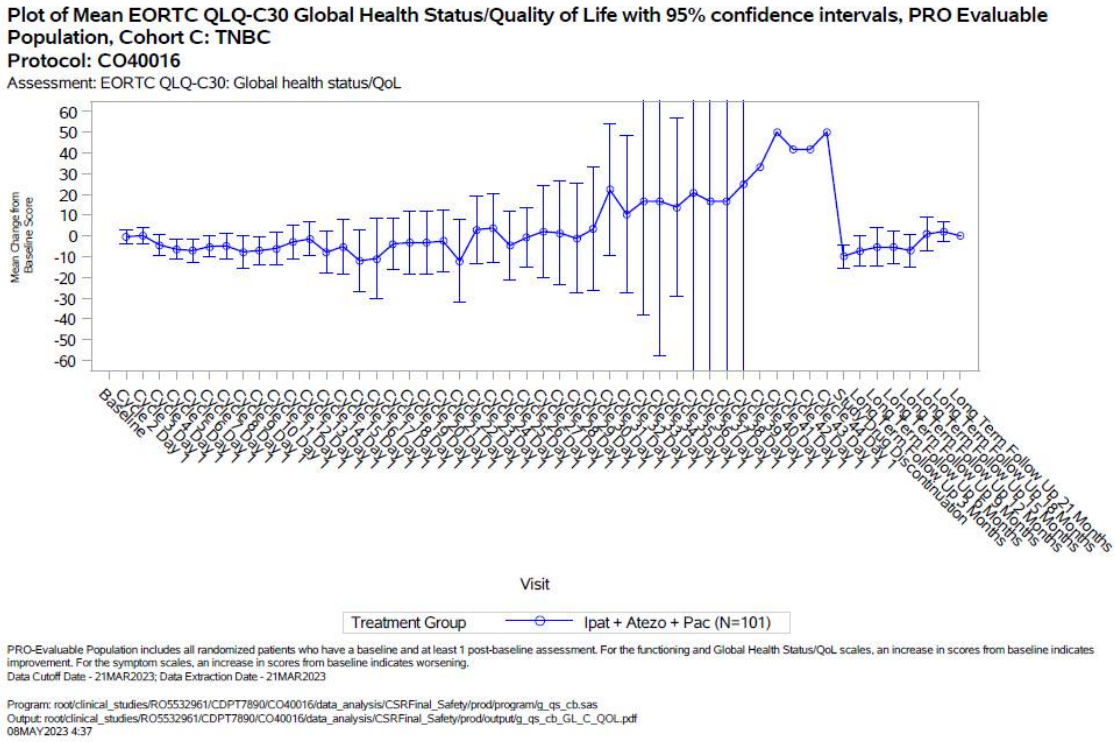
5.1.4.4.2 Secondary PRO Endpoint: GHS/QoL – EORTC QLQ-C30

Beyond Cycle 7, less than half of the PRO evaluable population were still on treatment (t_qs_cb_GL_C_QOL), precluding a meaningful analysis following the Cycle 7 assessment. Thus, interpretation will focus on patient-reported data through Cycle 7.

The mean GHS/QoL score at baseline was 74.92 (t_qs_cb_GL_C_QOL).

The mean change from baseline scores in GHS/QoL remained stable (i.e., within 8 points of the baseline score) through Cycle 7, with no clinically meaningful deterioration (i.e., a ≥10-point decrease from baseline in mean change score; Osoba et al. 1998) observed (Figure 7), indicating patients' baseline GHS/QoL was maintained during this time period.

Figure 7 Plot of Mean EORTC QLQ-C30 Global Health Status/Quality of Life Change from Baseline with 95% Confidence Intervals (PRO Evaluable Population)



EOTRC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; PRO = patient-reported outcome.

5.2 SAFETY

Results presented in this section are based on a snapshot of 21 March 2023.

Throughout this section, where treatment arms are not specifically stated for Cohorts A and B, the presentation of results is as follows: results in the Ipat + Pac arm are provided first followed by the Pbo + Pac arm.

5.2.1 Safety Summary

Ipatasertib in combination with paclitaxel (Cohorts A and B) or with atezolizumab and paclitaxel (Cohort C) was well tolerated, and the safety profile of the combination treatment regimen was consistent with the known risks of each individual study treatment component. No new safety concerns were identified. Overviews of the key safety results for Cohort A (Table 30), Cohort B (Table 31), and Cohort C (Table 32) are provided.

Cohort A

The key safety findings for Cohort A were:

- The median duration of ipatasertib/placebo treatment was 5.3 months in the Ipat+Pac arm and 5.7 months in the Pbo+Pac arm. The median duration of paclitaxel treatment was 5.1 months in the Ipat + Pac arm and 5.3 months in the Pbo + Pac arm.
- The most frequent AEs (by PT) of any grade (reported in ≥30% of patients) were diarrhea, alopecia, nausea, and vomiting in the Ipat + Pac arm and diarrhea, alopecia and constipation in the Pbo+Pac arm.
- Grade≥3 AEs were reported in a similar proportion of patients in the Ipat+Pac arm and the Pbo+Pac arm (50.6% vs. 46.0%). The most frequent Grade ≥3 AEs (by PT) with ≥5% incidence were diarrhea and neutropenia in the Ipat+Pac arm, and neutrophil count decreased in the Pbo+Pac arm.
- A total of 132 deaths were reported in the safety evaluable population (Ipat+Pac: 91 patients [54.8%] vs. Pbo+Pac: 41 patients [47.1%]). The primary cause of death was progressive disease.
- Grade 5 AEs were reported in 2 patients in both Ipat+Pac (1.2%) and Pbo+Pac (2.3%) arms. Of these, 1 AE (by PT) of tumor lysis syndrome in the Pbo+Pac arm was considered related to both placebo and paclitaxel by the investigator.
- SAEs were reported in a similar proportion of patients in the Ipat+Pac arm and the Pbo+Pac arm (20.5% vs. 23.0%). SAEs (by PT) reported in ≥1% of patients (i.e., ≥2 patients) in the Ipat+Pac arm were: diarrhea, febrile neutropenia, pulmonary embolism, pneumonia, nausea, and vomiting. SAEs (by PT) reported in more than 1 patient in the Pbo+Pac arm were: pneumonia and pleural effusion.
- The proportion of patients who experienced AEs leading to ipatasertib/placebo treatment discontinuation was higher in the Ipat+Pac arm compared with Pbo+Pac arm (10.2% vs. 6.9%)
- AEs leading to discontinuation of paclitaxel was reported in 15.1% of patients in the Ipat+Pac arm and 16.1% of patients in the Pbo + Pac arm.
- Selected AEs were reported in both treatment arms (Ipat+Pac: 94.6% vs. Pbo+Pac: 90.8%). Selected AEs of diarrhea, asthenia, nausea, rash, vomiting, hyperglycemia and oral mucositis were observed with a higher frequency (≥5% difference) in the Ipat+Pac arm compared with the Pbo+Pac arm. Peripheral neuropathy, neutropenia, erythropenia, hepatotoxicity, hyperlipidemia, pneumonia, thrombocytopenia, pneumonitis, colitis, and erythema multiforme were reported with < 5% difference between treatment arms. Of the safety evaluable patients, for selected AEs, 51.8% experienced a highest Grade of 1–2 in the Ipat + Pac arm, 57.5% experienced a highest Grade of 1–2 in the Pbo + Pac arm, 42.8% experienced a highest Grade of 3–4 in the Ipat + Pac arm, and 33.3% experienced a highest Grade of 3–4 in the Pbo + Pac arm.

Table 30 Safety Summary, Cohort A: TNBC Patients (Safety Evaluable Population)

Safety Summary, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one AE	84 (96.6%)	162 (97.6%)
Total number of AEs	976	2645
Total number of patients with at least one		
AE with fatal outcome	2 (2.3%)	2 (1.2%)
Serious AE	20 (23.0%)	34 (20.5%)
AE leading to discontinuation from Ipatasertib/placebo	6 (6.9%)	17 (10.2%)
AE leading to discontinuation from Paclitaxel	14 (16.1%)	25 (15.1%)
AE leading to discontinuation from any treatment	14 (16.1%)	31 (18.7%)
AE leading to Ipatasertib/placebo dose reduction	7 (8.0%)	46 (27.7%)
AE leading to Paclitaxel dose reduction	9 (10.3%)	34 (20.5%)
AE leading to dose reduction from any treatment	12 (13.8%)	64 (38.6%)
AE leading to Ipatasertib/placebo dose interruption	26 (29.9%)	74 (44.6%)
AE leading to Paclitaxel dose interruption	41 (47.1%)	85 (51.2%)
AE leading to dose interruption from any treatment	43 (49.4%)	98 (59.0%)
Grade >=3 AE	40 (46.0%)	84 (50.6%)
AE related to Ipatasertib/placebo	55 (63.2%)	152 (91.6%)
AE related to Paclitaxel	81 (93.1%)	152 (91.6%)
AE related to any treatment	83 (95.4%)	156 (94.0%)

Investigator text for AEs is coded using MedDRA version 25.1. Percentages are based on N in the column headings. Multiple occurrences of the same AE in one individual are counted only once except for 'Total number of AEs' row in which multiple occurrences of the same AE are counted separately.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Cohort B

The key safety findings for Cohort B were:

- The median duration of ipatasertib/placebo treatment was 8 months in the Ipat+Pac arm and 9.1 months in the Pbo+Pac arm. The median duration of paclitaxel treatment was 6.9 months in the Ipat + Pac arm and 8.8 months in the Pbo + Pac arm.
- The most frequent AEs (by PT) of any grade (reported in ≥30% of patients) were: diarrhea, alopecia, anemia, neuropathy peripheral, vomiting and nausea in the Ipat+Pac arm and diarrhea, alopecia, peripheral sensory neuropathy, and constipation in the Pbo+Pac arm.
- Grade≥3 AEs were reported in a higher proportion of patients in the Ipat+Pac arm and the Pbo+Pac arm (57.2% vs. 49.3%). The most frequent Grade ≥3 AEs (by PT) with ≥5% incidence were diarrhea, neutrophil count decreased, neuropathy peripheral and neutropenia in the Ipat+Pac arm, and neutrophil count decreased, peripheral sensory neuropathy, neutropenia, and hypertension in the Pbo+Pac arm.
- A total of 122 deaths were reported in the safety evaluable population (Ipat+Pac: 78 patients [53.8%] vs. Pbo+Pac: 44 patients [58.7%]). The primary cause of death was progressive disease.

- Grade 5 AEs were reported in 5 patients (3.4%) in the Ipat+Pac arm and 1 patient (1.3%) in the Pbo+Pac arm. Of these, SAE (by PT) of sepsis in the Pbo+Pac arm was considered related to paclitaxel and SAE of febrile neutropenia in the Ipat+Pac arm was considered related to ipatasertib and paclitaxel by the investigator.
- SAEs were reported in a higher proportion of patients in the Ipat+Pac arm compared with the Pbo+Pac arm (20.7% vs. 14.7%). SAEs (by PT) reported in ≥1% of patients (i.e., ≥2 patients) in the Ipat+Pac arm were: diarrhea, pneumonia, pneumonitis, febrile neutropenia, and neutropenia. No SAE (by PT) was reported in more than 1 patient in the Pbo+Pac arm.
- The proportion of patients who experienced AEs leading to ipatasertib/placebo treatment discontinuation was higher in the Ipat+Pac arm compared with Pbo+Pac arm (11.7% vs. 4.0%)
- AEs led to discontinuation of paclitaxel in 29% of patients in the Ipat+Pac arm and 16% of patients in the Pbo + Pac arm.
- Selected AEs were reported in both treatment arms (Ipat+Pac: 97.2% vs. Pbo+Pac: 97.3%). Selected AEs of diarrhea, nausea, rash, erythropenia, vomiting, and oral mucositis were observed with a higher frequency (≥5% difference) in the Ipat+Pac arm compared with the Pbo+Pac arm. Peripheral neuropathy, neutropenia, asthenia, hyperglycemia, hyperlipidemia, pneumonia, pneumonitis, and thrombocytopenia were reported with <5% difference between treatment arms. Of the safety evaluable patients, for selected AEs, 51.7% experienced a highest Grade of 1–2 in the Ipat+Pac arm, 65.3% experienced a highest Grade of 1–2 in the Pbo+Pac arm, 44.1% experienced a highest Grade of 3–4 in the Ipat+Pac arm, 32% experienced a highest Grade of 3–4 in the Pbo+Pac arm, and 1.4% experienced a highest Grade of 5 in the Ipat+Pac arm.

Table 31 Safety Summary, Cohort B: HR+/HER2- Patients (Safety Evaluable Population)

Safety Summary, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one AE	74 (98.7%)	144 (99.3%)
Total number of AEs	1195	2722
Total number of patients with at least one		
AE with fatal outcome	1 (1.3%)	5 (3.4%)
Serious AE	11 (14.7%)	30 (20.7%)
AE leading to discontinuation from Ipatasertib/placebo	3 (4.0%)	17 (11.7%)
AE leading to discontinuation from Paclitaxel	12 (16.0%)	42 (29.0%)
AE leading to discontinuation from any treatment	12 (16.0%)	48 (33.1%)
AE leading to Ipatasertib/placebo dose reduction	6 (8.0%)	50 (34.5%)
AE leading to Paclitaxel dose reduction	19 (25.3%)	39 (26.9%)
AE leading to dose reduction from any treatment	21 (28.0%)	68 (46.9%)
AE leading to Ipatasertib/placebo dose interruption	32 (42.7%)	67 (46.2%)
AE leading to Paclitaxel dose interruption	40 (53.3%)	77 (53.1%)
AE leading to dose interruption from any treatment	45 (60.0%)	86 (59.3%)
Grade >=3 AE	37 (49.3%)	83 (57.2%)
AE related to Ipatasertib/placebo	54 (72.0%)	134 (92.4%)
AE related to Paclitaxel	70 (93.3%)	138 (95.2%)
AE related to any treatment	70 (93.3%)	143 (98.6%)

Investigator text for AEs is coded using MedDRA version 25.1. Percentages are based on N in the column headings. Multiple occurrences of the same AE in one individual are counted only once except for 'Total number of AEs' row in which multiple occurrences of the same AE are counted separately.
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Cohort C

The key safety findings for Cohort C were:

- The median duration of ipatasertib, atezolizumab, and paclitaxel treatment were 6.2, 5.7, and 6.1 months, respectively.
- The most frequent AEs (by PT) of any grade (reported in ≥30% of patients) were diarrhea, alopecia, nausea, anemia, and rash.
- Grade ≥3 AEs were reported in 60.8% of patients. The most frequent Grade ≥3 AEs (by PT) with ≥5% incidence were alanine aminotransferase increased, aspartate aminotransferase increased, neuropathy peripheral, diarrhea and neutropenia.
- A total of 50 deaths were reported in the safety evaluable population. The primary cause of death was progressive disease.
- Grade 5 AEs were reported in 4 patients (3.9%). Of these, an SAE (by PT) of pulmonary embolism was considered related to atezolizumab by the investigator.
- SAEs (by PT) reported in ≥2 patients were diarrhea, pneumonia, urinary tract infection, pyrexia, fatigue, pneumonitis, cholecystitis, dehydration, tumor necrosis, rash, febrile neutropenia, and vomiting.

- The proportions of patients who experienced AEs leading to ipatasertib, atezolizumab, and paclitaxel treatment discontinuation were 10.8%, 13.7%, and 22.5%, respectively.
- The proportion of patients who experienced at least one selected AE was 99%. The most frequent (≥30%) selected AEs (by PT) were diarrhea, rash, nausea, and anemia. Of the safety evaluable patients, for selected AEs, 48% experienced a highest Grade of 1–2, 50% experienced a highest Grade of 3–4, and 1% experienced a highest Grade of 5.

Table 32 Safety Summary, Cohort C: TNBC Patients (Safety Evaluable Population)

Safety Summary, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one AE	102 (100%)
Total number of AEs	2019
Total number of patients with at least one	
AE with fatal outcome	4 (3.9%)
Serious AE	29 (28.4%)
AE leading to discontinuation from Ipatasertib	11 (10.8%)
AE leading to discontinuation from Paclitaxel	23 (22.5%)
AE leading to discontinuation from Atezolizumab	14 (13.7%)
AE leading to discontinuation from any treatment	30 (29.4%)
AE leading to Ipatasertib dose reduction	37 (36.3%)
AE leading to Paclitaxel dose reduction	25 (24.5%)
AE leading to dose reduction from any treatment	46 (45.1%)
AE leading to Ipatasertib dose interruption	59 (57.8%)
AE leading to Paclitaxel dose interruption	67 (65.7%)
AE leading to Atezolizumab dose interruption	53 (52.0%)
AE leading to dose interruption from any treatment	78 (76.5%)
Grade >=3 AE	62 (60.8%)
AE related to Ipatasertib	98 (96.1%)
AE related to Paclitaxel	96 (94.1%)
AE related to Atezolizumab	75 (73.5%)
AE related to any treatment	102 (100%)

Investigator text for AEs is coded using MedDRA version 25.1. Percentages are based on N in the column headings. Multiple occurrences of the same AE in one individual are counted only once except for 'Total number of AEs' row in which multiple occurrences of the same AE are counted separately.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_saf_sum.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_saf_sum_C_SE.out
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5.2.2 Adverse Events

5.2.2.1 Analysis of Adverse Events

5.2.2.1.1 Adverse Events by Incidence

Cohort A

Most patients in each treatment arm experienced at least one AE of any grade (Ipat+Pac: 162 patients [97.6%] vs. Pbo+Pac: 84 patients [96.6%]) (t_ae_A_SE). A total of 2645 and 976 AEs were reported in the Ipat+Pac arm and Pbo+Pac arm, respectively.

The SOCs in which AEs were most commonly reported (>50% of patients in either treatment arm) were: gastrointestinal disorders (Ipat+Pac: 91% vs. Pbo+Pac: 65.5%), skin and subcutaneous tissue disorders (62.7% vs. 59.8%), nervous system disorder (58.4% vs. 67.8%), general disorders and administration site conditions (57.8% vs. 49.4%). AEs (by PT) occurring in ≥10% of patients in either treatment arm are summarized in Table 33.

Table 33 Adverse Events Reported in≥10% of Patients in Either Treatment Arm (Cohort A, Safety Evaluable Population)

Adverse Events with an Incidence Rate of at Least 10% in Any Treatment Arm by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Diarrhoea	28 (32.2%)	141 (84.9%)
Alopecia	38 (43.7%)	78 (47.0%)
Nausea	22 (25.3%)	66 (39.8%)
Constipation	31 (35.6%)	49 (29.5%)
Anaemia	23 (26.4%)	44 (26.5%)
Vomiting	8 (9.2%)	54 (32.5%)
Neuropathy peripheral	20 (23.0%)	39 (23.5%)
Peripheral sensory neuropathy	19 (21.8%)	32 (19.3%)
Neutropenia	21 (24.1%)	28 (16.9%)
Fatigue	15 (17.2%)	31 (18.7%)
Asthenia	10 (11.5%)	35 (21.1%)
Hyperglycaemia	9 (10.3%)	31 (18.7%)
Decreased appetite	10 (11.5%)	29 (17.5%)
Headache	10 (11.5%)	28 (16.9%)
Rash	11 (12.6%)	26 (15.7%)
Neutrophil count decreased	10 (11.5%)	22 (13.3%)
Alanine aminotransferase increased	7 (8.0%)	23 (13.9%)
Arthralgia	12 (13.8%)	16 (9.6%)
Back pain	9 (10.3%)	16 (9.6%)
Oedema peripheral	7 (8.0%)	18 (10.8%)
Aspartate aminotransferase increased	6 (6.9%)	18 (10.8%)
Cough	10 (11.5%)	14 (8.4%)
Stomatitis	6 (6.9%)	18 (10.8%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_10P_A_SE.out
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Adverse events (by PT) reported more frequently in the Ipat+Pac arm compared with the Pbo+Pac arm (with ≥5% difference) were: diarrhaea (Ipat+Pac: 84.9% vs. Pbo+Pac: 32.2%), nausea (39.8% vs. 25.3%), vomiting (32.5% vs. 9.2%), asthenia (21.1% vs. 11.5%), hyperglycemia (18.7% vs. 10.3%), decreased appetite (17.5% vs. 11.5%), headache (16.9% vs. 11.5%), alanine aminotransferase increased (13.9% vs. 8.0%), urinary tract infection (7.8% vs. 2.3%), oropharyngeal pain (7.8% vs. 0%) (Table 34).

Table 34 Adverse Events with a Difference of≥5% Between Treatment Arms (Cohort A, Safety Evaluable Population)

Adverse Events with a Difference of at Least 2% between Treatment Arms by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Diarrhoea	28 (32.2%)	141 (84.9%)
Nausea	22 (25.3%)	66 (39.8%)
Constipation	31 (35.6%)	49 (29.5%)
Vomiting	8 (9.2%)	54 (32.5%)
Neutropenia	21 (24.1%)	28 (16.9%)
Asthenia	10 (11.5%)	35 (21.1%)
Hyperglycaemia	9 (10.3%)	31 (18.7%)
Decreased appetite	10 (11.5%)	29 (17.5%)
Headache	10 (11.5%)	28 (16.9%)
Alanine aminotransferase increased	7 (8.0%)	23 (13.9%)
Urinary tract infection	2 (2.3%)	13 (7.8%)
Dizziness	8 (9.2%)	6 (3.6%)
Oropharyngeal pain	0	13 (7.8%)
Polyneuropathy	7 (8.0%)	5 (3.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2D_A_SE.out
08MAY2023 6:25

Adapted from: t_ae_pt_2D_A_SE

A listing (l_ae_A_SE) of all AEs by patients is provided.

Cohort B

Most patients in each treatment arm experienced at least one AE of any grade (Ipat+Pac: 144 patients [99.3%] vs. Pbo+Pac: 74 patients [98.7%]) (t_ae_B_SE). A total of 2722 AEs and 1195 AEs were reported in the Ipat+Pac arm and Pbo+Pac arm, respectively.

The SOCs in which AEs were most commonly reported (>50% of patients in either treatment arm) were: gastrointestinal disorders (Ipat+Pac: 95.9% vs. Pbo+Pac: 74.7%), skin and subcutaneous tissue disorders (73.1% vs. 70.7%), nervous system disorder (75.9% vs. 72.0%), general disorders and administration site conditions (62.8% vs. 62.7%), infections and infestation (52.4% vs. 56.0%), musculoskeletal and connective tissue disorders (47.6% vs. 52.0%), investigations (42.8% vs. 56%).

Adverse events (by PT) occurring in ≥10% of patients in either treatment arm are summarized in Table 35.

Table 35 Adverse Events Reported in≥10% of Patients in Either Treatment Arm (Cohort B, Safety Evaluable Population)

Adverse Events with an Incidence Rate of at Least 10% in Any Treatment Arm by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Diarrhoea	30 (40.0%)	126 (86.9%)
Alopecia	44 (58.7%)	75 (51.7%)
Nausea	17 (22.7%)	60 (41.4%)
Constipation	26 (34.7%)	42 (29.0%)
Anaemia	15 (20.0%)	45 (31.0%)
Neuropathy peripheral	12 (16.0%)	46 (31.7%)
Neutropenia	18 (24.0%)	38 (26.2%)
Vomiting	6 (8.0%)	45 (31.0%)
Fatigue	19 (25.3%)	29 (20.0%)
Peripheral sensory neuropathy	23 (30.7%)	23 (15.9%)
Neutrophil count decreased	18 (24.0%)	23 (15.9%)
Asthenia	13 (17.3%)	27 (18.6%)
Rash	9 (12.0%)	31 (21.4%)
Arthralgia	10 (13.3%)	26 (17.9%)
Oedema peripheral	14 (18.7%)	21 (14.5%)
Alanine aminotransferase increased	15 (20.0%)	19 (13.1%)
Headache	8 (10.7%)	24 (16.6%)
Cough	6 (8.0%)	23 (15.9%)
Decreased appetite	7 (9.3%)	22 (15.2%)
Hyperglycaemia	10 (13.3%)	19 (13.1%)
Back pain	7 (9.3%)	21 (14.5%)
Pyrexia	4 (5.3%)	23 (15.9%)
Nasopharyngitis	7 (9.3%)	19 (13.1%)
Myalgia	9 (12.0%)	15 (10.3%)
Aspartate aminotransferase increased	10 (13.3%)	13 (9.0%)
Stomatitis	6 (8.0%)	16 (11.0%)
Urinary tract infection	5 (6.7%)	16 (11.0%)
Abdominal pain upper	5 (6.7%)	15 (10.3%)
Epistaxis	4 (5.3%)	15 (10.3%)
Pruritus	3 (4.0%)	15 (10.3%)
Nail discolouration	8 (10.7%)	9 (6.2%)
Leukopenia	8 (10.7%)	8 (5.5%)
Blood lactate dehydrogenase increased	8 (10.7%)	5 (3.4%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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08MAY2023 6:28

Adapted from: t_ae_pt_10P_B_SE

Adverse events (by PT) reported more frequently in the Ipat+Pac arm compared with the Pbo+Pac arm (with ≥5% difference) were: diarrhea (Ipat+Pac: 86.9% vs. Pbo+Pac: 40.0%), nausea (41.4% vs. 22.7%), anemia (31.0% vs. 20.0%), neuropathy peripheral (31.7% vs. 16.0%); vomiting (31.0% vs. 8.0%), rash (21.4% vs. 12.0%), headache (16.6% vs. 10.7%), cough (15.9% vs. 8.0%), decreased appetite (15.2% vs. 9.3%), back pain (14.5% vs. 9.3%), pyrexia (15.9% vs. 5.3%), epistaxis (10.3% vs. 5.3%), pruritus (10.3% vs. 4.0%) (Table 36).

Table 36 Adverse Events with a Difference of≥5% Between Treatment Arms (Cohort B, Safety Evaluable Population)

Adverse Events with a Difference of at Least 2% between Treatment Arms by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Diarrhoea	30 (40.0%)	126 (86.9%)
Alopecia	44 (58.7%)	75 (51.7%)
Nausea	17 (22.7%)	60 (41.4%)
Constipation	26 (34.7%)	42 (29.0%)
Anaemia	15 (20.0%)	45 (31.0%)
Neuropathy peripheral	12 (16.0%)	46 (31.7%)
Vomiting	6 (8.0%)	45 (31.0%)
Fatigue	19 (25.3%)	29 (20.0%)
Peripheral sensory neuropathy	23 (30.7%)	23 (15.9%)
Neutrophil count decreased	18 (24.0%)	23 (15.9%)
Rash	9 (12.0%)	31 (21.4%)
Alanine aminotransferase increased	15 (20.0%)	19 (13.1%)
Headache	8 (10.7%)	24 (16.6%)
Cough	6 (8.0%)	23 (15.9%)
Decreased appetite	7 (9.3%)	22 (15.2%)
Back pain	7 (9.3%)	21 (14.5%)
Pyrexia	4 (5.3%)	23 (15.9%)
Epistaxis	4 (5.3%)	15 (10.3%)
Pruritus	3 (4.0%)	15 (10.3%)
Leukopenia	8 (10.7%)	8 (5.5%)
Blood lactate dehydrogenase increased	8 (10.7%)	5 (3.4%)
Oropharyngeal pain	2 (2.7%)	11 (7.6%)
Blood alkaline phosphatase increased	7 (9.3%)	3 (2.1%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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Output:
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08MAY2023 6:26

Adapted from: t_ae_pt_2D_B_SE

A listing (l_ae_B_SE) of all AEs by patients is provided.

Cohort C

Most patients experienced at least one AE of any grade (102 patients [100%]) (t_ae_C_SE). A total of 2019 AEs were reported. A summary of AEs by PT is appended (t_ae_pt_C_SE).

The SOCs in which AEs were most commonly reported (>50% of patients) were: gastrointestinal disorders (91.2%) skin and subcutaneous tissue disorders (76.5%), nervous system disorder (66.7%), general disorders and administration site conditions (60.8%), blood and lymphatic system disorders (52%), and investigations (51%).

Adverse events (by PT) occurring in ≥10% of patients are summarized in Table 37.

Table 37 Adverse Events Reported in ≥10% of Patients (Cohort C, Safety Evaluable Population)

Adverse Events with an Incidence Rate of at Least 10% by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diarrhoea	86 (84.3%)
Alopecia	42 (41.2%)
Nausea	42 (41.2%)
Anaemia	34 (33.3%)
Rash	31 (30.4%)
Neuropathy peripheral	30 (29.4%)
Vomiting	29 (28.4%)
Alanine aminotransferase increased	26 (25.5%)
Neutropenia	25 (24.5%)
Fatigue	23 (22.5%)
Aspartate aminotransferase increased	22 (21.6%)
Hyperglycaemia	22 (21.6%)
Headache	21 (20.6%)
Asthenia	19 (18.6%)
Pruritus	17 (16.7%)
Cough	16 (15.7%)
Decreased appetite	14 (13.7%)
Arthralgia	13 (12.7%)
Constipation	13 (12.7%)
Abdominal pain	12 (11.8%)
Blood alkaline phosphatase increased	12 (11.8%)
Mucosal inflammation	12 (11.8%)
Pyrexia	12 (11.8%)
Leukopenia	11 (10.8%)

Investigator text for Aes encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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Output:
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08MAY2023 6:29 Page 1 of 1

A listing (l_ae_C_SE) of all AEs by patients is provided.

5.2.2.1.2 Adverse Events Related to Treatment Cohort A

Adverse Events Related to Ipatasertib/Placebo

Adverse events (any grade) considered by the investigator to be related to ipatasertib/placebo were reported in higher proportions of patients in the Ipat+Pac arm (152 patients [91.6%]) and the Pbo+Pac arm (63.2 patients [55%]) (t_ae_ctc_RELIPAT_A_SE).

The most common AEs (by PT, in ≥20% of patients in either arm) considered related to ipatasertib/placebo by the investigator were: diarrhea (Ipat+Pac: 81.3% vs. Pbo+Pac: 27.6%), nausea (29.5% vs. 10.3%), and vomiting (24.1% vs. 5.7%) (Table 38).

Table 38 Adverse Events Related to Ipatasertib/Placebo Treatment Reported in≥10% of Patients in Either Treatment Arm (Cohort A, Safety Evaluable Population)

Adverse Events Related to Ipatasertib/Placebo Treatment with an Incidence Rate of at Least 10% in Any Treatment Arm by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Diarrhoea	24 (27.6%)	135 (81.3%)
Nausea	9 (10.3%)	49 (29.5%)
Vomiting	5 (5.7%)	40 (24.1%)
Hyperglycaemia	7 (8.0%)	27 (16.3%)
Asthenia	5 (5.7%)	27 (16.3%)
Fatigue	6 (6.9%)	20 (12.0%)
Decreased appetite	2 (2.3%)	23 (13.9%)
Rash	6 (6.9%)	19 (11.4%)
Alanine aminotransferase increased	5 (5.7%)	18 (10.8%)

Investigator text for Aes encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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Output:
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Adverse Events Related to Paclitaxel

Adverse events (any grade) considered by the investigator to be related to paclitaxel were reported in similar proportions of patients in the Ipat+Pac arm (152 patients [91.6%]) and the Pbo+Pac arm (81 patients [93.1%]) (t_ae_ctc_RELPAC_A_SE).

The most common AEs (by PT, in ≥20% of patients in either arm) considered related to paclitaxel by the investigator were: alopecia (Ipat+Pac: 47% vs. Pbo+Pac: 43.7%), diarrhea (45.2% vs. 12.6%), nausea (33.1% vs. 17.2%), neuropathy peripheral (22.9% vs, 21.8%), anemia (22.3% vs. 21.8%), peripheral sensory neuropathy (18.7% vs. 21.8%), neutropenia (16.3% vs. 23%), and vomiting (24.7% vs. 4.6%) (Table 39).

Table 39 Adverse Events Related to Paclitaxel Treatment Reported in≥10% of Patients in Either Treatment Arm (Cohort A, Safety Evaluable Population)

Adverse Events Related to Paclitaxel Treatment with an Incidence Rate of at Least 10% in Any Treatment Arm by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Alopecia	38 (43.7%)	78 (47.0%)
Diarrhoea	11 (12.6%)	75 (45.2%)
Nausea	15 (17.2%)	55 (33.1%)
Neuropathy peripheral	19 (21.8%)	38 (22.9%)
Anaemia	19 (21.8%)	37 (22.3%)
Peripheral sensory neuropathy	19 (21.8%)	31 (18.7%)
Neutropenia	20 (23.0%)	27 (16.3%)
Vomiting	4 (4.6%)	41 (24.7%)
Fatigue	15 (17.2%)	23 (13.9%)
Asthenia	8 (9.2%)	29 (17.5%)
Neutrophil count decreased	10 (11.5%)	21 (12.7%)
Decreased appetite	7 (8.0%)	23 (13.9%)
Rash	6 (6.9%)	18 (10.8%)
Stomatitis	5 (5.7%)	18 (10.8%)

Investigator text for Aes encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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Output:
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08MAY2023 6:22 Page 1 of 1

Cohort B

Adverse Events Related to Ipatasertib/Placebo

Adverse events (any grade) considered by the investigator to be related to ipatasertib/placebo were reported in higher proportions of patients in the Ipat+Pac arm (134 patients [92.4%]) and the Pbo+Pac arm (54 patients [72.0%]) (t_ae_ctc_RELIPAT_B_SE).

The most common AEs (by PT, in ≥20% of patients in either arm) considered related to ipatasertib/placebo by the investigator were: diarrhea (Ipat+Pac: 83.4% vs. Pbo+Pac: 32.0%), nausea (29.7% vs. 12.0%), and vomiting (20.7% vs. 5.3%) (Table 40).

Table 40 Adverse Events Related to Ipatasertib/Placebo Treatment Reported in≥10% of Patients in Either Treatment Arm (Cohort B, Safety Evaluable Population)

Adverse Events Related to Ipatasertib/Placebo Treatment with an Incidence Rate of at Least 10% in Any Treatment Arm by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Diarrhoea	24 (32.0%)	121 (83.4%)
Nausea	9 (12.0%)	43 (29.7%)
Vomiting	4 (5.3%)	30 (20.7%)
Alopecia	14 (18.7%)	9 (6.2%)
Hyperglycaemia	7 (9.3%)	16 (11.0%)
Neutropenia	12 (16.0%)	11 (7.6%)
Rash	5 (6.7%)	17 (11.7%)
Anaemia	3 (4.0%)	18 (12.4%)
Alanine aminotransferase increased	9 (12.0%)	11 (7.6%)
Fatigue	8 (10.7%)	12 (8.3%)
Neutrophil count decreased	8 (10.7%)	12 (8.3%)

Investigator text for Aes encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_10P_RELIPAT_B_SE.out
08MAY2023 6:20 Page 1 of 1

Adverse Events Related to Paclitaxel

Adverse events (any grade) considered by the investigator to be related to paclitaxel were reported in similar proportions of patients in the Ipat+Pac arm (138 patients [95.2%]) and the Pbo+Pac arm (70 patients [93.3%]) (t_ae_ctc_RELPAC_B_SE).

The most common AEs (by PT, in ≥20% of patients in either arm) considered related to paclitaxel by the investigator were: alopecia (Ipat+Pac: 51.7% vs. Pbo+Pac: 57.3%), diarrhea (35.2% vs. 17.3%), neuropathy peripheral (31.7% vs. 13.3%), nausea (26.9% vs. 21.3%), neutropenia (24.8% vs. 22.7%), anemia (27.6% vs. 14.7%), peripheral sensory neuropathy (15.2% vs. 30.7%), neutrophil count decreased (15.9% vs. 24%), and fatigue (14.5% vs. 21.3%) (Table 41).

Table 41 Adverse Events Related to Paclitaxel Treatment Reported in≥10% of Patients in Either Treatment Arm (Cohort B, Safety Evaluable Population)

Adverse Events Related to Paclitaxel Treatment with an Incidence Rate of at Least 10% in Any Treatment Arm by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Alopecia	43 (57.3%)	75 (51.7%)
Diarrhoea	13 (17.3%)	51 (35.2%)
Neuropathy peripheral	10 (13.3%)	46 (31.7%)
Nausea	16 (21.3%)	39 (26.9%)
Neutropenia	17 (22.7%)	36 (24.8%)
Anaemia	11 (14.7%)	40 (27.6%)
Peripheral sensory neuropathy	23 (30.7%)	22 (15.2%)
Neutrophil count decreased	18 (24.0%)	23 (15.9%)
Fatigue	16 (21.3%)	21 (14.5%)
Asthenia	11 (14.7%)	21 (14.5%)
Vomiting	4 (5.3%)	25 (17.2%)
Oedema peripheral	11 (14.7%)	13 (9.0%)
Rash	3 (4.0%)	21 (14.5%)
Alanine aminotransferase increased	10 (13.3%)	13 (9.0%)
Decreased appetite	6 (8.0%)	15 (10.3%)
Aspartate aminotransferase increased	8 (10.7%)	10 (6.9%)
Nail discolouration	8 (10.7%)	9 (6.2%)

Investigator text for Aes encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date – 21MAR2023; Data Extraction Date – 21MAR2023

Program:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_10P_RELPAC_B_SE.out
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Cohort C

Adverse Events Related to Ipatasertib

Adverse events (any grade) considered by the investigator to be related to ipatasertib were reported in 96.1% of patients (t_ae_ctc_RELIPAT_C_SE). AEs related to ipatasertib by PT is appended (t_ae_pt_RELIPAT_C_SE).

The most common AEs (by PT, in ≥20% of patients) considered related to ipatasertib by the investigator were: diarrhea (83.3%), nausea (30.4%), and rash (22.5%) (Table 42).

Table 42 Adverse Events Related to Ipatasertib Treatment Reported in ≥10% of Patients (Cohort C, Safety Evaluable Population)

Adverse Events Related to Ipatasertib Treatment with an Incidence Rate of at Least 10% by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diarrhoea	85 (83.3%)
Nausea	31 (30.4%)
Rash	23 (22.5%)
Fatigue	18 (17.6%)
Hyperglycaemia	18 (17.6%)
Vomiting	18 (17.6%)
Alanine aminotransferase increased	16 (15.7%)
Asthenia	14 (13.7%)
Aspartate aminotransferase increased	13 (12.7%)
Neutropenia	12 (11.8%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_10P_RELIPAT_C_SE.out
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Adverse Events Related to Paclitaxel

The proportion of patients with AEs (any grade) considered by the investigator to be related to paclitaxel was 96 (94.1%) (t_ae_ctc_RELPAC_C_SE). AEs related to paclitaxel by PT is appended (t_ae_pt_RELPAC_C_SE).

The most common AEs (by PT, in ≥20% of patients in either arm) considered related to paclitaxel by the investigator were: alopecia (40.2%), diarrhea (45.1%), nausea (31.4%), anemia (30.4%), neuropathy peripheral (27.5%), and neutropenia (24.5%) (Table 43).

Table 43 Adverse Events Related to Paclitaxel Treatment Reported in ≥10% of Patients (Cohort C, Safety Evaluable Population)

Adverse Events Related to Paclitaxel Treatment with an Incidence Rate of at Least 10% by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diarrhoea	46 (45.1%)
Alopecia	41 (40.2%)
Nausea	32 (31.4%)
Anaemia	31 (30.4%)
Neuropathy peripheral	28 (27.5%)
Neutropenia	25 (24.5%)
Fatigue	20 (19.6%)
Vomiting	19 (18.6%)
Alanine aminotransferase increased	18 (17.6%)
Asthenia	18 (17.6%)
Aspartate aminotransferase increased	13 (12.7%)
Leukopenia	11 (10.8%)

Investigator text for Aes encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_10P_RELPAC_C_SE.out
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Adverse Events Related to Atezolizumab

The proportion of patients with AEs (any grade) considered by the investigator to be related to atezolizumab was 75 (73.5%) (t_ae_ctc_RELATZ_C_SE). AEs related to atezolizumab by PT is appended (t_ae_pt_RELATZ_C_SE).

The most common AE (by PT, in ≥20% of patients in either arm) considered related to atezolizumab by the investigator was: diarrhea (33.3%) (Table 44).

Table 44 Adverse Events Related to Atezolizumab Treatment Reported in ≥10% of Patients (Cohort C, Safety Evaluable Population)

Adverse Events Related to Atezolizumab Treatment with an Incidence Rate of at Least 10% by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diarrhoea	34 (33.3%)
Rash	20 (19.6%)
Alanine aminotransferase increased	15 (14.7%)
Nausea	15 (14.7%)
Aspartate aminotransferase increased	13 (12.7%)
Asthenia	11 (10.8%)

Investigator text for Aes encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_10P_RELATZ_C_SE.out
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5.2.2.1.3 Adverse Events by Intensity

Cohort A

The proportion of patients who experienced Grade ≥3 AEs were similar between the Ipat+Pac arm (84 patients [50.6%]) and the Pbo+Pac arm (40 patients [46.0%]) (t_ae_CTC35_A_SE). Among all AEs in the Ipat+Pac arm, 41.6% of patients had Grade 3 AEs, 7.8% had Grade 4 AEs and 1.2% had Grade 5 AEs. Among all AEs in the Pbo+Pac arm, 37.9% of patients had Grade 3 AEs, 5.7% had Grade 4 AEs and 2.3% had Grade 5 AEs (t_ae_ctc_A_SE).

The most common Grade ≥3 AEs (by PT) reported in ≥5% of patients in either treatment arm were: diarrhea (Ipat+Pac: 9.0% vs. Pbo+Pac: 2.3%), neutrophil count decreased (4.8% vs. 5.7%), neutropenia (7.2% vs. 4.6%) (t_ae_CTC35_A_SE).

Cohort B

The proportion of patients who experienced Grade ≥3 AEs were higher between the Ipat+Pac arm (83 patients [57.2%]) and the Pbo+Pac arm (37 patients [49.3%]) (t_ae_CTC35_B_SE). Among all AEs in the Ipat+Pac arm, 48.3% of patients had Grade 3 AEs, 5.5% had Grade 4 AEs and 3.4% had Grade 5 AEs. Among all AEs in the Pbo+Pac arm, 44% of patients had Grade 3 AEs, 4.0% had Grade 4 AEs and 1.3% had Grade 5 AEs (t_ae_ctc_B_SE).

The most common Grade ≥3 AEs (by PT) reported in ≥5% of patients in either treatment arm were: diarrhea (Ipat+Pac: 11.7% vs. Pbo+Pac: 1.3%), neutrophil count decreased (9.0% vs. 8.0%), neutropenia (8.3% vs. 9.3%), neuropathy peripheral (6.9% vs. 4.0%), peripheral sensory neuropathy (2.8% vs. 5.3%), and hypertension (1.4% vs. 5.3%) (t_ae_CTC35_B_SE).

Cohort C

The number of patients who experienced Grade ≥3 AEs was 62 (60.8%) (t_ae_CTC35_C_SE). Among all AEs, 51% of patients had Grade 3 AEs, 5.9% had Grade 4 AEs and 3.9% had Grade 5 AEs (t_ae_ctc_C_SE).

The most common Grade ≥3 AEs (by PT) reported in ≥5% of patients were: diarrhea (16.7%), alanine aminotransferase increased (7.8%), asparate aminotransferase increased (7.8%), neutropenia (5.9%), and neuropathy peripheral (6.9%) (t_ae_CTC35_C_SE).

5.2.2.2 Deaths

Cohort A

A total of 132 deaths were reported in the safety evaluable population (91 patients [54.8%] in the Ipat+Pac arm, 41 patients [47.1%] in the Pbo+Pac arm) (Table 45). Of these events, the primary cause of death in both treatment arms was progressive disease (Ipat+Pac: 80 patients [87.9% of all deaths within treatment arm] vs. Pbo+Pac: 34 patients [82.9% of all deaths within treatment arm]). Deaths due to AEs were reported in 2 patients each in the Ipat+Pac and Pbo+Pac arm.

There were an additional 14 patients (Ipat+Pac: 9 patients vs. Pbo+Pac: 5 patients) who died with the reason categorized as “other”, which were non-reportable AEs per protocol (i.e., outside of the protocol-specified AE reporting period, refer to Protocol v11, Section 5.4.2.2 and Section 5.6). In the Ipat+Pac arm, 1 patient died due to pulmonary embolism, 1 patient died due to Covid-19, 1 patient died due to Covid-19 infection, 4 patients died due to unknown cause, and 2 patients’ death were identified by public records after the patient had discontinued from the study, meaning the cause of death was not reported. In the Pbo +Pac arm, the “other” causes of death were respiratory failure (1 patient), sepsis (1 patient), unknown (2 patients), and death outside the study’s reporting period (1 patient).

The majority of deaths occurred more than 28 days after the last study drug administration (Ipat+Pac: 85 patients [93.4%] vs. Pbo+Pac: 40 patients [97.6%]).

A listing (l_dd_A_SE) of deaths is appended.

Narratives for patients who died are appended.

Table 45 Summary of Deaths by Treatment (Cohort A, Safety Evaluable Population)

Deaths by Study Treatment, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)	All Patients (N=253)
Total number of deaths	41 (47.1%)	91 (54.8%)	132 (52.2%)
Primary cause of death			
n	41	91	132
Adverse event	2 (4.9%)	2 (2.2%)	4 (3.0%)
Progressive disease	34 (82.9%)	80 (87.9%)	114 (86.4%)
Other	5 (12.2%)	9 (9.9%)	14 (10.6%)
Days from last study drug administration			
n	41	91	132
<=28 days	1 (2.4%)	6 (6.6%)	7 (5.3%)
>28 days	40 (97.6%)	85 (93.4%)	125 (94.7%)
Primary cause by days from last study drug administration			
<=28 days			
n	1	6	7
Adverse event	1 (100%)	2 (33.3%)	3 (42.9%)
Progressive disease	0	4 (66.7%)	4 (57.1%)
>28 days			
n	40	85	125
Adverse event	1 (2.5%)	0	1 (0.8%)
Progressive disease	34 (85.0%)	76 (89.4%)	110 (88.0%)
Other	5 (12.5%)	9 (10.6%)	14 (11.2%)

Percentages for Total Number of Deaths are relative to total N. All other percentages are relative to n within each category.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_dd.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_dd_A_SE.out
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In the safety evaluable population, fatal AEs were reported in 2 patients (1.2%) in the Ipat+Pac arm and 2 patients (2.3%) in the Pbo+Pac arm, respectively (Table 46).

In the Ipat+Pac arm, 1 patient died due to a fatal AE (PT) of pulmonary embolism and 1 patient died due to a fatal AE (PT) of cardiopulmonary failure. The events were not considered related to any study treatment by the investigator.

In the Pbo+Pac arm, 1 patient died due to a fatal AE (PT) of tumor lysis syndrome, which was considered related to both placebo and paclitaxel and 1 patient died due to gastric cancer (unrelated to any study treatment).

A listing (l_ae_FATAL_A_SE) of AEs resulting in death is appended.

Table 46 Adverse Events Resulting in Death (Cohort A, Safety Evaluable Population)

Adverse Events Resulting in Death, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one such adverse event	2 (2.3%)	2 (1.2%)
Overall total number of events	2	2
Cardiac disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Cardiopulmonary failure	0	1 (0.6%)
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Tumour lysis syndrome	1 (1.1%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Gastric cancer	1 (1.1%)	0
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Pulmonary embolism	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_FATAL_A_SE.out
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Cohort B

A total of 122 deaths were reported in the safety evaluable population (78 patients [53.8%] in the Ipat+Pac arm, 44 patients [58.7%] in the Pbo+Pac arm) (Table 47). Of these events, the primary cause of death in both treatment arms was progressive disease (Ipat+Pac: 70 patients [89.7% of all deaths within treatment arm] vs. Pbo+Pac: 37 patients [84.1% of all deaths within treatment arm]). Deaths due to AEs were reported in 5 patients in the Ipat+Pac arm and 1 patient in the Pbo+Pac arm.

There were an additional 9 patients (Ipat+Pac: 3 patients vs. Pbo+Pac: 6 patients) who died with the reason categorized as “other”, which were non-reportable AEs per protocol (i.e., outside of the protocol-specified AE reporting period, refer to Protocol v11, Section 5.4.2.2 and Section 5.6). In the Ipat+Pac arm, 1 patient died due to pulmonary embolism, and 2 patients’ death were identified by public records after the patient had discontinued from the study, meaning the cause of death was not reported. In the Pbo +Pac arm, the “other” causes of death in 6 patients (1 in each) were: infective

pneumonia related to to SARS-COV2, deep vein thrombosis, sepsis, death, post study reporting period, and unknown causes.

The majority of deaths occurred more than 28 days after the last study drug administration (Ipat+Pac: 66 patients [84.6%] vs. Pbo+Pac: 41 patients [95.3%]).

A listing (l_dd_B_SE) of deaths is appended.

Narratives for patients who died are appended.

Table 47 Summary of Deaths by Treatment (Cohort B, Safety Evaluable Population)

Deaths by Study Treatment, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)	All Patients (N=220)
Total number of deaths	44 (58.7%)	78 (53.8%)	122 (55.5%)
Primary cause of death			
n	44	78	122
Adverse event	1 (2.3%)	5 (6.4%)	6 (4.9%)
Progressive disease	37 (84.1%)	70 (89.7%)	107 (87.7%)
Other	6 (13.6%)	3 (3.8%)	9 (7.4%)
Days from last study drug administration			
n	43	78	121
<=28 days	2 (4.7%)	12 (15.4%)	14 (11.6%)
>28 days	41 (95.3%)	66 (84.6%)	107 (88.4%)
Primary cause by days from last study drug administration			
<=28 days			
n	2	12	14
Adverse event	1 (50.0%)	4 (33.3%)	5 (35.7%)
Progressive disease	1 (50.0%)	8 (66.7%)	9 (64.3%)
>28 days			
n	41	66	107
Adverse event	0	1 (1.5%)	1 (0.9%)
Progressive disease	36 (87.8%)	62 (93.9%)	98 (91.6%)
Other	5 (12.2%)	3 (4.5%)	8 (7.5%)

Percentages for Total Number of Deaths are relative to total N. All other percentages are relative to n within each category.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_dd.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_dd_B_SE.out
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In the safety evaluable population, fatal AEs were reported in 5 patients (3.4%) in the Ipat+Pac arm and 1 patient (1.3%) in the Pbo+Pac arm, respectively (Table 48).

In the Ipat+Pac arm, 2 fatal AEs (PT) of general physical health deterioration and road traffic accident were reported in 1 patient, and for the remaining 4 patients, each had one fatal AE of respiratory tract infection, febrile neutropenia (only fatal AE considered related to ipatasertib and paclitaxel by investigator), pneumonia and death.

In the Pbo+Pac arm, the 1 patient died due to a fatal AE (PT) of sepsis which was considered related to paclitaxel by the investigator.

A listing (l_ae_FATAL_B_SE) of AEs resulting in death is appended.

Table 48 Adverse Events Resulting in Death (Cohort B, Safety Evaluable Population)

Adverse Events Resulting in Death, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one such adverse event	1 (1.3%)	5 (3.4%)
Overall total number of events	1	6
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	0	2 (1.4%)
Total number of events	0	2
Death	0	1 (0.7%)
General physical health deterioration	0	1 (0.7%)
Infections and infestations		
Total number of patients with at least one such adverse event	1 (1.3%)	1 (0.7%)
Total number of events	1	1
Pneumonia	0	1 (0.7%)
Sepsis	1 (1.3%)	0
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Febrile neutropenia	0	1 (0.7%)
Injury, poisoning and procedural complications		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Road traffic accident	0	1 (0.7%)
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Respiratory distress	0	1 (0.7%)

Investigator text for Aes encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_FATAL_B_SE.out
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Cohort C

A total of 50 (49.0%) deaths were reported in the safety evaluable population (Table 49). Of these, the primary cause of death was progressive disease (38 patients [76.0% of all deaths]). Deaths due to AEs were reported in 4 patients (cardiac arrest, Covid-19, pulmonary embolism, and septic shock).

There were an additional 8 patients who died with the reason categorized as “other”, which were non-reportable AEs per protocol (i.e., outside of the protocol-specified AE

reporting period, refer to Protocol v11, Section 5.4.2.2 and Section 5.6). One patient died due to septic shock, 2 patients due to Covid-19 infection, 1 patient due to failure to thrive, 2 patients due to unknown causes and 2 patients' death were identified by public records after the patient had discontinued from the study, meaning the cause of death was not reported.

The majority of deaths occurred more than 28 days after the last study drug administration (43 patients [86.0%]).

One patient died due to an AE (pneumonia) after the 28-day reporting period for ipatasertib, which was not related to any study medications. All study medications had been previously discontinued due to the AE of pneumonitis, which was reported as related to atezolizumab.

A listing (l_dd_C_SE) of deaths is appended.

Narratives for patients who died are appended.

Table 49 Summary of Deaths by Treatment (Cohort C, Safety Evaluable Population)

Deaths by Study Treatment, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of deaths	50 (49.0%)
Primary cause of death	
n	50
Adverse event	4 (8.0%)
Progressive disease	38 (76.0%)
Other	8 (16.0%)
Days from last study drug administration	
n	50
<=28 days	7 (14.0%)
>28 days	43 (86.0%)
Primary cause by days from last study drug administration	
<=28 days	
n	7
Adverse event	3 (42.9%)
Progressive disease	4 (57.1%)
>28 days	
n	43
Adverse event	1 (2.3%)
Progressive disease	34 (79.1%)
Other	8 (18.6%)

Percentages for Total Number of Deaths are relative to total N. All other percentages are relative to n within each category.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_dd.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_dd_C_SE.out
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In the safety evaluable population, fatal AEs were reported in 4 patients (3.9%) (Table 50).

Four (1 in each patient) fatal AEs (PT) were: pulmonary embolism (considered related to atezolizumab by the investigator), suspected Covid-19, cardiac arrest, and pneumonia.

A listing (l_ae_FATAL_C_SE) of AEs resulting in death is appended.

Table 50 Adverse Events Resulting in Death (Cohort C, Safety Evaluable Population)

Adverse Events Resulting in Death, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	4 (3.9%)
Overall total number of events	4
Infections and infestations	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Pneumonia	1 (1.0%)
Suspected COVID-19	1 (1.0%)
Cardiac disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Cardiac arrest	1 (1.0%)
Respiratory, thoracic and mediastinal disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Pulmonary embolism	1 (1.0%)

Investigator text for Aes encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_FATAL_C_SE.out
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5.2.2.3 Serious Adverse Events

Cohort A

A similar proportion of patients in the Ipat+Pac arm (34 patients [20.5%]) and Pbo+Pac arm (20 patients [23.0%]) experienced SAEs (t_ae_SER_A_SE).

Serious adverse events (by PT) reported in ≥1% of patients (i.e., ≥2 patients) in the Ipat+Pac arm were: diarrhea (3.6%), febrile neutropenia (1.8%), pulmonary embolism (1.8%), pneumonia (1.2%), nausea (1.2%), and vomiting (1.2%). Six SAEs (by PT) were reported in more than 1 patient in the Pbo+Pac arm: pneumonia (4.6%), and pleural

effusion (2.3%) (t_ae_pt_1P_SER_A_SE). Diarrhea and pneumonia were SAEs that occurred with a ≥2% difference between treatment arms (t_ae_pt_2D_SER_A_SE).

The proportions of patients with SAEs considered related to ipatasertib/placebo by the investigator was higher in the Ipat+Pac arm (Ipat + Pac: 15 patients [9.0%] vs. Pbo+Pac: 3 patients [3.4%]).

In the Ipat+Pac arm, SAEs related to ipatasertib (by PT) reported in ≥1% of patients (i.e., ≥2 patients) was diarrhea (3.6%) (t_ae_ctc_SER_RELIPAT_A_SE). SAEs related to paclitaxel (by PT) reported in ≥1% of patients were nausea (1.2%), vomiting (1.2%), and febrile neutropenia (1.8%) (t_ae_ctc_SER_RELPAC_A_SE).

In the Pbo+Pac arm, there were no SAEs related to placebo reported by the investigator in ≥2 patients. SAEs related to paclitaxel were reported by the investigator in 2 patients (2.3%) for pneumonia (PT).

One SAE considered related to ipatasertib/placebo (by PT) and occurring in ≥2% of patients in either treatment arm was diarrhea (Ipat+Pac: 6 patients [3.6%] vs. Pbo+Pac: 0 patient) (t_ae_pt_2P_SER_RELIPAT_A_SE). One SAE considered related to paclitaxel (by PT) and occurring in ≥2% of patients in either treatment arm was pneumonia (Ipat+Pac: 0 patient vs. Pbo+Pac: 2 patients [2.3%]) (t_ae_pt_2P_SER_RELPAC_A_SE).

A summary of SAEs by highest NCI CTCAE grade (t_ae_ctc_SER_A_SE) and a listing of SAEs by patient (l_ae_ser_A_SE) are provided.

Narratives for patients who experienced SAEs during the study are appended.

Cohort B

A higher proportion of patients in the Ipat+Pac arm (30 patients [20.7%]) and Pbo+Pac arm (11 patients [14.7%]) experienced SAEs (t_ae_SER_B_SE).

Serious adverse events (by PT) reported in ≥1% of patients (i.e., ≥2 patients) in the Ipat+Pac arm were: diarrhea (2.8%), febrile neutropenia (1.4%), pneumonia (1.4%), neutropenia (1.4%), and pneumonitis (1.4%). No SAE (by PT) was reported in more than 1 patient in the Pbo+Pac arm(t_ae_pt_1P_SER_B_SE). There were no SAEs that occurred with a ≥2% difference between treatment arms (t_ae_pt_2D_SER_B_SE).

The proportions of patients with SAEs considered related to ipatasertib/placebo by the investigator was similar in the Ipat+Pac arm and Pbo+Pac arm (Ipat + Pac: 9 patients [6.2%] vs. Pbo+Pac: 4 patients [5.3%]).

In the Ipat+Pac arm, SAEs related to ipatasertib (by PT) reported in ≥1% of patients (i.e., ≥2 patients) were diarrhea (2.8%) and febrile neutropenia (1.4%) (t_ae_ctc_SER_RELIPAT_B_SE). SAEs related to paclitaxel (by PT) reported in ≥1% of patients were febrile neutropenia (1.4%) and neutropenia (1.4%) (t_ae_ctc_SER_RELPAC_B_SE).

In the Pbo+Pac arm, no SAEs related to placebo or paclitaxel were reported by the investigator in ≥2 patients.

One SAE considered related to ipatasertib/placebo (by PT) and occurring in ≥2% of patients in either treatment arm was diarrhea (Ipat+Pac: 4 patients [2.8%] vs. Pbo+Pac: 1 patient [1.3%]) (t_ae_pt_2P_SER_RELIPAT_B_SE). There were no SAEs (by PT) considered related to paclitaxel that were occurring in ≥2% of patients in either treatment arm (t_ae_pt_2P_SER_RELPAC_B_SE).

A summary of SAEs by highest NCI CTCAE grade (t_ae_ctc_SER_B_SE) and a listing of SAEs by patient (l_ae_ser_B_SE) are provided.

Narratives for patients who experienced SAEs during the study are appended.

Cohort C

The total number of patients with at least one SAE was 29 (28.4%) (t_ae_SER_C_SE).

Serious adverse events (by PT) reported in ≥2 patients were: diarrhea (3.9%), pyrexia (3.9%), pneumonia (2.9%), urinary tract infection (2.9%), cholecystitis (2.0%), dehydration (2.0%), fatigue (2.0%), febrile neutropenia (2.0%), pneumonitis (2.0%), rash (2.0%), tumor necrosis (2.0%), and vomiting (2.0%) (t_ae_pt_1P_SER_C_SE).

Twelve patients (11.8%) experienced SAEs considered related to ipatasertib by the investigator.

Serious adverse events related to ipatasertib (by PT) and reported in ≥2 patients were diarrhea (2.9%), dehydration (2.0%), and tumor necrosis (2.0%) (t_ae_ctc_SER_RELIPAT_C_SE). SAEs related to paclitaxel (by PT) reported in ≥2 patients were diarrhea (2.0%), febrile neutropenia (2.0%), urinary tract infection (2.0%), dehydration (2.0%), and tumor necrosis (2.0%) (t_ae_ctc_SER_RELPAC_C_SE). SAEs related to atezolizumab (by PT) reported in ≥2 patients were diarrhea (2.0%), pneumonitis (2.0%), dehydration (2.0%), tumor necrosis (2.0%), rash (2.0%) (t_ae_ctc_SER_RELATZ_C_SE).

One SAE considered related to ipatasertib (by PT) and occurring in ≥2% of patients in either treatment arm was diarrhea (3 patients [2.9%]) (t_ae_pt_2P_SER_RELIPAT_C_SE). There were no SAEs (by PT) considered related to paclitaxel or atezolizumab that were occurring in ≥2% of patients in either treatment arm (t_ae_pt_2P_SER_RELPAC_C_SE, t_ae_pt_2P_SER_RELATZ_C_SE).

A summary of SAEs by highest NCI CTCAE grade (t_ae_ctc_SER_C_SE), by PT (t_ae_pt_SER_C_SE), and a listing of SAEs by patient (l_ae_ser_C_SE) are provided.

Narratives for patients who experienced SAEs during the study are appended.

5.2.2.4 Adverse Events That Led to Withdrawal of Treatment Cohort A

The proportion of patients who experienced AEs leading to ipatasertib/placebo treatment discontinuation was higher in the Ipat+Pac (17 patients [10.2%]) and Pbo+Pac arm (6 patients [6.9%]) (t_ae_DSCIPAT_A_SE).

Adverse events (by PT) leading to ipatasertib discontinuation occurring in ≥1% of patients (i.e., ≥2 patients) in the Ipat+Pac arm were diarrhea (3.6%), pulmonary embolism (1.2%), hyperglycemia (1.2%) (Table 51). In the Pbo+Pac arm, AE (by PT) leading to placebo discontinuation in more than 1 patient was neuropathy peripheral (2.3%).

Among AEs leading to ipatasertib/placebo discontinuation, Grade 3 events were reported in 6% of patients in the Ipat+Pac arm and 4.6% of patients in the Pbo+Pac arm, respectively (t_ae_ctc_DSCIPAT_A_SE). One (0.6%) patient in the Ipat+Pac arm had Grade 5 AE (PT: pulmonary embolism) leading to treatment discontinuation of both ipatasertib and paclitaxel (see Deaths). Two patients in the Ipat+Pac arm had Grade 4 events (PTs: large intestine perforation and neutrophil count decreased). The rest of AEs leading to ipatasertib/placebo discontinuation were reported as Grade 2.

Table 51 Adverse Events Leading to Ipatasertib/Placebo Discontinuation (Cohort A, Safety Evaluable Population)

Adverse Events Leading to Ipatasertib/Placebo Discontinuation by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Diarrhoea	0	6 (3.6%)
Hyperglycaemia	0	2 (1.2%)
Neuropathy peripheral	2 (2.3%)	0
Pulmonary embolism	0	2 (1.2%)
Alanine aminotransferase increased	0	1 (0.6%)
Anaphylactic shock	1 (1.1%)	0
Aspartate aminotransferase increased	0	1 (0.6%)
Atrial fibrillation	1 (1.1%)	0
Dyspnoea	1 (1.1%)	0
Erythema	1 (1.1%)	0
Erythema multiforme	0	1 (0.6%)
Fatigue	0	1 (0.6%)
Haematuria	1 (1.1%)	0
Hypersensitivity	1 (1.1%)	0
Hypotension	0	1 (0.6%)
Large intestine perforation	0	1 (0.6%)
Neutrophil count decreased	0	1 (0.6%)
Ocular hyperaemia	1 (1.1%)	0
Peritonitis	0	1 (0.6%)
Pneumonia	0	1 (0.6%)
Pneumothorax	1 (1.1%)	0
Rash	0	1 (0.6%)
Tumour lysis syndrome	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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Output:
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Adverse events leading to discontinuation of paclitaxel was reported in 25 patients (15.1%) in the Ipat + Pac arm and in 14 patients (16.1%) in the Pbo+Pac arm (t_ae_DSCPAC_A_SE). The most common AEs leading to paclitaxel discontinuation were reported in the SOC of nervous system disorders (Ipat+Pac: 7.8% vs. Pbo+Pac: 10.3%).

The AEs (by PT) leading to paclitaxel discontinuation occurring in ≥ 2 of patients in either treatment arm were: neuropathy peripheral (Ipat + Pac: 4.8% vs. Pbo+Pac: 4.6%), peripheral sensory neuropathy (2.4% vs. 2.3%), polyneuropathy (0.6% vs. 3.4%), diarrhea (1.8% vs. 0), and pulmonary embolism (1.2% vs. 0) (Table 52).

Among patients with AEs leading to paclitaxel discontinuation, the majority (11.4%) had Grade ≥ 3 AEs by highest NCI CTCAE grade in the Ipat+Pac arm (t_ae_ctc_DSCPAC_A_SE). One patient (0.6%) in the Ipat+Pac arm had Grade 5 AE (PT: pulmonary embolism) leading to treatment discontinuation of both ipatasertib and paclitaxel (see Deaths). One patient (1.1%) in the Pbo+Pac arm had Grade 5 AE (PT: tumor lysis syndrome) leading to paclitaxel and placebo discontinuation.

Table 52 Adverse Events Leading to Paclitaxel Discontinuation (Cohort A, Safety Evaluable Population)

Adverse Events Leading to Paclitaxel Discontinuation by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Neuropathy peripheral	4 (4.6%)	8 (4.8%)
Peripheral sensory neuropathy	2 (2.3%)	4 (2.4%)
Polyneuropathy	3 (3.4%)	1 (0.6%)
Diarrhoea	0	3 (1.8%)
Hypersensitivity	1 (1.1%)	1 (0.6%)
Pulmonary embolism	0	2 (1.2%)
Anaphylactic shock	1 (1.1%)	0
Atrial fibrillation	1 (1.1%)	0
Dyspnoea	1 (1.1%)	0
Erythema	1 (1.1%)	0
Fatigue	1 (1.1%)	0
Haematuria	1 (1.1%)	0
Large intestine perforation	0	1 (0.6%)
Neutropenia	0	1 (0.6%)
Neutrophil count decreased	0	1 (0.6%)
Ocular hyperaemia	1 (1.1%)	0
Oedema	0	1 (0.6%)
Onycholysis	0	1 (0.6%)
Paronychia	0	1 (0.6%)
Peripheral motor neuropathy	0	1 (0.6%)
Pneumonia	0	1 (0.6%)
Pneumothorax	1 (1.1%)	0
Rash	0	1 (0.6%)
Toxic neuropathy	0	1 (0.6%)
Tumour lysis syndrome	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSCPAC_A_SE.out
08MAY2023 6:17 Page 1 of 1

A listing (l_ae_DSCANY_A_SE) of all AEs leading to any study treatment discontinuation is appended.

Narratives for patients who experienced AEs leading to study treatment discontinuation are appended.

Cohort B

The proportion of patients who experienced AEs leading to ipatasertib/placebo treatment discontinuation was higher in the Ipat+Pac arm (17 patients [11.7%]) compared with Pbo+Pac arm (3 patients [4%]) (t_ae_DSCIPAT_B_SE).

Adverse events (by PT) leading to ipatasertib discontinuation occurring in ≥1% of patients (i.e., ≥2 patients) in the Ipat+Pac arm were diarrhea (2.8%), febrile neutropenia (1.4%), and hyperglycemia (1.4%) (Table 53). In the Pbo+Pac arm, no AEs (by PT) leading to placebo discontinuation were reported in more than 1 patient.

Among AEs leading to ipatasertib/placebo discontinuation, Grade 3 events were reported in 4.8% of patients in the Ipat+Pac arm and 2.7% of patients in the Pbo+Pac arm (t_ae_ctc_DSCIPAT_B_SE). Three (2.1%) patients in the Ipat+Pac arm had Grade 5 AEs (PT: febrile neutropenia, death, pneumonia) leading to treatment discontinuation of both ipatasertib and paclitaxel (see Deaths). No patients in the Ipat+Pac arm had Grade 4 events that led to discontinuation of study treatment. The rest of AEs leading to ipatasertib/placebo discontinuation were reported as Grade 1 or Grade 2.

Table 53 Adverse Events Leading to Ipatasertib/Placebo Discontinuation (Cohort B, Safety Evaluable Population)

Adverse Events Leading to Ipatasertib/Placebo Discontinuation by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Diarrhoea	1 (1.3%)	4 (2.8%)
Febrile neutropenia	0	2 (1.4%)
Hyperglycaemia	0	2 (1.4%)
Abdominal discomfort	0	1 (0.7%)
Alanine aminotransferase increased	0	1 (0.7%)
COVID-19	0	1 (0.7%)
Cerebrovascular accident	0	1 (0.7%)
Death	0	1 (0.7%)
Dyspnoea	0	1 (0.7%)
Fatigue	1 (1.3%)	0
Flushing	0	1 (0.7%)
Hypertransaminasaemia	0	1 (0.7%)
Neutropenia	0	1 (0.7%)
Peripheral sensory neuropathy	1 (1.3%)	0
Pneumonia	0	1 (0.7%)
Pneumonitis	0	1 (0.7%)
Stomatitis	0	1 (0.7%)
Vomiting	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSCIPAT_B_SE.out
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Adverse events leading to discontinuation of paclitaxel were reported in 42 patients (29%) in the Ipat+Pac arm and in 12 patients (16%) in the Pbo+Pac arm (t_ae_DSCPAC_B_SE). The most common AEs leading to paclitaxel discontinuation were reported in the SOC of nervous system disorders (Ipat+Pac: 16.6% vs. Pbo+Pac: 9.3%).

The AEs (by PT) leading to paclitaxel discontinuation occurring in ≥ 2 of patients in either treatment arm were: neuropathy peripheral (Ipat + Pac: 6.9% vs. Pbo+Pac: 1.3%), peripheral sensory neuropathy (4.8% vs. 6.7%), neurotoxicity (1.4% vs. 0), polyneuropathy (1.4% vs. 0), febrile neutropenia (2.1% vs. 0), neutropenia (2.1% vs. 0), and neutrophil count decreased (1.2% vs. 2.7%) (Table 54).

Among patients with AEs leading to paclitaxel discontinuation, the majority (15.2%) had Grade ≥ 3 AEs by highest NCI CTCAE grade in the Ipat+Pac arm (t_ae_ctc_DSCPAC_B_SE). Three patients (2.1%) in the Ipat+Pac arm (PTs: febrile neutropenia, death, pneumonia) and 1 patient (1.3%) in Pbo+Pac arm (PT: sepsis) had Grade 5 AEs leading to study treatment discontinuation (see Deaths).

Table 54 Adverse Events Leading to Paclitaxel Discontinuation (Cohort B, Safety Evaluable Population)

Adverse Events Leading to Paclitaxel Discontinuation by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Peripheral sensory neuropathy	5 (6.7%)	7 (4.8%)
Neuropathy peripheral	1 (1.3%)	10 (6.9%)
Neutrophil count decreased	2 (2.7%)	2 (1.4%)
Febrile neutropenia	0	3 (2.1%)
Neutropenia	0	3 (2.1%)
Fatigue	1 (1.3%)	1 (0.7%)
Neurotoxicity	0	2 (1.4%)
Paraesthesia	1 (1.3%)	1 (0.7%)
Polyneuropathy	0	2 (1.4%)
Abdominal discomfort	0	1 (0.7%)
Anaemia	0	1 (0.7%)
Asthenia	0	1 (0.7%)
COVID-19	0	1 (0.7%)
Cerebrovascular accident	0	1 (0.7%)
Death	0	1 (0.7%)
Diarrhoea	0	1 (0.7%)
Dizziness	0	1 (0.7%)
Dyspnoea	0	1 (0.7%)
Flushing	0	1 (0.7%)
Hyperglycaemia	0	1 (0.7%)
Hypertransaminasaemia	0	1 (0.7%)
Leukopenia	0	1 (0.7%)
Nausea	0	1 (0.7%)
Oedema	1 (1.3%)	0
Pneumonia	0	1 (0.7%)
Pneumonitis	0	1 (0.7%)
Rash	0	1 (0.7%)
Scleroderma	0	1 (0.7%)
Sepsis	1 (1.3%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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A listing (l_ae_DSCANY_B_SE) of all AEs leading to any study treatment discontinuation is appended.

Narratives for patients who experienced AEs leading to study treatment discontinuation are appended.

Cohort C

The total number of patients with at least one AE leading to ipatasertib treatment discontinuation was 11 (10.8%) (t_ae_DSCIPAT_C_SE).

Adverse events (by PT) leading to ipataserib discontinuation occurring in ≥2 patients were aspartate aminotransferase increased, alanine aminotransferase increased, and autoimmune hepatitis (Table 55).

Among AEs leading to ipatasertib discontinuation, Grade 3 events were reported in 6.9% of patients (t_ae_ctc_DSCIPAT_C_SE). Two (2.0%) patients had Grade 5 AE (PTs: pulmonary embolism, suspected Covid-19) leading to treatment discontinuation of ipatasertib, atezolizumab, and paclitaxel (see Deaths). One patient had Grade 4 event (PT: diabetic ketoacidosis). The remaining one AE leading to ipatasertib discontinuation was reported as Grade 1.

Table 55 Adverse Events Leading to Ipatasertib Discontinuation (Cohort C, Safety Evaluable Population)

Adverse Events Leading to Ipatasertib Discontinuation by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Aspartate aminotransferase increased	3 (2.9%)
Alanine aminotransferase increased	2 (2.0%)
Autoimmune hepatitis	2 (2.0%)
Blood alkaline phosphatase increased	1 (1.0%)
Diabetic ketoacidosis	1 (1.0%)
Hyperglycaemia	1 (1.0%)
Hypersensitivity	1 (1.0%)
Large intestine perforation	1 (1.0%)
Pneumonitis	1 (1.0%)
Pulmonary embolism	1 (1.0%)
Suspected COVID-19	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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Output:
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The total number of patients with at least one AE leading to discontinuation of paclitaxel was 23(22.5%) (t_ae_DSCPAC_C_SE). The most common AEs leading to paclitaxel discontinuation were reported in the SOC of nervous system disorders (11.8%).

The AEs (by PT) leading to paclitaxel discontinuation occurring in ≥ 2 of patients were: neuropathy peripheral (6.9%), and polyneuropathy (2%), (Table 56).

Among patients with AEs leading to paclitaxel discontinuation, 10.8% had Grade ≥ 3 AEs by highest NCI CTCAE grade (t_ae_ctc_DSCPAC_C_SE). Two patients (2.0%) had Grade 5 AE

(PTs: pulmonary embolism, suspected Covid-19) leading to treatment discontinuation of ipatasertib, atezolizumab, and paclitaxel (see Deaths).

Table 56 Adverse Events Leading to Paclitaxel Discontinuation (Cohort C, Safety Evaluable Population)

Adverse Events Leading to Paclitaxel Discontinuation by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Neuropathy peripheral	7 (6.9%)
Polyneuropathy	2 (2.0%)
Aspartate aminotransferase increased	1 (1.0%)
Autoimmune hepatitis	1 (1.0%)
Dyspnoea	1 (1.0%)
Encephalopathy	1 (1.0%)
Fatigue	1 (1.0%)
Flushing	1 (1.0%)
Hypersensitivity	1 (1.0%)
Large intestine perforation	1 (1.0%)
Neutrophil count decreased	1 (1.0%)
Peripheral motor neuropathy	1 (1.0%)
Peripheral sensory neuropathy	1 (1.0%)
Pneumonia	1 (1.0%)
Pneumonitis	1 (1.0%)
Pulmonary embolism	1 (1.0%)
Suspected COVID-19	1 (1.0%)

Investigator text for Aes encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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The total number of patients with at least one AE leading to discontinuation of atezolizumab was 14 (13.7%) (t_ae_DSCATZ_C_SE). The most common AEs leading to atezolizumab discontinuation were reported in the SOCs: hepatobiliary disorder and investigations (2.9% in each).

The AEs (by PT) leading to atezolizumab discontinuation occurring in ≥ 2 of patients were: autoimmune hepatitis (2.9%), alanine aminotransferase increased (2.9%), and aspartate aminotransferase increased (2.0%) (Table 57).

Among patients with AEs leading to atezolizumab discontinuation, the majority (11.8%) had Grade ≥ 3 AEs by highest NCI CTCAE grade (t_ae_ctc_DSCATZ_C_SE). Two patients (2.0%) had Grade 5 AE (PTs: pulmonary embolism, suspected Covid-19) leading to treatment discontinuation of ipatasertib, atezolizumab, and paclitaxel (see Deaths).

Table 57 Adverse Events Leading to Atezolizumab Discontinuation (Cohort C, Safety Evaluable Population)

Adverse Events Leading to Atezolizumab Discontinuation by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Alanine aminotransferase increased	3 (2.9%)
Autoimmune hepatitis	3 (2.9%)
Aspartate aminotransferase increased	2 (2.0%)
Blood alkaline phosphatase increased	1 (1.0%)
Diarrhoea	1 (1.0%)
Dystonia	1 (1.0%)
Hypersensitivity	1 (1.0%)
Large intestine perforation	1 (1.0%)
Mixed connective tissue disease	1 (1.0%)
Pneumonia	1 (1.0%)
Pneumonitis	1 (1.0%)
Pulmonary embolism	1 (1.0%)
Suspected COVID-19	1 (1.0%)

Investigator text for Aes encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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Output:
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A listing (l_ae_DSCANY_C_SE) of all AEs leading to any study treatment discontinuation is appended.

Narratives for patients who experienced AEs leading to study treatment discontinuation are appended.

5.2.2.5 Adverse Events That Led to Dose Modification

Cohort A

A higher proportion of patients experienced AEs leading to ipatasertib/placebo dose reduction in the Ipat+Pac arm (46 patients [27.7%]) compared with the Pbo+Pac arm (7 patients [8%]), with the difference mainly due to the SOC of gastrointestinal disorders (Ipat+Pac arm: 16.9% vs. Pbo+Pac arm: 2.3%) (t_ae_DSRIPAT_A_SE).

The most commonly reported (≥2% of patients in either arm) AEs by PT leading to dose reduction of ipatasertib/placebo were diarrhea (13.9% vs. 2.3%), hyperglycemia (2.4% vs. 2.3%), alanine aminotransferase increased (2.4% vs. 1.1%), aspartate aminotransferase increased (2.4% vs. 1.1%), neutropenia (2.4% vs. 0), and neutrophil count decreased (1.2% vs. 2.3%) (Table 58). There were 15.1% of patients in the Ipat+Pac arm and 4.6% of patients in the Pbo+Pac arm that experienced Grade 3–4 AEs leading to ipatasertib/placebo dose reduction (t_ae_ctc_DSRIPAT_A_SE).

Table 58 Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo (Cohort A, Safety Evaluable Population)

Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Diarrhoea	2 (2.3%)	23 (13.9%)
Hyperglycaemia	2 (2.3%)	4 (2.4%)
Alanine aminotransferase increased	1 (1.1%)	4 (2.4%)
Aspartate aminotransferase increased	1 (1.1%)	4 (2.4%)
Neutropenia	0	4 (2.4%)
Neutrophil count decreased	2 (2.3%)	2 (1.2%)
Febrile neutropenia	0	3 (1.8%)
Nausea	0	3 (1.8%)
Decreased appetite	0	2 (1.2%)
Rash	0	2 (1.2%)
Abdominal pain	0	1 (0.6%)
Colitis	0	1 (0.6%)
Eschar	0	1 (0.6%)
Fatigue	0	1 (0.6%)
Neuropathy peripheral	0	1 (0.6%)
Stomatitis	0	1 (0.6%)
Weight decreased	0	1 (0.6%)
White blood cell count decreased	1 (1.1%)	0

Investigator text for Aes encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSRIPAT_A_SE.out
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A higher proportion of patients experienced AEs leading to ipatasertib/placebo dose interruption in the Ipat+Pac arm: (73 patients [44%]) compared with the Pbo+Pac arm (26 patients [29.9%]), with only the SOC of gastrointestinal disorders with a ≥ 5% difference between treatment arms (Ipat+Pac: 13.9% vs. Pbo+Pac: 3.4%) (t_ae_DSIIPAT_A_SE). The most commonly reported (≥5% of patients in either arm) AEs by PTs leading to dose interruption of ipatasertib/placebo was diarrhea (8.4% vs. 0), neutropenia (6% vs. 4.6%) (t_ae_pt_DSIIPAT_A_SE). There were 19.3% of patients in the Ipat+Pac arm and 23% of patients in the Pbo+Pac arm that experienced Grade 3-4 AEs leading to ipatasertib/placebo dose interruption (t_ae_ctc_DSIIPAT_A_SE).

A higher proportion of patients experienced AEs leading to paclitaxel dose reduction in the Ipat+Pac arm (34 patients [20.5%]) compared with Pbo+Pac arm (9 patients [10.3%]) (t_ae_DSRPAC_A_SE). Overall, the most commonly reported (≥2% of patients in either arm) AEs by PTs leading to dose reduction of paclitaxel were neuropathy peripheral (3% vs. 1.1%), peripheral sensory neuropathy (3% vs. 2.3%), neutropenia (3% vs. 0), and neutrophil count decreased (1.8% vs. 2.3%) (Table 59). There were 9.6% of patients in the Ipat+Pac arm and 3.4% of patients in the Pbo+Pac arm that experienced Grade 3–4 AEs leading to paclitaxel dose reduction (t_ae_ctc_DSRPAC_A_SE).

Table 59 Adverse Events Leading to Dose Reduction of Paclitaxel (Cohort A, Safety Evaluable Population)

Adverse Events Leading to Dose Reduction of Paclitaxel by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Peripheral sensory neuropathy	2 (2.3%)	5 (3.0%)
Neuropathy peripheral	1 (1.1%)	5 (3.0%)
Neutropenia	0	5 (3.0%)
Neutrophil count decreased	2 (2.3%)	3 (1.8%)
Alanine aminotransferase increased	0	3 (1.8%)
Aspartate aminotransferase increased	0	2 (1.2%)
Diarrhoea	0	2 (1.2%)
Fatigue	1 (1.1%)	1 (0.6%)
Febrile neutropenia	0	2 (1.2%)
Anaemia	0	1 (0.6%)
Asthenia	0	1 (0.6%)
Decreased appetite	0	1 (0.6%)
Eschar	0	1 (0.6%)
Hyperglycaemia	0	1 (0.6%)
Hypotension	0	1 (0.6%)
Ill-defined disorder	1 (1.1%)	0
Neurotoxicity	0	1 (0.6%)
Oedema	0	1 (0.6%)
Oedema peripheral	1 (1.1%)	0
Oliguria	0	1 (0.6%)
Paraesthesia	0	1 (0.6%)
Peripheral motor neuropathy	0	1 (0.6%)
Toxicity to various agents	1 (1.1%)	0
White blood cell count decreased	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSRPAC_A_SE.out
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A similar proportion of patients experienced AEs leading to paclitaxel dose interruption in both treatment arms (Ipat+Pac: 85 patients [51.2%] vs. Pbo+Pac: 41 patients [47.1%]), with only the SOC of gastrointestinal disorders with a ≥ 5% difference between treatment arms (Ipat+Pac: 10.2% vs. Pbo + Pac: 2.3%) (t_ae_DSIPAC_A_SE). The most commonly reported (≥5% of patients in either arm) AEs by PTs leading to dose interruption of paclitaxel was neutropenia (12% vs. 14.9%) and neutrophil count decreased (9.0% vs. 9.2%) (t_ae_pt_DSIPAC_A_SE). There were 21.7% of patients in the Ipat+Pac arm and 26.4% of patients in the Pbo+Pac arm that experienced Grade 3–4 AEs leading to paclitaxel dose interruption (t_ae_ctc_DSIPAC_A_SE).

A listing (l_ae_DSMANY_A_SE) of all AEs leading to dose reduction or interruption of any study treatment is appended.

Cohort B

A higher proportion of patients experienced AEs leading to ipatasertib/placebo dose reduction in the Ipat+Pac arm (50 patients [34.5%]) compared with the Pbo+Pac arm

(6 patients [8%]), with the difference mainly due to the SOC of gastrointestinal disorders (Ipat+Pac arm: 24.1% vs. Pbo+Pac arm: 1.3%) (t_ae_DSRIPAT_B_SE).

The most commonly reported (≥2% of patients in either arm) AEs by PT leading to dose reduction of ipatasertib/placebo were diarrhea (22.8% vs. 0), neutropenia (1.4% vs. 2.7%), hyperglycemia (2.1% vs. 0), and neutrophil count decreased (4.1% vs. 4%) (Table 60). There were 17.9% of patients in the Ipat+Pac arm and 6.7% of patients in the Pbo+Pac arm that experienced Grade 3-4 AEs leading to ipatasertib/placebo dose reduction (t_ae_ctc_DSRIPAT_B_SE).

Table 60 Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo (Cohort B, Safety Evaluable Population)

Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Diarrhoea	0	33 (22.8%)
Neutrophil count decreased	3 (4.0%)	6 (4.1%)
Neutropenia	2 (2.7%)	2 (1.4%)
Hyperglycaemia	0	3 (2.1%)
Nausea	1 (1.3%)	2 (1.4%)
Alanine aminotransferase increased	0	2 (1.4%)
Decreased appetite	0	2 (1.4%)
Leukopenia	0	2 (1.4%)
Rash	0	2 (1.4%)
Rash maculo-papular	0	2 (1.4%)
Aphthous ulcer	0	1 (0.7%)
Aspartate aminotransferase increased	0	1 (0.7%)
Asthenia	1 (1.3%)	0
Blood creatine phosphokinase increased	0	1 (0.7%)
Erythema multiforme	0	1 (0.7%)
Fatigue	1 (1.3%)	0
Febrile neutropenia	0	1 (0.7%)
Gamma-glutamyltransferase increased	0	1 (0.7%)
Oedema peripheral	0	1 (0.7%)
Peripheral sensory neuropathy	0	1 (0.7%)
Pneumonitis	0	1 (0.7%)
Rash erythematous	0	1 (0.7%)
Vomiting	0	1 (0.7%)
White blood cell count decreased	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSRIPAT_B_SE.out
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A similar proportion of patients experienced AEs leading to ipatasertib/placebo dose interruption in the Ipat+Pac arm: (67 patients [46.2%]) compared with the Pbo+Pac arm (32 patients [42.7%]), with only the SOC of gastrointestinal disorders with a ≥ 5% difference between treatment arms (Ipat+Pac: 20.0% vs. Pbo+Pac: 4.0%) (t_ae_DSIIPAT_B_SE). The most commonly reported (≥5% of patients in either arm) AEs by PTs leading to dose interruption of ipatasertib/placebo was diarrhea (9.7% vs. 0%), neutrophil count decreased (7.6% vs. 8.0%), and neutropenia (4.8% vs. 8%)

(t_ae_pt_DSIIPAT_B_SE). There were 24.8% of patients in the Ipat+Pac arm and 25.3% of patients in the Pbo+Pac arm that experienced Grade 3–4 AEs leading to ipatasertib/placebo dose interruption (t_ae_ctc_DSIIPAT_B_SE).

A similar proportion of patients experienced AEs leading to paclitaxel dose reduction in the Ipat+Pac arm (39 patients [26.9%]) compared with Pbo+Pac arm (19 patients [25.3%]) (t_ae_DSRPAC_B_SE). Overall, the most commonly reported (≥2% of patients in either arm) AEs (by PTs) leading to dose reduction of paclitaxel were neuropathy peripheral (6.2% vs. 2.7%), peripheral sensory neuropathy (3.4% vs. 2.7%), polyneuropathy (2.1% vs. 1.3%), neutrophil count decreased (5.5% vs. 4%), neutropenia (3.4% vs. 4%), asthenia (0 vs. 2.7%), diarrhea (2.8% vs. 0), and cystitis (0 vs. 2.7%) (Table 61). There were 11% of patients in the Ipat+Pac arm and 8% of patients in the Pbo+Pac arm that experienced Grade 3-4 AEs leading to paclitaxel dose reduction (t_ae_ctc_DSRPAC_B_SE).

Table 61 Adverse Events Leading to Dose Reduction of Paclitaxel (Cohort B, Safety Evaluable Population)

Adverse Events Leading to Dose Reduction of Paclitaxel by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Neuropathy peripheral	2 (2.7%)	9 (6.2%)
Neutrophil count decreased	3 (4.0%)	8 (5.5%)
Neutropenia	3 (4.0%)	5 (3.4%)
Peripheral sensory neuropathy	2 (2.7%)	5 (3.4%)
Diarrhoea	0	4 (2.8%)
Polyneuropathy	1 (1.3%)	3 (2.1%)
Oedema peripheral	1 (1.3%)	2 (1.4%)
Anaemia	1 (1.3%)	1 (0.7%)
Asthenia	2 (2.7%)	0
Cystitis	2 (2.7%)	0
Neurotoxicity	1 (1.3%)	1 (0.7%)
Alanine aminotransferase increased	1 (1.3%)	0
Decreased appetite	0	1 (0.7%)
Gait disturbance	1 (1.3%)	0
Nausea	0	1 (0.7%)
Oedema	1 (1.3%)	0
Paronychia	0	1 (0.7%)
Peripheral motor neuropathy	0	1 (0.7%)
Pneumonitis	0	1 (0.7%)
Poisoning	1 (1.3%)	0
White blood cell count decreased	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSRPAC_B_SE.out
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A similar proportion of patients experienced AEs leading to paclitaxel dose interruption in both treatment arms (Ipat+Pac: 77 patients [53.1%] vs. Pbo+Pac: 40 patients [53.3%]), with only the SOC of gastrointestinal disorders with a ≥ 5% difference between treatment

arms (Ipat+Pac: 16.6% vs. Pbo+Pac: 2.7%) (t_ae_DSIPAC_B_SE). The most commonly reported (≥5% of patients in either arm) AEs by PTs leading to dose interruption of paclitaxel were neutropenia (13.1% vs. 13.3%), neutrophil count decreased (11.7% vs. 17.3%), and diarrhea (6.9% vs. 0) (t_ae_pt_DSIPAC_B_SE). There were 31% of patients in the Ipat+Pac arm and 28% of patients in the Pbo+Pac arm that experienced Grade 3–4 AEs leading to paclitaxel dose interruption (t_ae_ctc_DSIPAC_B_SE).

A listing (l_ae_DSMANY_B_SE) of all AEs leading to dose reduction or interruption of any study treatment is appended.

Cohort C

The total number of patients who experienced at least one AE leading to ipatasertib dose reduction was 37 (36.3%), mainly due to the SOC of gastrointestinal disorders (t_ae_DSRIPAT_C_SE).

The most commonly reported (≥2% of patients) AEs (by PT) leading to dose reduction of ipatasertib were diarrhea (20.6%), nausea (3.9%), hyperglycemia (4.9%), neutrophil count decreased (2.9%), and neutropenia (2.0%) (Table 62). There were 21.6% of patients that experienced Grade 3–4 AEs leading to ipatasertib dose reduction (t_ae_ctc_DSRIPAT_C_SE).

Table 62 Adverse Events Leading to Dose Reduction of Ipatasertib (Cohort C, Safety Evaluable Population)

Adverse Events Leading to Dose Reduction of Ipatasertib by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diarrhoea	21 (20.6%)
Hyperglycaemia	5 (4.9%)
Nausea	4 (3.9%)
Neutrophil count decreased	3 (2.9%)
Neutropenia	2 (2.0%)
Alanine aminotransferase increased	1 (1.0%)
Aspartate aminotransferase increased	1 (1.0%)
Blood triglycerides increased	1 (1.0%)
Dizziness	1 (1.0%)
Febrile neutropenia	1 (1.0%)
Gastroenteritis	1 (1.0%)
Hyperbilirubinaemia	1 (1.0%)
Lipase increased	1 (1.0%)
Rash	1 (1.0%)
Visual impairment	1 (1.0%)
Vomiting	1 (1.0%)

Investigator text for Aes encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
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Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSRIPAT_C_SE.out
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The total number of patients who experienced at least one AE leading to ipatasertib dose interruption was 59 (57.8%), mainly due to the SOC of gastrointestinal disorders (t_ae_DSIIPAT_C_SE). The most commonly reported (≥5% of patients) AEs (by PTs) leading to dose interruption of ipatasertib were diarrhea (14.7%), neutropenia (9.8%), alanine aminotransferase increased (5.9%), aspartate aminotransferase increased (5.9%), pyrexia (5.9%), and rash (5.9%) (t_ae_pt_DSIIPAT_C_SE). There were 31.4% of patients that experienced Grade 3–4 AEs leading to ipatasertib dose interruption (t_ae_ctc_DSIIPAT_C_SE).

The total number of patients who experienced at least one AE leading to paclitaxel dose reduction was 25 (24.5%) (t_ae_DSRPAC_C_SE). Overall, the most commonly reported (≥2% of patients) AEs by PTs leading to dose reduction of paclitaxel were neuropathy peripheral (7.8%), polyneuropathy (2.9%), neutrophil count decreased (2.9%), alanine aminotransferase increased (2.0%), neutropenia (2.9%), and diarrhea (2.0%) (Table 63). There were 7.8% of patients that experienced Grade 3–4 AEs leading to paclitaxel dose reduction (t_ae_ctc_DSRPAC_C_SE).

Table 63 Adverse Events Leading to Dose Reduction of Paclitaxel (Cohort C, Safety Evaluable Population)

Adverse Events Leading to Dose Reduction of Paclitaxel by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Neuropathy peripheral	8 (7.8%)
Neutropenia	3 (2.9%)
Neutrophil count decreased	3 (2.9%)
Polyneuropathy	3 (2.9%)
Alanine aminotransferase increased	2 (2.0%)
Diarrhoea	2 (2.0%)
Anaemia	1 (1.0%)
Aspartate aminotransferase increased	1 (1.0%)
Dizziness	1 (1.0%)
Nail disorder	1 (1.0%)
Oedema peripheral	1 (1.0%)
Visual impairment	1 (1.0%)
Weight decreased	1 (1.0%)

Investigator text for Aes encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSRPAC_C_SE.out
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The total number of patients who experienced at least one AE leading to paclitaxel dose interruption was 67 (65.7%), mainly due to the SOC of blood and lymphatic system disorders and infections and infestations (t_ae_DSIPAC_C_SE). The most commonly reported (≥5% of patients) AEs (by PTs) leading to dose interruption of paclitaxel were neutropenia (15.7%), diarrhea (8.8%), alanine aminotransferase increased (7.8%), aspartate aminotransferase increased (6.9%), pyrexia (6.9%) and neutrophil count

decreased (5.9%) (t_ae_pt_DSIPAC_C_SE). There were 35.3% of patients that experienced Grade 3–4 AEs leading to paclitaxel dose interruption (t_ae_ctc_DSIPAC_C_SE).

The total number of patients who experienced at least one AE leading to atezolizumab dose interruption was 53 (52%), mainly due to the SOC of infections and infestations (t_ae_DSIATZ_C_SE). The most commonly reported (≥5% of patients) AEs (by PTs) leading to dose interruption of atezolizumab were neutropenia (6.9%), aspartate aminotransferase increased (6.9%), pyrexia (5.9%) and rash (5.9%) (t_ae_pt_DSIATZ_C_SE). There were 26.5% of patients that experienced Grade 3–4 AEs leading to atezolizumab dose interruption (t_ae_ctc_DSIATZ_C_SE).

A listing (l_ae_DSMANY_C_SE) of all AEs leading to dose reduction or interruption of any study treatment is appended.

5.2.2.6 Selected Adverse Events

Selected AEs in the study included identified and potential toxicities based on nonclinical toxicology information, clinical experience with ipatasertib, and AEs known to be associated with the PI3K/Akt pathway inhibitor class.

Selected AEs were identified by grouping MedDRA Standardized MedDRA Queries and PTs of similar medical concept together to AE grouped terms (see Safety Analysis). The list of Selected AE definition (MedDRA_GroupTerms_Selected_AE_CO40016) is provided.

An overview of selected AEs of the safety evaluable population is provided for Cohort A (Table 64), Cohort B (Table 65), and Cohort C (Table 66). Selected AEs were reported in both treatment arms of Cohort A (Ipat+Pac: 94.6% vs. Pbo+Pac: 90.8%) and Cohort B (Ipat+Pac: 97.2% vs. Pbo+Pac: 97.3%). For Cohort C, selected AEs were reported in 99% of patients, and results for immune-mediated selected AEs associated with atezolizumab (i.e., immune-mediated rash, immune-mediated pneumonitis, etc.) are appended (t_aesi_C_SE, t_aesi_ctc_C_SE).

In the following Sections 5.2.2.6.1 to 5.2.2.6.17, results are discussed as clinically relevant for each selected AE category. However, complete analyses were conducted for all selected AE categories, and are appended.

Listings of all selected AEs for Cohort A (l_aesi_A_SE), Cohort B (l_aesi_B_SE), and Cohort C (l_aesi_C_SE) are appended.

Table 64 Overview of Selected Adverse Events (Cohort A, Safety Evaluable Population)

Summary of Selected Adverse Events, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one selected AE	79 (90.8%)	157 (94.6%)
Total number of selected AEs	404	1435
Total number of patients with at least one		
Selected AEs with fatal outcome	0	0
Serious Selected AEs	7 (8.0%)	17 (10.2%)
Selected AEs leading to discontinuation from Ipatasertib/placebo	3 (3.4%)	13 (7.8%)
Selected AEs leading to discontinuation from Paclitaxel	11 (12.6%)	20 (12.0%)
Selected AEs leading to discontinuation from any treatment	11 (12.6%)	27 (16.3%)
Selected AEs leading to Ipatasertib/placebo dose reduction	7 (8.0%)	44 (26.5%)
Selected AEs leading to Paclitaxel dose reduction	6 (6.9%)	32 (19.3%)
Selected AEs leading to dose reduction from any treatment	10 (11.5%)	61 (36.7%)
Selected AEs leading to Ipatasertib/placebo dose interruption	15 (17.2%)	51 (30.7%)
Selected AEs leading to Paclitaxel dose interruption	27 (31.0%)	62 (37.3%)
Selected AEs leading to dose interruption from any treatment	30 (34.5%)	73 (44.0%)
Grade >=3 Selected AEs	29 (33.3%)	71 (42.8%)
Selected AEs related to Ipatasertib/placebo	50 (57.5%)	151 (91.0%)
Selected AEs related to Paclitaxel	74 (85.1%)	143 (86.1%)
Selected AEs related to any treatment	79 (90.8%)	154 (92.8%)
Selected Adverse Events		
Hyperglycemia	10 (11.5%)	31 (18.7%)
Pneumonitis	1 (1.1%)	3 (1.8%)
Erythropenia	23 (26.4%)	45 (27.1%)
Thrombocytopenia	4 (4.6%)	2 (1.2%)
Peripheral neuropathy	49 (56.3%)	86 (51.8%)
Rash	19 (21.8%)	50 (30.1%)
Diarrhea	28 (32.2%)	141 (84.9%)
Vomiting	8 (9.2%)	54 (32.5%)
Nausea	22 (25.3%)	66 (39.8%)
Asthenia	25 (28.7%)	63 (38.0%)
Oral mucositis	8 (9.2%)	30 (18.1%)
Colitis	1 (1.1%)	1 (0.6%)
Hyperlipidemia	5 (5.7%)	13 (7.8%)
Hepatotoxicity	12 (13.8%)	29 (17.5%)
Neutropenia	31 (35.6%)	51 (30.7%)
Erythema multiforme	0	1 (0.6%)
Pneumonia	5 (5.7%)	8 (4.8%)

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. Multiple occurrences of the same AE in one individual are counted only once except for 'Total number of selected AEs' row in which multiple occurrences of the same AE are counted separately.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi_sum.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_sum_A_SE.out
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Table 65 Overview of Selected Adverse Events (Cohort B, Safety Evaluable Population)

Summary of Selected Adverse Events, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one selected AE	73 (97.3%)	141 (97.2%)
Total number of selected AEs	584	1419
Total number of patients with at least one		
Selected AEs with fatal outcome	0	2 (1.4%)
Serious Selected AEs	3 (4.0%)	12 (8.3%)
Selected AEs leading to discontinuation from Ipatasertib/placebo	3 (4.0%)	12 (8.3%)
Selected AEs leading to discontinuation from Paclitaxel	10 (13.3%)	35 (24.1%)
Selected AEs leading to discontinuation from any treatment	11 (14.7%)	41 (28.3%)
Selected AEs leading to Ipatasertib/placebo dose reduction	6 (8.0%)	47 (32.4%)
Selected AEs leading to Paclitaxel dose reduction	16 (21.3%)	38 (26.2%)
Selected AEs leading to dose reduction from any treatment	18 (24.0%)	66 (45.5%)
Selected AEs leading to Ipatasertib/placebo dose interruption	19 (25.3%)	52 (35.9%)
Selected AEs leading to Paclitaxel dose interruption	30 (40.0%)	61 (42.1%)
Selected AEs leading to dose interruption from any treatment	32 (42.7%)	70 (48.3%)
Grade >=3 Selected AEs	24 (32.0%)	66 (45.5%)
Selected AEs related to Ipatasertib/placebo	49 (65.3%)	133 (91.7%)
Selected AEs related to Paclitaxel	67 (89.3%)	132 (91.0%)
Selected AEs related to any treatment	70 (93.3%)	140 (96.6%)
Selected Adverse Events		
Hyperglycemia	10 (13.3%)	23 (15.9%)
Pneumonitis	0	6 (4.1%)
Erythropenia	16 (21.3%)	47 (32.4%)
Thrombocytopenia	1 (1.3%)	3 (2.1%)
Peripheral neuropathy	49 (65.3%)	94 (64.8%)
Rash	18 (24.0%)	47 (32.4%)
Diarrhea	30 (40.0%)	126 (86.9%)
Vomiting	6 (8.0%)	45 (31.0%)
Nausea	17 (22.7%)	60 (41.4%)
Asthenia	31 (41.3%)	55 (37.9%)
Oral mucositis	9 (12.0%)	27 (18.6%)
Colitis	0	2 (1.4%)
Hyperlipidemia	8 (10.7%)	17 (11.7%)
Hepatotoxicity	21 (28.0%)	25 (17.2%)
Neutropenia	33 (44.0%)	59 (40.7%)
Erythema multiforme	0	1 (0.7%)
Pneumonia	4 (5.3%)	6 (4.1%)

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. Multiple occurrences of the same AE in one individual are counted only once except for 'Total number of selected AEs' row in which multiple occurrences of the same AE are counted separately.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi_sum.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_sum_B_SE.out
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Table 66 Overview of Selected Adverse Events (Cohort C, Safety Evaluable Population)

Summary of Selected Adverse Events, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one selected AE	101 (99.0%)
Total number of selected AEs	1115
Total number of patients with at least one	
Selected AEs with fatal outcome	1 (1.0%)
Serious Selected AEs	13 (12.7%)
Selected AEs leading to discontinuation from Ipatasertib/ placebo	5 (4.9%)
Selected AEs leading to discontinuation from Paclitaxel	15 (14.7%)
Selected AEs leading to discontinuation from any treatment	19 (18.6%)
Selected AEs leading to Ipatasertib/placebo dose reduction	36 (35.3%)
Selected AEs leading to Paclitaxel dose reduction	23 (22.5%)
Selected AEs leading to dose reduction from any treatment	45 (44.1%)
Selected AEs leading to Ipatasertib/placebo dose interruption	48 (47.1%)
Selected AEs leading to Paclitaxel dose interruption	51 (50.0%)
Selected AEs leading to dose interruption from any treatment	64 (62.7%)
Grade >=3 Selected AEs	52 (51.0%)
Selected AEs related to Ipatasertib/placebo	96 (94.1%)
Selected AEs related to Paclitaxel	94 (92.2%)
Selected AEs related to any treatment	101 (99.0%)
Selected Adverse Events	
Hyperglycemia	24 (23.5%)
Pneumonitis	9 (8.8%)
Erythropenia	34 (33.3%)
Thrombocytopenia	3 (2.9%)
Peripheral neuropathy	53 (52.0%)
Rash	46 (45.1%)
Diarrhea	86 (84.3%)
Vomiting	29 (28.4%)
Nausea	42 (41.2%)
Asthenia	40 (39.2%)
Oral mucositis	21 (20.6%)
Colitis	0
Hyperlipidemia	14 (13.7%)
Hepatotoxicity	35 (34.3%)
Neutropenia	34 (33.3%)
Erythema multiforme	0
Pneumonia	7 (6.9%)

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. Multiple occurrences of the same AE in one individual are counted only once except for 'Total number of selected AEs' row in which multiple occurrences of the same AE are counted separately.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi_sum.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_sum_C_SE.out
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5.2.2.6.1 Diarrhea

Cohort A

The proportion of patients with selected AEs in the diarrhea category was higher in the Ipat+Pac arm compared with the Pbo+Pac arm (141 patients [84.9%] vs. 28 patients [32.2%]) (t_aesi_A_SE).

The majority of patients who experienced diarrhea had events that were Grade 1–2 in intensity. Grade 3 diarrhea events were reported in 15 patients (9.0%) in the Ipat+Pac

arm and 2 patients (2.3%) in the Pbo+Pac arm, respectively. No events of Grade 4 or Grade 5 intensity were reported in either treatment arm (t_aesi_ctc_A_SE).

Most diarrhea events (PT: diarrhea) were non-serious, with SAEs (Grade 2 or 3) occurring in 6 patients (3.6%) in the Ipat+Pac arm and no patient in the Pbo+Pac arm (t_aesi_ctc_SER_A_SE, l_aesi_A_SE).

A low number of patients discontinued ipatasertib/placebo treatment due to diarrhea (Ipat+Pac: 6 patients [3.6%] vs. Pbo+Pac: 0 patient) (t_aesi_ctc_DSCIPAT_A_SE). Three patients (1.8%) in the Ipat+Pac arm discontinued paclitaxel treatment due to diarrhea (t_aesi_ctc_DSCPAC_A_SE). In the Ipat+Pac arm, diarrhea led to ipatasertib dose reduction and dose interruption in 13.9% of patients and in 8.4% of patients, respectively. Diarrhea led to paclitaxel dose reduction in 1.2% of patients and dose interruption in 4.2% of patients (t_aesi_ctc_DSRPAC_A_SE, t_aesi_ctc_DSRIPAT_A_SE, t_aesi_ctc_DSIIPAT_A_SE, t_aesi_ctc_DSIPAC_A_SE).

Overall, the vast majority of diarrhea events had resolved (97.7% vs. 96.4%) (t_aesiout_A_SE).

In this study, to improve diarrhea management and patient experiences, if allowed locally, prophylactic loperamide (racecadotril as used in Europe) for diarrhea management was mandated in the first cycle, dose adjusted as necessary, and continued as per investigator judgment (see Prior and Concomitant Therapy). A similar proportion of patients in each treatment arm received at least one dose of prophylactic loperamide during the study period (Ipat+Pac: 83.3% vs. Pbo+Pac: 87.4%) (see Prior And Concomitant Therapy, t_cm_lop_A_IT).

Narratives for patients who experienced Grade ≥3 diarrhea events are appended.

Cohort B

The proportion of patients with selected AEs in the diarrhea category was higher in the Ipat+Pac arm compared with the Pbo+Pac arm (126 patients [86.9%] vs. 30 patients [40.0%]) (t_aesi_B_SE).

The majority of patients who experienced diarrhea had events that were Grade 1–2 in intensity. Grade 3 diarrhea were reported in 11.7% of patients in the Ipat+Pac arm and 1.3% of patients in the Pbo+Pac arm, respectively. No events of Grade 4 or Grade 5 intensity were reported in either treatment arm (t_aesi_ctc_B_SE).

Most diarrhea events were non-serious, with SAEs (Grade 3 or 4) occurring in 4 patients (2.8%) in the Ipat+Pac arm and 1 patient (1.3%) in the Pbo+Pac arm (t_aesi_ctc_SER_B_SE).

A low number of patients discontinued ipatasertib/placebo treatment due to diarrhea (Ipat+Pac: 4 patients [2.8%] vs. Pbo+Pac: 1 patient [1.3%]) (t_aesi_ctc_DSCIPAT_B_SE). One patient (0.7%) in the Ipat+Pac arm discontinued paclitaxel treatment due to diarrhea

(t_aesi_ctc_DSCPAC_B_SE). In the Ipat+Pac arm, diarrhea led to ipatasertib dose reduction and dose interruption in 22.8% of patients and in 9.7% of patients, respectively. Diarrhea led to paclitaxel dose reduction in 2.8% of patients and dose interruption in 6.9% of patients (t_aesi_ctc_DSRPAC_B_SE, t_aesi_ctc_DSRIPAT_B_SE, t_aesi_ctc_DSIIPAT_B_SE, t_aesi_ctc_DSIPAC_B_SE).

Overall, the vast majority of diarrhea events had resolved (97.6% vs. 98.5%) (t_aesiout_B_SE).

In this study, to improve diarrhea management and patient experiences, if allowed locally, prophylactic loperamide (racecadotril as used in Europe) for diarrhea management was mandated in the first cycle, dose adjusted as necessary, and continued as per investigator judgment (see Prior and Concomitant Therapy). A similar proportion of patients in each treatment arm received at least one dose of prophylactic loperamide during the study period (Ipat+Pac: 79.5% vs. Pbo+Pac: 77.6%) (see Prior And Concomitant Therapy, t_cm_lop_B_IT).

Narratives for patients who experienced Grade ≥3 diarrhea events are appended.

Cohort C

The number of patients with selected AEs in the diarrhea category was 86 patients [84.3%] (t_aesi_C_SE).

The majority of patients who experienced diarrhea had events that were Grade 1–2 in intensity. Grade 3 diarrhea was reported in 16.7% of patients. No events of Grade 4 or Grade 5 intensity were reported (t_aesi_ctc_C_SE).

Most diarrhea events were non-serious, with SAEs (Grade 1 and Grade 3) occurring in 4 patients (3.9%) (t_aesi_ctc_SER_C_SE). No patients had discontinued ipatasertib or paclitaxel treatment due to diarrhea (t_aesi_ctc_DSCIPAT_C_SE, t_aesi_ctc_DSCPAC_C_SE). One patient (1.0%) discontinued atezolizumab treatment due to diarrhea (t_aesi_ctc_DSCATZ_C_SE). Diarrhea led to ipatasertib dose reduction and dose interruption in 20.6% of patients and in 14.7% of patients, respectively. Diarrhea led to paclitaxel dose reduction in 2.0% of patients and dose interruption in 8.8% of patients. Diarrhea led to atezolizumab interruption in 4.9% of patients (t_aesi_ctc_DSRPAC_C_SE, t_aesi_ctc_DSRIPAT_C_SE, t_aesi_ctc_DSIIPAT_C_SE, t_aesi_ctc_DSIPAC_C_SE, t_aesi_ctc_DSIATZ_C_SE).

Overall, the vast majority of diarrhea events had resolved (97.2%) (t_aesiout_C_SE).

In this study, to improve diarrhea management and patient experiences, if allowed locally, prophylactic loperamide (racecadotril as used in Europe) for diarrhea management was mandated in the first cycle, dose adjusted as necessary, and continued as per investigator judgment (see Prior and Concomitant Therapy). The

proportion of patients who received at least one dose of prophylactic loperamide during the study period was 83.3% (see Prior And Concomitant Therapy, t_cm_lop_C_IT).

Narratives for patients who experienced Grade ≥3 diarrhea events are appended.

5.2.2.6.2 Rash

Cohort A

The proportion of patients with selected AEs of rash was higher in the Ipat+Pac arm compared with the Pbo+Pac arm (50 patients [30.1%] vs. 19 patients [21.8%], respectively). The most commonly reported PT within this category was rash (15.7% vs. 12.6%) (t_aesi_A_SE).

The majority of rash events were Grade 1 or Grade 2, with Grade 3 events reported in 1.2% of patients in the Ipat+Pac arm and 1.1% of patients in the Pbo+Pac arm. No events of Grade 4 or Grade 5 intensity were reported in either treatment arm (t_aesi_ctc_A_SE). One patient in the Ipat+Pac arm discontinued ipatasertib due to rash (t_aesi_ctc_DSCIPAT_A_SE). One patient each in the Ipat+Pac arm and Pbo+Pac arm also discontinued paclitaxel due to rash (t_aesi_ctc_DSCPAC_A_SE).

There were no serious events of rash reported (t_aesi_ctc_SER_A_SE). Two patients (1.2%) had ipatasertib dose reduction and 6 patients (3.6%) had ipatasertib dose interruption in the Ipat+Pac arm due to rash (t_aesi_ctc_DSRIPAT_A_SE, t_aesi_ctc_DSIIPAT_A_SE). No rash events led to paclitaxel dose reduction in any patients (t_aesi_ctc_DSRPAC_A_SE). Paclitaxel dose interruption due to rash was reported in 4.2% of patients in the Ipat+Pac arm and was not reported in any patients in the Pbo+Pac arm (t_aesi_ctc_DSIPAC_A_SE).

Overall, the majority of rash events in both treatment arms had resolved (Ipat+Pac: 88.6% vs. Pbo+Pac: 87.5%) (t_aesiout_A_SE).

Narratives for patients who experienced Grade ≥3 rash events are appended.

Cohort B

The proportion of patients with selected AEs in the rash category was higher in the Ipat+Pac arm compared with the Pbo+Pac arm (47 patients [32.4%] vs. 18 patients [24.0%]). The most commonly reported PT within this category was rash (21.4% vs. 12.0%) (t_aesi_B_SE).

The majority of the rash events were Grade 1 or Grade 2, with Grade 3 events reported in 4.1% of patients in the Ipat+Pac arm. No events of Grade 4 or Grade 5 intensity were reported in either treatment arm (t_aesi_ctc_B_SE). No patients discontinued ipatasertib due to rash (t_aesi_ctc_DSCIPAT_B_SE). One patient in the Ipat+Pac arm discontinued paclitaxel due to rash (t_aesi_ctc_DSCPAC_B_SE).

There were no serious rash events reported (t_aesi_ctc_SER_B_SE). Five patients (3.4%) had ipatasertib dose reduction and 8 patients (5.5%) had ipatasertib dose interruption in

the Ipat+Pac arm due to rash (t_aesi_ctc_DSRIPAT_B_SE, t_aesi_ctc_DSIIPAT_B_SE). No rash events led to paclitaxel dose reduction in any patients (t_aesi_ctc_DSRPAC_B_SE). Paclitaxel dose interruption due to rash were reported in 4.8% of patients in the Ipat+Pac arm and 4.0% patients in the Pbo+Pac arm, respectively (t_aesi_ctc_DSIPAC_B_SE).

Overall, the majority of rash events in both treatment arms had resolved (Ipat+Pac: 91.0% vs. Pbo+Pac: 90.3%) (t_aesiout_B_SE).

Narratives for patients who experienced Grade ≥3 rash events are appended.

Cohort C

The proportion of patients with selected AEs in the rash category was 45.1%. The most commonly reported PT within this category was rash (30.4%) (t_aesi_C_SE).

The majority of rash events were Grade 1 or Grade 2, with Grade 3 events reported in 4.9% of patients. No events of Grade 4 or Grade 5 intensity were reported (t_aesi_ctc_C_SE). No patients discontinued ipatasertib, atezolizumab, or paclitaxel due to rash (t_aesi_ctc_DSCIPAT_C_SE, t_aesi_ctc_DSCATZ_C_SE, t_aesi_ctc_DSCPAC_C_SE).

Two serious rash events (Grade 2 or Grade 3) were reported (t_aesi_ctc_SER_C_SE). One patient (1.0%) had ipatasertib dose reduction and 10 patients (9.8%) had ipatasertib dose interruption due to rash (t_aesi_ctc_DSRIPAT_C_SE, t_aesi_ctc_DSIIPAT_C_SE). No rash events led to paclitaxel dose reduction in any patients (t_aesi_ctc_DSRPAC_C_SE). Paclitaxel dose interruption due to rash was reported in 6.9% of patients (t_aesi_ctc_DSIPAC_C_SE). Atezolizumab dose interruption due to rash was reported in 9.8% of patients (t_aesi_ctc_DSIATZ_C_SE).

Overall, the majority of the rash events had resolved (87.9%) (t_aesiout_C_SE).

Narratives for patients who experienced Grade ≥3 rash events are appended.

5.2.2.6.3 Hyperglycemia

Cohort A

The proportions of patients with selected AEs in the category of hyperglycemia was higher in the Ipat+Pac arm compared with the Pbo+Pac arm (31 patients [18.7%] vs. 10 patients [11.5%]). In the safety evaluable population, the PTs reported within this category were hyperglycemia (18.7% vs. 10.3%), glucose tolerance impaired (1.2% vs. 0), blood glucose increased (0 vs. 1.1%), glycosylated hemoglobin abnormal (0.6% vs. 0) and diabetes mellitus (0.6% vs. 0) (t_aesi_A_SE).

The majority of cases of hyperglycemia were Grade 1 and 2. Grade 3–4 hyperglycemia was reported in 1.8% of patients in the Ipat+Pac arm. In the Ipat+Pac arm, 2 patients experienced Grade 3 hyperglycemia and 1 patient experienced Grade 4 hyperglycemia. No events of Grade 5 intensity were reported in either treatment arm (t_aesi_ctc_A_SE).

One patient (0.6%) in the Ipat+Pac arm experienced a serious hyperglycemia event (Grade 4, PT: hyperglycemia) (t_aesi_SER_A_SE, t_aesi_ctc_SER_A_SE).

In the Ipat+Pac arm, 2 patients discontinued from ipatasertib treatment due to hyperglycemia. No patients discontinued paclitaxel treatment due to hyperglycemia (t_aesi_ctc_DSCIPAT_A_SE, t_aesi_ctc_DSCPAC_A_SE).

In the Ipat+Pac arm, hyperglycemia led to ipatasertib dose reduction and dose interruption in 4 patients (2.4%) and 8 patients (4.8%), respectively, and paclitaxel dose reduction and dose interruption in 1 patient (0.6%) and 2 patients (1.2%), respectively (t_aesi_ctc_DSRIPAT_A_SE, t_aesi_ctc_DSIIPAT_A_SE, t_aesi_ctc_DSRPAC_A_SE, t_aesi_ctc_DSIPAC_A_SE). In the Pbo+Pac arm, hyperglycemia led to paclitaxel dose interruption in 2.3% of patients (t_aesi_ctc_DSIPAC_A_SE).

Overall, the majority of hyperglycemia events had resolved (Ipat+Pac: 87.1% vs. Pbo+Pac: 70.6%).

Narratives for patients who experienced Grade ≥3 hyperglycemia events are appended.

Cohort B

The proportions of patients with selected AEs in the category of hyperglycemia were similar in the Ipat+Pac arm compared with the Pbo+Pac arm (23 patients [15.9%] vs. 10 patients [13.3%]). In the safety evaluable population, the PTs reported within this category were hyperglycemia (13.1% vs. 13.3%), blood glucose increased (1.4% vs. 0), diabetes mellitus (0.7% vs. 0), glycosylated hemoglobin increased (0.7% vs. 0), and type 2 diabetes mellitus (0.7% vs. 0) (t_aesi_B_SE).

The majority of cases of hyperglycemia were Grade 1 and 2. Grade 3 hyperglycemia was reported in 2.1% of patients in the Ipat+Pac arm. No events of Grade 4 or 5 intensity were reported in either treatment arm (t_aesi_ctc_B_SE).

One patient (0.7%) in the Ipat+Pac arm experienced a serious hyperglycemia event (Grade 3, PT: hyperglycemia) (t_aesi_SER_B_SE, t_aesi_ctc_SER_B_SE).

In the Ipat+Pac arm, 2 patients (1.4%) discontinued from ipatasertib treatment due to hyperglycemia (t_aesi_ctc_DSCIPAT_B_SE). One patient (0.7%) in the Ipat+Pac arm and none in the Pbo+Pac arm discontinued paclitaxel due to hyperglycemia (t_aesi_ctc_DSCPAC_B_SE).

In the Ipat+Pac arm, hyperglycemia led to ipatasertib dose reduction and dose interruption in 3 patients (2.1%) and 5 patients (3.4%), respectively (t_aesi_ctc_DSRIPAT_B_SE, t_aesi_ctc_DSIIPAT_B_SE). No paclitaxel dose reduction due to hyperglycemia was reported. Paclitaxel dose interruption due to hyperglycemia was reported in 2 patients (1.4%) in the Ipat+Pac arm (t_aesi_ctc_DSRPAC_B_SE, t_aesi_ctc_DSIPAC_B_SE).

Overall, the majority of hyperglycemia events had resolved (Ipat+Pac: 85.3% vs. Pbo+Pac: 97.4%) (t_aesiout_B_SE).

Narratives for patients who experienced Grade ≥3 hyperglycemia events are appended.

Cohort C

The number of patients with selected AEs in the category of hyperglycemia was 24 patients (23.5%). In the safety evaluable population, the PTs reported within this category were hyperglycemia (21.6%), blood glucose increased (2.0%), diabetes mellitus (1.0%), diabetic ketoacidosis (1.0%), type 1 diabetes mellitus (1.0%), glycosylated hemoglobin increased (1.0%) (t_aesi_C_SE).

The majority of cases of hyperglycemia were Grade 1 and 2. Grade 3 and 4 hyperglycemia events were reported in 3.9% and 1.0% of patients, respectively. No event of Grade 5 intensity was reported (t_aesi_ctc_C_SE).

One patient (1.0%) experienced a serious hyperglycemia event (Grade 4, PT: diabetic ketoacidosis) (t_aesi_SER_C_SE, t_aesi_ctc_SER_C_SE).

One patient (1.0%) discontinued from ipatasertib treatment due to hyperglycemia (t_aesi_ctc_DSCIPAT_C_SE). No patients discontinued paclitaxel or atezolizumab due to hyperglycemia (t_aesi_ctc_DSCPAC_C_SE, t_aesi_ctc_DSCATZ_C_SE).

Hyperglycemia led to ipatasertib dose reduction and dose interruption in 5 patients (4.9%) and 6 patients (5.9%), respectively (t_aesi_ctc_DSRIPAT_C_SE, t_aesi_ctc_DSIIPAT_C_SE). No paclitaxel dose reduction due to hyperglycemia was reported. Paclitaxel dose interruption due to hyperglycemia was reported in 2 patients (2.0%) (t_aesi_ctc_DSRPAC_C_SE, t_aesi_ctc_DSIPAC_C_SE). Atezolizumab dose interruption due to hyperglycemia was reported in 3 patients (2.9%) (t_aesi_ctc_DSIATZ_C_SE).

Overall, the majority of hyperglycemia events had resolved (83.3%) (t_aesiout_C_SE).

Narratives for patients who experienced Grade ≥3 hyperglycemia events are appended.

5.2.2.6.4 Nausea

Cohort A

The proportion of patients with selected AEs in the nausea category was higher in the Ipat+Pac arm compared with the Pbo+Pac arm (66 patients [39.8%] vs. 22 patients [25.3%]) (t_aesi_A_SE).

Two events of nausea (both Grade 3) were reported as serious in the Ipat+Pac arm. Most nausea events were non-serious (t_aesi_ctc_SER_A_SE), and were Grade 1 or Grade 2, with Grade 3 events reported in 5 patients (3%) in the Ipat+Pac arm (t_aesi_ctc_A_SE). No events of Grade 4 or Grade 5 intensity were reported in either treatment arm. No patients were discontinued from any treatment in either treatment arm

(t_aesi_ctc_DSCIPAT_A_SE, t_aesi_ctc_DSCPAC_A_SE). Ipatasertib dose interruption and reduction due to nausea was reported in 4 patients (2.4%) and 3 patients (1.8%), respectively (t_aesi_ctc_DSIIPAT_A_SE, t_aesi_ctc_DSRIPAT_A_SE). Paclitaxel dose interruption due to nausea was reported in 8 patients (4.8%) in the Ipat+Pac arm (t_aesi_ctc_DSIPAC_A_SE). No paclitaxel dose reduction due to nausea was reported (t_aesi_ctc_DSRPAC_A_SE).

Overall, the majority of nausea events in both treatment arms had resolved (Ipat+Pac: 89.8% vs. Pbo+Pac: 93.1%) (t_aesiout_A_SE).

Cohort B

The proportion of patients with selected AEs in the nausea category was higher in the Ipat+Pac arm compared with the Pbo+Pac arm (60 patients [41.4%] vs. 17 patients [22.7%]) (t_aesi_B_SE).

No events of nausea were reported as serious (t_aesi_SER_B_SE). Most nausea events were Grade 1 or Grade 2, with Grade 3 events reported in 2 patients (1.4%) in the Ipat+Pac arm (t_aesi_ctc_B_SE). No events of Grade 4 or Grade 5 intensity were reported in either treatment arm. No patients were discontinued from ipatasertib or placebo due to nausea in either treatment arm (t_aesi_ctc_DSCIPAT_B_SE). Paclitaxel discontinuation due to nausea was reported in 0.7% of patients in the Ipat+Pac arm (t_aesi_ctc_DSCPAC_B_SE). In the Ipat+Pac arm, nausea led to ipatasertib dose reduction and dose interruption in 2 patients (1.4%) and in 3 patients (2.1%), respectively. Nausea led to paclitaxel dose reduction in 1 patient (0.7%) and dose interruption in 2 patients (1.4%) in the Ipat+Pac arm (t_aesi_ctc_DSRPAC_B_SE, t_aesi_ctc_DSRIPAT_B_SE, t_aesi_ctc_DSIIPAT_B_SE, t_aesi_ctc_DSIPAC_B_SE).

Overall, the majority of nausea events in both treatment arms had resolved (Ipat+Pac: 89.4% vs. Pbo+Pac: 85.7%) (t_aesiout_B_SE).

Cohort C

The number of patients with selected AEs in the nausea category was 42 patients (41.2%) (t_aesi_C_SE).

One event of nausea (Grade 3) was reported as serious (t_aesi_SER_C_SE). Most nausea events were Grade 1 or Grade 2, with Grade 3 events reported in 2 patients (2%) (t_aesi_ctc_C_SE). No events of Grade 4 or Grade 5 intensity were reported. No patients were discontinued from any treatment (t_aesi_ctc_DSCIPAT_C_SE, t_aesi_ctc_DSCPAC_C_SE, t_aesi_ctc_DSCATZ_C_SE). Ipatasertib dose reduction and interruption due to nausea were reported in 4 patients (3.9%) and 5 patients (4.9%), respectively. Atezolizumab dose interruption due to nausea was reported in 3 patients (2.9%). No paclitaxel dose reduction was reported, but paclitaxel dose interruption due to nausea was reported in 4 patients (3.9%) (t_aesi_ctc_DSRIPAT_C_SE, t_aesi_ctc_DSIIPAT_C_SE, t_aesi_ctc_DSIATZ_C_SE, t_aesi_ctc_DSRPAC_C_SE, t_aesi_ctc_DSIPAC_C_SE).

Overall, the majority of nausea events had resolved (80.3%) (t_aesiout_C_SE).

5.2.2.6.5 Vomiting

Cohort A

The proportion of patients with selected AEs in the vomiting category was higher in the Ipat+Pac arm compared with the Pbo+Pac arm (54 patients [32.5%] vs. 8 patients [9.2%]) (t_aesi_A_SE).

The majority of the reported events of vomiting were Grade 1 or Grade 2. Grade 3 and Grade 4 events were reported in 4 patients (2.4%) and 1 patient (1.1%), respectively, in the Ipat + Pac arm and Pbo+Pac arm (t_aesi_ctc_A_SE).

Two events of vomiting (Grade 3 or 4) were reported as serious in the Ipat+Pac arm (t_aesi_SER_A_SE, t_aesi_ctc_SER_A_SE). No patients in the Ipat + Pac or Pbo + Pac arm discontinued any drug due to vomiting (t_aesi_ctc_DSCIPAT_A_SE, t_aesi_ctc_DSCPAC_A_SE). In the Ipat+Pac arm, vomiting led to ipatasertib and paclitaxel dose interruption in 3 patients each (1.8%) (t_aesi_ctc_DSIIPAT_A_SE, t_aesi_ctc_DSIPAC_A_SE). No patients had treatment dose reduction due to vomiting in either treatment arms (t_aesi_ctc_DSRIPAT_A_SE, t_aesi_ctc_DSRPAC_A_SE).

Overall, the majority of vomiting events had resolved (Ipat+Pac: 97.6% vs. Pbo+Pac: 100%) (t_aesiout_A_SE).

Cohort B

The proportion of patients with selected AEs in the vomiting category was higher in the Ipat+Pac arm compared with the Pbo+Pac arm (45 patients [31.0%] vs. 6 patients [8.0%]) (t_aesi_B_SE).

The majority of reported events of vomiting were Grade 1 or Grade 2. Grade 3–4 events were reported in 3 patients (2.1%) in the Ipat + Pac arm and were not reported in the Pbo+Pac arm (t_aesi_ctc_B_SE). No Grade 5 event of vomiting was reported.

No serious events of vomiting were reported (t_aesi_SER_B_SE). One patient in the Ipat + Pac arm discontinued ipatasertib due to vomiting. No patients were discontinued from paclitaxel due to vomiting (t_aesi_ctc_DSCIPAT_B_SE, t_aesi_ctc_DSCPAC_B_SE). In the Ipat+Pac arm, vomiting led to ipatasertib dose interruption in 7 patients (4.8%); and paclitaxel dose interruption in 4 patients (2.8%) (t_aesi_ctc_DSIIPAT_B_SE, t_aesi_ctc_DSIPAC_B_SE). Ipatasertib dose reduction was reported in one patient (0.7%) in the Ipat+Pac arm (t_aesi_ctc_DSRIPAT_B_SE). Paclitaxel dose interruption due to vomiting was reported in 4 patients (2.8%) in the Ipat+Pac arm (t_aesi_ctc_DSIPAC_B_SE). No paclitaxel dose reduction due to vomiting was reported in either treatment arm (t_aesi_ctc_DSRPAC_B_SE).

Overall, the majority of vomiting events had resolved (Ipat+Pac: 97.0% vs. Pbo+Pac: 100%) (t_aesiout_B_SE).

Cohort C

The number of patients with selected AEs in the vomiting category was 29 patients (28.4%) (t_aesi_C_SE).

The majority of reported events of vomiting were Grade 1 or Grade 2. Grade 3 events were reported in 2 patients (2.0%) (t_aesi_ctc_C_SE). No Grade 4 or 5 event of vomiting was reported.

Two serious events of vomiting (Grade 1 and Grade 3) were reported (t_aesi_SER_C_SE, t_aesi_ctc_SER_C_SE). No patients were discontinued from any study drug due to vomiting (t_aesi_ctc_DSCIPAT_C_SE, t_aesi_ctc_DSCPAC_C_SE, t_aesi_ctc_DSCATZ_C_SE). Vomiting led to ipatasertib dose interruption in 2 patients (2.0%) and paclitaxel dose interruption in 1 patient (1.0%). No atezolizumab dose interruption due to vomiting were reported (t_aesi_ctc_DSIIPAT_C_SE, t_aesi_ctc_DSIPAC_C_SE, t_aesi_ctc_DSIATZ_C_SE). Ipatasertib dose reduction was reported in 1 patient (1.0%) (t_aesi_ctc_DSRIPAT_C_SE). No paclitaxel dose reduction due to vomiting was reported (t_aesi_ctc_DSRPAC_C_SE).

All of the vomiting events resolved (t_aesiout_C_SE).

5.2.2.6.6 Asthenia

Cohort A

The proportions of patients with selected AEs in the asthenia category was higher in the Ipat+Pac arm compared with the Pbo+Pac arm (63 patients [38.0%] vs. 25 patients [28.7%]) (t_aesi_A_SE).

The majority of asthenia events were Grade 1 or Grade 2. Grade 3 asthenia events were reported in 7.2% of patients in the Ipat+Pac arm and 3.4% of patients in the Pbo+Pac arm. No events of Grade 4 or Grade 5 intensity were reported in either treatment arm (t_aesi_ctc_A_SE).

One Grade 3 asthenia event (PT: fatigue) was reported as serious in the Ipat+Pac arm and the event had resolved (t_aesi_SER_A_SE). Ipatasertib treatment discontinuation due to asthenia was reported in 1 patient (0.6%) in the Ipat+Pac arm(t_aesi_ctc_DSCIPAT_A_SE). Paclitaxel treatment discontinuation due to asthenia was reported in 1 patient (1.1%) in the Pbo+Pac arm and none in the Ipat+Pac arm (t_aesi_ctc_DSCPAC_A_SE). Ipatasertib dose reduction due to asthenia was reported in 1 (0.6%) patient in the Ipat+Pac arm only (t_aesi_ctc_DSRIPAT_A_SE). Ipatasertib/placebo dose interruption due to asthenia was reported in 3 patients (1.8%) and 1 patient (1.1%) in the Ipat+Pac arm and Pbo+Pac arm, respectively (t_aesi_ctc_DSIIPAT_A_SE). Paclitaxel dose reduction due to asthenia was reported in 2 (1.2%) and 1 (1.1%) patients in the Ipat+Pac arm and Pbo+Pac arm, respectively (t_aesi_ctc_DSRPAC_A_SE). Paclitaxel dose interruption due to asthenia was reported in 6 (3.6%) and 2 (2.3%) of patients in the Ipat+Pac arm and Pbo+Pac arm, respectively (t_aesi_ctc_DSIPAC_A_SE)

Overall, 52.7% and 50% of AEs of asthenia resolved in the Ipat+Pac and Pbo+Pac arms, respectively (t_aesiout_A_SE).

Cohort B

The proportions of patients with selected AEs in the asthenia category was lower in the Ipat+Pac arm compared with the Pbo+Pac arm (55 patients [37.9%] vs. 31 patients [41.3%]) (t_aesi_B_SE).

The majority of asthenia events were Grade 1 or Grade 2. Grade 3 asthenia events were reported in 1.4% of patients in the Ipat+Pac arm and 5.3% of patients in the Pbo+Pac arm. No events of Grade 4 or Grade 5 intensity were reported in either treatment arm (t_aesi_ctc_B_SE).

One Grade 3 asthenia event (PT: fatigue) was reported as serious in the Pbo+Pac arm and the event had resolved (t_aesi_SER_B_SE, t_aesi_ctc_SER_B_SE). Ipatasertib treatment discontinuation due to asthenia was reported in none of the patients in the Ipat+Pac arm (t_aesi_ctc_DSCIPAT_B_SE). Paclitaxel treatment discontinuation due to asthenia was reported in 1 patient each in the Pbo+Pac arm (1.3%) and in the Ipat+Pac arm (0.7%) (t_aesi_ctc_DSCPAC_B_SE). Ipatasertib dose reduction due to asthenia was reported in none of the patients in the Ipat+Pac arm (t_aesi_ctc_DSRIPAT_B_SE). Ipataserti dose interruption due to asthenia was reported in 3 patients each in the Ipat+Pac arm (2.1%) (t_aesi_ctc_DSIIPAT_B_SE). Paclitaxel dose reduction due to asthenia was reported in 2 patients (2.7%) in the Pbo+Pac arm and none in the Ipat+Pac arm (t_aesi_ctc_DSRPAC_B_SE). Paclitaxel dose interruption due to asthenia was reported in 5 patients (3.4%) in the Ipat+Pac arm and 4 patients (5.3%) in the Pbo+Pac arm (t_aesi_ctc_DSIPAC_B_SE)

Overall, 63.9% and 64.6% of AEs of asthenia resolved in the Ipat+Pac and Pbo+Pac arms, respectively (t_aesiout_B_SE).

Cohort C

The number of patients with selected AEs in the asthenia category was 40 patients (39.2%) (t_aesi_C_SE).

The majority of asthenia events were Grade 1 or Grade 2. Grade 3 asthenia events were reported in 3.9% of patients. No events of Grade 4 or Grade 5 intensity were reported (t_aesi_ctc_C_SE).

One Grade 2 and one Grade 3 asthenia events (PT: fatigue) were reported as serious and both events had resolved (t_aesi_SER_C_SE, t_aesi_ctc_SER_C_SE). No ipatasertib or atezolizumab treatment discontinuation due to asthenia was reported (t_aesi_ctc_DSCIPAT_C_SE, t_aesi_ctc_DSCATZ_C_SE). Paclitaxel treatment discontinuation due to asthenia was reported in 1 patient (1.0%) (t_aesi_ctc_DSCPAC_C_SE). No ipatasertib or paclitaxel dose reduction due to asthenia was reported (t_aesi_ctc_DSRIPAT_C_SE,

t_aesi_ctc_DSRPAC_C_SE). Ipatasertib and paclitaxel dose interruption due to asthenia were reported in 2 (2.0%) and 6 (5.9%) patients, respectively (t_aesi_ctc_DSIIPAT_C_SE, t_aesi_ctc_DSIPAC_C_SE). Atezolizumab dose interruption due to asthenia was reported in 3 patients (2.9%) (t_aesi_ctc_DSIATZ_C_SE).

Overall, 57.6% of AEs of asthenia resolved (t_aesiout_C_SE).

5.2.2.6.7 Oral Mucositis

Cohort A

The proportion of patients with selected AEs in the category of oral mucositis was higher in the Ipat+Pac arm compared with the Pbo+Pac arm (30 patients [18.1%] vs. 8 patients [9.2%]). The most commonly reported PT within this category was stomatitis (10.8% vs. 6.9%) (t_aesi_A_SE). All oral mucositis events were Grade 1 or Grade 2 except for one Grade 3 event in Ipat+Pac arm (t_aesi_ctc_A_SE).

There were no serious oral mucositis events reported (t_aesi_SER_A_SE). No patients were discontinued from any study treatment in either treatment arm (t_aesi_ctc_DSCIPAT_A_SE, t_aesi_ctc_DSCPAC_A_SE). Ipatasertib dose interruption and reduction due to oral mucositis was reported in 2 patients (1.2%) and 1 patient (0.6%), respectively (t_aesi_ctc_DSIIPAT_A_SE, t_aesi_ctc_DSRIPAT_A_SE). Paclitaxel dose interruption due to oral mucositis was reported in 2 patients (1.2%) in the Ipat+Pac arm (t_aesi_ctc_DSIPAC_A_SE). No paclitaxel dose reduction due to oral mucositis was reported in either treatment arm (t_aesi_ctc_DSRPAC_A_SE).

Overall, the majority of the oral mucositis events in both the treatment arms had resolved (Ipat+Pac: 93.3% vs. Pbo+Pac: 100%) (t_aesiout_A_SE).

Cohort B

The proportion of patients with selected AEs in the category of oral mucositis was higher in the Ipat+Pac arm as compared with the Pbo+Pac arm (27 patients [18.6%] vs. 9 patients [12.0%]). The most commonly reported PT within this category was stomatitis (11.0% vs. 8.0%) (t_aesi_B_SE). All oral mucositis events were Grade 1 or Grade 2 (t_aesi_ctc_B_SE).

There were no serious oral mucositis events reported (t_aesi_SER_B_SE). One patient (0.7%) was discontinued from ipatasertib treatment in the Ipat+Pac arm due to oral mucositis (t_aesi_ctc_DSCIPAT_B_SE). No patients were discontinued from paclitaxel treatment in either treatment arm due to oral mucositis (t_aesi_ctc_DSCPAC_B_SE). No ipatasertib or paclitaxel dose reduction due to oral mucositis was reported (t_aesi_ctc_DSRIPAT_B_SE, t_aesi_ctc_DSRPAC_B_SE). Ipatasertib dose interruption due to oral mucositis was reported in 2 patients (1.4%) in the Ipat+Pac arm (t_aesi_ctc_DSIIPAT_B_SE). Paclitaxel dose interruption due to oral mucositis was reported in 1 patient (1.3%) in the Pbo+Pac arm only (t_aesi_ctc_DSIPAC_B_SE).

Overall, the majority of oral mucositis events in both treatment arms had resolved (Ipat+Pac: 93.2% vs. Pbo+Pac: 92.3%) (t_aesiout_B_SE).

Cohort C

The proportion of patients with selected AEs in the category of oral mucositis was 20.6%. The most commonly reported PT within this category was mucosal inflammation (11.8%) (t_aesi_C_SE). All oral mucositis events were Grade 1 or Grade 2 (t_aesi_ctc_C_SE).

There were no serious oral mucositis events reported (t_aesi_SER_C_SE). No patients were discontinued from any study treatment (t_aesi_ctc_DSCIPAT_C_SE, t_aesi_ctc_DSCATZ_C_SE, t_aesi_ctc_DSCPAC_C_SE). No ipatasertib or atezolizumab dose interruptions were reported due to oral mucositis (t_aesi_ctc_DSIIPAT_C_SE, t_aesi_ctc_DSIATZ_C_SE). Paclitaxel dose interruption due to oral mucositis was reported in 1 patient (1.0%) (t_aesi_ctc_DSIPAC_C_SE). No ipatasertib or paclitaxel dose reduction was reported due to oral mucositis (t_aesi_ctc_DSRIPAT_C_SE, t_aesi_ctc_DSRPAC_C_SE).

Overall, the majority of oral mucositis events had resolved (91.3%) (t_aesiout_C_SE).

5.2.2.6.8 Erythema Multiforme

Cohort A

Selected AEs in the category of erythema multiforme was reported in 1 patient (0.6%) in the Ipat+Pac arm (PT: erythema multiforme) (t_aesi_A_SE). The event was reported as serious Grade 3, led to discontinuation of ipatasertib treatment and had resolved (t_aesi_ctc_SER_A_SE, t_aesiout_A_SE, l_aesi_A_SE).

Cohort B

Selected AEs in the category of erythema multiforme was reported in 1 patient (0.7%) in the Ipat+Pac arm (PT: erythema multiforme) (t_aesi_B_SE). The event was reported as serious Grade 3, led to dose reduction of ipatasertib treatment and had resolved (l_aesi_B_SE).

Cohort C

No selected AEs in the category of erythema multiforme were reported in Cohort C (t_aesi_C_SE, l_aesi_C_SE).

5.2.2.6.9 Neutropenia

Cohort A

The proportion of patients with selected AEs in the category of neutropenia was higher in Pbo+Pac arm than Ipat+Pac arm (Ipat+Pac: 51 patients [30.7%] vs. Pbo+Pac: 31 patients [35.6%]) (t_aesi_A_SE).

The majority of neutropenia events were Grade 1 or 2. Grade 3 neutropenia events were reported in 18 (10.8%) and 8 (9.2%) patients in the Ipat+Pac arm and Pbo+Pac arm, respectively. Grade 4 neutropenia events were reported in 5 (3.0%) and 1 (1.1%) patients in the Ipat+Pac arm and Pbo+Pac arm, respectively (t_aesi_ctc_A_SE). A total of

4 (2.4%) patients in the Ipat+Pac arm (2 each of Grade 3 and Grade 4) and 1 (1.1%) patient in the Pbo+Pac arm (Grade 4) experienced serious neutropenia events that had resolved (t_aesi_SER_A_SE). No Grade 5 neutropenia event was reported.

One patient (0.6%) in the Ipat+Pac arm discontinued ipatersertib treatment due to neutropenia (t_aesi_ctc_DSCIPAT_A_SE). Two patients (1.2%) in the Ipat+Pac arm discontinued paclitaxel treatment due to neutropenia (t_aesi_ctc_DSCPAC_A_SE). Ipatasertib dose interruption due to neutropenia was reported in 15 (9.0%) patients in the Ipat+Pac arm (t_aesi_ctc_DSIIPAT_A_SE). Ipatasertib dose reduction due to neutropenia was reported in 9 (5.4%) patients in the Ipat+Pac arm (t_aesi_ctc_DSRIPAT_A_SE). Paclitaxel dose interruption due to neutropenia was reported in 34 (20.5%) and 21 (24.1%) patients in the Ipat+Pac arm and Pbo+Pac arm, respectively (t_aesi_ctc_DSIPAC_A_SE). Paclitaxel dose reduction due to neutropenia was reported in 10 (6.0%) and 2 (2.3%) patients in the Ipat+Pac arm and Pbo+Pac arm, respectively (t_aesi_ctc_DSRPAC_A_SE).

Overall, the majority of neutropenia events had resolved (Ipat+Pac: 95.9% vs. Pbo+Pac: 98.4%) (t_aesiout_A_SE).

See Hematology for laboratory assessment of neutrophil counts.

Cohort B

The proportions of patients with selected AEs in the category of neutropenia were similar between treatment arms (Ipat+Pac: 59 patients [40.7%] vs. Pbo+Pac: 33 patients [44.0%]) (t_aesi_B_SE).

The majority of neutropenia events were Grade 1 or 2. Grade 3 neutropenia events were reported in 21 (14.5%) and 10 (13.3%) patients in the Ipat+Pac arm and Pbo+Pac arm, respectively. Grade 4 neutropenia events were reported in 4 (2.8%) and 2 (2.7%) patients in the Ipat+Pac arm and Pbo+Pac arm, respectively. One Grade 5 neutropenia event (PT: febrile neutropenia) considered related to ipatasertib and paclitaxel was reported (t_aesi_ctc_B_SE, l_aesi_B_SE). A total of 3 (2.1%) patients in the Ipat+Pac arm experienced serious neutropenia events (Grade 3: 2 patients [1.4%]; Grade 5: 1 patient [0.7%]) (t_aesi_ctc_SER_B_SE).

Three patients (2.1%) in the Ipat+Pac arm discontinued ipatasertib treatment due to neutropenia (t_aesi_ctc_DSCIPAT_B_SE). Eight patients (5.5%) in the Ipat+Pac arm and 2 patients (2.7%) in the Pbo+Pac arm discontinued paclitaxel treatment due to neutropenia (t_aesi_ctc_DSCPAC_B_SE). Ipatasertib dose interruption due to neutropenia was reported in 18 (12.4%) patients in the Ipat+Pac arm (t_aesi_ctc_DSIIPAT_B_SE). Ipatasertib dose reduction due to neutropenia was reported in 9 (6.2%) patients in the Ipat+Pac arm (t_aesi_ctc_DSRIPAT_B_SE). Paclitaxel dose interruption due to neutropenia was reported in 35 (24.1%) and 22 (29.3%) patients in the Ipat+Pac arm and Pbo+Pac arm, respectively (t_aesi_ctc_DSIPAC_B_SE). Paclitaxel dose reduction due to neutropenia was reported in

13 (9.0%) and 6 (8.0%) patients in the Ipat+Pac arm and Pbo+Pac arm, respectively (t_aesi_ctc_DSRPAC_B_SE).

Overall, the majority of neutropenia events had resolved (Ipat+Pac: 98.5% vs. Pbo+Pac: 96.7%) (t_aesiout_B_SE).

See Hematology for laboratory assessment of neutrophil counts.

Cohort C

The number of patients with selected AEs in the category of neutropenia was 34 patients (33.3%) (t_aesi_C_SE).

The majority of neutropenia events were Grade 1 or 2. Grade 3 neutropenia events were reported in 8 (7.8%) patients. Grade 4 neutropenia events were reported in 3 (2.9%) patients. No Grade 5 neutropenia event was reported (t_aesi_ctc_C_SE). A total of 2 (2.0%) patients experienced serious neutropenia events (PT: febrile neutropenia) of Grade 3 and Grade 4, both of which had resolved (t_aesi_SER_C_SE, l_aesi_C_SE).

No ipatasertib or atezolizumab treatment discontinuation due to neutropenia was reported (t_aesi_ctc_DSCIPAT_C_SE, t_aesi_ctc_DSCATZ_C_SE). One patient (1.0%) in the Ipat+Pac arm discontinued paclitaxel treatment due to neutropenia (t_aesi_ctc_DSCPAC_C_SE). Ipatasertib, paclitaxel, and atezolizumab dose interruption due to neutropenia was reported in 14 (13.7%), 22 (21.6%), and 10 (9.8%) patients, respectively (t_aesi_ctc_DSIIPAT_C_SE, t_aesi_ctc_DSIPAC_C_SE, t_aesi_ctc_DSIATZ_C_SE). Ipatasertib and paclitaxel dose reduction due to neutropenia was reported in 6 (5.9%) and 6 (5.9%) patients, respectively (t_aesi_ctc_DSRIPAT_C_SE, t_aesi_ctc_DSRPAC_C_SE).

The majority of neutropenia events had resolved (99.4%) (t_aesiout_C_SE).

See Hematology for laboratory assessment of neutrophil counts.

5.2.2.6.10 Erythropenia

Cohort A

The proportion of patients with selected AEs in the erythropenia category was similar between the Ipat+Pac arm and the Pbo+Pac arm (45 patients [27.1%] vs. 23 patients [26.4%]). The most commonly reported PT in this selected AE was anemia (26.5% vs. 26.4%) (t_aesi_A_SE).

Most erythropenia events were Grade 1 or Grade 2. Grade 3 erythropenia (PT: anemia) was reported in 4 patients (2.4%) in the Ipat+Pac arm and 2 patients (2.3%) in the Pbo+Pac arm. Only 1 Grade 4 erythropenia (PT: anemia) was reported in 1 patient (1.1%) in the Pbo+Pac arm. No events of Grade 5 intensity were reported in either treatment arm (t_aesi_ctc_A_SE).

One Grade 3 erythropenia event (PT: anemia) in the Ipat+Pac arm was reported as serious and it resolved (t_aesi_SER_A_SE). One Grade 4 erythropenia event (PT: anemia) in the Pbo+Pac arm was reported as serious and it resolved (t_aesi_SER_A_SE).

No patient was discontinued from any treatment in either treatment arm (t_aesi_ctc_DSCIPAT_A_SE, t_aesi_ctc_DSCPAC_A_SE). No ipatasertib dose reduction due to erythropenia was reported (t_aesi_ctc_DSRIPAT_A_SE). Ipatasertib dose interruption due to erythropenia was reported in 3 (1.8%) patients in the Ipat+Pac arm (t_aesi_ctc_DSIIPAT_A_SE). Paclitaxel dose interruption due to erythropenia was reported in 7 (4.2%) and 1 (1.1%) patients in the Ipat+Pac arm and Pbo+Pac arm, respectively (t_aesi_ctc_DSIPAC_A_SE). Paclitaxel dose reduction due to erythropenia was reported in 1 patient (0.6%) in the Ipat+Pac arm only (t_aesi_ctc_DSRPAC_A_SE).

Overall, the majority of erythropenia events had resolved (Ipat+Pac: 59.7% vs. Pbo+Pac: 66.7%) (t_aesiout_A_SE).

See Hematology for laboratory assessment of red blood cell count, hematocrit and hemoglobin.

Cohort B

The proportion of patients with selected AEs in the erythropenia category was higher in the Ipat+Pac arm than the Pbo+Pac arm (47 patients [32.4%] vs. 16 patients [21.3%]). The most commonly reported PT in this selected AE was anemia (31.0% vs. 20.0%) (t_aesi_B_SE).

No events of erythropenia were reported as serious (t_aesi_SER_B_SE). Most erythropenia events were Grade 1 or Grade 2. Grade 3 erythropenia (PT: anemia) was reported in 2 patients (1.4%) in the Ipat+Pac arm. No events of Grade 4 or 5 intensity were reported in either treatment arm (t_aesi_ctc_B_SE).

No patient was discontinued from ipatasertib treatment in either treatment arm (t_aesi_ctc_DSCIPAT_B_SE). One patient (0.7%) was discontinued from paclitaxel treatment in the Ipat+Pac arm (t_aesi_ctc_DSCPAC_B_SE). Ipatasertib and paclitaxel dose interruption due to erythropenia was reported in 1 patient (0.7%) each in the Ipat+Pac arm (t_aesi_ctc_DSIIPAT_B_SE, t_aesi_ctc_DSIPAC_B_SE). No ipatasertib dose reduction due to erythropenia was reported (t_aesi_ctc_DSRIPAT_B_SE). Paclitaxel dose reduction due to erythropenia was reported in 1 patient (0.7%) in the Ipat+Pac arm (t_aesi_ctc_DSRPAC_B_SE).

Overall, the majority of the erythropenia events had resolved (Ipat+Pac: 77.4% vs. Pbo+Pac: 83.9%) (t_aesiout_B_SE).

See Hematology for laboratory assessment of red blood cell count, hematocrit and hemoglobin.

Cohort C

The number of patients with selected AEs in the erythropenia category was 34 patients (33.3%). The most commonly reported PT in this selected AE was anemia (33.3%) (t_aesi_C_SE).

No events of erythropenia were reported as serious (t_aesi_SER_C_SE). Most erythropenia events were Grade 1 or Grade 2. Grade 3 erythropenia (PT: anemia) was reported in 2 patients (2.0%). No events of Grade 4 or Grade 5 intensity were reported in either treatment arm (t_aesi_ctc_C_SE).

No patient was discontinued from any treatment (t_aesi_ctc_DSCIPAT_C_SE, t_aesi_ctc_DSCPAC_C_SE, t_aesi_ctc_DSCATZ_C_SE). No ipatasertib dose reduction due to erythropenia was reported (t_aesi_ctc_DSRIPAT_C_SE). Paclitaxel dose reduction due to erythropenia was reported in 1 patient (1.0%) (t_aesi_ctc_DSRPAC_C_SE). No ipatasertib or atezolizumab dose interruption due to erythropenia was reported (t_aesi_ctc_DSIIPAT_C_SE, t_aesi_ctc_DSIATZ_C_SE). Paclitaxel dose interruption due to erythropenia was reported in 2 patients (2.0%) (t_aesi_ctc_DSIPAC_C_SE).

The majority of erythropenia events had resolved (67.9%) (t_aesiout_C_SE).

See Hematology for laboratory assessment of red blood cell count, hematocrit and hemoglobin.

5.2.2.6.11 Hepatotoxicity

Cohort A

Selected AEs in the category of hepatotoxicity were reported in 29 patients (17.5%) in the Ipat+Pac arm and 12 patients (13.8%) in the Pbo+Pac arm. The most commonly reported PTs in this category were alanine aminotransferase increased (13.9% vs. 8.0%), aspartate aminotransferase increased (10.8% vs. 6.9%) and blood alkaline phosphatase increased (5.4% vs. 1.1%) (t_aesi_A_SE).

The majority of hepatotoxicity events were Grade 1 or 2. Grade 3 hepatotoxicity were reported in 4.8% of patients the Ipat+Pac arm and 3.4% of patients in the Pbo+Pac arm. Grade 4 hepatoxicity was reported in one patient in the Ipat+Pac arm and no patient in the Pbo+Pac arm. No Grade 5 hepatotoxicity events were reported (t_aesi_ctc_A_SE).

No hepatotoxicity events were reported as serious (t_aesi_SER_A_SE). One patient (0.6%) in the Ipat+Pac arm discontinued ipatasertib treatment due to Grade 3 hepatotoxicity (PT: alanine aminotransferase increased and aspartate aminotransferase increased) (t_aesi_ctc_DSCIPAT_A_SE, l_aesi_A_SE). No patients discontinued paclitaxel treatment due to hepatotoxicity (t_aesi_ctc_DSCPAC_A_SE). Ipatasertib dose reduction due to hepatotoxicity was reported in 5 (3.0%) in the Ipat+Pac arm (t_aesi_ctc_DSRIPAT_A_SE). Ipatasertib dose interruption due to hepatotoxicity was reported in 1 patient (0.6%) in Ipat+Pac arm (t_aesi_ctc_DSIIPAT_A_SE). Paclitaxel dose reduction due to hepatotoxicity was reported in

3 (1.8%) patients in the Ipat+Pac arm only (t_aesi_ctc_DSRPAC_A_SE). Paclitaxel dose interruption due to hepatotoxicity was reported in 2 (1.2%) and 4 (4.6%) patients in the Ipat+Pac arm and Pbo+Pac arm, respectively (t_aesi_ctc_DSIPAC_A_SE).

The majority of hepatotoxicity events had resolved (Ipat+Pac: 74.3% vs Pbo+Pac: 91.9%) (t_aesiout_A_SE).

Narratives for patients who experienced Grade ≥3 hepatotoxicity events are appended.

Cohort B

Selected AEs in the category of hepatotoxicity were reported in 25 patients (17.2%) in the Ipat+Pac arm and 21 patients (28.0%) in the Pbo+Pac arm. The most commonly reported PTs in this category were alanine aminotransferase increased (13.1% vs. 20.0%), aspartate aminotransferase increased (9.0% vs. 13.3%), and hyperbilirubinaemia (4.1% vs. 5.3%) (t_aesi_B_SE).

The majority of hepatotoxicity events were Grade 1 or 2. Grade 3 hepatotoxicity were reported in 5.5% of patients the Ipat+Pac arm and 4.0% of patients in the Pbo+Pac arm. No Grade 4 or 5 hepatotoxicity events were reported (t_aesi_ctc_B_SE).

No hepatotoxicity events were reported as serious (t_aesi_SER_B_SE). One patient (0.7%) in the Ipat+Pac arm discontinued ipatasertib treatment due to Grade 3 hepatotoxicity (PT: alanine aminotransferase increased) (t_aesi_ctc_DSCIPAT_B_SE, l_aesi_B_SE). No patients discontinued paclitaxel treatment due to hepatotoxicity (t_aesi_ctc_DSCPAC_B_SE). Ipatasertib dose reduction due to hepatotoxicity was reported in 2 (1.4%) patients in the Ipat+Pac arm only (t_aesi_ctc_DSRIPAT_B_SE). Ipatasertib dose interruption due to hepatotoxicity was reported in 5 (3.4%) patients in the Ipat+Pac arm (t_aesi_ctc_DSIIPAT_B_SE). Paclitaxel dose reduction due to hepatoxicity was reported in 1 (1.3%) patient in the Pbo+Pac arm only (t_aesi_ctc_DSRPAC_B_SE). Paclitaxel dose interruption due to hepatotoxicity was reported in 8 (5.5%) and 4 (5.3%) patients in the Ipat+Pac arm and Pbo+Pac arm, respectively (t_aesi_ctc_DSIPAC_B_SE).

The majority of hepatotoxicity events had resolved (Ipat+Pac: 82.9% vs Pbo+Pac: 88.7%) (t_aesiout_B_SE).

Narratives for patients who experienced Grade ≥3 hepatotoxicity events are appended.

Cohort C

Selected AEs in the category of hepatotoxicity were reported in 35 patients (34.3%). The most commonly reported PTs in this category were alanine aminotransferase increased (25.5%), aspartate aminotransferase increased (21.6%), and hyperbilirubinaemia (5.9%) (t_aesi_C_SE).

The majority of hepatotoxicity events were Grade 1 or 2. Grade 3 hepatotoxicity were reported in 13.7% of patients. No Grade 4 or 5 hepatotoxicity events were reported (t_aesi_ctc_C_SE).

Two Grade 3 hepatotoxicity events were reported as serious and had resolved (PT: alanine aminotransferase increased and aspartate aminotransferase increased) (t_aesi_SER_C_SE, l_aesi_C_SE). Ipatasertib, atezolizumab, and paclitaxel discontinuation due to hepatotoxicity was reported in 3 (2.9%), 3 (2.9%), and 1 (1.0%) patients, respectively (t_aesi_ctc_DSCIPAT_C_SE, t_aesi_ctc_DSCATZ_C_SE, t_aesi_ctc_DSCPAC_C_SE). Ipatasertib and paclitaxel dose reduction due to hepatotoxicity was reported in 1 (1.0%) and 2 (2.0%) patients, respectively (t_aesi_ctc_DSRIPAT_C_SE, t_aesi_ctc_DSRPAC_C_SE). Ipatasertib, atezolizumab, and paclitaxel dose interruption due to hepatotoxicity was reported in 7 (6.9%), 8 (7.8%), and 8 (7.8%) patients, respectively (t_aesi_ctc_DSIIPAT_C_SE, t_aesi_ctc_DSIATZ_C_SE, t_aesi_ctc_DSIPAC_C_SE).

The majority of hepatotoxicity events had resolved (85.9%) (t_aesiout_C_SE).

Narratives for patients who experienced Grade ≥3 hepatotoxicity events are appended.

5.2.2.6.12 Hyperlipidemia

Cohort A

The proportions of patients with selected AEs in the hyperlipidemia category were similar between treatment arms (Ipat+Pac: 13 patients [7.8%] vs. Pbo+Pac: 5 patients [5.7%]) (t_aesi_A_SE).

The majority of hyperlipidemia events were Grade 1 or 2 (t_aesi_ctc_A_SE). One patient (0.6%) in the Ipat+Pac arm had Grade 3 hyperlipidemia (PT: hypertriglyceridemia) that had not resolved (l_aesi_A_SE). No Grade 4 or 5 hyperlipidemia event was reported.

No events of hyperlipidemia were reported as serious (t_aesi_SER_A_SE). No patients had discontinuation of any study treatment due to hyperlipidemia (t_aesi_ctc_DSCIPAT_A_SE, t_aesi_ctc_DSCPAC_A_SE). No ipatasertib or paclitaxel dose reduction due to hyperlipidemia was reported (t_aesi_ctc_DSRIPAT_A_SE, t_aesi_ctc_DSRPAC_A_SE). Ipatasertib dose interruption due to hyperlipidemia was reported in 2 (1.2%) patients in the Ipat+Pac arm only (t_aesi_ctc_DSIIPAT_A_SE). Paclitaxel dose interruption due to hyperlipidemia was reported in 1 (0.6%) patient in the Ipat+Pac arm (t_aesi_ctc_DSIPAC_A_SE).

Overall, 36.4% and 40% of hyperlipidemia events in the Ipat+Pac arm and Pbo+Pac arm, respectively, had resolved (t_aesiout_A_SE).

Cohort B

The proportions of patients with selected AEs in the hyperlipidemia category were similar between treatment arms (Ipat+Pac: 17 patients [11.7%] vs. Pbo+Pac: 8 patients [10.7%]) (t_aesi_B_SE).

The majority of hyperlipidemia events were Grade 1 or 2 (t_aesi_ctc_B_SE). One patient (0.7%) in the Ipat+Pac arm had Grade 3 hyperlipidemia (PT: hypertriglyceridemia) and 1 patient (1.3%) in the Pbo+Pac arm had Grade 4 hyperlipidemia (PT: hypertriglyceridemia) that had both resolved (l_aesi_B_SE). No Grade 5 hyperlipidemia was reported.

No events of hyperlipidemia were reported as serious (t_aesi_SER_B_SE). No patients had discontinuation of any study treatment due to hyperlipidemia (t_aesi_ctc_DSCIPAT_B_SE, t_aesi_ctc_DSCPAC_B_SE). No ipatasertib dose interruption due to hyperlipidemia was reported (t_aesi_ctc_DSIIPAT_B_SE). Paclitaxel dose interruption due to hyperlipidemia was reported in 1 patient (1.3%) in the Pbo+Pac arm (t_aesi_ctc_DSIPAC_B_SE). No ipatasertib or paclitaxel dose reduction due to hyperlipidemia was reported (t_aesi_ctc_DSRIPAT_B_SE, t_aesi_ctc_DSRPAC_B_SE).

Overall, the majority of the hyperlipidemia events had resolved (Ipat+Pac: 64.5% vs. Pbo+Pac: 76.9%) (t_aesiout_B_SE).

Cohort C

The selected AEs in the hyperlipidemia category were reported in 14 patients (13.7%) (t_aesi_C_SE).

The majority of hyperlipidemia events were Grade 1 or 2 (t_aesi_ctc_C_SE). One patient (1.0%) had a Grade 3 hyperlipidemia event (PT: blood cholesterol increased) and the same patient had a Grade 4 hyperlipidemia (PT: blood triglycerides increased) event, both of which had not resolved (l_aesi_C_SE). No Grade 5 hyperlipidemia event was reported (t_aesi_ctc_C_SE).

No events of hyperlipidemia were reported as serious (t_aesi_SER_C_SE). No patients had discontinuation of any study treatment due to hyperlipidemia (t_aesi_ctc_DSCIPAT_C_SE, t_aesi_ctc_DSCPAC_C_SE, t_aesi_ctc_DSCATZ_C_SE). No ipatasertib, atezolizumab, or paclitaxel dose interruption due to hyperlipidemia was reported (t_aesi_ctc_DSIIPAT_C_SE, t_aesi_ctc_DSIATZ_C_SE, t_aesi_ctc_DSIPAC_C_SE). Ipatasertib dose reduction due to hyperlipidemia was reported in 1 patient (1.0%) (t_aesi_ctc_DSRIPAT_C_SE). No paclitaxel dose reduction due to hyperlipidemia was reported (t_aesi_ctc_DSRPAC_C_SE).

Half of the hyperlipidemia events had resolved (50%) (t_aesiout_C_SE).

5.2.2.6.13 Pneumonitis

Cohort A

The proportions of patients with selected AEs in the pneumonitis category were similar between treatment arms (Ipat+Pac: 3 patients [1.8%] vs. Pbo+Pac: 1 patient [1.1%]) (t_aesi_A_SE). All the events were Grade 1 and non-serious (t_aesi_ctc_A_SE, t_aesi_SER_A_SE). No patients had discontinuation of any study treatment due to pneumonitis (t_aesi_ctc_DSCIPAT_A_SE, t_aesi_ctc_DSCPAC_A_SE). Ipatasertib dose interruption due to

pneumonitis was reported in 2 patients (1.2%) (t_aesi_ctc_DSIIPAT_A_SE). Paclitaxel dose interruption due to pneumonitis was reported in 1 patient (0.6%) in the Ipat+Pac arm (t_aesi_ctc_DSIPAC_A_SE). No dose reduction due to pneumonitis was reported for any study treatment (t_aesi_ctc_DSRIPAT_A_SE, t_aesi_ctc_DSRPAC_A_SE).

Overall, the majority of pneumonitis events had resolved (Ipat+Pac: 66.7% vs. Pbo+Pac: 100%) (t_aesiout_A_SE).

Narratives for patients who experienced Grade ≥2 pneumonitis events are appended.

Cohort B

The proportion of patients with selected AEs in the pneumonitis category was higher in the Ipat+Pac arm (6 patients [4.1%]) than in the Pbo+Pac arm (0 patient) (t_aesi_B_SE).

The majority of pneumonitis events were Grade 1 or 2. Two serious events of pneumonitis (Grade 2 and 3) were reported in the Ipat+Pac arm and had resolved (t_aesi_ctc_B_SE, l_aesi_B_SE).

Ipatasertib and paclitaxel discontinuation due to pneumonitis was reported in 1 patient (0.7%) each in the Ipat+Pac arm (t_aesi_ctc_DSCIPAT_B_SE, t_aesi_ctc_DSCPAC_B_SE). Ipatasertib dose interruption due to pneumonitis was reported in 1 patient (0.7%) (t_aesi_ctc_DSIIPAT_B_SE). Paclitaxel dose interruption due to pneumonitis was reported in 1 patient (0.7%) in the Ipat+Pac arm (t_aesi_ctc_DSIPAC_B_SE). Ipatasertib dose reduction due to pneumonitis was reported in 1 patient (0.7%) (t_aesi_ctc_DSRIPAT_B_SE). Paclitaxel dose reduction due to pneumonitis was reported in 1 patient (0.7%) in the Ipat+Pac arm (t_aesi_ctc_DSRPAC_B_SE).

Overall, the majority of pneumonitis events in the Ipat+Pac arm had resolved (66.7%) (t_aesiout_B_SE).

Narratives for patients who experienced Grade ≥2 pneumonitis events are appended.

Cohort C

Selected AEs in the pneumonitis category were reported in 9 patients (8.8%) (t_aesi_C_SE).

The majority of pneumonitis events were Grade 1 or 2 (t_aesi_ctc_C_SE). Two serious Grade 2 pneumonitis events (PT: pneumonitis and immune-mediated lung disease) and one serious Grade 3 pneumonitis (PT: pneumonitis) were reported. All serious events of pneumonitis had resolved (t_aesi_SER_C_SE, t_aesi_ctc_SER_C_SE, l_aesi_C_SE).

Ipatasertib, atezolizumab, and paclitaxel treatment discontinuation due to pneumonitis was reported in 1 patient (1.0%) each (t_aesi_ctc_DSCIPAT_C_SE, t_aesi_ctc_DSCATZ_C_SE, t_aesi_ctc_DSCPAC_C_SE). Ipatasertib, paclitaxel, and atezolizumab dose interruption due to pneumonitis was reported in 4 patients (3.9%), 3 patients (2.9%), and 6 patients (5.9%),

respectively (t_aesi_ctc_DSIIPAT_C_SE, t_aesi_ctc_DSIPAC_C_SE, t_aesi_ctc_DSIATZ_C_SE). No dose reductions due to pneumonitis were reported for any study treatment (t_aesi_ctc_DSRIPAT_C_SE, t_aesi_ctc_DSRPAC_C_SE).

Overall, the majority of pneumonitis events had resolved (66.7%) (t_aesiout_C_SE).

Narratives for patients who experienced Grade ≥2 pneumonitis events are appended.

5.2.2.6.14 Thrombocytopenia

Cohort A

Selected AEs in the category of thrombocytopenia were reported in 2 patients (1.2%) in the Ipat+Pac arm and 4 patients (4.6%) in the Pbo+Pac arm(t_aesi_A_SE).

One patient (1.1%) in the Pbo+Pac arm experienced Grade 3 thrombocytopenia (PT: thrombocytopenia) and the rest of the thrombocytopenia events were Grade 1–2 in intensity (t_aesi_ctc_A_SE). The Grade 3 thrombocytopenia was reported as serious that led to paclitaxel dose interruption and had not resolved (l_aesi_A_SE, t_aesi_ctc_DSIPAC_A_SE).

No thrombocytopenia events led to discontinuation of any study treatments in either treatment arm (t_aesi_ctc_DSCIPAT_A_SE, t_aesi_ctc_DSCPAC_A_SE). No ipatasertib dose interruption or dose reduction of any study drug due to thrombocytopenia was reported (t_aesi_ctc_DSIIPAT_A_SE, t_aesi_ctc_DSRIPAT_A_SE, t_aesi_ctc_DSRPAC_A_SE).

Overall, the proportion of the thrombocytopenia events that had resolved in the Ipat+Pac arm and Pbo+Pac arm were 100% and 20%, respectively.

Cohort B

Selected AEs in the category of thrombocytopenia were reported in 3 patients (2.1%) in the Ipat+Pac arm and 1 patient (1.3%) in the Pbo+Pac arm (t_aesi_B_SE).

One patient (0.7%) in the Ipat+Pac arm experienced Grade 3 thrombocytopenia (PT: thrombocytopenia) and the rest of the thrombocytopenia events were Grade 1 in intensity (t_aesi_ctc_B_SE). No thrombocytopenia events were reported as serious (t_aesi_SER_B_SE).

No thrombocytopenia events led to discontinuation of any study treatments in either treatment arm (t_aesi_ctc_DSCIPAT_B_SE, t_aesi_ctc_DSCPAC_B_SE). No ipatasertib dose interruption or reduction due to thrombocytopenia was reported (t_aesi_ctc_DSIIPAT_B_SE, t_aesi_ctc_DSRIPAT_B_SE). Paclitaxel dose interruptions due to thrombocytopenia were reported in 2 patients (1.4%) in the Ipat+Pac arm (t_aesi_ctc_DSIPAC_B_SE). No paclitaxel dose reduction was reported (t_aesi_ctc_DSRPAC_B_SE).

Overall, the majority of thrombocytopenia events had resolved (Ipat+Pac: 75% vs. Pbo+Pac arm: 100%) (t_aesiout_B_SE).

Cohort C

Selected AEs in the category of thrombocytopenia were reported in 3 patients (2.9%) (t_aesi_C_SE).

One patient (1.0%) experienced Grade 3 thrombocytopenia (PT: platelet count decreased) and the remaining two events of thrombocytopenia were Grade 1 in intensity (t_aesi_ctc_C_SE). No thrombocytopenia events were reported as serious (t_aesi_SER_C_SE).

No thrombocytopenia events led to discontinuation or dose reduction of any study treatments (t_aesi_ctc_DSCIPAT_C_SE, t_aesi_ctc_DSCATZ_C_SE, t_aesi_ctc_DSCPAC_C_SE). No ipatasertib or atezolizumab dose interruption was reported (t_aesi_ctc_DSIIPAT_C_SE, t_aesi_ctc_DSIATZ_C_SE). Paclitaxel dose interruption due to thrombocytopenia was reported in 1 patient (1.0%) (t_aesi_ctc_DSIPAC_C_SE). No dose reduction of any study treatment due to thrombocytopenia was reported (t_aesi_ctc_DSRIPAT_C_SE, t_aesi_ctc_DSRPAC_C_SE).

Overall, all thrombocytopenia events had resolved (t_aesiout_C_SE).

See Hematology for laboratory assessment of thrombocytes.

5.2.2.6.15 Colitis

Cohort A

Selected AEs in the category of colitis were reported in one patient (0.6%) in the Ipat+Pac arm and one patient in the Pbo+Pac arm (1.1%) (t_aesi_A_SE) and both events were Grade 3 in intensity (t_aesi_ctc_A_SE).

One patient had a serious Grade 3 colitis event (PT: colitis) in the Pbo + Pac arm that led to dose interruption of placebo and paclitaxel (l_aesi_A_SE, t_aesi_ctc_DSIIPAT_A_SE, t_aesi_ctc_DSIPAC_A_SE). No other paclitaxel dose interruption was reported and no ipatasertib dose interruption was reported (t_aesi_ctc_DSIPAC_A_SE, t_aesi_ctc_DSIIPAT_A_SE). No study treatment discontinuation due to colitis was reported (t_aesi_ctc_DSCIPAT_A_SE, t_aesi_ctc_DSCPAC_A_SE). Ipatasertib dose reduction due to colitis was reported in 1 patient (0.6%) (t_aesi_ctc_DSRIPAT_A_SE). No paclitaxel dose reduction due to colitis was reported (t_aesi_ctc_DSRPAC_A_SE).

All colitis events had resolved (t_aesiout_A_SE).

Narratives for patients who experienced Grade ≥ 2 colitis/enterocolitis events are appended.

Cohort B

Selected AEs in the category of colitis were reported in 2 patients (1.4%) in the Ipat+Pac arm and none in the Pbo+Pac arm (t_aesi_B_SE).

One patient (0.7%) had a serious Grade 3 colitis event (PT: enterocolitis) in the Ipat+Pac arm (t_aesi_ctc_SER_B_SE). No study treatment discontinuation due to colitis was reported

(t_aesi_ctc_DSCIPAT_B_SE, t_aesi_ctc_DSCPAC_B_SE). Ipatasertib and paclitaxel dose interruptions due to colitis were each reported in 2 patients (1.4%) (t_aesi_ctc_DSIIPAT_B_SE, t_aesi_ctc_DSIPAC_B_SE). No ipatasertib or paclitaxel dose reduction due to colitis was reported (t_aesi_ctc_DSRIPAT_B_SE, t_aesi_ctc_DSRPAC_B_SE).

All colitis events had resolved (t_aesiout_B_SE).

Narratives for patients who experienced Grade ≥ 2 colitis/enterocolitis events are appended.

Cohort C

No selected AEs in the category of colitis were reported in Cohort C (t_aesi_C_SE).

5.2.2.6.16 Peripheral Neuropathy

Cohort A

The proportions of patients with selected AEs in the category of peripheral neuropathy were similar between treatment arms (Ipat+Pac: 86 patients [51.8%] vs. Pbo+Pac: 49 patients [56.3%]) (t_aesi_A_SE).

The majority of peripheral neuropathy events were Grade 1 or Grade 2. Grade 3 events were reported among 9.6% of patients in the Ipat + Pac arm and 5.7% of patients in the Pbo + Pac arm, respectively. No events of Grade 4 or Grade 5 intensity were reported in either treatment arm (t_aesi_ctc_A_SE). No peripheral neuropathy events were reported as serious (t_aesi_SER_A_SE). Paclitaxel treatment discontinuation due to peripheral neuropathy was reported in 13 patients (7.8%) in the Ipat+Pac arm and 9 patients (10.3%) in the Pbo+Pac arm. No patients discontinued ipatasertib in the Ipat+Pac arm due to peripheral neuropathy. (t_aesi_ctc_DSCPAC_A_SE, t_aesi_ctc_DSCIPAT_A_SE). Ipatasertib dose interruption due to peripheral neuropathy was reported in 2 patients (1.2%) in the Ipat+Pac arm (t_aesi_ctc_DSIIPAT_A_SE). Paclitaxel dose interruption due to peripheral neuropathy was reported in 4 patients (2.4%) in the Ipat+Pac arm and 2 patients (2.3%) in the Pbo+Pac arm (t_aesi_ctc_DSIPAC_A_SE). Ipatasertib dose reduction due to peripheral neuropathy was reported in 1 patient (0.6%) (t_aesi_ctc_DSRIPAT_A_SE). Paclitaxel dose reduction due to peripheral neuropathy was reported in 13 patients (7.8%) in the Ipat+Pac arm and 3 patients (3.4%) in the Pbo+Pac arm (t_aesi_ctc_DSRPAC_A_SE).

Overall, 36.6% of peripheral neuropathy events resolved in the Ipat+Pac arm and 29.3% in the Pbo+Pac arm (t_aesiout_A_SE).

Cohort B

The proportions of patients with selected AEs in the category of peripheral neuropathy were similar between treatment arms (Ipat+Pac: 94 patients [64.8%] vs. Pbo+Pac: 49 patients [65.3%]) (t_aesi_B_SE).

The majority of peripheral neuropathy events were Grade 1 or Grade 2. Grade 3 events were reported among 10.3% of patients in the Ipat + Pac arm and 9.3% of patients in the

Pbo + Pac arm, respectively. No events of Grade 4 or Grade 5 intensity were reported in either treatment arm (t_aesi_ctc_B_SE). No peripheral neuropathy events were reported as serious (t_aesi_SER_B_SE). No patients in the Ipat + Pac arm discontinued ipatasertib treatment due to peripheral neuropathy. Twenty-two patients (15.2%) and 7 patients (9.3%) discontinued paclitaxel due to peripheral neuropathy in the Ipat+Pac arm and Pbo+Pac arm, respectively (t_aesi_ctc_DSCPAC_B_SE, t_aesi_ctc_DSCIPAT_B_SE). Ipatasertib dose interruptions due to peripheral neuropathy was reported in 3 patients (2.1%) in the Ipat+Pac arm (t_aesi_ctc_DSIIPAT_B_SE). Paclitaxel dose interruption due to peripheral neuropathy was reported in 7 patients (4.8%) in the Ipat+Pac arm and 3 patients (4.0%) in the Pbo+Pac arm (t_aesi_ctc_DSIPAC_B_SE). Ipatasertib dose reduction due to peripheral neuropathy was reported in 1 patient (0.7%) (t_aesi_ctc_DSRPAC_B_SE). Paclitaxel dose reduction due to peripheral neuropathy was reported in 19 patient (13.1%) in the Ipat+Pac arm and 7 patients (9.3%) in the Pbo+Pac arm (t_aesi_ctc_DSRPAC_B_SE).

Overall, 31.6% of peripheral neuropathy events resolved in the Ipat+Pac arm and 26.6% in the Pbo+Pac arm (t_aesiout_B_SE).

Cohort C

Selected AEs in the category of peripheral neuropathy were reported in 53 patients (52.0%) (t_aesi_C_SE).

The majority of peripheral neuropathy events were Grade 1 or Grade 2. Grade 3 events were reported among 8.8% of patients. No events of Grade 4 or Grade 5 intensity were reported (t_aesi_ctc_C_SE). No peripheral neuropathy events were reported as serious (t_aesi_SER_C_SE). No patients discontinued ipatasertib or atezolizumab treatment due to peripheral neuropathy (t_aesi_ctc_DSCIPAT_C_SE, t_aesi_ctc_DSCATZ_C_SE). Eleven patients (10.8%) discontinued paclitaxel treatment due to peripheral neuropathy (t_aesi_ctc_DSCPAC_C_SE). No ipatasertib or atezolizumab dose interruption due to peripheral neuropathy was reported but paclitaxel dose interruption due to peripheral neuropathy was reported in 2 patients (2.0%) (t_aesi_ctc_DSIATZ_C_SE, t_aesi_ctc_DSIIPAT_C_SE, t_aesi_ctc_DSIPAC_C_SE). No ipatasertib dose reduction due to peripheral neuropathy was reported but paclitaxel dose reduction due to peripheral neuropathy was reported in 11 patients (10.8%) (t_aesi_ctc_DSRPAC_C_SE).

Overall, 29.2% of the peripheral neuropathy events resolved (t_aesiout_C_SE).

5.2.2.6.17 Pneumonia

Cohort A

The proportions of patients with selected AEs in the pneumonia category were similar between treatment arms (Ipat+Pac: 8 patients [4.8%] vs. Pbo+Pac: 5 patients [5.7%]) (t_aesi_A_SE).

Three patients (1.8%) in the Ipat+Pac arm experienced Grade 3 pneumonia. One patient (1.1%) in the Pbo+Pac arm experienced Grade 4 pneumonia. No Grade 5 pneumonia events were reported (t_aesi_ctc_A_SE).

Serious pneumonia events were experienced by 3 patients in the Ipat+Pac arm (all Grade 3) and 4 patients in the Pbo+Pac arm (Grade 3: 3 patients [3.4%], Grade 4: 1 patient [1.1%]) (t_aesi_ctc_SER_A_SE).

In the Ipat+Pac arm, 1 patient discontinued ipatasertib due to pneumonia. One patient also discontinued paclitaxel due to pneumonia. No patients led to discontinuation of any study treatment in the Pbo+Pac arm due to pneumonia (t_aesi_ctc_DSCIPAT_A_SE, t_aesi_ctc_DSCPAC_A_SE). Ipatasertib dose interruption due to pneumonia was reported in 3 patients (1.8%) in the Ipat+Pac arm, while paclitaxel dose interruption due to pneumonia was reported in 3 patients in each arm (Ipat+Pac: 1.8% vs. Pbo+Pac: 3.4%) (t_aesi_ctc_DSIIPAT_A_SE, t_aesi_ctc_DSIPAC_A_SE). No dose reduction of any study treatment was reported due to pneumonia (t_aesi_ctc_DSRIPAT_A_SE, t_aesi_ctc_DSRPAC_A_SE).

The majority of pneumonia events had resolved (87.5% vs 100%) (t_aesiout_A_SE).

Cohort B

The proportions of patients with selected AEs in the pneumonia category were similar between treatment arms (Ipat+Pac: 6 patients [4.1%] vs. Pbo+Pac: 4 patients [5.3%]) (t_aesi_B_SE).

The majority of pneumonia events were Grade 1 or Grade 2. Serious pneumonia events (PT: pneumonia) were experienced by 2 patients (1.4%) in the Ipat+Pac arm (Grade 2 and Grade 5) and 1 patient (1.3%) (Grade 3) in the Pbo+Pac arm (t_aesi_SER_B_SE). For the one patient (0.7%) in the Ipat+Pac arm who experienced the Grade 5 pneumonia event, it was determined as not related to study treatment by the investigator (t_aesi_ctc_B_SE, l_aesi_B_SE, t_aesi_ctc_DSCIPAT_B_SE, t_aesi_ctc_DSCPAC_B_SE). Paclitaxel dose interruption due to pneumonia was reported in 3 patients (4%) in the Pbo+Pac arm (t_aesi_ctc_DSIIPAT_B_SE, t_aesi_ctc_DSIPAC_B_SE). No ipatasertib dose interruption and no dose reduction of any study treatment due to pneumonia was reported (t_aesi_ctc_DSRIPAT_B_SE, t_aesi_ctc_DSRPAC_B_SE).

Except for the one Grade 5 event (see Deaths), all other events of pneumonia had resolved (t_aesiout_B_SE).

Cohort C

Selected AEs in the pneumonia category was reported in 7 patients (6.9%) (t_aesi_C_SE).

The majority of pneumonia events were reported as Grade 1 or Grade 2 in intensity. A serious Grade 2 and a serious Grade 3 pneumonia event were reported in 1 patient (1.0%) each. One Grade 5 pneumonia event was reported after the 28-day reporting period for ipatasertib, which was not related to any study medications. All study

medications had been previously discontinued due to the AE of pneumonitis, which was reported as related to atezolizumab (see Safety Analysis for AE reporting period) (t_aesi_ctc_C_SE, t_aesi_SER_C_SE, l_aesi_C_SE).

No patients discontinued ipatasertib due to pneumonia. (t_aesi_ctc_DSCIPAT_C_SE, t_aesi_ctc_DSCATZ_C_SE, t_aesi_ctc_DSCPAC_C_SE). Ipatasertib and paclitaxel dose interruption due to pneumonia was reported in 1 patient (1.0%) and 3 patients (2.9%), respectively (t_aesi_ctc_DSIIPAT_C_SE, t_aesi_ctc_DSIPAC_C_SE). No atezolizumab dose interruption due to pneumonia was reported (t_aesi_ctc_DSIATZ_C_SE). No ipatasertib or paclitaxel dose reduction was reported (t_aesi_ctc_DSRIPAT_C_SE, t_aesi_ctc_DSRPAC_C_SE).

The majority of the pneumonia events had resolved (85.7%) (t_aesiout_C_SE).

5.2.3 Clinical Laboratory Evaluation

Cohort A

Overall, few patients experienced clinically relevant shifts from baseline (defined as those who did not have a baseline NCI CTCAE grade of Grade 3–4 for the specific laboratory abnormality and shifted to Grade 3–4 postbaseline) during study treatment (Table 67).

The most common clinically relevant shifts were hematologic toxicities (see Hematology) and abnormalities in liver function tests (see Chemistry).

In general, laboratory abnormalities observed in the study are consistent with the safety profile of known risks of each individual study drug.

A summary of safety laboratory tests with highest NCI CTCAE grade postbaseline (t_lb_cb_grdmax_A_SE), and a listing (l_lb_mabn_A_SE) of laboratory abnormalities are appended.

Table 67 Summary of Clinically Relevant Shifts from Baseline in Laboratory Safety Parameters (Cohort A, Safety Evaluable Population)

Laboratory Test Shifts to NCI-CTCAE Grade 3-4 Post-Baseline, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Laboratory Test	Direction of Abnormality	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Chemistry			
Albumin	Low	0/86	2/166 (1.2%)
Alkaline Phosphatase	High	0/85	0/165
SGPT/ALT	High	3/85 (3.5%)	10/166 (6.0%)
SGOT/AST	High	3/86 (3.5%)	5/166 (3.0%)
Calcium	Low	1/86 (1.2%)	1/166 (0.6%)
	High	0/86	1/166 (0.6%)
Triglycerides, Fasting	High	1/74 (1.4%)	4/152 (2.6%)
Amylase, Fasting	High	1/74 (1.4%)	1/153 (0.7%)
Lipase, Total, Fasting	High	2/73 (2.7%)	6/152 (3.9%)
Creatinine	High	1/86 (1.2%)	0/166
Cholesterol, Fasting	High	0/74	1/152 (0.7%)
Glucose, Fasting	Low	0/83	0/162
	High	0/83	2/162 (1.2%)
Glucose	Low	0/21	0/ 28
	High	0/21	2/ 28 (7.1%)
Magnesium	Low	0/86	0/166
	High	1/86 (1.2%)	5/166 (3.0%)
Phosphorus	Low	1/86 (1.2%)	6/165 (3.6%)
Potassium	Low	1/86 (1.2%)	2/166 (1.2%)
	High	2/86 (2.3%)	1/165 (0.6%)
Sodium	Low	6/85 (7.1%)	8/163 (4.9%)
	High	0/86	0/166
Bilirubin	High	0/86	0/166
Coagulation			
International Normalized Ratio	High	0/62	2/133 (1.5%)
Activated Partial Thromboplastin Time	High	1/62 (1.6%)	1/128 (0.8%)
Hematology			
Hemoglobin	Low	4/86 (4.7%)	6/166 (3.6%)
	High	0/86	0/166
Lymphocytes Abs	Low	4/84 (4.8%)	18/165 (10.9%)
	High	1/86 (1.2%)	0/166
Neutrophils, Total, Abs	Low	9/86 (10.5%)	25/166 (15.1%)
Platelet	Low	1/86 (1.2%)	1/166 (0.6%)
Total Leukocyte Count	Low	4/86 (4.7%)	13/166 (7.8%)
	High	1/86 (1.2%)	1/166 (0.6%)

For each patient, baseline is the last observation prior to initiation of study drug. For each laboratory test, patients with at least 1 post-baseline assessment are included in the analysis. For each cell, the denominator is the number of patients with baseline extended NCI-CTCAE v4 Grade 0-2 in the specified direction of abnormality, or Grade 1-4 in the opposite direction of abnormality. Patients with missing baseline values are included in the denominator.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_sabn.sas
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08MAY2023 8:08 Page 1 of 1

Cohort B

Overall, few patients experienced clinically relevant shifts from baseline (defined as those who did not have a baseline NCI CTCAE grade of Grade 3–4 for the specific laboratory abnormality and shifted to Grade 3–4 postbaseline) during study treatment (Table 68).

The most common clinically relevant shifts were hematologic toxicities (see Hematology) and abnormalities in liver function tests (see Chemistry).

In general, laboratory abnormalities observed in the study are consistent with the safety profile of known risks of each individual study drug.

A summary of safety laboratory tests with highest NCI CTCAE grade postbaseline (t_lb_cb_grdmax_B_SE), and a listing (l_lb_mabn_B_SE) of laboratory abnormalities are appended.

Table 68 Summary of Clinically Relevant Shifts from Baseline in Laboratory Safety Parameters (Cohort B, Safety Evaluable Population)

Laboratory Test Shifts to NCI-CTCAE Grade 3-4 Post-Baseline, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Laboratory Test	Direction of Abnormality	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Chemistry			
Albumin	Low	0/74	1/144 (0.7%)
Alkaline Phosphatase	High	6/73 (8.2%)	6/142 (4.2%)
SGPT/ALT	High	6/73 (8.2%)	12/144 (8.3%)
SGOT/AST	High	8/74 (10.8%)	11/142 (7.7%)
Calcium	Low	0/74	1/144 (0.7%)
	High	3/74 (4.1%)	1/144 (0.7%)
Triglycerides, Fasting	High	1/71 (1.4%)	2/133 (1.5%)
Amylase, Fasting	High	0/69	2/134 (1.5%)
Lipase, Total, Fasting	High	2/65 (3.1%)	7/132 (5.3%)
Creatinine	High	1/75 (1.3%)	4/144 (2.8%)
Cholesterol, Fasting	High	0/71	0/135
Glucose, Fasting	Low	0/73	0/144
	High	0/73	2/144 (1.4%)
Glucose	Low	0/ 8	0/ 32
	High	0/ 8	1/ 32 (3.1%)
Magnesium	Low	1/73 (1.4%)	1/143 (0.7%)
	High	4/73 (5.5%)	3/143 (2.1%)
Phosphorus	Low	3/73 (4.1%)	5/142 (3.5%)
Potassium	Low	0/74	4/144 (2.8%)
	High	1/75 (1.3%)	0/144
Sodium	Low	3/75 (4.0%)	6/144 (4.2%)
	High	0/75	0/144
Bilirubin	High	3/74 (4.1%)	3/144 (2.1%)
Coagulation			
International Normalized Ratio	High	0/63	0/110
Activated Partial Thromboplastin Time	High	0/60	0/106
Hematology			
Hemoglobin	Low	4/75 (5.3%)	7/144 (4.9%)
	High	0/75	0/144
Lymphocytes Abs	Low	10/74 (13.5%)	20/139 (14.4%)
	High	0/74	0/143
Neutrophils, Total, Abs	Low	12/74 (16.2%)	25/144 (17.4%)
Platelet	Low	1/75 (1.3%)	1/144 (0.7%)
Total Leukocyte Count	Low	9/75 (12.0%)	20/144 (13.9%)
	High	0/75	0/144

For each patient, baseline is the last observation prior to initiation of study drug. For each laboratory test, patients with at least 1 post-baseline assessment are included in the analysis. For each cell, the denominator is the number of patients with baseline extended NCI-CTCAE v4 Grade 0-2 in the specified direction of abnormality, or Grade 1-4 in the opposite direction of abnormality. Patients with missing baseline values are included in the denominator.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_sabn.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_sabn_B_SE.out
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Cohort C

Overall, few patients experienced clinically relevant shifts from baseline (defined as those who did not have a baseline NCI CTCAE grade of Grade 3–4 for the specific

laboratory abnormality and shifted to Grade 3–4 postbaseline) during study treatment (Table 69).

The most common clinically relevant shifts were hematologic toxicities (see Hematology) and abnormalities in liver function tests (see Chemistry).

In general, laboratory abnormalities observed in the study are consistent with the safety profile of known risks of each individual study drug.

A summary of safety laboratory tests with highest NCI CTCAE grade postbaseline (t_lb_cb_grdmax_C_SE), and a listing (l_lb_mabn_C_SE) of laboratory abnormalities are appended.

Table 69 Summary of Clinically Relevant Shifts from Baseline in Laboratory Safety Parameters (Cohort C, Safety Evaluable Population)

Laboratory Test Shifts to NCI-CTCAE Grade 3-4 Post-Baseline, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Laboratory Test	Direction of Abnormality	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Chemistry		
Albumin	Low	1/102 (1.0%)
Alkaline Phosphatase	High	6/102 (5.9%)
SGPT/ALT	High	13/102 (12.7%)
SGOT/AST	High	11/102 (10.8%)
Calcium	Low	1/102 (1.0%)
	High	1/102 (1.0%)
Triglycerides, Fasting	High	2/ 93 (2.2%)
Amylase, Fasting	High	1/ 93 (1.1%)
Lipase, Total, Fasting	High	3/ 91 (3.3%)
Creatinine	High	3/102 (2.9%)
Cholesterol, Fasting	High	2/ 93 (2.2%)
Glucose, Fasting	Low	0/ 98
	High	4/ 98 (4.1%)
Glucose	Low	1/ 37 (2.7%)
	High	1/ 37 (2.7%)
Magnesium	Low	1/102 (1.0%)
	High	3/101 (3.0%)
Phosphorus	Low	2/101 (2.0%)
Potassium	Low	6/102 (5.9%)
	High	2/102 (2.0%)
Sodium	Low	9/102 (8.8%)
	High	0/102
Bilirubin	High	3/102 (2.9%)
Coagulation		
International Normalized Ratio	High	0/ 80
Activated Partial Thromboplastin Time	High	0/ 77
Hematology		
Hemoglobin	Low	4/102 (3.9%)
	High	0/102
Lymphocytes Abs	Low	17/102 (16.7%)
	High	0/102
Neutrophils, Total, Abs	Low	11/102 (10.8%)
Platelet	Low	1/102 (1.0%)
Total Leukocyte Count	Low	10/102 (9.8%)
	High	0/102

For each patient, baseline is the last observation prior to initiation of study drug. For each laboratory test, patients with at least 1 post-baseline assessment are included in the analysis. For each cell, the denominator is the number of patients with baseline extended NCI-CTCAE v4 Grade 0-2 in the specified direction of abnormality, or Grade 1-4 in the opposite direction of abnormality. Patients with missing baseline values are included in the denominator.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_sabn.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_sabn_C_SE.out
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5.2.3.1 Hematology

Cohort A

The most common clinically relevant shifts from baseline in hematology parameters (≥5% incidence in either arm) were: low values for absolute neutrophils (Ipat+Pac: 15.1% vs. Pbo+Pac: 10.5%), lymphocytes (10.9% vs. 4.8%), and leukocytes (7.8% vs. 4.7%) (Table 67).

Aside from low absolute neutrophil, lymphocyte, and leukocyte counts, no other hematology parameter had clinically relevant shifts that were more frequently reported (i.e., with ≥2% difference) in the Ipat+Pac arm compared with the Pbo+Pac arm.

Laboratory hematology shifts in NCI CTCAE grade postbaseline in the high (t_lb_shift_high_HEM_A_SE) or low direction (t_lb_shift_low_HEM_A_SE) are appended.

Cohort B

The most common clinically relevant shifts from baseline in hematology parameters (≥5% incidence in either arm) were: low values for absolute neutrophils (Ipat+Pac: 17.4% vs. Pbo+Pac: 16.2%), lymphocytes (14.4% vs. 13.5%), leukocytes (13.9% vs. 12.0%), and hemoglobin (4.9% vs. 5.3%) (Table 68).

None of the hematology parameters had clinically relevant shifts that were more frequently reported (i.e., with ≥2% difference) in the Ipat+Pac arm compared with the Pbo+Pac arm.

Laboratory hematology shifts in NCI CTCAE grade postbaseline in the high (t_lb_shift_high_HEM_B_SE) or low direction (t_lb_shift_low_HEM_B_SE) are appended.

Cohort C

The most common clinically relevant shifts from baseline in hematology parameters (≥5% incidence) were: low values for absolute neutrophils (10.8%), lymphocytes (16.7%), and leukocytes (9.8%) (Table 69).

Aside from low absolute neutrophil and lymphocyte counts, no other hematology parameter had clinically relevant shifts.

Laboratory hematology shifts in NCI CTCAE grade postbaseline in the high (t_lb_shift_high_HEM_C_SE) or low direction (t_lb_shift_low_HEM_C_SE) are appended.

5.2.3.2 Chemistry

Cohort A

The most common clinically relevant shift from baseline in laboratory chemistry parameters (≥5% incidence in either arm) were: elevated serum glutamic-pyruvic transaminase/alanine aminotransferase (SGPT/ALT) (Ipat+Pac: 6.0% vs Pbo+Pac: 3.5%), elevated glucose (7.1% vs. 0), and low sodium (4.9% vs. 7.1%) (Table 67).

The incidences of other clinically relevant shifts in laboratory chemistry parameters were comparable between the treatment arms. Aside from elevated SGPT/ALT and low phosphorus, no other chemistry parameters had clinically significant shifts that were more frequently reported (i.e., with ≥2% difference) in the Ipat+Pac arm compared with the Pbo+Pac arm.

Laboratory chemistry shifts in NCI CTCAE grade postbaseline in the high (t_lb_shift_high_CHEM_A_SE) or low direction (t_lb_shift_low_CHEM_A_SE) are appended.

Cohort B

The most common clinically relevant shift from baseline in laboratory chemistry parameters (≥5% incidence in either arm) were: elevated alkaline phosphatase (Ipat+Pac: 4.2% vs. Pbo+Pac: 8.2%), elevated SGPT/ALT (8.3% vs 8.2%), elevated serum glutamic-oxaloacetic transaminase/aspartate aminotransferase (SGOT/AST) (7.7% vs. 10.8%), elevated fasting lipase (5.3% vs. 3.1%), and elevated magnesium level (2.1% vs. 5.5%) (Table 68).

The incidences of other clinically relevant shifts in laboratory chemistry parameters were comparable between the treatment arms. Aside from fasting lipase, no other chemistry parameters had clinically significant shifts that were more frequently reported (i.e., with ≥2% difference) in the Ipat+Pac arm compared with the Pbo+Pac arm.

Laboratory chemistry shifts in NCI CTCAE grade postbaseline in the high (t_lb_shift_high_CHEM_B_SE) or low direction (t_lb_shift_low_CHEM_B_SE) are appended.

Cohort C

The most common clinically relevant shift from baseline in laboratory chemistry parameters (≥5% incidence) were: elevated alkaline phosphatase (5.9%), elevated SGPT/ALT (12.7%), elevated SGOT/AST (10.8%), low potassium level (5.9%), and low sodium level (8.8%) (Table 69).

No other chemistry parameters had clinically significant shifts.

Laboratory chemistry shifts in NCI CTCAE grade postbaseline in the high (t_lb_shift_high_CHEM_C_SE) or low direction (t_lb_shift_low_CHEM_C_SE) are appended.

5.2.3.2.1 Hy's Law

Cohort A

There were no cases of drug-induced liver injury (by PT) or AESI of potential drug-induced liver injury as defined by Hy's law reported by investigators.

Potential Hy's law cases were identified for review based on the following criteria: any patient with elevated ALT or AST (>3x upper limit of normal [ULN]) and with elevated total bilirubin (>2x ULN) within 7 days after the AST/ALT increase. No cases of potential hy's law were identified using these laboratory criteria.

A summary and listing of patients meeting laboratory criteria for Hy's law are appended (t_lb_hy_A_SE, l_lb_hy_A_SE).

Cohort B

There were no cases of drug-induced liver injury (by PT) or AESI of potential drug-induced liver injury as defined by Hy's law reported by investigators.

Potential Hy's law cases were identified for review based on the following criteria: any patient with elevated ALT or AST (>3x ULN) and with elevated total bilirubin (>2x ULN) within 7 days after the AST/ALT increase.

A total of 9 patients (Ipat+Pac: 4 patients vs. Pbo+Pac: 5 patients) were identified as potential Hy's law cases (Table 70). A detailed medical review showed that none of these cases met the criteria of Hy's law.

A listing of patients meeting laboratory criteria for Hy's law is appended (l_lb_hy_B_SE).

Table 70 Summary of Patient Laboratory Criteria for Hy's Law (Cohort B, Safety Evaluable Population)

Hy`s Law, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hy's Law Laboratory Criteria Met	5 (6.7%)	4 (2.8%)

ALT = Alanine Aminotransferase, AST = Aspartate Aminotransferase, TBILI = Bilirubin, ULN = Upper Limit Normal. Patients who met Hy's Law Criteria reported at least one TBILI > 2 x ULN within 7 days after latest ALT or AST > 3 x ULN. Local lab reference ranges are used to assess Hy's Law criteria.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_hy.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_hy_B_SE.out
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Cohort C

There were no cases of drug-induced liver injury (by PT) or AESI of potential drug-induced liver injury as defined by Hy's law reported by investigators.

Potential Hy's law cases were identified for review based on the following criteria: any patient with elevated ALT or AST (>3x ULN) and with elevated total bilirubin (>2x ULN) within 7 days after the AST/ALT increase.

A total of 2 patients were identified as potential Hy's law cases (Table 71). A detailed medical review showed that none of these cases met the criteria of Hy's law.

A listing of patients meeting laboratory criteria for Hy's law is appended (l_lb_hy_C_SE).

Table 71 Summary of Patient Laboratory Criteria for Hy's Law (Cohort C, Safety Evaluable Population)

Hy`s Law, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hy's Law Laboratory Criteria Met	2 (2.0%)

ALT = Alanine Aminotransferase, AST = Aspartate Aminotransferase, TBILI = Bilirubin, ULN = Upper Limit Normal. Patients who met Hy's Law Criteria reported at least one TBILI > 2 x ULN within 7 days after latest ALT or AST > 3 x ULN. Local lab reference ranges are used to assess Hy's Law criteria.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_hy.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_hy_C_SE.out
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5.2.3.3 Coagulation

Cohort A

Clinically relevant shifts in NCI CTCAE grade from baseline for laboratory coagulation parameters were reported for elevated international normalized ratio (Ipat+Pac: 1.5% vs. Pbo+Pac: 0) and elevated activated partial thromboplastin time (0.8% vs. 1.6%) (Table 67).

Laboratory coagulation shift in NCI CTCAE grade postbaseline in the high direction (t_lb_shift_high_COAG_A_SE) is appended.

Cohort B

There were no clinically relevant shifts in NCI CTCAE grade from baseline for any laboratory coagulation parameters (Table 68).

Laboratory coagulation shift in NCI CTCAE grade postbaseline in the high direction (t_lb_shift_high_COAG_B_SE) is appended.

Cohort C

There were no clinically relevant shifts in NCI CTCAE grade from baseline for any laboratory coagulation parameters (Table 69).

Laboratory coagulation shifts in NCI CTCAE grade postbaseline in the high direction (t_lb_shift_high_COAG_C_SE) is appended.

5.2.4 Other Safety Evaluation

5.2.4.1 Vital Signs

There were no clinically relevant differences between the treatment arms with respect to vital sign parameters during the study in all cohorts.

A summary of vital signs by visit (with change from baseline) for each cohort (t_vs_cb_A_SE; t_vs_cb_B_SE; t_vs_cb_C_SE) is appended.

5.2.4.2 Electrocardiograms (ECG)

Cohort A

One patient in the Pbo+Pac arm had clinically significant abnormal electrocardiogram (ECG) recordings reported postbaseline at the study drug discontinuation visit and no AE was reported for this (t_eg_shift_A_SE).

One patient in the Ipat+Pac arm had clinically significant abnormal ECG recordings reported postbaseline. The patient had an SAE of Grade 1 atrial fibrillation which was considered related to ipatasertib and study disease. Atrial fibrillation was treated with a beta blocker, and ipatasertib and paclitaxel were interrupted due to the event. Subsequent ECG recordings were assessed as abnormal, but non-clinically significant.

Cohort B

One patient in the Pbo+Pac arm had clinically significant abnormal ECG recordings reported during study treatment (Day 337) with a corresponding AE of Grade 1 sinus tachycardia (t_eg_shift_B_SE). The AE had resolved without requiring treatment discontinuation or dose modification. Another patient had clinically significant abnormal ECG recordings (Day 582), but subsequent ECG recording was abnormal but not clinically signficant.

In the Ipat+Pac arm, one patient had clinically significant abnormal ECG recordings reported during study treatment (Day 157); this patient had abnormal but not clinically significant ECGs on Day 153 associated with an AE of Grade 2 sinus tachycardia (Day 155); this event had not resolved. Another patient had clinically significant abnormal ECG recordings at study drug discontinuation (Day 262) with no corresponding AEs reported.

Cohort C

Two patients had clinically significant abnormal ECG recordings reported postbaseline (t_eg_shift_C_SE). One patient had clinically significant ECG abnormality recording on Day 62, with no corresponding AE reported. Another patient had an AE of Grade 1 sinus tachycardia which had not resolved.

5.2.4.3 ECOG Performance Status

ECOG PS at baseline and shifts in ECOG PS from baseline were for Cohort A and B were reported in the primary CSR for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941), respectively.

For Cohort C, patients either had a baseline ECOG PS of 0 or 1. No patient had a baseline ECOG PS of ≥2 (Table 16).

5.2.4.4 Pregnancies

No pregnancies were reported in the study. At the time of the primary analyses, false pregnancy tests were reported for 1 patient and 2 patients in Cohorts A (see Report No. 1101889) and B (see Report No. 1100941), respectively, and there are no changes. No positive pregnancy tests were reported for Cohort C (l_lb_preg_C_SE).

5.3 PHARMACOKINETICS

Ipatasertib

Plasma samples for PK characterization of ipatasertib and its metabolite G-037720, were analyzed on Day 1 and Day 15 of Cycle 1 and on Day 15 of Cycle 3 from all patients who received ipatasertib. Patients who had at least one evaluable plasma sample were included in this PK analysis. In this study, there were 101 PK-evaluable patients.

Twelve samples were excluded from the descriptive statistics. These samples had concentrations that were below the limit of quantification post the first dose for ipatasertib and G-037720, which was considered pharmacokinetically not feasible.

A summary of plasma concentrations of ipatasertib and G-037720 at the nominal times of collection is shown in Table 72 and Table 73, respectively. The geometric mean plasma concentration of ipatasertib at 1–3 hours post dose ($C_{1\text{-}3hr}$) (geometric mean coefficient of variation [geoCV%]) increased from 175 ng/mL (183%) on Day 1 of Cycle 1 to 233 ng/mL (161.6%) on Day 15 of Cycle 1 upon multiple dosing to steady state. The geometric mean (geoCV%) plasma concentration of ipatasertib at 2–4 hours postdose at steady state ($C_{2\text{-}4hr,ss}$) on Day 15 of Cycle 3 was 207 ng/mL (197.6%). The geometric mean (geoCV%) predose concentrations at steady state ($C_{min,ss}$) on Day 15 of Cycles 1 and 3 were comparable (48.5 ng/mL [156.9%] and 46 ng/mL [120.3%], respectively).

The geometric mean plasma concentration of G-037720 at 1–3 hours post dose ($C_{1\text{-}3hr}$) (geoCV%) increased from 67.3 ng/mL (222.3%) on Day 1 of Cycle 1 to 96.8 ng/mL (140.7%) on Day 15 of Cycle 1 upon multiple dosing. The geometric mean (geoCV%) plasma concentration of G-037720 at 2–4 hours postdose at steady state ($C_{2\text{-}4hr,ss}$) on Day 15 of Cycle 3 was 96.5 ng/mL (167.9%). The geometric mean (geoCV%) predose concentrations at steady state ($C_{min,ss}$) on Day 15 of Cycles 1 and 3 were comparable (26.9 ng/mL [133.2%] and 24.5 ng/mL [87%], respectively).

Table 72 Ipatasertib Plasma Concentrations at Nominal Sampling Times (PK Evaluable Population)

	Day 1 of Cycle 1	Day 15 of Cycle 1		Day 15 of Cycle 3	
	$C_{1\text{-}3hr}$	$C_{min,ss}$	$C_{1\text{-}3hr,ss}$	$C_{min,ss}$	$C_{2\text{-}4hr,ss}$
N	94	83	82	67	62
Geomean (ng/mL)	175	48.5	233	46	207
geoCV%	183%	156.9%	161.6%	120.3%	197.6%

$C_{1\text{-}3hr}$ = plasma concentration at 1–3 hours post ipatasertib dose; $C_{1\text{-}3hr,ss}$ = plasma concentration at 1–3 hours post ipatasertib dose at steady state; $C_{2\text{-}4hr,ss}$ = plasma concentration at 2–4 hours post ipatasertib dose at steady state; $C_{min,ss}$ = trough concentration at steady state, geoCV% = geometric mean coefficient of variations; Geomean = geometric mean; N = Number of patients; PK = pharmacokinetic.

Source: t_pkc.

Table 73 G-037720 Plasma Concentrations at Nominal Sampling Times (PK Evaluable Population)

	Day 1 of Cycle 1	Day 15 of Cycle 1		Day 15 of Cycle 3	
	$C_{1\text{-}3hr}$	$C_{min,ss}$	$C_{1\text{-}3hr,ss}$	$C_{min,ss}$	$C_{2\text{-}4hr,ss}$
N	91	83	82	66	62
Geomean (ng/mL)	67.3	26.9	96.8	24.5	96.5
geoCV%	222.3%	133.2%	140.7%	87%	167.9%

$C_{1\text{-}3hr}$ = plasma concentration at 1–3 hours post ipatasertib dose; $C_{1\text{-}3hr,ss}$ = plasma concentration at 1–3 hours post ipatasertib dose at steady state; $C_{2\text{-}4hr,ss}$ = plasma concentration at 2–4 hours post ipatasertib dose at steady state; $C_{min,ss}$ = trough concentration at steady state, geoCV% = geometric mean coefficient of variations; Geomean = geometric mean; N = Number of patients; PK = pharmacokinetic.

Source: t_pkc_met.

Atezolizumab

A summary of serum concentrations of atezolizumab at the nominal times of collection is shown in t_pkc_atzo.

5.4 IMMUNOGENICITY

Atezolizumab

The incidence of treatment-emergent ADAs was 17.8% (18/101) in the treatment-emergent ADA-evaluable population (Table 74).

A bioanalytical report (CO40016 ADA ICON 188357 Final BAR) including immunogenicity data is appended.

Table 74 Baseline Prevalence and Postbaseline Incidence of Atezolizumab Anti-Drug Antibodies

Baseline Prevalence and Post-Baseline Incidence of Anti-Drug Antibodies (ADAs) to Atezolizumab (RO5541267)
Safety Population
Protocol: CO40016

	COHORT C IPATASERTIB + ATEZOLIZUMAB + PACLITAXEL (n=102)
Baseline Prevalence of ADAs	
Baseline evaluable patients	99
Patients with a positive sample at baseline	0 (0.0%)
Patients with no positive samples at baseline	99
Incidence of Treatment Emergent ADAs	
Post-baseline evaluable patients	101
Patients positive for Treatment Emergent ADA	18 (17.8%)
Treatment-induced ADA	18
Treatment-enhanced ADA	0
Patients negative for Treatment Emergent ADA	83
Treatment unaffected	0

ADA = Anti-Drug Antibodies (is also referred to as ATA, or Anti-Therapeutic Antibodies).
Baseline evaluable patient = a patient with an ADA assay result from a baseline sample.
Post-baseline evaluable patient = a patient with an ADA assay result from at least one post-baseline sample.
Number of patients positive for Treatment Emergent ADA = the number (and percentage) of post-baseline evaluable patients determined to have treatment-induced ADA or treatment-enhanced ADA during the study period.
Treatment-induced ADA = a patient with negative or missing baseline ADA result(s) and at least one positive post-baseline ADA result.
Treatment-enhanced ADA = a patient with positive ADA result at baseline who has one or more post-baseline titer results that are at least 0.60 t.u. greater than the baseline titer result.
Number of patients negative for Treatment Emergent ADA = number of post-baseline evaluable patients with negative or missing baseline ADA result(s) and all negative post-baseline results, or a patient who is treatment unaffected.
Treatment unaffected = A post-baseline evaluable patient with a positive ADA result at baseline and (a) where all post-baseline titer results are less than 0.60 t.u. greater than the baseline titer result, OR (b) where all post-baseline results are negative or missing.
For any positive sample with titer result less than the minimum reportable titer or any positive sample where a titer cannot be obtained, titer value is imputed as equal to the minimum reportable titer.

Program:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/PK_Final_CSR_CohortC/prod/program/t_ata1.sas
Output:
root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/PK_Final_CSR_CohortC/prod/output/t_ata1.out
24JUN2023 0:07 Page 1 of 1

5.5 SUMMARY OF EVALUATION OF RESPONSE TO STUDY TREATMENT

Study CO40016 was designed to assess the efficacy and safety of ipatasertib in combination with paclitaxel in patients with *PIK3CA/AKT1/PTEN*-altered locally advanced unresectable or metastatic TNBC (Cohort A) or HR+/HER2− breast cancer (Cohort B) with no prior systemic treatment in the locally advanced/metastatic setting. Study CO40016 included a single-arm open-label cohort (Cohort C) to assess the safety and efficacy of ipatasertib in combination with atezolizumab and paclitaxel in TNBC

patients without *PIK3CA/AKT1/PTEN*-altered tumors. The primary endpoint was INV-assessed PFS per RECIST v1.1 and the key secondary endpoint was OS.

Efficacy

As discussed in the primary CSR for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941), Study CO40016 did not meet its primary endpoint, PFS. As such, the final OS analysis results were considered descriptive and there was no clinically meaningful benefit observed in OS with ipatasertib in combination with paclitaxel over paclitaxel alone in patients with *PIK3CA/AKT1/PTEN*-altered, locally advanced or metastatic TNBC (Cohort A) or HR+/HER2- breast cancer (Cohort B). While efficacy results for Cohort C were descriptive in nature, the median duration of PFS and OS were consistent with the Ipat+Pac arm in Cohort A.

Patient-Reported Outcomes

For Cohort C, the patient experience was characterized through prespecified patient-reported endpoints of mean and mean changes from baseline in health-related QoL (HRQoL) through the GHS/QoL scale of the EORTC QLQ-C30 questionnaire. Completion rates at baseline (Cycle 1, Day 1) was high at 100% and remained high through Cycle 7, with mean change from baseline remaining within 8 points of the baseline score. Patients' baseline HRQoL was maintained while receiving treatment, with no clinically meaningful deterioration in patients' GHS/QoL observed. Patient-reported outcome results demonstrated that adding ipatasertib in combination with atezolizumab and paclitaxel for the treatment of patients with locally advanced unresectable or metastatic TNBC did not result in a detrimental effect to patients' overall HRQoL.

Safety

The safety profile of ipatasertib in combination with paclitaxel remained consistent with the safety profile reported in the primary CSR for Cohorts A and B. The safety profile of ipatasertib in combination with atezolizumab and paclitaxel (Cohort C) was consistent with the known risks of each individual study drug and no new safety signals were identified across cohorts.

<u>Cohort A</u>

- Most patients in each treatment arm experienced at least one AE of any grade (Ipat+Pac: 162 patients [97.6%] vs. Pbo+Pac: 84 patients [96.6%]).
- Grade ≥3 AEs were reported in a similar proportion of patients between treatment arms for Cohort A (Ipat + Pac: 84 patients [50.6%] vs. Pbo + Pac: 40 patients [46.0%]).
- The most common Grade ≥3 AEs (by PT) reported in ≥5% of patients in either treatment arm were: diarrhea (Ipat+Pac: 9% vs. Pbo+Pac: 2.3%), neutrophil count decreased (4.8% vs. 5.7%), and neutropenia (7.2% vs. 4.6%)

- A total of 132 deaths were reported in the safety evaluable population (Ipat+Pac: 91 patients [54.8%] vs. Pbo+Pac: 41 patients [47.1%]). The primary cause of death was progressive disease. Deaths due to AEs were reported in 2 patients in each treatment arm.
- Grade 5 AEs occurred in a low number of patients (Ipat+Pac: 2 patients [1.2%] vs. Pbo+Pac: 2 patients [2.3%]). Of these Grade 5 AEs, one AE (PT: tumor lysis syndrome) in the Pbo + Pac arm was considered related to both placebo and paclitaxel.
- Similar proportions of SAEs were reported between the Ipat + Pac arm (20.5%) and the Pbo + Pac arm (23%). SAEs (by PT) reported in ≥1% of patients (i.e., ≥2 patients) in the Ipat + Pac arm were: diarrhea, febrile neutropenia, pulmonary embolism, pneumonia, nausea, and vomiting. Two SAEs (by PT) were reported in more than 1 patient in the Pbo + Pac arm: pneumonia and pleural effusion.
- The proportion of patients with AEs leading to ipatasertib/placebo treatment discontinuation was higher in the Ipat+Pac arm compared with the Pbo+Pac arm (Ipat+Pac: 10.2% vs. Pbo+Pac: 6.9%). AEs (by PT) leading to ipatasertib treatment discontinuation occurring in ≥1% of patients (i.e., ≥2 patients) in the Ipat + Pac arm were diarrhea, pulmonary embolism, and hyperglycemia.
- The proportions of patients with AEs leading to paclitaxel treatment discontinuation in the Ipat+Pac arm and in the Pbo+Pac arm were 15.1% and 16.1%, respectively. AEs (by PT) leading to paclitaxel treatment discontinuation occurring in ≥2 patients in either treatment arm were neuropathy peripheral, peripheral sensory neuropathy, polyneuropathy, diarrhea, and pulmonary embolism.
- The incidence of selected AEs was consistent with known safety profile of ipatasertib, and in general were manageable and reversible. Selected AEs were reported in both treatment arms (Ipat+Pac: 94.6% vs. Pbo+Pac: 90.8%).

Cohort B

- Most patients in each treatment arm experienced at least one AE of any grade (144 patients [99.3%] vs. 74 patients [98.7%]).
- Grade ≥3 AEs were reported in a higher proportion of patients in the Ipat+Pac arm compared with the Pbo+Pac arm (83 patients [57.2%] vs. 37 patients [49.3%]).
- The most common Grade ≥3 AEs (by PT) reported in ≥5% of patients in either treatment arm were: diarrhea (Ipat+Pac: 11.7% vs. Pbo+Pac: 1.3%), neutrophil count decreased (9% vs. 8%), neutropenia (8.3% vs. 9.3%), neuropathy peripheral (6.9% vs. 4%), peripheral sensory neuropathy (2.8% vs. 5.3%), and hypertension (1.4% vs. 5.3%).
- A total of 122 deaths were reported in the safety evaluable population (Ipat+Pac: 78 patients [53.8%] vs. Pbo+Pac: 44 patients [58.7%]). The primary cause of death was progressive disease. Deaths due to AEs were reported in 5 patients in the Ipat+Pac arm and 1 patient in the Pbo+Pac arm.
- Grade 5 AEs occurred in a low number of patients (5 patients [3.4%] vs. 1 patient [1.3%]). Of these Grade 5 AEs, one AE (PT: febrile neutropenia) in the Ipat+Pac

arm was considered related to ipatasertib and paclitaxel and led to ipatasertib and paclitaxel treatment discontinuation, and one AE (PT: sepsis) in the Pbo+Pac arm considered related to paclitaxel and led to paclitaxel treatment discontinuation, the rest of the events were not considered related to any study treatment by the investigator.

- A higher proportion of SAEs was reported in the Ipat + Pac arm (20.7%) compared with the Pbo + Pac arm (14.7%). SAEs (by PT) reported in ≥1% of patients (i.e., ≥2 patients) in the Ipat + Pac arm were: diarrhea, febrile neutropenia, pneumonia, neutropenia, and pneumonitis. No SAE (by PT) was reported in more than 1 patient in the Pbo+Pac arm.
- The proportions of patients with AEs leading to ipatasertib/placebo treatment discontinuation were higher in the Ipat+Pac arm (11.7%) compared with the Pbo+Pac arm (4%). AEs (by PT) leading to ipatasertib treatment discontinuation occurring in ≥1% of patients (i.e., ≥ 2 patients) in the Ipat + Pac arm were diarrhea, febrile neutropenia, and hyperglycemia.
- The proportions of patients with AEs leading to paclitaxel treatment discontinuation in the Ipat+Pac arm and in the Pbo+Pac arm were 29% and 16%, respectively. AEs (by PT) leading to paclitaxel treatment discontinuation occurring in ≥2 of patients in either treatment arm were neuropathy peripheral, peripheral sensory neuropathy, neurotoxicity, polyneuropathy, febrile neutropenia, neutropenia, and neutrophil count decreased.
- The incidence of selected AEs was consistent with known safety profile of ipatasertib, and in general were manageable and reversible. Selected AEs were reported in both treatment arms (Ipat+Pac: 97.2% vs. Pbo+Pac: 97.3%).

Cohort C

- All patients experienced at least one AE of any grade.
- Grade ≥3 AEs were reported in 62 patients [60.8%]. The most frequent Grade ≥3 AEs (by PT) with ≥5% incidence were alanine aminotransferase increased, aspartate aminotransferase increased, neuropathy peripheral, diarrhea and neutropenia.
- A total of 50 deaths were reported in the safety evaluable population. The primary cause of death was progressive disease. Deaths due to AEs were reported in 4 patients.
- Grade 5 AEs occurred in a low number of patients (4 patients [3.9%]). Of these Grade 5 AEs, one AE (PT: pulmonary embolism) was considered related to atezolizumab.
- The proportion of patients with at least one SAE was 28.4%. SAEs (by PT) reported in ≥2 patients) were: diarrhea, pyrexia, pneumonia, urinary tract infection, cholecystitis, dehydration, fatigue, febrile neutropenia, pneumonitis, rash, tumor necrosis, and vomiting.
- The proportion of patients with AEs leading to ipatasertib treatment discontinuation was 10.8%. AEs (by PT) leading to ipatasertib treatment discontinuation occurring

in ≥2 patients were aspartate aminotransferase increased, alanine aminotransferase increased, autoimmune hepatitis.

- The proportion of patients with AEs leading to paclitaxel treatment discontinuation was 22.5%. AEs (by PT) leading to paclitaxel treatment discontinuation occurring in ≥2 of patients were neuropathy peripheral and polyneuropathy.
- The proportion of patients with AEs leading to atezolizumab treatment discontinuation was 13.7%. The AEs (by PT) leading to atezolizumab treatment discontinuation occurring in ≥2 of patients were autoimmune hepatitis, alanine aminotransferase increased, and aspartate aminotransferase increased.
- The incidence of selected AEs was consistent with known safety profile of ipatasertib, and in general were manageable and reversible. Selected AEs were reported in 99% of patients.

Pharmacokinetics

Concentrations of ipatasertib and its metabolite, G-037720, increased after multiple dosing compared with that following a single dose. This is consistent with what is expected for ipatasertib given its half-life and the once daily dosing regimen. The steady state plasma exposures of ipatasertib and G-037720 were comparable on Cycle 1 Day 15 and Cycle 3 Day 15. The variability of ipatasertib and G-037720 concentrations at each time point observed in this study is high, partially due to the wide window of time (time range) allowed for sample collection for PK analysis.

6. CONCLUSIONS

In Study CO40016, Cohorts A and B did not meet their primary endpoint: Ipatasertib in combination with paclitaxel did not demonstrate a statistically significant and clinically meaningful improvement in investigator-assessed PFS compared with paclitaxel alone in patients with *PIK3CA/AKT1/PTEN*-altered, locally advanced or metastatic TNBC or HR+/HER2- breast cancer. The final OS results were consistent with those of the primary endpoint, with no clinically meaningful benefit observed for ipatasertib in combination with paclitaxel over paclitaxel alone for both Cohorts A and B. The efficacy results from Cohort C (ipatasertib in combination with paclitaxel and atezolizumab) were consistent with the results in the ipatasertib and paclitaxel arm in Cohort A. For patient-reported GHS/QOL, the result of adding ipatasertib to paclitaxel and atezolizumab (Cohort C) was consistent with that of adding ipatasertib to paclitaxel alone (Cohorts A and B), such that it did not result in a detrimental effect to patients' overall HRQoL.

The safety profile of the combination of ipatasertib with either paclitaxel alone (Cohort A and B) or with atezolizumab and paclitaxel (Cohort C) was consistent with the known risks of each individual study treatment component. No new safety signals were identified.

7. REFERENCES

Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumours. Nature 2012;490:61–70.

Cardoso F, Costa A, Senkus E, et al. 3rd ESO-ESMO international consensus guidelines for Advanced Breast Cancer (ABC 3). Ann Oncol 2017;28:16–33.

Fayers PM, Aaronson NK, Bjordal K, et al. on behalf of the EORTC Quality of Life Group. The EORTC QLQ-C30 scoring manual (3rd ed). Brussels: European Organisation for Research and Treatment of Cancer, 2001.

Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136:E359–86.

Jemal A, Bray F, Center MM, et al. Global cancer statistics. Cancer J Clin 2011;61:69–90.

Lin K, Lin J, Wu WI, et al. An ATP-site on-off switch that restricts phosphatase accessibility of Akt. Sci Signal 2012;5:ra37.

Miles DW, Cameron D, Bondarenko I, et al. Bevacizumab plus paclitaxel versus placebo plus paclitaxel as first-line therapy for HER2-negative metastatic breast cancer (MERiDiAN): a double-blind placebo-controlled randomised phase III trial with prospective biomarker evaluation. Eur J Cancer 2017;70:146–155.

Miles DW, Diéras V, Cortés J, et al. First-line bevacizumab in combination with chemotherapy for HER2-negative metastatic breast cancer: pooled and subgroup analyses of data from 2447 patients. Ann Oncol 2013;24:2773–80.

[NCCN] National Comprehensive Cancer Network. NCCN guidelines: breast cancer, version 1 [resource on the Internet]. 2017 [cited 12 March 2017]. Available from: https://www.nccn.org/professionals/physician_gls/f_guidelines.asp#breast.

Osoba D, Rodrigues G, Myles J, et al. Interpreting the significance of changes in healthrelated quality of life score. J Clin Oncol 1998;16:139-44.

Robert NJ, Diéras V, Glaspy J, et al. RIBBON-1: randomized, double-blind, placebocontrolled, phase III trial of chemotherapy with or without bevacizumab for first-line treatment of human epidermal growth factor receptor 2-negative, locally recurrent or metastatic breast cancer. J Clin Oncol 2011;29:1252–60.

Rodler E, Korde L, Gralow J. Current treatment options in triple negative breast cancer. Breast Dis 2010;32:99–122.

Vuylsteke P, Huizing M, Petrakova K, et al. Pictilisib PI3Kinase inhibitor (a phosphatidylinositol 3-kinase [PI3K] inhibitor) plus paclitaxel for the treatment of hormone receptor-positive, HER2-negative, locally recurrent, or metastatic breast cancer: interim analysis of the multicentre, placebo-controlled, phase II randomised PEGGY study. Ann Oncol 2016;27:2059–66.

List of Referenced Studies

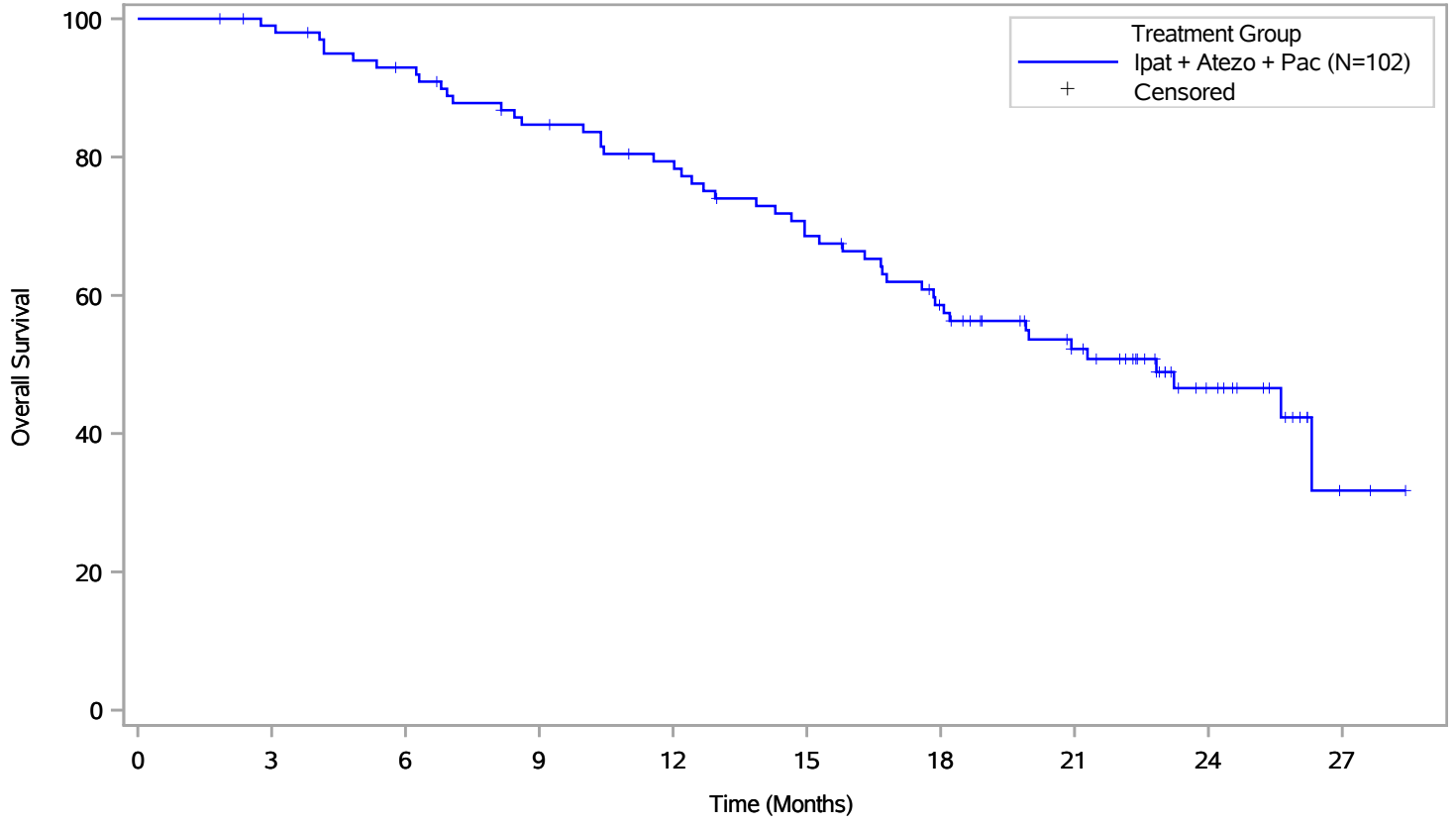
Final Clinical Study Report – Protocol No. GO29227 – A randomized, phase II, multicenter, placebo-controlled study of ipatasertib (GDC-0068), an inhibitor of Akt, in combination with paclitaxel as front-line treatment for patients with metastatic triple-negative breast cancer. Report No. 1099589. March, 2020.

Interim Clinical Study Report – Protocol No. GO27845 – A phase Ib, open-label, dose-escalation study of the safety and pharmacology of GDC-0068 in combination with docetaxel, fluoropyrimidine plus oxaliplatin, paclitaxel, or enzalutamide in patients with advanced solid tumors. Report No. 1074119. June 2017.

Primary Clinical Study Report: Study CO40016, (Cohort A–Triple Negative Breast Cancer). A double-blind, placebo-controlled, randomized phase III study of ipatasertib in combination with paclitaxel as a treatment for patients with *PIK3CA/AKT1/PTEN*-altered, locally advanced or metastatic, triple-negative breast cancer or hormone receptor–positive, HER2-negative breast cancer. Report No. 1101889. November 2020.

Primary Clinical Study Report: Study CO40016, (Cohort B-Hormone Receptor Positive, HER2-Negative Breast Cancer). A double-blind, placebo-controlled, randomized phase III study of ipatasertib in combination with paclitaxel as a treatment for patients with *PIK3CA/AKT1/PTEN*-altered, locally advanced or metastatic, triple-negative breast cancer or hormone receptor–positive, HER2-negative breast cancer. Report No 1100941. July, 2020.

Kaplan-Meier Plot of Overall Survival, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016



Patients remaining at risk										
Ipat + Atezo + Pac	102	99	91	81	74	63	51	37	17	2

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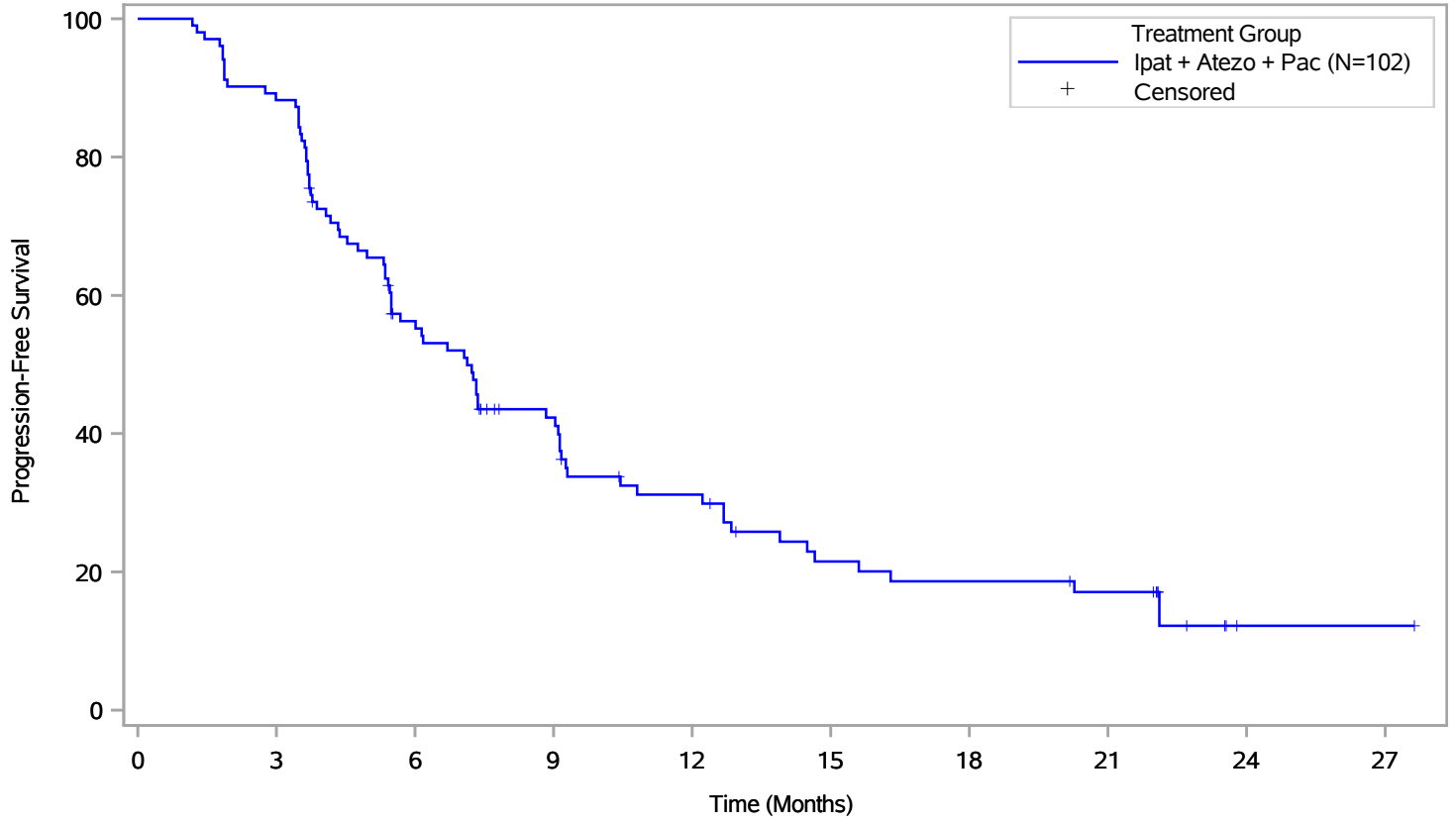
Kaplan-Meier Plot of Progression-Free Survival (Investigator), Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016



Patients remaining at risk										
Ipat + Atezo + Pac	102	90	53	35	24	15	13	11	1	1

Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

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Adverse Events, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one adverse event	84 (96.6%)	162 (97.6%)
Overall total number of events	976	2645
Gastrointestinal disorders		
Total number of patients with at least one adverse event	57 (65.5%)	151 (91.0%)
Total number of events	181	894
Diarrhoea	28 (32.2%)	141 (84.9%)
Nausea	22 (25.3%)	66 (39.8%)
Constipation	31 (35.6%)	49 (29.5%)
Vomiting	8 (9.2%)	54 (32.5%)
Abdominal pain upper	8 (9.2%)	16 (9.6%)
Stomatitis	6 (6.9%)	18 (10.8%)
Abdominal pain	5 (5.7%)	15 (9.0%)
Dyspepsia	4 (4.6%)	14 (8.4%)
Haemorrhoids	2 (2.3%)	5 (3.0%)
Abdominal discomfort	3 (3.4%)	3 (1.8%)
Flatulence	1 (1.1%)	5 (3.0%)
Abdominal distension	0	5 (3.0%)
Gastrooesophageal reflux disease	0	4 (2.4%)
Toothache	2 (2.3%)	2 (1.2%)
Periodontal disease	0	3 (1.8%)
Cheilitis	0	2 (1.2%)
Colitis	1 (1.1%)	1 (0.6%)
Dry mouth	1 (1.1%)	1 (0.6%)
Tongue ulceration	0	2 (1.2%)
Anal inflammation	0	1 (0.6%)
Chapped lips	0	1 (0.6%)
Dental caries	0	1 (0.6%)
Dysphagia	0	1 (0.6%)
Enteritis	0	1 (0.6%)
Food poisoning	1 (1.1%)	0
Gastritis	0	1 (0.6%)
Gastrointestinal pain	1 (1.1%)	0
Gingival pain	0	1 (0.6%)
Large intestine perforation	0	1 (0.6%)
Mouth ulceration	0	1 (0.6%)
Oesophagitis	1 (1.1%)	0
Pancreatitis	0	1 (0.6%)
Proctalgia	0	1 (0.6%)
Tongue oedema	0	1 (0.6%)
Upper gastrointestinal haemorrhage	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Nervous system disorders		
Total number of patients with at least one adverse event	59 (67.8%)	97 (58.4%)
Total number of events	100	214
Neuropathy peripheral	20 (23.0%)	39 (23.5%)
Peripheral sensory neuropathy	19 (21.8%)	32 (19.3%)
Headache	10 (11.5%)	28 (16.9%)
Dysgeusia	8 (9.2%)	10 (6.0%)
Dizziness	8 (9.2%)	6 (3.6%)
Polyneuropathy	7 (8.0%)	5 (3.0%)
Paraesthesia	2 (2.3%)	8 (4.8%)
Syncope	0	5 (3.0%)
Sciatica	1 (1.1%)	3 (1.8%)
Neurotoxicity	1 (1.1%)	2 (1.2%)
Tremor	1 (1.1%)	2 (1.2%)
Dysaesthesia	1 (1.1%)	1 (0.6%)
Memory impairment	0	2 (1.2%)
Peripheral motor neuropathy	0	2 (1.2%)
Taste disorder	1 (1.1%)	1 (0.6%)
Ageusia	0	1 (0.6%)
Altered state of consciousness	0	1 (0.6%)
Anosmia	1 (1.1%)	0
Ataxia	0	1 (0.6%)
Balance disorder	1 (1.1%)	0
Cranial nerve disorder	0	1 (0.6%)
Disturbance in attention	1 (1.1%)	0
Encephalopathy	0	1 (0.6%)
Head discomfort	1 (1.1%)	0
Hemiparaesthesia	1 (1.1%)	0
Hypersomnia	1 (1.1%)	0
Loss of consciousness	0	1 (0.6%)
Migraine	0	1 (0.6%)
Neuralgia	0	1 (0.6%)
Paralysis recurrent laryngeal nerve	0	1 (0.6%)
Parosmia	0	1 (0.6%)
Presyncope	0	1 (0.6%)
Radicular pain	0	1 (0.6%)
Radiculopathy	0	1 (0.6%)
Seizure	0	1 (0.6%)
Stupor	1 (1.1%)	0
Toxic neuropathy	0	1 (0.6%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Skin and subcutaneous tissue disorders		
Total number of patients with at least one adverse event	52 (59.8%)	104 (62.7%)
Total number of events	104	202
Alopecia	38 (43.7%)	78 (47.0%)
Rash	11 (12.6%)	26 (15.7%)
Pruritus	7 (8.0%)	15 (9.0%)
Nail discolouration	4 (4.6%)	6 (3.6%)
Dermatitis acneiform	1 (1.1%)	7 (4.2%)
Erythema	5 (5.7%)	3 (1.8%)
Dermatitis allergic	0	6 (3.6%)
Eczema	3 (3.4%)	3 (1.8%)
Onychoclasis	3 (3.4%)	2 (1.2%)
Onycholysis	1 (1.1%)	4 (2.4%)
Rash maculo-papular	0	5 (3.0%)
Dermatitis	2 (2.3%)	2 (1.2%)
Dry skin	4 (4.6%)	0
Nail disorder	2 (2.3%)	2 (1.2%)
Hyperhidrosis	1 (1.1%)	2 (1.2%)
Nail dystrophy	1 (1.1%)	2 (1.2%)
Dermatitis contact	0	2 (1.2%)
Hand dermatitis	1 (1.1%)	1 (0.6%)
Nail toxicity	1 (1.1%)	1 (0.6%)
Onychomadesis	2 (2.3%)	0
Skin hyperpigmentation	0	2 (1.2%)
Acne	0	1 (0.6%)
Blister	1 (1.1%)	0
Dermatitis diaper	0	1 (0.6%)
Drug eruption	0	1 (0.6%)
Erythema multiforme	0	1 (0.6%)
Haemorrhage subcutaneous	1 (1.1%)	0
Hyperkeratosis	1 (1.1%)	0
Nail ridging	1 (1.1%)	0
Onychalgia	1 (1.1%)	0
Onychomalacia	1 (1.1%)	0
Pain of skin	1 (1.1%)	0
Palmar-plantar erythrodysaesthesia syndrome	0	1 (0.6%)
Pigmentation disorder	1 (1.1%)	0
Rash papular	1 (1.1%)	0
Scab	0	1 (0.6%)
Skin exfoliation	0	1 (0.6%)
Skin ulcer	1 (1.1%)	0
Solar dermatitis	0	1 (0.6%)
Urticaria	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
General disorders and administration site conditions		
Total number of patients with at least one adverse event	43 (49.4%)	96 (57.8%)
Total number of events	72	188
Fatigue	15 (17.2%)	31 (18.7%)
Asthenia	10 (11.5%)	35 (21.1%)
Oedema peripheral	7 (8.0%)	18 (10.8%)
Pyrexia	6 (6.9%)	16 (9.6%)
Mucosal inflammation	2 (2.3%)	11 (6.6%)
Influenza like illness	1 (1.1%)	8 (4.8%)
Oedema	2 (2.3%)	5 (3.0%)
Pain	1 (1.1%)	6 (3.6%)
Non-cardiac chest pain	2 (2.3%)	4 (2.4%)
Chest pain	1 (1.1%)	4 (2.4%)
Malaise	2 (2.3%)	3 (1.8%)
Axillary pain	2 (2.3%)	2 (1.2%)
Chills	1 (1.1%)	2 (1.2%)
Face oedema	1 (1.1%)	2 (1.2%)
Chest discomfort	2 (2.3%)	0
Infusion site extravasation	2 (2.3%)	0
Peripheral swelling	1 (1.1%)	1 (0.6%)
Cyst	1 (1.1%)	0
Discomfort	0	1 (0.6%)
Generalised oedema	0	1 (0.6%)
Hyperthermia	0	1 (0.6%)
Hypothermia	1 (1.1%)	0
Ill-defined disorder	1 (1.1%)	0
Infusion site pain	0	1 (0.6%)
Localised oedema	0	1 (0.6%)
Mucosal dryness	1 (1.1%)	0
Swelling face	0	1 (0.6%)
Tenderness	1 (1.1%)	0
Treatment noncompliance	0	1 (0.6%)
Infections and infestations		
Total number of patients with at least one adverse event	29 (33.3%)	81 (48.8%)
Total number of events	60	144
Upper respiratory tract infection	3 (3.4%)	12 (7.2%)
Urinary tract infection	2 (2.3%)	13 (7.8%)
Nasopharyngitis	3 (3.4%)	11 (6.6%)
Cystitis	3 (3.4%)	8 (4.8%)
Pneumonia	5 (5.7%)	6 (3.6%)
COVID-19	0	8 (4.8%)
Conjunctivitis	1 (1.1%)	4 (2.4%)
Pharyngitis	2 (2.3%)	3 (1.8%)
Bronchitis	1 (1.1%)	3 (1.8%)
Fungal skin infection	1 (1.1%)	3 (1.8%)
Oral candidiasis	3 (3.4%)	1 (0.6%)
Oral herpes	0	4 (2.4%)
Herpes zoster	1 (1.1%)	2 (1.2%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Influenza	2 (2.3%)	1 (0.6%)
Nail infection	0	3 (1.8%)
Parasitic gastroenteritis	1 (1.1%)	2 (1.2%)
Rash pustular	0	3 (1.8%)
Rhinitis	0	3 (1.8%)
Sinusitis	0	3 (1.8%)
Skin infection	2 (2.3%)	1 (0.6%)
Cellulitis	1 (1.1%)	1 (0.6%)
Device related infection	1 (1.1%)	1 (0.6%)
Erysipelas	1 (1.1%)	1 (0.6%)
Laryngitis	1 (1.1%)	1 (0.6%)
Mastitis	0	2 (1.2%)
Paronychia	0	2 (1.2%)
Respiratory tract infection viral	0	2 (1.2%)
Tooth infection	1 (1.1%)	1 (0.6%)
Viral infection	1 (1.1%)	1 (0.6%)
Vulvovaginal candidiasis	0	2 (1.2%)
Abscess jaw	0	1 (0.6%)
Acarodermatitis	1 (1.1%)	0
Anal abscess	0	1 (0.6%)
Bacterial infection	0	1 (0.6%)
Bronchiolitis	0	1 (0.6%)
COVID-19 pneumonia	0	1 (0.6%)
Chronic sinusitis	0	1 (0.6%)
Ear, nose and throat infection	0	1 (0.6%)
Empyema	1 (1.1%)	0
Enteritis infectious	0	1 (0.6%)
Erythrasma	0	1 (0.6%)
Folliculitis	0	1 (0.6%)
Fungal infection	1 (1.1%)	0
Fungal oesophagitis	1 (1.1%)	0
Furuncle	0	1 (0.6%)
Helicobacter infection	0	1 (0.6%)
Herpes simplex	1 (1.1%)	0
Hordeolum	0	1 (0.6%)
Lower respiratory tract infection	1 (1.1%)	0
Mucosal infection	1 (1.1%)	0
Periodontitis	0	1 (0.6%)
Peritonitis	0	1 (0.6%)
Pneumonia klebsiella	0	1 (0.6%)
Pustule	1 (1.1%)	0
Respiratory tract infection	1 (1.1%)	0
Subglottic laryngitis	1 (1.1%)	0
Tinea pedis	0	1 (0.6%)
Tonsillitis	0	1 (0.6%)
Tooth abscess	1 (1.1%)	0
Vaginal abscess	1 (1.1%)	0
Vaginal infection	1 (1.1%)	0
Vascular access site infection	0	1 (0.6%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Vascular device infection	1 (1.1%)	0
Viral sinusitis	0	1 (0.6%)
Vulvitis	1 (1.1%)	0
Vulvovaginal mycotic infection	1 (1.1%)	0
Blood and lymphatic system disorders		
Total number of patients with at least one adverse event	41 (47.1%)	67 (40.4%)
Total number of events	96	195
Anaemia	23 (26.4%)	44 (26.5%)
Neutropenia	21 (24.1%)	28 (16.9%)
Leukopenia	4 (4.6%)	7 (4.2%)
Lymphopenia	2 (2.3%)	3 (1.8%)
Thrombocytopenia	4 (4.6%)	1 (0.6%)
Febrile neutropenia	0	4 (2.4%)
Leukocytosis	1 (1.1%)	1 (0.6%)
Thrombocytosis	0	2 (1.2%)
Anaemia macrocytic	0	1 (0.6%)
Eosinophilia	0	1 (0.6%)
Lymph node pain	0	1 (0.6%)

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Adverse Events, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Investigations		
Total number of patients with at least one adverse event	24 (27.6%)	83 (50.0%)
Total number of events	91	230
Neutrophil count decreased	10 (11.5%)	22 (13.3%)
Alanine aminotransferase increased	7 (8.0%)	23 (13.9%)
Aspartate aminotransferase increased	6 (6.9%)	18 (10.8%)
White blood cell count decreased	7 (8.0%)	11 (6.6%)
Weight decreased	3 (3.4%)	12 (7.2%)
Blood lactate dehydrogenase increased	4 (4.6%)	7 (4.2%)
Blood alkaline phosphatase increased	1 (1.1%)	9 (5.4%)
Blood cholesterol increased	2 (2.3%)	6 (3.6%)
Blood creatinine increased	0	6 (3.6%)
Blood urea increased	3 (3.4%)	3 (1.8%)
Gamma-glutamyltransferase increased	1 (1.1%)	4 (2.4%)
Lipase increased	0	5 (3.0%)
Lymphocyte count decreased	2 (2.3%)	2 (1.2%)
Weight increased	1 (1.1%)	3 (1.8%)
Amylase increased	1 (1.1%)	2 (1.2%)
Blood phosphorus increased	1 (1.1%)	1 (0.6%)
Haemoglobin decreased	0	2 (1.2%)
Low density lipoprotein increased	1 (1.1%)	1 (0.6%)
Blood bilirubin increased	0	1 (0.6%)
Blood calcium decreased	0	1 (0.6%)
Blood chloride decreased	1 (1.1%)	0
Blood glucose increased	1 (1.1%)	0
Blood magnesium decreased	0	1 (0.6%)
Blood pressure increased	0	1 (0.6%)
Blood triglycerides increased	0	1 (0.6%)
Body temperature increased	0	1 (0.6%)
Eastern Cooperative Oncology Group performance status worsened	0	1 (0.6%)
Electrocardiogram QT prolonged	1 (1.1%)	0
Glycosylated haemoglobin abnormal	0	1 (0.6%)
Haematocrit decreased	1 (1.1%)	0
Influenza A virus test positive	0	1 (0.6%)
Platelet count decreased	0	1 (0.6%)
Platelet count increased	0	1 (0.6%)
Vitamin B12 decreased	0	1 (0.6%)
White blood cell count increased	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Metabolism and nutrition disorders		
Total number of patients with at least one adverse event	25 (28.7%)	74 (44.6%)
Total number of events	55	144
Hyperglycaemia	9 (10.3%)	31 (18.7%)
Decreased appetite	10 (11.5%)	29 (17.5%)
Hypertriglyceridaemia	2 (2.3%)	9 (5.4%)
Hypokalaemia	3 (3.4%)	5 (3.0%)
Hypoalbuminaemia	3 (3.4%)	4 (2.4%)
Hypomagnesaemia	1 (1.1%)	6 (3.6%)
Hyperkalaemia	1 (1.1%)	3 (1.8%)
Hyponatraemia	2 (2.3%)	2 (1.2%)
Hypophosphataemia	3 (3.4%)	1 (0.6%)
Hypercholesterolaemia	1 (1.1%)	2 (1.2%)
Dyslipidaemia	0	2 (1.2%)
Electrolyte imbalance	0	2 (1.2%)
Glucose tolerance impaired	0	2 (1.2%)
Hyperamylasaemia	1 (1.1%)	1 (0.6%)
Hypocalcaemia	1 (1.1%)	1 (0.6%)
Increased appetite	1 (1.1%)	1 (0.6%)
Dehydration	0	1 (0.6%)
Diabetes mellitus	0	1 (0.6%)
Food aversion	1 (1.1%)	0
Gout	0	1 (0.6%)
Hypercreatininaemia	0	1 (0.6%)
Hyperlipasaemia	1 (1.1%)	0
Hyperlipidaemia	0	1 (0.6%)
Lipoedema	0	1 (0.6%)
Tumour lysis syndrome	1 (1.1%)	0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Musculoskeletal and connective tissue disorders		
Total number of patients with at least one adverse event	34 (39.1%)	54 (32.5%)
Total number of events	58	118
Arthralgia	12 (13.8%)	16 (9.6%)
Back pain	9 (10.3%)	16 (9.6%)
Myalgia	5 (5.7%)	16 (9.6%)
Pain in extremity	4 (4.6%)	14 (8.4%)
Bone pain	0	7 (4.2%)
Muscle spasms	1 (1.1%)	4 (2.4%)
Musculoskeletal pain	3 (3.4%)	2 (1.2%)
Neck pain	2 (2.3%)	3 (1.8%)
Muscular weakness	3 (3.4%)	1 (0.6%)
Musculoskeletal chest pain	1 (1.1%)	3 (1.8%)
Spinal pain	0	3 (1.8%)
Spinal disorder	1 (1.1%)	1 (0.6%)
Flank pain	1 (1.1%)	0
Intervertebral disc compression	1 (1.1%)	0
Joint swelling	0	1 (0.6%)
Limb discomfort	0	1 (0.6%)
Myosclerosis	1 (1.1%)	0
Osteoarthritis	0	1 (0.6%)
Osteonecrosis of jaw	1 (1.1%)	0
Pathological fracture	0	1 (0.6%)
Spondylolysis	0	1 (0.6%)
Tendon disorder	1 (1.1%)	0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one adverse event	27 (31.0%)	48 (28.9%)
Total number of events	52	96
Cough	10 (11.5%)	14 (8.4%)
Dyspnoea	7 (8.0%)	8 (4.8%)
Epistaxis	3 (3.4%)	12 (7.2%)
Oropharyngeal pain	0	13 (7.8%)
Dysphonia	3 (3.4%)	3 (1.8%)
Nasal congestion	2 (2.3%)	4 (2.4%)
Productive cough	1 (1.1%)	5 (3.0%)
Rhinitis allergic	3 (3.4%)	3 (1.8%)
Dyspnoea exertional	3 (3.4%)	2 (1.2%)
Pleural effusion	2 (2.3%)	1 (0.6%)
Pulmonary embolism	0	3 (1.8%)
Rhinorrhoea	0	3 (1.8%)
Haemoptysis	1 (1.1%)	0
Hypoxia	1 (1.1%)	0
Laryngeal inflammation	0	1 (0.6%)
Lung infiltration	0	1 (0.6%)
Nasal dryness	0	1 (0.6%)
Nasal inflammation	1 (1.1%)	0
Nasal mucosa atrophy	1 (1.1%)	0
Pneumonitis	0	1 (0.6%)
Pneumothorax	1 (1.1%)	0
Pulmonary hypertension	0	1 (0.6%)
Respiratory disorder	1 (1.1%)	0
Rhinalgia	0	1 (0.6%)
Tachypnoea	0	1 (0.6%)
Throat tightness	1 (1.1%)	0
Upper-airway cough syndrome	0	1 (0.6%)
Wheezing	1 (1.1%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Injury, poisoning and procedural complications		
Total number of patients with at least one adverse event	15 (17.2%)	24 (14.5%)
Total number of events	27	34
Accidental overdose	3 (3.4%)	6 (3.6%)
Fall	2 (2.3%)	3 (1.8%)
Product dose omission issue	2 (2.3%)	3 (1.8%)
Vascular access site pain	3 (3.4%)	1 (0.6%)
Infusion related reaction	1 (1.1%)	2 (1.2%)
Ligament sprain	1 (1.1%)	1 (0.6%)
Procedural pain	1 (1.1%)	1 (0.6%)
Spinal fracture	1 (1.1%)	1 (0.6%)
Tooth fracture	0	2 (1.2%)
Wound	0	2 (1.2%)
Brachial plexus injury	1 (1.1%)	0
Eschar	0	1 (0.6%)
Extra dose administered	0	1 (0.6%)
Fracture	0	1 (0.6%)
Inappropriate schedule of product administration	1 (1.1%)	0
Intentional product misuse	0	1 (0.6%)
Radiation inflammation	0	1 (0.6%)
Radiation pneumonitis	1 (1.1%)	0
Recall phenomenon	1 (1.1%)	0
Rib fracture	0	1 (0.6%)
Skin abrasion	0	1 (0.6%)
Skin laceration	1 (1.1%)	0
Splinter	0	1 (0.6%)
Thermal burn	0	1 (0.6%)
Toxicity to various agents	1 (1.1%)	0
Psychiatric disorders		
Total number of patients with at least one adverse event	11 (12.6%)	26 (15.7%)
Total number of events	12	27
Insomnia	5 (5.7%)	10 (6.0%)
Anxiety	2 (2.3%)	8 (4.8%)
Depression	1 (1.1%)	5 (3.0%)
Depressed mood	0	2 (1.2%)
Dyssomnia	0	1 (0.6%)
Mental disorder	1 (1.1%)	0
Panic attack	1 (1.1%)	0
Restlessness	1 (1.1%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Vascular disorders		
Total number of patients with at least one adverse event	9 (10.3%)	26 (15.7%)
Total number of events	11	49
Hypertension	3 (3.4%)	6 (3.6%)
Lymphoedema	0	7 (4.2%)
Hypotension	2 (2.3%)	3 (1.8%)
Flushing	1 (1.1%)	3 (1.8%)
Phlebitis	2 (2.3%)	2 (1.2%)
Hot flush	0	3 (1.8%)
Venous thrombosis	1 (1.1%)	1 (0.6%)
Deep vein thrombosis	1 (1.1%)	0
Embolism	0	1 (0.6%)
Haematoma	0	1 (0.6%)
Hyperaemia	0	1 (0.6%)
Hypertensive crisis	0	1 (0.6%)
Hypertensive urgency	0	1 (0.6%)
Thrombophlebitis	0	1 (0.6%)
Varicose vein	0	1 (0.6%)
Vasculitis	0	1 (0.6%)
Venous occlusion	0	1 (0.6%)
Venous thrombosis limb	0	1 (0.6%)
Eye disorders		
Total number of patients with at least one adverse event	7 (8.0%)	22 (13.3%)
Total number of events	10	27
Vision blurred	1 (1.1%)	4 (2.4%)
Dry eye	0	3 (1.8%)
Blepharitis	1 (1.1%)	1 (0.6%)
Lacrimation increased	0	2 (1.2%)
Ocular hyperaemia	2 (2.3%)	0
Visual acuity reduced	0	2 (1.2%)
Visual impairment	1 (1.1%)	1 (0.6%)
Chalazion	1 (1.1%)	0
Conjunctival haemorrhage	0	1 (0.6%)
Conjunctival irritation	0	1 (0.6%)
Conjunctival oedema	0	1 (0.6%)
Conjunctivitis allergic	0	1 (0.6%)
Cystoid macular oedema	1 (1.1%)	0
Epiretinal membrane	0	1 (0.6%)
Eye disorder	1 (1.1%)	0
Eye pain	0	1 (0.6%)
Eye pruritus	0	1 (0.6%)
Glaucoma	0	1 (0.6%)
Macular oedema	0	1 (0.6%)
Periorbital oedema	0	1 (0.6%)
Periorbital swelling	0	1 (0.6%)
Photopsia	1 (1.1%)	0
Retinal vascular disorder	1 (1.1%)	0
Strabismus	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Renal and urinary disorders		
Total number of patients with at least one adverse event	4 (4.6%)	16 (9.6%)
Total number of events	6	21
Dysuria	2 (2.3%)	7 (4.2%)
Haematuria	1 (1.1%)	1 (0.6%)
Proteinuria	1 (1.1%)	1 (0.6%)
Anuria	0	1 (0.6%)
Haemoglobinuria	1 (1.1%)	0
Oliguria	0	1 (0.6%)
Renal failure	0	1 (0.6%)
Renal impairment	0	1 (0.6%)
Strangury	0	1 (0.6%)
Tubulointerstitial nephritis	0	1 (0.6%)
Urinary incontinence	0	1 (0.6%)
Urinary retention	0	1 (0.6%)
Urine flow decreased	0	1 (0.6%)
Reproductive system and breast disorders		
Total number of patients with at least one adverse event	4 (4.6%)	14 (8.4%)
Total number of events	4	16
Breast pain	3 (3.4%)	9 (5.4%)
Amenorrhoea	0	1 (0.6%)
Breast discomfort	1 (1.1%)	0
Menopausal symptoms	0	1 (0.6%)
Pelvic pain	0	1 (0.6%)
Vaginal discharge	0	1 (0.6%)
Vulvovaginal burning sensation	0	1 (0.6%)
Ear and labyrinth disorders		
Total number of patients with at least one adverse event	2 (2.3%)	13 (7.8%)
Total number of events	2	18
Vertigo	1 (1.1%)	9 (5.4%)
Ear pain	1 (1.1%)	2 (1.2%)
Tinnitus	0	2 (1.2%)
Cerumen impaction	0	1 (0.6%)
Hypoacusis	0	1 (0.6%)
Cardiac disorders		
Total number of patients with at least one adverse event	6 (6.9%)	5 (3.0%)
Total number of events	8	5
Sinus tachycardia	2 (2.3%)	2 (1.2%)
Tachycardia	3 (3.4%)	0
Atrial fibrillation	1 (1.1%)	1 (0.6%)
Bradycardia	1 (1.1%)	0
Cardiopulmonary failure	0	1 (0.6%)
Extrasystoles	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Immune system disorders		
Total number of patients with at least one adverse event	6 (6.9%)	5 (3.0%)
Total number of events	7	10
Hypersensitivity	5 (5.7%)	5 (3.0%)
Anaphylactic shock	1 (1.1%)	0
Drug hypersensitivity	0	1 (0.6%)
Seasonal allergy	1 (1.1%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Total number of patients with at least one adverse event	4 (4.6%)	7 (4.2%)
Total number of events	7	9
Cancer pain	1 (1.1%)	2 (1.2%)
Infected neoplasm	1 (1.1%)	1 (0.6%)
Gastric cancer	1 (1.1%)	0
Lymphangiosis carcinomatosa	1 (1.1%)	0
Schwannoma	0	1 (0.6%)
Tumour haemorrhage	0	1 (0.6%)
Tumour necrosis	0	1 (0.6%)
Tumour pain	1 (1.1%)	0
Tumour ulceration	0	1 (0.6%)
Hepatobiliary disorders		
Total number of patients with at least one adverse event	3 (3.4%)	1 (0.6%)
Total number of events	12	1
Hyperbilirubinaemia	3 (3.4%)	0
Cholecystitis acute	0	1 (0.6%)
No Coding available		
Total number of patients with at least one adverse event	1 (1.1%)	1 (0.6%)
Total number of events	1	2
No Coding available	1 (1.1%)	1 (0.6%)
Product issues		
Total number of patients with at least one adverse event	0	1 (0.6%)
Total number of events	0	1
Device occlusion	0	1 (0.6%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Adverse Events, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one such adverse event	74 (98.7%)	144 (99.3%)
Overall total number of events	1195	2722

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	56 (74.7%)	139 (95.9%)
Total number of events	190	838
Diarrhoea	30 (40.0%)	126 (86.9%)
Nausea	17 (22.7%)	60 (41.4%)
Constipation	26 (34.7%)	42 (29.0%)
Vomiting	6 (8.0%)	45 (31.0%)
Stomatitis	6 (8.0%)	16 (11.0%)
Abdominal pain upper	5 (6.7%)	15 (10.3%)
Abdominal pain	7 (9.3%)	12 (8.3%)
Dyspepsia	4 (5.3%)	9 (6.2%)
Flatulence	4 (5.3%)	7 (4.8%)
Gastrooesophageal reflux disease	4 (5.3%)	4 (2.8%)
Mouth ulceration	1 (1.3%)	5 (3.4%)
Abdominal distension	1 (1.3%)	4 (2.8%)
Gastritis	2 (2.7%)	3 (2.1%)
Toothache	2 (2.7%)	3 (2.1%)
Abdominal discomfort	1 (1.3%)	3 (2.1%)
Aphthous ulcer	0	4 (2.8%)
Haemorrhoids	0	4 (2.8%)
Haematochezia	1 (1.3%)	2 (1.4%)
Oral pain	0	3 (2.1%)
Ascites	1 (1.3%)	1 (0.7%)
Chronic gastritis	0	2 (1.4%)
Dry mouth	0	2 (1.4%)
Enterocolitis	0	2 (1.4%)
Paraesthesia oral	0	2 (1.4%)
Abdominal hernia	0	1 (0.7%)
Abdominal pain lower	1 (1.3%)	0
Anal haemorrhage	0	1 (0.7%)
Angular cheilitis	0	1 (0.7%)
Dental caries	1 (1.3%)	0
Dental discomfort	0	1 (0.7%)
Dental necrosis	0	1 (0.7%)
Eructation	0	1 (0.7%)
Faeces discoloured	0	1 (0.7%)
Faeces soft	0	1 (0.7%)
Food poisoning	0	1 (0.7%)
Hyperchlorhydria	0	1 (0.7%)
Hypoaesthesia oral	0	1 (0.7%)
Intestinal obstruction	0	1 (0.7%)
Lip dry	0	1 (0.7%)
Odynophagia	0	1 (0.7%)
Periodontal disease	1 (1.3%)	0
Proctalgia	0	1 (0.7%)
Tongue erythema	0	1 (0.7%)
Tongue exfoliation	0	1 (0.7%)
Tongue ulceration	0	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Nervous system disorders		
Total number of patients with at least one such adverse event	54 (72.0%)	110 (75.9%)
Total number of events	95	214
Neuropathy peripheral	12 (16.0%)	46 (31.7%)
Peripheral sensory neuropathy	23 (30.7%)	23 (15.9%)
Headache	8 (10.7%)	24 (16.6%)
Paraesthesia	6 (8.0%)	13 (9.0%)
Polyneuropathy	6 (8.0%)	12 (8.3%)
Dysgeusia	4 (5.3%)	11 (7.6%)
Dizziness	3 (4.0%)	10 (6.9%)
Neurotoxicity	2 (2.7%)	3 (2.1%)
Hypoaesthesia	2 (2.7%)	2 (1.4%)
Peripheral motor neuropathy	0	4 (2.8%)
Amnesia	0	2 (1.4%)
Disturbance in attention	1 (1.3%)	1 (0.7%)
Lethargy	1 (1.3%)	1 (0.7%)
Post herpetic neuralgia	0	2 (1.4%)
Radiculopathy	1 (1.3%)	1 (0.7%)
Sciatica	1 (1.3%)	1 (0.7%)
Taste disorder	0	2 (1.4%)
Anosmia	0	1 (0.7%)
Ataxia	0	1 (0.7%)
Cerebral ischaemia	0	1 (0.7%)
Cerebrovascular accident	0	1 (0.7%)
Cognitive disorder	0	1 (0.7%)
Dysaesthesia	1 (1.3%)	0
Epilepsy	0	1 (0.7%)
Facial paralysis	0	1 (0.7%)
Head discomfort	0	1 (0.7%)
Hypertonia	0	1 (0.7%)
Hypotonia	1 (1.3%)	0
Memory impairment	1 (1.3%)	0
Muscle spasticity	1 (1.3%)	0
Muscle tone disorder	1 (1.3%)	0
Neuritis	0	1 (0.7%)
Radicular pain	1 (1.3%)	0
Somnolence	0	1 (0.7%)
Tension headache	0	1 (0.7%)
Skin and subcutaneous tissue disorders		
Total number of patients with at least one such adverse event	53 (70.7%)	106 (73.1%)
Total number of events	115	259
Alopecia	44 (58.7%)	75 (51.7%)
Rash	9 (12.0%)	31 (21.4%)
Pruritus	3 (4.0%)	15 (10.3%)
Nail discolouration	8 (10.7%)	9 (6.2%)
Rash maculo-papular	4 (5.3%)	7 (4.8%)
Dry skin	5 (6.7%)	5 (3.4%)
Erythema	3 (4.0%)	5 (3.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Nail disorder	3 (4.0%)	3 (2.1%)
Onycholysis	1 (1.3%)	5 (3.4%)
Dermatitis acneiform	2 (2.7%)	3 (2.1%)
Dermatitis	1 (1.3%)	3 (2.1%)
Dermatitis contact	1 (1.3%)	3 (2.1%)
Nail dystrophy	3 (4.0%)	1 (0.7%)
Onychomadesis	0	4 (2.8%)
Dermatitis allergic	2 (2.7%)	1 (0.7%)
Dermatitis bullous	1 (1.3%)	2 (1.4%)
Drug eruption	0	3 (2.1%)
Eczema	0	3 (2.1%)
Palmar-plantar erythrodysaesthesia syndrome	1 (1.3%)	2 (1.4%)
Urticaria	0	3 (2.1%)
Eczema asteatotic	0	2 (1.4%)
Nail ridging	1 (1.3%)	1 (0.7%)
Onychoclasis	1 (1.3%)	1 (0.7%)
Photosensitivity reaction	0	2 (1.4%)
Skin disorder	0	2 (1.4%)
Skin hyperpigmentation	0	2 (1.4%)
Skin lesion	0	2 (1.4%)
Skin ulcer	2 (2.7%)	0
Blister	1 (1.3%)	0
Butterfly rash	0	1 (0.7%)
Dermal cyst	1 (1.3%)	0
Erythema multiforme	0	1 (0.7%)
Hyperhidrosis	0	1 (0.7%)
Ingrowing nail	0	1 (0.7%)
Nail bed inflammation	0	1 (0.7%)
Nail toxicity	0	1 (0.7%)
Onychalgia	1 (1.3%)	0
Pain of skin	0	1 (0.7%)
Papule	0	1 (0.7%)
Periarticular thenar erythema with onycholysis	1 (1.3%)	0
Polymorphic light eruption	0	1 (0.7%)
Rash erythematous	0	1 (0.7%)
Rash papular	0	1 (0.7%)
Rash pruritic	0	1 (0.7%)
Sclerema	1 (1.3%)	0
Skin discolouration	0	1 (0.7%)
Skin exfoliation	0	1 (0.7%)
Skin reaction	1 (1.3%)	0
Stasis dermatitis	0	1 (0.7%)
Urticaria contact	1 (1.3%)	0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	47 (62.7%)	91 (62.8%)
Total number of events	103	206
Fatigue	19 (25.3%)	29 (20.0%)
Asthenia	13 (17.3%)	27 (18.6%)
Oedema peripheral	14 (18.7%)	21 (14.5%)
Pyrexia	4 (5.3%)	23 (15.9%)
Oedema	4 (5.3%)	9 (6.2%)
Mucosal inflammation	3 (4.0%)	8 (5.5%)
Chest pain	2 (2.7%)	6 (4.1%)
Influenza like illness	1 (1.3%)	7 (4.8%)
Malaise	3 (4.0%)	5 (3.4%)
Chest discomfort	1 (1.3%)	4 (2.8%)
Pain	1 (1.3%)	4 (2.8%)
Peripheral swelling	2 (2.7%)	2 (1.4%)
Treatment noncompliance	0	3 (2.1%)
Chills	0	2 (1.4%)
Face oedema	0	2 (1.4%)
Generalised oedema	0	2 (1.4%)
Infusion site extravasation	1 (1.3%)	1 (0.7%)
Catheter site erythema	0	1 (0.7%)
Death	0	1 (0.7%)
Extravasation	0	1 (0.7%)
Feeling drunk	1 (1.3%)	0
Gait disturbance	1 (1.3%)	0
General physical health deterioration	0	1 (0.7%)
Hyperthermia	1 (1.3%)	0
Hypothermia	1 (1.3%)	0
Localised oedema	0	1 (0.7%)
Non-cardiac chest pain	0	1 (0.7%)
Swelling face	0	1 (0.7%)
Thirst	0	1 (0.7%)
Infections and infestations		
Total number of patients with at least one such adverse event	42 (56.0%)	76 (52.4%)
Total number of events	81	171
Nasopharyngitis	7 (9.3%)	19 (13.1%)
Upper respiratory tract infection	7 (9.3%)	14 (9.7%)
Urinary tract infection	5 (6.7%)	16 (11.0%)
Cystitis	6 (8.0%)	7 (4.8%)
Pneumonia	4 (5.3%)	6 (4.1%)
Influenza	2 (2.7%)	6 (4.1%)
Paronychia	1 (1.3%)	7 (4.8%)
Pharyngitis	2 (2.7%)	5 (3.4%)
Bronchitis	2 (2.7%)	4 (2.8%)
Herpes zoster	1 (1.3%)	5 (3.4%)
Rhinitis	0	6 (4.1%)
Cellulitis	2 (2.7%)	3 (2.1%)
Folliculitis	1 (1.3%)	4 (2.8%)

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Conjunctivitis	2 (2.7%)	2 (1.4%)
Gingivitis	1 (1.3%)	2 (1.4%)
Lower respiratory tract infection	0	3 (2.1%)
Oral herpes	0	3 (2.1%)
Sinusitis	0	3 (2.1%)
Vaginal infection	1 (1.3%)	2 (1.4%)
COVID-19	1 (1.3%)	1 (0.7%)
Erysipelas	1 (1.3%)	1 (0.7%)
Escherichia urinary tract infection	1 (1.3%)	1 (0.7%)
Furuncle	0	2 (1.4%)
Respiratory tract infection	0	2 (1.4%)
Respiratory tract infection viral	2 (2.7%)	0
Skin infection	1 (1.3%)	1 (0.7%)
Tonsillitis	1 (1.3%)	1 (0.7%)
Tooth abscess	2 (2.7%)	0
Tracheitis	2 (2.7%)	0
Wound infection	1 (1.3%)	1 (0.7%)
Abdominal abscess	0	1 (0.7%)
Appendicitis	0	1 (0.7%)
Candida infection	1 (1.3%)	0
Colonic abscess	1 (1.3%)	0
Diarrhoea infectious	0	1 (0.7%)
Enterovirus infection	1 (1.3%)	0
Fungal skin infection	0	1 (0.7%)
Herpes ophthalmic	0	1 (0.7%)
Herpes simplex	0	1 (0.7%)
Herpes virus infection	0	1 (0.7%)
Hordeolum	0	1 (0.7%)
Infection	0	1 (0.7%)
Laryngitis	0	1 (0.7%)
Laryngitis fungal	1 (1.3%)	0
Lymphangitis	1 (1.3%)	0
Nail infection	0	1 (0.7%)
Nasal vestibulitis	1 (1.3%)	0
Onychomycosis	1 (1.3%)	0
Oral infection	1 (1.3%)	0
Otitis externa	0	1 (0.7%)
Otitis media acute	0	1 (0.7%)
Periodontitis	0	1 (0.7%)
Pharyngotonsillitis	1 (1.3%)	0
Pulpitis dental	0	1 (0.7%)
Sepsis	1 (1.3%)	0
Tinea infection	1 (1.3%)	0
Tinea pedis	0	1 (0.7%)
Tracheobronchitis	1 (1.3%)	0
Vascular access site infection	0	1 (0.7%)
Viral infection	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Musculoskeletal and connective tissue disorders		
Total number of patients with at least one such adverse event	39 (52.0%)	69 (47.6%)
Total number of events	68	157
Arthralgia	10 (13.3%)	26 (17.9%)
Back pain	7 (9.3%)	21 (14.5%)
Myalgia	9 (12.0%)	15 (10.3%)
Pain in extremity	6 (8.0%)	13 (9.0%)
Bone pain	4 (5.3%)	9 (6.2%)
Muscle spasms	5 (6.7%)	3 (2.1%)
Arthritis	2 (2.7%)	3 (2.1%)
Muscular weakness	3 (4.0%)	2 (1.4%)
Neck pain	1 (1.3%)	4 (2.8%)
Musculoskeletal chest pain	1 (1.3%)	3 (2.1%)
Spinal pain	1 (1.3%)	2 (1.4%)
Musculoskeletal pain	1 (1.3%)	1 (0.7%)
Osteonecrosis of jaw	0	2 (1.4%)
Pain in jaw	1 (1.3%)	1 (0.7%)
Pathological fracture	1 (1.3%)	1 (0.7%)
Bone swelling	0	1 (0.7%)
Costochondritis	1 (1.3%)	0
Flank pain	1 (1.3%)	0
Fracture pain	0	1 (0.7%)
Joint swelling	0	1 (0.7%)
Musculoskeletal stiffness	1 (1.3%)	0
Osteoarthritis	1 (1.3%)	0
Rhabdomyolysis	0	1 (0.7%)
Scleroderma	0	1 (0.7%)
Spinal osteoarthritis	0	1 (0.7%)
Synovitis	1 (1.3%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Investigations		
Total number of patients with at least one such adverse event	42 (56.0%)	62 (42.8%)
Total number of events	184	265
Neutrophil count decreased	18 (24.0%)	23 (15.9%)
Alanine aminotransferase increased	15 (20.0%)	19 (13.1%)
Aspartate aminotransferase increased	10 (13.3%)	13 (9.0%)
White blood cell count decreased	5 (6.7%)	10 (6.9%)
Blood lactate dehydrogenase increased	8 (10.7%)	5 (3.4%)
Blood alkaline phosphatase increased	7 (9.3%)	3 (2.1%)
Blood cholesterol increased	3 (4.0%)	6 (4.1%)
Weight decreased	2 (2.7%)	7 (4.8%)
Lipase increased	3 (4.0%)	5 (3.4%)
Amylase increased	1 (1.3%)	5 (3.4%)
Blood creatinine increased	2 (2.7%)	3 (2.1%)
Gamma-glutamyltransferase increased	2 (2.7%)	3 (2.1%)
Blood triglycerides increased	0	4 (2.8%)
Blood albumin decreased	1 (1.3%)	2 (1.4%)
Blood urea increased	1 (1.3%)	2 (1.4%)
Haemoglobin decreased	1 (1.3%)	2 (1.4%)
Low density lipoprotein increased	1 (1.3%)	2 (1.4%)
Weight increased	3 (4.0%)	0
Blood bilirubin increased	0	2 (1.4%)
Blood glucose increased	0	2 (1.4%)
Blood bicarbonate increased	0	1 (0.7%)
Blood creatine phosphokinase increased	0	1 (0.7%)
Blood fibrinogen increased	1 (1.3%)	0
Blood thyroid stimulating hormone increased	0	1 (0.7%)
C-reactive protein increased	0	1 (0.7%)
Eastern Cooperative Oncology Group performance status worsened	0	1 (0.7%)
Glycosylated haemoglobin increased	0	1 (0.7%)
Haematocrit decreased	0	1 (0.7%)
Heart rate increased	0	1 (0.7%)
Lymphocyte count decreased	0	1 (0.7%)
Platelet count decreased	1 (1.3%)	0
SARS-CoV-2 test positive	0	1 (0.7%)
Very low density lipoprotein increased	1 (1.3%)	0
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	28 (37.3%)	68 (46.9%)
Total number of events	103	183
Anaemia	15 (20.0%)	45 (31.0%)
Neutropenia	18 (24.0%)	38 (26.2%)
Leukopenia	8 (10.7%)	8 (5.5%)
Febrile neutropenia	0	3 (2.1%)
Thrombocytopenia	0	3 (2.1%)
Haemolysis	0	1 (0.7%)
Lymphadenitis	0	1 (0.7%)
Lymphadenopathy	0	1 (0.7%)
Lymphopenia	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	18 (24.0%)	57 (39.3%)
Total number of events	32	131
Cough	6 (8.0%)	23 (15.9%)
Epistaxis	4 (5.3%)	15 (10.3%)
Oropharyngeal pain	2 (2.7%)	11 (7.6%)
Dyspnoea	2 (2.7%)	10 (6.9%)
Pneumonitis	0	6 (4.1%)
Rhinorrhoea	0	6 (4.1%)
Haemoptysis	1 (1.3%)	2 (1.4%)
Nasal congestion	0	3 (2.1%)
Productive cough	1 (1.3%)	2 (1.4%)
Pulmonary embolism	3 (4.0%)	0
Upper respiratory tract inflammation	1 (1.3%)	2 (1.4%)
Catarrh	0	2 (1.4%)
Dysphonia	0	2 (1.4%)
Oropharyngeal discomfort	1 (1.3%)	1 (0.7%)
Pleural effusion	0	2 (1.4%)
Rhinitis allergic	0	2 (1.4%)
Asthma	1 (1.3%)	0
Bronchitis chronic	1 (1.3%)	0
Chronic obstructive pulmonary disease	1 (1.3%)	0
Diaphragmatic disorder	1 (1.3%)	0
Nasal dryness	0	1 (0.7%)
Nasal septum ulceration	1 (1.3%)	0
Paranasal sinus discomfort	0	1 (0.7%)
Pleuritic pain	0	1 (0.7%)
Pulmonary hypertension	0	1 (0.7%)
Respiratory disorder	1 (1.3%)	0
Respiratory distress	0	1 (0.7%)
Sinus pain	0	1 (0.7%)
Upper-airway cough syndrome	0	1 (0.7%)
Vasomotor rhinitis	1 (1.3%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	24 (32.0%)	49 (33.8%)
Total number of events	83	110
Decreased appetite	7 (9.3%)	22 (15.2%)
Hyperglycaemia	10 (13.3%)	19 (13.1%)
Hypertriglyceridaemia	5 (6.7%)	7 (4.8%)
Hypokalaemia	2 (2.7%)	6 (4.1%)
Hypercholesterolaemia	2 (2.7%)	4 (2.8%)
Dehydration	0	4 (2.8%)
Hypocalcaemia	1 (1.3%)	3 (2.1%)
Hypophosphataemia	1 (1.3%)	3 (2.1%)
Hypercalcaemia	2 (2.7%)	1 (0.7%)
Hypercreatininaemia	2 (2.7%)	1 (0.7%)
Hyperuricaemia	1 (1.3%)	1 (0.7%)
Hypoglycaemia	1 (1.3%)	1 (0.7%)
Hypomagnesaemia	0	2 (1.4%)
Hyponatraemia	0	2 (1.4%)
Calcium deficiency	1 (1.3%)	0
Diabetes mellitus	0	1 (0.7%)
Dyslipidaemia	0	1 (0.7%)
Fluid retention	0	1 (0.7%)
Hyperlipidaemia	0	1 (0.7%)
Hypernatraemia	0	1 (0.7%)
Hypoalbuminaemia	0	1 (0.7%)
Type 2 diabetes mellitus	0	1 (0.7%)
Vitamin D deficiency	1 (1.3%)	0
Vascular disorders		
Total number of patients with at least one such adverse event	15 (20.0%)	30 (20.7%)
Total number of events	26	36
Hypertension	4 (5.3%)	8 (5.5%)
Lymphoedema	5 (6.7%)	6 (4.1%)
Flushing	2 (2.7%)	4 (2.8%)
Hot flush	1 (1.3%)	4 (2.8%)
Phlebitis	1 (1.3%)	3 (2.1%)
Lymphostasis	3 (4.0%)	0
Hypotension	0	2 (1.4%)
Orthostatic hypotension	0	2 (1.4%)
Thrombosis	1 (1.3%)	1 (0.7%)
Venous thrombosis limb	1 (1.3%)	1 (0.7%)
Deep vein thrombosis	0	1 (0.7%)
Embolism	0	1 (0.7%)
Haemorrhage	0	1 (0.7%)
Hypertensive crisis	1 (1.3%)	0
Peripheral venous disease	1 (1.3%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Injury, poisoning and procedural complications		
Total number of patients with at least one such adverse event	12 (16.0%)	28 (19.3%)
Total number of events	21	44
Product dose omission issue	3 (4.0%)	6 (4.1%)
Accidental overdose	1 (1.3%)	6 (4.1%)
Fall	2 (2.7%)	2 (1.4%)
Vascular access site pain	0	4 (2.8%)
Contusion	0	2 (1.4%)
Incorrect dose administered	0	2 (1.4%)
Poisoning	2 (2.7%)	0
Thermal burn	0	2 (1.4%)
Arthropod bite	0	1 (0.7%)
Breast injury	1 (1.3%)	0
Femoral neck fracture	0	1 (0.7%)
Femur fracture	1 (1.3%)	0
Foot fracture	0	1 (0.7%)
Fracture	1 (1.3%)	0
Limb injury	1 (1.3%)	0
Medication error	0	1 (0.7%)
Radiation skin injury	1 (1.3%)	0
Road traffic accident	0	1 (0.7%)
Spinal fracture	1 (1.3%)	0
Traumatic haematoma	0	1 (0.7%)
Vascular access site discharge	0	1 (0.7%)
Vascular access site erythema	0	1 (0.7%)
Vascular access site swelling	0	1 (0.7%)
Wrist fracture	0	1 (0.7%)
Wrong schedule	0	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_B_SE.out
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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Eye disorders		
Total number of patients with at least one such adverse event	8 (10.7%)	18 (12.4%)
Total number of events	12	28
Dry eye	1 (1.3%)	6 (4.1%)
Lacrimation increased	3 (4.0%)	3 (2.1%)
Cataract	3 (4.0%)	2 (1.4%)
Conjunctival haemorrhage	1 (1.3%)	1 (0.7%)
Visual acuity reduced	0	2 (1.4%)
Visual impairment	0	2 (1.4%)
Chalazion	0	1 (0.7%)
Diplopia	0	1 (0.7%)
Eye discharge	0	1 (0.7%)
Eye pruritus	0	1 (0.7%)
Eyelid oedema	0	1 (0.7%)
Hypermetropia	0	1 (0.7%)
Keratitis	0	1 (0.7%)
Macular degeneration	0	1 (0.7%)
Ocular hypertension	0	1 (0.7%)
Retinal oedema	1 (1.3%)	0
Vision blurred	1 (1.3%)	0
Vitreous degeneration	0	1 (0.7%)
Vitreous floaters	1 (1.3%)	0
Psychiatric disorders		
Total number of patients with at least one such adverse event	12 (16.0%)	12 (8.3%)
Total number of events	13	16
Insomnia	6 (8.0%)	6 (4.1%)
Anxiety	2 (2.7%)	3 (2.1%)
Depression	1 (1.3%)	3 (2.1%)
Affect lability	0	1 (0.7%)
Anxiety disorder	0	1 (0.7%)
Confusional state	1 (1.3%)	0
Imperception	0	1 (0.7%)
Irritability	1 (1.3%)	0
Sleep disorder	1 (1.3%)	0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Renal and urinary disorders		
Total number of patients with at least one such adverse event	5 (6.7%)	12 (8.3%)
Total number of events	7	13
Pollakiuria	1 (1.3%)	4 (2.8%)
Dysuria	1 (1.3%)	3 (2.1%)
Hydronephrosis	2 (2.7%)	0
Urinary retention	0	2 (1.4%)
Acute kidney injury	1 (1.3%)	0
Chromaturia	1 (1.3%)	0
Haematuria	0	1 (0.7%)
Oliguria	0	1 (0.7%)
Renal failure	0	1 (0.7%)
Renal impairment	0	1 (0.7%)
Ureterolithiasis	1 (1.3%)	0
Hepatobiliary disorders		
Total number of patients with at least one such adverse event	6 (8.0%)	10 (6.9%)
Total number of events	42	19
Hyperbilirubinaemia	4 (5.3%)	6 (4.1%)
Hypertransaminasaemia	0	3 (2.1%)
Cholecystitis acute	1 (1.3%)	1 (0.7%)
Cholestasis	1 (1.3%)	0
Hepatic cytolysis	1 (1.3%)	0
Hepatic function abnormal	1 (1.3%)	0
Hepatic pain	0	1 (0.7%)
Hepatic vein thrombosis	0	1 (0.7%)
Cardiac disorders		
Total number of patients with at least one such adverse event	4 (5.3%)	11 (7.6%)
Total number of events	7	14
Palpitations	1 (1.3%)	4 (2.8%)
Sinus tachycardia	1 (1.3%)	3 (2.1%)
Angina unstable	0	1 (0.7%)
Cardiac failure	1 (1.3%)	0
Coronary artery disease	1 (1.3%)	0
Extrasystoles	0	1 (0.7%)
Left ventricular hypertrophy	1 (1.3%)	0
Metabolic cardiomyopathy	1 (1.3%)	0
Supraventricular extrasystoles	0	1 (0.7%)
Supraventricular tachycardia	0	1 (0.7%)
Ventricular arrhythmia	1 (1.3%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Reproductive system and breast disorders		
Total number of patients with at least one such adverse event	3 (4.0%)	7 (4.8%)
Total number of events	3	7
Breast pain	0	3 (2.1%)
Breast discharge	1 (1.3%)	0
Breast ulceration	0	1 (0.7%)
Erectile dysfunction	0	1 (0.7%)
Menstruation irregular	1 (1.3%)	0
Pelvic pain	0	1 (0.7%)
Postmenopausal haemorrhage	1 (1.3%)	0
Vulvovaginal pruritus	0	1 (0.7%)
Ear and labyrinth disorders		
Total number of patients with at least one such adverse event	3 (4.0%)	6 (4.1%)
Total number of events	3	6
Vertigo	2 (2.7%)	4 (2.8%)
Deafness	0	1 (0.7%)
Ear pain	0	1 (0.7%)
Tinnitus	1 (1.3%)	0
Immune system disorders		
Total number of patients with at least one such adverse event	0	4 (2.8%)
Total number of events	0	4
Allergic oedema	0	1 (0.7%)
Contrast media allergy	0	1 (0.7%)
Drug hypersensitivity	0	1 (0.7%)
Hypersensitivity	0	1 (0.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Total number of patients with at least one such adverse event	3 (4.0%)	0
Total number of events	7	0
Ear neoplasm	1 (1.3%)	0
Tumour necrosis	1 (1.3%)	0
Tumour pain	1 (1.3%)	0
Tumour ulceration	1 (1.3%)	0
No Coding available		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
No Coding available	0	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Adverse Events, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	102 (100%)
Overall total number of events	2019
Gastrointestinal disorders	
Total number of patients with at least one such adverse event	93 (91.2%)
Total number of events	537
Diarrhoea	86 (84.3%)
Nausea	42 (41.2%)
Vomiting	29 (28.4%)
Constipation	13 (12.7%)
Abdominal pain	12 (11.8%)
Stomatitis	7 (6.9%)
Abdominal pain upper	6 (5.9%)
Dyspepsia	6 (5.9%)
Dry mouth	5 (4.9%)
Gastrooesophageal reflux disease	5 (4.9%)
Toothache	4 (3.9%)
Abdominal discomfort	3 (2.9%)
Flatulence	3 (2.9%)
Haemorrhoids	2 (2.0%)
Mouth ulceration	2 (2.0%)
Abdominal distension	1 (1.0%)
Breath odour	1 (1.0%)
Dental caries	1 (1.0%)
Dental discomfort	1 (1.0%)
Dysphagia	1 (1.0%)
Epigastric discomfort	1 (1.0%)
Gastrointestinal disorder	1 (1.0%)
Gastrooesophageal sphincter insufficiency	1 (1.0%)
Gingival pain	1 (1.0%)
Intestinal mucosal atrophy	1 (1.0%)
Large intestine perforation	1 (1.0%)
Oesophagitis	1 (1.0%)
Oral discomfort	1 (1.0%)
Oral pain	1 (1.0%)
Paraesthesia oral	1 (1.0%)
Proctalgia	1 (1.0%)
Retching	1 (1.0%)

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Adverse Events, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Skin and subcutaneous tissue disorders	
Total number of patients with at least one such adverse event	78 (76.5%)
Total number of events	162
Alopecia	42 (41.2%)
Rash	31 (30.4%)
Pruritus	17 (16.7%)
Rash maculo-papular	5 (4.9%)
Dermatitis acneiform	3 (2.9%)
Erythema	3 (2.9%)
Hand dermatitis	3 (2.9%)
Acne	2 (2.0%)
Dermatitis allergic	2 (2.0%)
Hyperhidrosis	2 (2.0%)
Nail disorder	2 (2.0%)
Nail dystrophy	2 (2.0%)
Rash erythematous	2 (2.0%)
Rash papular	2 (2.0%)
Skin hyperpigmentation	2 (2.0%)
Dermatitis contact	1 (1.0%)
Dry skin	1 (1.0%)
Eczema	1 (1.0%)
Madarosis	1 (1.0%)
Miliaria	1 (1.0%)
Nail bed tenderness	1 (1.0%)
Nail discolouration	1 (1.0%)
Nail ridging	1 (1.0%)
Night sweats	1 (1.0%)
Onychalgia	1 (1.0%)
Onychoclasis	1 (1.0%)
Onycholysis	1 (1.0%)
Onychomadesis	1 (1.0%)
Perioral dermatitis	1 (1.0%)
Rash pruritic	1 (1.0%)
Scar pain	1 (1.0%)
Seborrhoeic dermatitis	1 (1.0%)
Skin exfoliation	1 (1.0%)
Skin lesion	1 (1.0%)
Urticaria	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Nervous system disorders	
Total number of patients with at least one such adverse event	68 (66.7%)
Total number of events	149
Neuropathy peripheral	30 (29.4%)
Headache	21 (20.6%)
Dizziness	10 (9.8%)
Peripheral sensory neuropathy	8 (7.8%)
Polyneuropathy	8 (7.8%)
Dysgeusia	6 (5.9%)
Hypoaesthesia	5 (4.9%)
Paraesthesia	5 (4.9%)
Tremor	3 (2.9%)
Balance disorder	2 (2.0%)
Cognitive disorder	2 (2.0%)
Encephalopathy	2 (2.0%)
Lethargy	2 (2.0%)
Peripheral motor neuropathy	2 (2.0%)
Amnesia	1 (1.0%)
Burning sensation mucosal	1 (1.0%)
Cerebrovascular insufficiency	1 (1.0%)
Dystonia	1 (1.0%)
Hypersomnia	1 (1.0%)
Memory impairment	1 (1.0%)
Migraine	1 (1.0%)
Neurotoxicity	1 (1.0%)
Posterior reversible encephalopathy syndrome	1 (1.0%)
Somnolence	1 (1.0%)
Taste disorder	1 (1.0%)
Thoracic radiculopathy	1 (1.0%)
Transient ischaemic attack	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
General disorders and administration site conditions	
Total number of patients with at least one such adverse event	62 (60.8%)
Total number of events	137
Fatigue	23 (22.5%)
Asthenia	19 (18.6%)
Mucosal inflammation	12 (11.8%)
Pyrexia	12 (11.8%)
Oedema peripheral	7 (6.9%)
Chills	5 (4.9%)
Pain	5 (4.9%)
Chest pain	4 (3.9%)
Influenza like illness	3 (2.9%)
Oedema	3 (2.9%)
Non-cardiac chest pain	2 (2.0%)
Thirst	2 (2.0%)
Axillary pain	1 (1.0%)
Chest discomfort	1 (1.0%)
Facial pain	1 (1.0%)
General physical health deterioration	1 (1.0%)
Generalised oedema	1 (1.0%)
Hyperthermia	1 (1.0%)
Mass	1 (1.0%)
Peripheral swelling	1 (1.0%)
Sensation of foreign body	1 (1.0%)
Vascular device occlusion	1 (1.0%)
Blood and lymphatic system disorders	
Total number of patients with at least one such adverse event	53 (52.0%)
Total number of events	231
Anaemia	34 (33.3%)
Neutropenia	25 (24.5%)
Leukopenia	11 (10.8%)
Lymphopenia	3 (2.9%)
Febrile neutropenia	2 (2.0%)
Eosinophilia	1 (1.0%)
Lymphadenopathy	1 (1.0%)
Thrombocytopenia	1 (1.0%)
Thrombocytosis	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Investigations	
Total number of patients with at least one such adverse event	52 (51.0%)
Total number of events	258
Alanine aminotransferase increased	26 (25.5%)
Aspartate aminotransferase increased	22 (21.6%)
Blood alkaline phosphatase increased	12 (11.8%)
Neutrophil count decreased	8 (7.8%)
Blood lactate dehydrogenase increased	7 (6.9%)
Weight decreased	7 (6.9%)
Weight increased	6 (5.9%)
Blood cholesterol increased	5 (4.9%)
White blood cell count decreased	5 (4.9%)
Blood bilirubin increased	4 (3.9%)
Blood triglycerides increased	4 (3.9%)
Lipase increased	4 (3.9%)
Low density lipoprotein increased	4 (3.9%)
Blood glucose increased	2 (2.0%)
Blood thyroid stimulating hormone increased	2 (2.0%)
High density lipoprotein increased	2 (2.0%)
Platelet count decreased	2 (2.0%)
Amylase increased	1 (1.0%)
Anti-GAD antibody positive	1 (1.0%)
Anti-islet cell antibody positive	1 (1.0%)
Basophil percentage increased	1 (1.0%)
Blood chloride decreased	1 (1.0%)
Blood lactate dehydrogenase decreased	1 (1.0%)
Blood pressure increased	1 (1.0%)
Carbon dioxide decreased	1 (1.0%)
Eosinophil percentage increased	1 (1.0%)
Faecal volume increased	1 (1.0%)
Gamma-glutamyltransferase increased	1 (1.0%)
Glomerular filtration rate decreased	1 (1.0%)
Glycosylated haemoglobin increased	1 (1.0%)
Haematocrit decreased	1 (1.0%)
Immature granulocyte count increased	1 (1.0%)
Immature granulocyte percentage increased	1 (1.0%)
Lymphocyte count decreased	1 (1.0%)
Mean cell volume decreased	1 (1.0%)
Metamyelocyte percentage increased	1 (1.0%)
Monocyte percentage decreased	1 (1.0%)
Oxygen saturation decreased	1 (1.0%)
Prothrombin time prolonged	1 (1.0%)
Red blood cell count decreased	1 (1.0%)
Tri-iodothyronine increased	1 (1.0%)
White blood cell count increased	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Infections and infestations	
Total number of patients with at least one such adverse event	50 (49.0%)
Total number of events	90
Urinary tract infection	10 (9.8%)
Upper respiratory tract infection	8 (7.8%)
Pneumonia	6 (5.9%)
Nasopharyngitis	5 (4.9%)
COVID-19	4 (3.9%)
Herpes zoster	4 (3.9%)
Influenza	4 (3.9%)
Rhinitis	4 (3.9%)
Conjunctivitis	3 (2.9%)
Oral candidiasis	3 (2.9%)
Cystitis	2 (2.0%)
Mastitis	2 (2.0%)
Paronychia	2 (2.0%)
Respiratory tract infection viral	2 (2.0%)
Skin infection	2 (2.0%)
Tooth infection	2 (2.0%)
Bronchitis	1 (1.0%)
Cellulitis	1 (1.0%)
Emphysematous cystitis	1 (1.0%)
Fungal skin infection	1 (1.0%)
Furuncle	1 (1.0%)
Gastroenteritis	1 (1.0%)
Gastroenteritis norovirus	1 (1.0%)
Gingivitis	1 (1.0%)
Hordeolum	1 (1.0%)
Nail infection	1 (1.0%)
Oral herpes	1 (1.0%)
Pharyngitis	1 (1.0%)
Pneumonia viral	1 (1.0%)
Postoperative wound infection	1 (1.0%)
Rash pustular	1 (1.0%)
Suspected COVID-19	1 (1.0%)
Tonsillitis	1 (1.0%)
Tooth abscess	1 (1.0%)
Urethritis	1 (1.0%)
Urogenital infection fungal	1 (1.0%)
Wound infection	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Adverse Events, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Metabolism and nutrition disorders	
Total number of patients with at least one such adverse event	50 (49.0%)
Total number of events	124
Hyperglycaemia	22 (21.6%)
Decreased appetite	14 (13.7%)
Hypokalaemia	8 (7.8%)
Hypoalbuminaemia	5 (4.9%)
Hypercholesterolaemia	4 (3.9%)
Hypertriglyceridaemia	4 (3.9%)
Hyponatraemia	4 (3.9%)
Dehydration	3 (2.9%)
Dyslipidaemia	3 (2.9%)
Hypercalcaemia	3 (2.9%)
Hyperkalaemia	3 (2.9%)
Hypercreatininaemia	2 (2.0%)
Hypomagnesaemia	2 (2.0%)
Alkalosis	1 (1.0%)
Diabetes mellitus	1 (1.0%)
Diabetic ketoacidosis	1 (1.0%)
Fluid retention	1 (1.0%)
Hyperphosphataemia	1 (1.0%)
Hypocalcaemia	1 (1.0%)
Hypophosphataemia	1 (1.0%)
Increased appetite	1 (1.0%)
Polydipsia	1 (1.0%)
Type 1 diabetes mellitus	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Respiratory, thoracic and mediastinal disorders	
Total number of patients with at least one such adverse event	48 (47.1%)
Total number of events	83
Cough	16 (15.7%)
Dyspnoea	9 (8.8%)
Epistaxis	8 (7.8%)
Pneumonitis	7 (6.9%)
Oropharyngeal pain	6 (5.9%)
Dysphonia	3 (2.9%)
Pulmonary embolism	3 (2.9%)
Respiratory disorder	3 (2.9%)
Rhinorrhoea	3 (2.9%)
Dyspnoea exertional	2 (2.0%)
Nasal congestion	2 (2.0%)
Pleural effusion	2 (2.0%)
Productive cough	2 (2.0%)
Rhinitis allergic	2 (2.0%)
Bronchospasm	1 (1.0%)
Immune-mediated lung disease	1 (1.0%)
Lung infiltration	1 (1.0%)
Nasal crusting	1 (1.0%)
Pleuritic pain	1 (1.0%)
Pneumothorax	1 (1.0%)
Wheezing	1 (1.0%)
Musculoskeletal and connective tissue disorders	
Total number of patients with at least one such adverse event	37 (36.3%)
Total number of events	67
Arthralgia	13 (12.7%)
Back pain	10 (9.8%)
Myalgia	10 (9.8%)
Muscle spasms	5 (4.9%)
Pain in extremity	4 (3.9%)
Musculoskeletal chest pain	3 (2.9%)
Bone pain	2 (2.0%)
Spinal pain	2 (2.0%)
Joint swelling	1 (1.0%)
Mixed connective tissue disease	1 (1.0%)
Musculoskeletal pain	1 (1.0%)
Musculoskeletal stiffness	1 (1.0%)
Myositis	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Vascular disorders	
Total number of patients with at least one such adverse event	24 (23.5%)
Total number of events	27
Flushing	8 (7.8%)
Hypertension	8 (7.8%)
Hot flush	4 (3.9%)
Lymphoedema	3 (2.9%)
Embolism	1 (1.0%)
Jugular vein thrombosis	1 (1.0%)
Phlebitis	1 (1.0%)
Injury, poisoning and procedural complications	
Total number of patients with at least one such adverse event	23 (22.5%)
Total number of events	35
Accidental overdose	6 (5.9%)
Fall	2 (2.0%)
Infusion related reaction	2 (2.0%)
Procedural pain	2 (2.0%)
Contusion	1 (1.0%)
Incorrect dose administered	1 (1.0%)
Injury	1 (1.0%)
Intentional overdose	1 (1.0%)
Intentional product misuse	1 (1.0%)
Ligament sprain	1 (1.0%)
Overdose	1 (1.0%)
Product dose omission in error	1 (1.0%)
Product dose omission issue	1 (1.0%)
Rib fracture	1 (1.0%)
Vascular access site inflammation	1 (1.0%)
Vascular access site pain	1 (1.0%)
Wound	1 (1.0%)
Wound secretion	1 (1.0%)
Psychiatric disorders	
Total number of patients with at least one such adverse event	20 (19.6%)
Total number of events	24
Insomnia	10 (9.8%)
Anxiety	5 (4.9%)
Depression	5 (4.9%)
Depressed mood	1 (1.0%)
Irritability	1 (1.0%)
Sleep disorder	1 (1.0%)
Stress	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Eye disorders	
Total number of patients with at least one such adverse event	18 (17.6%)
Total number of events	20
Dry eye	5 (4.9%)
Vision blurred	4 (3.9%)
Periorbital oedema	2 (2.0%)
Abnormal sensation in eye	1 (1.0%)
Eye disorder	1 (1.0%)
Eye irritation	1 (1.0%)
Eyelid function disorder	1 (1.0%)
Foreign body sensation in eyes	1 (1.0%)
Lacrimation increased	1 (1.0%)
Retinal tear	1 (1.0%)
Visual impairment	1 (1.0%)
Vitreous detachment	1 (1.0%)
Hepatobiliary disorders	
Total number of patients with at least one such adverse event	13 (12.7%)
Total number of events	20
Hyperbilirubinaemia	6 (5.9%)
Autoimmune hepatitis	3 (2.9%)
Cholecystitis	2 (2.0%)
Cholestasis	1 (1.0%)
Hypertransaminasaemia	1 (1.0%)
Reproductive system and breast disorders	
Total number of patients with at least one such adverse event	11 (10.8%)
Total number of events	14
Breast pain	4 (3.9%)
Vulvovaginal dryness	2 (2.0%)
Amenorrhoea	1 (1.0%)
Artificial menopause	1 (1.0%)
Breast discharge	1 (1.0%)
Vaginal discharge	1 (1.0%)
Vulvovaginal discomfort	1 (1.0%)
Vulvovaginal pruritus	1 (1.0%)
Endocrine disorders	
Total number of patients with at least one such adverse event	8 (7.8%)
Total number of events	8
Hypothyroidism	6 (5.9%)
Autoimmune hypothyroidism	1 (1.0%)
Hyperthyroidism	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Total number of patients with at least one such adverse event	8 (7.8%)
Total number of events	9
Tumour necrosis	2 (2.0%)
Tumour pain	2 (2.0%)
Infected neoplasm	1 (1.0%)
Paraneoplastic syndrome	1 (1.0%)
Tumour fistulisation	1 (1.0%)
Tumour inflammation	1 (1.0%)
Ear and labyrinth disorders	
Total number of patients with at least one such adverse event	6 (5.9%)
Total number of events	7
Hypoacusis	2 (2.0%)
Tinnitus	2 (2.0%)
Vertigo	2 (2.0%)
Ear pain	1 (1.0%)
Immune system disorders	
Total number of patients with at least one such adverse event	6 (5.9%)
Total number of events	6
Hypersensitivity	2 (2.0%)
Seasonal allergy	2 (2.0%)
Contrast media allergy	1 (1.0%)
Contrast media reaction	1 (1.0%)
Cardiac disorders	
Total number of patients with at least one such adverse event	5 (4.9%)
Total number of events	5
Cardiac arrest	1 (1.0%)
Myocarditis	1 (1.0%)
Sinus tachycardia	1 (1.0%)
Tachycardia	1 (1.0%)
Ventricular extrasystoles	1 (1.0%)
Renal and urinary disorders	
Total number of patients with at least one such adverse event	4 (3.9%)
Total number of events	6
Acute kidney injury	3 (2.9%)
Urge incontinence	1 (1.0%)
Urinary incontinence	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
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Adverse Events, AEs Associated with COVID-19, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one such adverse event	9 (5.4%)
Overall total number of events	14
Infections and infestations	
Total number of patients with at least one such adverse event	9 (5.4%)
Total number of events	11
COVID-19	8 (4.8%)
COVID-19 pneumonia	1 (0.6%)
Rhinitis	1 (0.6%)
Upper respiratory tract infection	1 (0.6%)
Blood and lymphatic system disorders	
Total number of patients with at least one such adverse event	1 (0.6%)
Total number of events	2
Neutropenia	1 (0.6%)
Investigations	
Total number of patients with at least one such adverse event	1 (0.6%)
Total number of events	1
Neutrophil count decreased	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_COVAS_A_SE.out
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Adverse Events, AEs Associated with COVID-19, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one such adverse event	1 (1.3%)	2 (1.4%)
Overall total number of events	2	6
Investigations		
Total number of patients with at least one such adverse event	1 (1.3%)	2 (1.4%)
Total number of events	1	3
Blood creatinine increased	0	1 (0.7%)
SARS-CoV-2 test positive	0	1 (0.7%)
White blood cell count decreased	1 (1.3%)	0
Infections and infestations		
Total number of patients with at least one such adverse event	1 (1.3%)	1 (0.7%)
Total number of events	1	1
COVID-19	1 (1.3%)	1 (0.7%)
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Abdominal pain	0	1 (0.7%)
Vascular disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Venous thrombosis limb	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_COVAS_B_SE.out
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Adverse Events, AEs Associated with COVID-19, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	5 (4.9%)
Overall total number of events	12
Infections and infestations	
Total number of patients with at least one such adverse event	5 (4.9%)
Total number of events	5
COVID-19	4 (3.9%)
Suspected COVID-19	1 (1.0%)
Blood and lymphatic system disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Neutropenia	1 (1.0%)
General disorders and administration site conditions	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	2
Chest pain	1 (1.0%)
Investigations	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	2
Blood alkaline phosphatase increased	1 (1.0%)
High density lipoprotein increased	1 (1.0%)
Respiratory, thoracic and mediastinal disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	2
Dyspnoea exertional	1 (1.0%)
Nasal congestion	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	84 (96.6%)	162 (97.6%)
	Grade 1-2	44 (50.6%)	78 (47.0%)
	1	10 (11.5%)	9 (5.4%)
	2	34 (39.1%)	69 (41.6%)
	Grade 3-4	38 (43.7%)	82 (49.4%)
	3	33 (37.9%)	69 (41.6%)
	4	5 (5.7%)	13 (7.8%)
	Grade 5	2 (2.3%)	2 (1.2%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	57 (65.5%)	151 (91.0%)
	Grade 1-2	50 (57.5%)	130 (78.3%)
	1	35 (40.2%)	53 (31.9%)
	2	15 (17.2%)	77 (46.4%)
	Grade 3-4	7 (8.0%)	21 (12.7%)
	3	7 (8.0%)	19 (11.4%)
	4	0	2 (1.2%)
Diarrhoea	- Any Grade -	28 (32.2%)	141 (84.9%)
	Grade 1-2	26 (29.9%)	126 (75.9%)
	1	18 (20.7%)	67 (40.4%)
	2	8 (9.2%)	59 (35.5%)
	Grade 3-4	2 (2.3%)	15 (9.0%)
	3	2 (2.3%)	15 (9.0%)
Nausea	- Any Grade -	22 (25.3%)	66 (39.8%)
	Grade 1-2	22 (25.3%)	61 (36.7%)
	1	17 (19.5%)	46 (27.7%)
	2	5 (5.7%)	15 (9.0%)
	Grade 3-4	0	5 (3.0%)
	3	0	5 (3.0%)
Constipation	- Any Grade -	31 (35.6%)	49 (29.5%)
	Grade 1-2	30 (34.5%)	49 (29.5%)
	1	25 (28.7%)	41 (24.7%)
	2	5 (5.7%)	8 (4.8%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Vomiting	- Any Grade -	8 (9.2%)	54 (32.5%)
	Grade 1-2	7 (8.0%)	50 (30.1%)
	1	6 (6.9%)	41 (24.7%)
	2	1 (1.1%)	9 (5.4%)
	Grade 3-4	1 (1.1%)	4 (2.4%)
	3	1 (1.1%)	3 (1.8%)
	4	0	1 (0.6%)
Abdominal pain upper	- Any Grade -	8 (9.2%)	16 (9.6%)
	Grade 1-2	8 (9.2%)	16 (9.6%)
	1	8 (9.2%)	12 (7.2%)
	2	0	4 (2.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Stomatitis	- Any Grade -	6 (6.9%)	18 (10.8%)
	Grade 1-2	6 (6.9%)	18 (10.8%)
	1	5 (5.7%)	10 (6.0%)
	2	1 (1.1%)	8 (4.8%)
Abdominal pain	- Any Grade -	5 (5.7%)	15 (9.0%)
	Grade 1-2	4 (4.6%)	13 (7.8%)
	1	3 (3.4%)	9 (5.4%)
	2	1 (1.1%)	4 (2.4%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	1 (1.1%)	2 (1.2%)
Dyspepsia	- Any Grade -	4 (4.6%)	14 (8.4%)
	Grade 1-2	4 (4.6%)	14 (8.4%)
	1	4 (4.6%)	11 (6.6%)
	2	0	3 (1.8%)
Haemorrhoids	- Any Grade -	2 (2.3%)	5 (3.0%)
	Grade 1-2	2 (2.3%)	5 (3.0%)
	1	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	4 (2.4%)
Abdominal discomfort	- Any Grade -	3 (3.4%)	3 (1.8%)
	Grade 1-2	3 (3.4%)	3 (1.8%)
	1	3 (3.4%)	3 (1.8%)
Flatulence	- Any Grade -	1 (1.1%)	5 (3.0%)
	Grade 1-2	1 (1.1%)	5 (3.0%)
	1	1 (1.1%)	4 (2.4%)
	2	0	1 (0.6%)
Abdominal distension	- Any Grade -	0	5 (3.0%)
	Grade 1-2	0	5 (3.0%)
	1	0	4 (2.4%)
	2	0	1 (0.6%)
Gastrooesophageal reflux disease	- Any Grade -	0	4 (2.4%)
	Grade 1-2	0	4 (2.4%)
	1	0	3 (1.8%)
	2	0	1 (0.6%)
Toothache	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
Periodontal disease	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	3 (1.8%)
Cheilitis	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Colitis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Dry mouth	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Tongue ulceration	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Anal inflammation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Chapped lips	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Dental caries	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Dysphagia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Enteritis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Food poisoning	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Gastritis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Gastrointestinal pain	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Gingival pain	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Large intestine perforation	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Mouth ulceration	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Oesophagitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Pancreatitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Proctalgia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Tongue oedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Upper gastrointestinal haemorrhage	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Nervous system disorders			
- Overall -	- Any Grade -	59 (67.8%)	97 (58.4%)
	Grade 1-2	54 (62.1%)	79 (47.6%)
	1	40 (46.0%)	48 (28.9%)
	2	14 (16.1%)	31 (18.7%)
	Grade 3-4	5 (5.7%)	18 (10.8%)
	3	5 (5.7%)	18 (10.8%)
Neuropathy peripheral	- Any Grade -	20 (23.0%)	39 (23.5%)
	Grade 1-2	17 (19.5%)	31 (18.7%)
	1	13 (14.9%)	19 (11.4%)
	2	4 (4.6%)	12 (7.2%)
	Grade 3-4	3 (3.4%)	8 (4.8%)
	3	3 (3.4%)	8 (4.8%)
Peripheral sensory neuropathy	- Any Grade -	19 (21.8%)	32 (19.3%)
	Grade 1-2	17 (19.5%)	27 (16.3%)
	1	13 (14.9%)	18 (10.8%)
	2	4 (4.6%)	9 (5.4%)
	Grade 3-4	2 (2.3%)	5 (3.0%)
	3	2 (2.3%)	5 (3.0%)
Headache	- Any Grade -	10 (11.5%)	28 (16.9%)
	Grade 1-2	10 (11.5%)	28 (16.9%)
	1	10 (11.5%)	18 (10.8%)
	2	0	10 (6.0%)
Dysgeusia	- Any Grade -	8 (9.2%)	10 (6.0%)
	Grade 1-2	8 (9.2%)	10 (6.0%)
	1	7 (8.0%)	10 (6.0%)
	2	1 (1.1%)	0
Dizziness	- Any Grade -	8 (9.2%)	6 (3.6%)
	Grade 1-2	8 (9.2%)	6 (3.6%)
	1	6 (6.9%)	5 (3.0%)
	2	2 (2.3%)	1 (0.6%)
Polyneuropathy	- Any Grade -	7 (8.0%)	5 (3.0%)
	Grade 1-2	7 (8.0%)	4 (2.4%)
	1	4 (4.6%)	4 (2.4%)
	2	3 (3.4%)	0
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Paraesthesia	- Any Grade -	2 (2.3%)	8 (4.8%)
	Grade 1-2	2 (2.3%)	7 (4.2%)
	1	2 (2.3%)	3 (1.8%)
	2	0	4 (2.4%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Syncope	- Any Grade -	0	5 (3.0%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Sciatica	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	1 (1.1%)	0
	2	0	3 (1.8%)
Neurotoxicity	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	1 (1.1%)	1 (0.6%)
	2	0	1 (0.6%)
Tremor	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	1 (1.1%)	2 (1.2%)
Dysaesthesia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Memory impairment	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Peripheral motor neuropathy	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Taste disorder	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Ageusia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Altered state of consciousness	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Anosmia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Ataxia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Balance disorder	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Cranial nerve disorder	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Disturbance in attention	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Encephalopathy	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Head discomfort	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Hemiparaesthesia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Hypersomnia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Loss of consciousness	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Migraine	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Neuralgia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Paralysis recurrent laryngeal nerve	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Parosmia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Presyncope	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Radicular pain	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Radiculopathy	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Seizure	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Stupor	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Toxic neuropathy	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	52 (59.8%)	104 (62.7%)
	Grade 1-2	50 (57.5%)	101 (60.8%)
	1	18 (20.7%)	36 (21.7%)
	2	32 (36.8%)	65 (39.2%)
	Grade 3-4	2 (2.3%)	3 (1.8%)
	3	2 (2.3%)	3 (1.8%)
Alopecia	- Any Grade -	38 (43.7%)	78 (47.0%)
	Grade 1-2	38 (43.7%)	78 (47.0%)
	1	8 (9.2%)	19 (11.4%)
	2	30 (34.5%)	59 (35.5%)
Rash	- Any Grade -	11 (12.6%)	26 (15.7%)
	Grade 1-2	11 (12.6%)	24 (14.5%)
	1	9 (10.3%)	20 (12.0%)
	2	2 (2.3%)	4 (2.4%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Pruritus	- Any Grade -	7 (8.0%)	15 (9.0%)
	Grade 1-2	7 (8.0%)	15 (9.0%)
	1	5 (5.7%)	12 (7.2%)
	2	2 (2.3%)	3 (1.8%)
Nail discolouration	- Any Grade -	4 (4.6%)	6 (3.6%)
	Grade 1-2	4 (4.6%)	6 (3.6%)
	1	4 (4.6%)	6 (3.6%)
Dermatitis acneiform	- Any Grade -	1 (1.1%)	7 (4.2%)
	Grade 1-2	1 (1.1%)	7 (4.2%)
	1	1 (1.1%)	7 (4.2%)
Erythema	- Any Grade -	5 (5.7%)	3 (1.8%)
	Grade 1-2	4 (4.6%)	3 (1.8%)
	1	4 (4.6%)	2 (1.2%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Dermatitis allergic	- Any Grade -	0	6 (3.6%)
	Grade 1-2	0	6 (3.6%)
	1	0	4 (2.4%)
	2	0	2 (1.2%)
Eczema	- Any Grade -	3 (3.4%)	3 (1.8%)
	Grade 1-2	3 (3.4%)	3 (1.8%)
	1	2 (2.3%)	3 (1.8%)
	2	1 (1.1%)	0
Onychoclasis	- Any Grade -	3 (3.4%)	2 (1.2%)
	Grade 1-2	3 (3.4%)	2 (1.2%)
	1	3 (3.4%)	2 (1.2%)
Onycholysis	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	4 (2.4%)
	1	0	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Rash maculo-papular	- Any Grade -	0	5 (3.0%)
	Grade 1-2	0	5 (3.0%)
	1	0	4 (2.4%)
	2	0	1 (0.6%)
Dermatitis	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	2 (2.3%)	1 (0.6%)
	2	0	1 (0.6%)
Dry skin	- Any Grade -	4 (4.6%)	0
	Grade 1-2	4 (4.6%)	0
	1	4 (4.6%)	0
Nail disorder	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	2 (2.3%)	1 (0.6%)
	2	0	1 (0.6%)
Hyperhidrosis	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	1 (1.1%)	1 (0.6%)
	2	0	1 (0.6%)
Nail dystrophy	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	0	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
Dermatitis contact	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Hand dermatitis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Nail toxicity	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Onychomadesis	- Any Grade -	2 (2.3%)	0
	Grade 1-2	2 (2.3%)	0
	1	2 (2.3%)	0
Skin hyperpigmentation	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Acne	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Blister	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Dermatitis diaper	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Drug eruption	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Erythema multiforme	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Haemorrhage subcutaneous	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Hyperkeratosis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Nail ridging	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Onychalgia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Onychomalacia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Pain of skin	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Palmar-plantar erythrodysaesthesia syndrome	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Pigmentation disorder	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Rash papular	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Scab	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Skin exfoliation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Skin ulcer	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Solar dermatitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Urticaria	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
General disorders and administration site conditions			
- Overall -	- Any Grade -	43 (49.4%)	96 (57.8%)
	Grade 1-2	40 (46.0%)	81 (48.8%)
	1	25 (28.7%)	47 (28.3%)
	2	15 (17.2%)	34 (20.5%)
	Grade 3-4	3 (3.4%)	15 (9.0%)
	3	3 (3.4%)	15 (9.0%)
Fatigue	- Any Grade -	15 (17.2%)	31 (18.7%)
	Grade 1-2	13 (14.9%)	25 (15.1%)
	1	11 (12.6%)	20 (12.0%)
	2	2 (2.3%)	5 (3.0%)
	Grade 3-4	2 (2.3%)	6 (3.6%)
	3	2 (2.3%)	6 (3.6%)
Asthenia	- Any Grade -	10 (11.5%)	35 (21.1%)
	Grade 1-2	9 (10.3%)	29 (17.5%)
	1	5 (5.7%)	17 (10.2%)
	2	4 (4.6%)	12 (7.2%)
	Grade 3-4	1 (1.1%)	6 (3.6%)
	3	1 (1.1%)	6 (3.6%)
Oedema peripheral	- Any Grade -	7 (8.0%)	18 (10.8%)
	Grade 1-2	7 (8.0%)	17 (10.2%)
	1	2 (2.3%)	12 (7.2%)
	2	5 (5.7%)	5 (3.0%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Pyrexia	- Any Grade -	6 (6.9%)	16 (9.6%)
	Grade 1-2	6 (6.9%)	16 (9.6%)
	1	5 (5.7%)	12 (7.2%)
	2	1 (1.1%)	4 (2.4%)
Mucosal inflammation	- Any Grade -	2 (2.3%)	11 (6.6%)
	Grade 1-2	2 (2.3%)	10 (6.0%)
	1	2 (2.3%)	7 (4.2%)
	2	0	3 (1.8%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Influenza like illness	- Any Grade -	1 (1.1%)	8 (4.8%)
	Grade 1-2	1 (1.1%)	8 (4.8%)
	1	0	5 (3.0%)
	2	1 (1.1%)	3 (1.8%)
Oedema	- Any Grade -	2 (2.3%)	5 (3.0%)
	Grade 1-2	2 (2.3%)	5 (3.0%)
	1	2 (2.3%)	3 (1.8%)
	2	0	2 (1.2%)
Pain	- Any Grade -	1 (1.1%)	6 (3.6%)
	Grade 1-2	1 (1.1%)	6 (3.6%)
	1	0	6 (3.6%)
	2	1 (1.1%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Non-cardiac chest pain	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	1	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	2 (1.2%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Chest pain	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	4 (2.4%)
	1	1 (1.1%)	1 (0.6%)
	2	0	3 (1.8%)
Malaise	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	1	2 (2.3%)	3 (1.8%)
Axillary pain	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
Chills	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	1 (1.1%)	2 (1.2%)
Face oedema	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	1 (1.1%)	2 (1.2%)
Chest discomfort	- Any Grade -	2 (2.3%)	0
	Grade 1-2	2 (2.3%)	0
	1	2 (2.3%)	0
Infusion site extravasation	- Any Grade -	2 (2.3%)	0
	Grade 1-2	2 (2.3%)	0
	1	1 (1.1%)	0
	2	1 (1.1%)	0
Peripheral swelling	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	0
	2	0	1 (0.6%)
Cyst	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Discomfort	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Generalised oedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Hyperthermia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hypothermia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0

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Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Ill-defined disorder	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Infusion site pain	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Localised oedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Mucosal dryness	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Swelling face	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Tenderness	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Infections and infestations			
- Overall -	- Any Grade -	29 (33.3%)	81 (48.8%)
	Grade 1-2	23 (26.4%)	76 (45.8%)
	1	4 (4.6%)	28 (16.9%)
	2	19 (21.8%)	48 (28.9%)
	Grade 3-4	6 (6.9%)	5 (3.0%)
	3	5 (5.7%)	5 (3.0%)
	4	1 (1.1%)	0
Upper respiratory tract infection	- Any Grade -	3 (3.4%)	12 (7.2%)
	Grade 1-2	3 (3.4%)	12 (7.2%)
	1	2 (2.3%)	4 (2.4%)
	2	1 (1.1%)	8 (4.8%)
Urinary tract infection	- Any Grade -	2 (2.3%)	13 (7.8%)
	Grade 1-2	2 (2.3%)	12 (7.2%)
	1	0	1 (0.6%)
	2	2 (2.3%)	11 (6.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Nasopharyngitis	- Any Grade -	3 (3.4%)	11 (6.6%)
	Grade 1-2	3 (3.4%)	11 (6.6%)
	1	1 (1.1%)	6 (3.6%)
	2	2 (2.3%)	5 (3.0%)
Cystitis	- Any Grade -	3 (3.4%)	8 (4.8%)
	Grade 1-2	3 (3.4%)	8 (4.8%)
	1	1 (1.1%)	5 (3.0%)
	2	2 (2.3%)	3 (1.8%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Pneumonia	- Any Grade -	5 (5.7%)	6 (3.6%)
	Grade 1-2	1 (1.1%)	4 (2.4%)
	1	0	1 (0.6%)
	2	1 (1.1%)	3 (1.8%)
	Grade 3-4	4 (4.6%)	2 (1.2%)
	3	3 (3.4%)	2 (1.2%)
	4	1 (1.1%)	0
COVID-19	- Any Grade -	0	8 (4.8%)
	Grade 1-2	0	8 (4.8%)
	1	0	7 (4.2%)
	2	0	1 (0.6%)
Conjunctivitis	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	4 (2.4%)
	1	0	1 (0.6%)
	2	1 (1.1%)	3 (1.8%)
Pharyngitis	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	1	0	1 (0.6%)
	2	2 (2.3%)	2 (1.2%)
Bronchitis	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	0	1 (0.6%)
	2	1 (1.1%)	2 (1.2%)
Fungal skin infection	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	0	3 (1.8%)
	2	1 (1.1%)	0
Oral candidiasis	- Any Grade -	3 (3.4%)	1 (0.6%)
	Grade 1-2	3 (3.4%)	1 (0.6%)
	1	0	1 (0.6%)
	2	3 (3.4%)	0
Oral herpes	- Any Grade -	0	4 (2.4%)
	Grade 1-2	0	4 (2.4%)
	1	0	2 (1.2%)
	2	0	2 (1.2%)
Herpes zoster	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
Influenza	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 1-2	2 (2.3%)	1 (0.6%)
	2	2 (2.3%)	1 (0.6%)
Nail infection	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	1 (0.6%)
	2	0	2 (1.2%)
Parasitic gastroenteritis	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	1 (1.1%)	2 (1.2%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Rash pustular	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Rhinitis	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Sinusitis	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
Skin infection	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 1-2	2 (2.3%)	1 (0.6%)
	1	1 (1.1%)	0
	2	1 (1.1%)	1 (0.6%)
Cellulitis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Device related infection	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
Erysipelas	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
Laryngitis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
Mastitis	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Paronychia	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Respiratory tract infection viral	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Tooth infection	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
Viral infection	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Vulvovaginal candidiasis	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Abscess jaw	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Acarodermatitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Anal abscess	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Bacterial infection	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Bronchiolitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Chronic sinusitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Ear, nose and throat infection	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Empyema	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Enteritis infectious	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Erythrasma	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Folliculitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Fungal infection	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Fungal oesophagitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Furuncle	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Helicobacter infection	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Herpes simplex	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Hordeolum	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Lower respiratory tract infection	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Mucosal infection	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Periodontitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Peritonitis	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Pneumonia klebsiella	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Pustule	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Respiratory tract infection	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Subglottic laryngitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Tinea pedis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Tonsillitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Tooth abscess	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Vaginal abscess	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Vaginal infection	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0

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Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Vascular access site infection	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Vascular device infection	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Viral sinusitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Vulvitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Vulvovaginal mycotic infection	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	41 (47.1%)	67 (40.4%)
	Grade 1-2	34 (39.1%)	48 (28.9%)
	1	10 (11.5%)	21 (12.7%)
	2	24 (27.6%)	27 (16.3%)
	Grade 3-4	7 (8.0%)	19 (11.4%)
	3	6 (6.9%)	16 (9.6%)
	4	1 (1.1%)	3 (1.8%)
Anaemia	- Any Grade -	23 (26.4%)	44 (26.5%)
	Grade 1-2	20 (23.0%)	40 (24.1%)
	1	9 (10.3%)	21 (12.7%)
	2	11 (12.6%)	19 (11.4%)
	Grade 3-4	3 (3.4%)	4 (2.4%)
	3	2 (2.3%)	4 (2.4%)
	4	1 (1.1%)	0
Neutropenia	- Any Grade -	21 (24.1%)	28 (16.9%)
	Grade 1-2	17 (19.5%)	16 (9.6%)
	1	4 (4.6%)	3 (1.8%)
	2	13 (14.9%)	13 (7.8%)
	Grade 3-4	4 (4.6%)	12 (7.2%)
	3	3 (3.4%)	10 (6.0%)
	4	1 (1.1%)	2 (1.2%)
Leukopenia	- Any Grade -	4 (4.6%)	7 (4.2%)
	Grade 1-2	3 (3.4%)	7 (4.2%)
	1	2 (2.3%)	3 (1.8%)
	2	1 (1.1%)	4 (2.4%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Lymphopenia	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Thrombocytopenia	- Any Grade -	4 (4.6%)	1 (0.6%)
	Grade 1-2	3 (3.4%)	1 (0.6%)
	1	1 (1.1%)	0
	2	2 (2.3%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Febrile neutropenia	- Any Grade -	0	4 (2.4%)
	Grade 3-4	0	4 (2.4%)
	3	0	3 (1.8%)
	4	0	1 (0.6%)
Leukocytosis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Thrombocytosis	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Anaemia macrocytic	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Eosinophilia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Lymph node pain	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Investigations			
- Overall -	- Any Grade -	24 (27.6%)	83 (50.0%)
	Grade 1-2	15 (17.2%)	61 (36.7%)
	1	8 (9.2%)	31 (18.7%)
	2	7 (8.0%)	30 (18.1%)
	Grade 3-4	9 (10.3%)	22 (13.3%)
	3	9 (10.3%)	18 (10.8%)
	4	0	4 (2.4%)
Neutrophil count decreased	- Any Grade -	10 (11.5%)	22 (13.3%)
	Grade 1-2	5 (5.7%)	14 (8.4%)
	1	1 (1.1%)	2 (1.2%)
	2	4 (4.6%)	12 (7.2%)
	Grade 3-4	5 (5.7%)	8 (4.8%)
	3	5 (5.7%)	6 (3.6%)
	4	0	2 (1.2%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Alanine aminotransferase increased	- Any Grade -	7 (8.0%)	23 (13.9%)
	Grade 1-2	4 (4.6%)	15 (9.0%)
	1	4 (4.6%)	8 (4.8%)
	2	0	7 (4.2%)
	Grade 3-4	3 (3.4%)	8 (4.8%)
	3	3 (3.4%)	8 (4.8%)
Aspartate aminotransferase increased	- Any Grade -	6 (6.9%)	18 (10.8%)
	Grade 1-2	3 (3.4%)	13 (7.8%)
	1	2 (2.3%)	7 (4.2%)
	2	1 (1.1%)	6 (3.6%)
	Grade 3-4	3 (3.4%)	5 (3.0%)
	3	3 (3.4%)	5 (3.0%)
White blood cell count decreased	- Any Grade -	7 (8.0%)	11 (6.6%)
	Grade 1-2	5 (5.7%)	8 (4.8%)
	1	2 (2.3%)	3 (1.8%)
	2	3 (3.4%)	5 (3.0%)
	Grade 3-4	2 (2.3%)	3 (1.8%)
	3	2 (2.3%)	3 (1.8%)
Weight decreased	- Any Grade -	3 (3.4%)	12 (7.2%)
	Grade 1-2	3 (3.4%)	12 (7.2%)
	1	2 (2.3%)	8 (4.8%)
	2	1 (1.1%)	4 (2.4%)
Blood lactate dehydrogenase increased	- Any Grade -	4 (4.6%)	7 (4.2%)
	Grade 1-2	4 (4.6%)	7 (4.2%)
	1	4 (4.6%)	5 (3.0%)
	2	0	2 (1.2%)
Blood alkaline phosphatase increased	- Any Grade -	1 (1.1%)	9 (5.4%)
	Grade 1-2	1 (1.1%)	9 (5.4%)
	1	1 (1.1%)	8 (4.8%)
	2	0	1 (0.6%)
Blood cholesterol increased	- Any Grade -	2 (2.3%)	6 (3.6%)
	Grade 1-2	2 (2.3%)	6 (3.6%)
	1	2 (2.3%)	5 (3.0%)
	2	0	1 (0.6%)
Blood creatinine increased	- Any Grade -	0	6 (3.6%)
	Grade 1-2	0	6 (3.6%)
	1	0	5 (3.0%)
	2	0	1 (0.6%)
Blood urea increased	- Any Grade -	3 (3.4%)	3 (1.8%)
	Grade 1-2	3 (3.4%)	3 (1.8%)
	1	3 (3.4%)	3 (1.8%)
Gamma-glutamyltransferase increased	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Lipase increased	- Any Grade -	0	5 (3.0%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Lymphocyte count decreased	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	0
	4	0	1 (0.6%)
Weight increased	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	0	2 (1.2%)
	2	1 (1.1%)	1 (0.6%)
Amylase increased	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	1 (1.1%)	2 (1.2%)
Blood phosphorus increased	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Haemoglobin decreased	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Low density lipoprotein increased	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Blood bilirubin increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Blood calcium decreased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Blood chloride decreased	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Blood glucose increased	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Blood magnesium decreased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Blood pressure increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Blood triglycerides increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Body temperature increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Eastern Cooperative Oncology Group performance status worsened	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Electrocardiogram QT prolonged	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Glycosylated haemoglobin abnormal	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Haematocrit decreased	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Influenza A virus test positive	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Platelet count decreased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Platelet count increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Vitamin B12 decreased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
White blood cell count increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	25 (28.7%)	74 (44.6%)
	Grade 1-2	20 (23.0%)	63 (38.0%)
	1	13 (14.9%)	34 (20.5%)
	2	7 (8.0%)	29 (17.5%)
	Grade 3-4	4 (4.6%)	11 (6.6%)
	3	3 (3.4%)	10 (6.0%)
	4	1 (1.1%)	1 (0.6%)
	Grade 5	1 (1.1%)	0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hyperglycaemia	- Any Grade -	9 (10.3%)	31 (18.7%)
	Grade 1-2	9 (10.3%)	28 (16.9%)
	1	5 (5.7%)	17 (10.2%)
	2	4 (4.6%)	11 (6.6%)
	Grade 3-4	0	3 (1.8%)
	3	0	2 (1.2%)
	4	0	1 (0.6%)
Decreased appetite	- Any Grade -	10 (11.5%)	29 (17.5%)
	Grade 1-2	10 (11.5%)	28 (16.9%)
	1	7 (8.0%)	18 (10.8%)
	2	3 (3.4%)	10 (6.0%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hypertriglyceridaemia	- Any Grade -	2 (2.3%)	9 (5.4%)
	Grade 1-2	2 (2.3%)	6 (3.6%)
	1	2 (2.3%)	0
	2	0	6 (3.6%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Hypokalaemia	- Any Grade -	3 (3.4%)	5 (3.0%)
	Grade 1-2	2 (2.3%)	5 (3.0%)
	1	2 (2.3%)	5 (3.0%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Hypoalbuminaemia	- Any Grade -	3 (3.4%)	4 (2.4%)
	Grade 1-2	3 (3.4%)	4 (2.4%)
	1	2 (2.3%)	3 (1.8%)
	2	1 (1.1%)	1 (0.6%)
Hypomagnesaemia	- Any Grade -	1 (1.1%)	6 (3.6%)
	Grade 1-2	1 (1.1%)	6 (3.6%)
	1	1 (1.1%)	4 (2.4%)
	2	0	2 (1.2%)
Hyperkalaemia	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	0	2 (1.2%)
	2	1 (1.1%)	0
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hyponatraemia	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
Hypophosphataemia	- Any Grade -	3 (3.4%)	1 (0.6%)
	Grade 1-2	3 (3.4%)	1 (0.6%)
	1	1 (1.1%)	0
	2	2 (2.3%)	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hypercholesterolaemia	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	0
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Dyslipidaemia	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Electrolyte imbalance	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Glucose tolerance impaired	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hyperamylasaemia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Hypocalcaemia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Increased appetite	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Dehydration	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Diabetes mellitus	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Food aversion	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Gout	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hypercreatininaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Hyperlipasaemia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	4	1 (1.1%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hyperlipidaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Lipoedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Tumour lysis syndrome	- Any Grade -	1 (1.1%)	0
	Grade 5	1 (1.1%)	0
Musculoskeletal and connective tissue disorders			
- Overall -	- Any Grade -	34 (39.1%)	54 (32.5%)
	Grade 1-2	32 (36.8%)	53 (31.9%)
	1	21 (24.1%)	32 (19.3%)
	2	11 (12.6%)	21 (12.7%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
	4	1 (1.1%)	0
Arthralgia	- Any Grade -	12 (13.8%)	16 (9.6%)
	Grade 1-2	11 (12.6%)	16 (9.6%)
	1	5 (5.7%)	10 (6.0%)
	2	6 (6.9%)	6 (3.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Back pain	- Any Grade -	9 (10.3%)	16 (9.6%)
	Grade 1-2	9 (10.3%)	16 (9.6%)
	1	8 (9.2%)	6 (3.6%)
	2	1 (1.1%)	10 (6.0%)
Myalgia	- Any Grade -	5 (5.7%)	16 (9.6%)
	Grade 1-2	5 (5.7%)	16 (9.6%)
	1	5 (5.7%)	14 (8.4%)
	2	0	2 (1.2%)
Pain in extremity	- Any Grade -	4 (4.6%)	14 (8.4%)
	Grade 1-2	4 (4.6%)	14 (8.4%)
	1	2 (2.3%)	10 (6.0%)
	2	2 (2.3%)	4 (2.4%)
Bone pain	- Any Grade -	0	7 (4.2%)
	Grade 1-2	0	6 (3.6%)
	1	0	5 (3.0%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Muscle spasms	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	4 (2.4%)
	1	0	3 (1.8%)
	2	1 (1.1%)	1 (0.6%)
Musculoskeletal pain	- Any Grade -	3 (3.4%)	2 (1.2%)
	Grade 1-2	3 (3.4%)	2 (1.2%)
	1	2 (2.3%)	2 (1.2%)
	2	1 (1.1%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Neck pain	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	1	2 (2.3%)	3 (1.8%)
Muscular weakness	- Any Grade -	3 (3.4%)	1 (0.6%)
	Grade 1-2	3 (3.4%)	1 (0.6%)
	1	3 (3.4%)	0
	2	0	1 (0.6%)
Musculoskeletal chest pain	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	1 (1.1%)	1 (0.6%)
	2	0	2 (1.2%)
Spinal pain	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Spinal disorder	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Flank pain	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Intervertebral disc compression	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	4	1 (1.1%)	0
Joint swelling	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Limb discomfort	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Myosclerosis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Osteoarthritis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Osteonecrosis of jaw	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Pathological fracture	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Spondylolysis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Tendon disorder	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0

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Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	27 (31.0%)	48 (28.9%)
	Grade 1-2	20 (23.0%)	43 (25.9%)
	1	11 (12.6%)	33 (19.9%)
	2	9 (10.3%)	10 (6.0%)
	Grade 3-4	7 (8.0%)	4 (2.4%)
	3	7 (8.0%)	2 (1.2%)
	4	0	2 (1.2%)
	Grade 5	0	1 (0.6%)
Cough	- Any Grade -	10 (11.5%)	14 (8.4%)
	Grade 1-2	10 (11.5%)	14 (8.4%)
	1	6 (6.9%)	9 (5.4%)
	2	4 (4.6%)	5 (3.0%)
Dyspnoea	- Any Grade -	7 (8.0%)	8 (4.8%)
	Grade 1-2	4 (4.6%)	7 (4.2%)
	1	4 (4.6%)	5 (3.0%)
	2	0	2 (1.2%)
	Grade 3-4	3 (3.4%)	1 (0.6%)
	3	3 (3.4%)	0
	4	0	1 (0.6%)
Epistaxis	- Any Grade -	3 (3.4%)	12 (7.2%)
	Grade 1-2	3 (3.4%)	12 (7.2%)
	1	3 (3.4%)	11 (6.6%)
	2	0	1 (0.6%)
Oropharyngeal pain	- Any Grade -	0	13 (7.8%)
	Grade 1-2	0	13 (7.8%)
	1	0	12 (7.2%)
	2	0	1 (0.6%)
Dysphonia	- Any Grade -	3 (3.4%)	3 (1.8%)
	Grade 1-2	3 (3.4%)	3 (1.8%)
	1	3 (3.4%)	2 (1.2%)
	2	0	1 (0.6%)
Nasal congestion	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	2 (2.3%)	4 (2.4%)
	1	1 (1.1%)	3 (1.8%)
	2	1 (1.1%)	1 (0.6%)
Productive cough	- Any Grade -	1 (1.1%)	5 (3.0%)
	Grade 1-2	1 (1.1%)	5 (3.0%)
	1	0	5 (3.0%)
	2	1 (1.1%)	0
Rhinitis allergic	- Any Grade -	3 (3.4%)	3 (1.8%)
	Grade 1-2	3 (3.4%)	3 (1.8%)
	1	2 (2.3%)	3 (1.8%)
	2	1 (1.1%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Dyspnoea exertional	- Any Grade -	3 (3.4%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	1 (1.1%)	2 (1.2%)
	2	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Pleural effusion	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
Pulmonary embolism	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
	Grade 5	0	1 (0.6%)
Rhinorrhoea	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	3 (1.8%)
Haemoptysis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Hypoxia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Laryngeal inflammation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Lung infiltration	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Nasal dryness	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Nasal inflammation	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Nasal mucosa atrophy	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Pneumonitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Pneumothorax	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Pulmonary hypertension	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Respiratory disorder	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Rhinalgia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Tachypnoea	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Throat tightness	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Upper-airway cough syndrome	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Wheezing	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Psychiatric disorders			
- Overall -	- Any Grade -	11 (12.6%)	26 (15.7%)
	Grade 1-2	10 (11.5%)	26 (15.7%)
	1	8 (9.2%)	18 (10.8%)
	2	2 (2.3%)	8 (4.8%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Insomnia	- Any Grade -	5 (5.7%)	10 (6.0%)
	Grade 1-2	5 (5.7%)	10 (6.0%)
	1	4 (4.6%)	7 (4.2%)
	2	1 (1.1%)	3 (1.8%)
Anxiety	- Any Grade -	2 (2.3%)	8 (4.8%)
	Grade 1-2	2 (2.3%)	8 (4.8%)
	1	1 (1.1%)	4 (2.4%)
	2	1 (1.1%)	4 (2.4%)
Depression	- Any Grade -	1 (1.1%)	5 (3.0%)
	Grade 1-2	0	5 (3.0%)
	1	0	4 (2.4%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Depressed mood	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Dyssomnia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Mental disorder	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Panic attack	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Restlessness	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Vascular disorders			
- Overall -	- Any Grade -	9 (10.3%)	26 (15.7%)
	Grade 1-2	9 (10.3%)	20 (12.0%)
	1	5 (5.7%)	11 (6.6%)
	2	4 (4.6%)	9 (5.4%)
	Grade 3-4	0	6 (3.6%)
	3	0	6 (3.6%)
Hypertension	- Any Grade -	3 (3.4%)	6 (3.6%)
	Grade 1-2	3 (3.4%)	4 (2.4%)
	1	1 (1.1%)	1 (0.6%)
	2	2 (2.3%)	3 (1.8%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Lymphoedema	- Any Grade -	0	7 (4.2%)
	Grade 1-2	0	6 (3.6%)
	1	0	6 (3.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hypotension	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	2 (2.3%)	1 (0.6%)
	1	1 (1.1%)	0
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Flushing	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	0	1 (0.6%)
	2	1 (1.1%)	2 (1.2%)
Phlebitis	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	2 (2.3%)	1 (0.6%)
	2	0	1 (0.6%)
Hot flush	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	1 (0.6%)
	2	0	2 (1.2%)
Venous thrombosis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	0
	2	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Deep vein thrombosis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Embolism	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Haematoma	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Hyperaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hypertensive crisis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hypertensive urgency	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Thrombophlebitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Varicose vein	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Vasculitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Venous occlusion	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Venous thrombosis limb	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Eye disorders			
- Overall -	- Any Grade -	7 (8.0%)	22 (13.3%)
	Grade 1-2	5 (5.7%)	20 (12.0%)
	1	5 (5.7%)	16 (9.6%)
	2	0	4 (2.4%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	2 (1.2%)
Vision blurred	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	4 (2.4%)
	1	1 (1.1%)	2 (1.2%)
	2	0	2 (1.2%)
Dry eye	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	3 (1.8%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Blepharitis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Lacrimation increased	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Ocular hyperaemia	- Any Grade -	2 (2.3%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Visual acuity reduced	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Visual impairment	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	0
	2	0	1 (0.6%)
Chalazion	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Conjunctival haemorrhage	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Conjunctival irritation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Conjunctival oedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Conjunctivitis allergic	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Cystoid macular oedema	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Epiretinal membrane	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Eye disorder	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Eye pain	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Eye pruritus	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Glaucoma	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Macular oedema	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Periorbital oedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Periorbital swelling	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Photopsia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Retinal vascular disorder	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Strabismus	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Injury, poisoning and procedural complications			
- Overall -	- Any Grade -	11 (12.6%)	18 (10.8%)
	Grade 1-2	9 (10.3%)	15 (9.0%)
	1	7 (8.0%)	10 (6.0%)
	2	2 (2.3%)	5 (3.0%)
	Grade 3-4	2 (2.3%)	3 (1.8%)
	3	1 (1.1%)	3 (1.8%)
	4	1 (1.1%)	0
Fall	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	1	2 (2.3%)	1 (0.6%)
	2	0	2 (1.2%)
Accidental overdose	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	1 (1.1%)	3 (1.8%)
Vascular access site pain	- Any Grade -	3 (3.4%)	1 (0.6%)
	Grade 1-2	3 (3.4%)	1 (0.6%)
	1	2 (2.3%)	1 (0.6%)
	2	1 (1.1%)	0
Infusion related reaction	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	1 (1.1%)	1 (0.6%)
	2	0	1 (0.6%)
Ligament sprain	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Procedural pain	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Spinal fracture	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	0	1 (0.6%)
	4	1 (1.1%)	0
Tooth fracture	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Wound	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Brachial plexus injury	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Eschar	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Fracture	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Intentional product misuse	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Radiation inflammation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Radiation pneumonitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Recall phenomenon	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Rib fracture	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Skin abrasion	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Skin laceration	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Splinter	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Thermal burn	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Toxicity to various agents	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Renal and urinary disorders			
- Overall -	- Any Grade -	4 (4.6%)	16 (9.6%)
	Grade 1-2	4 (4.6%)	16 (9.6%)
	1	4 (4.6%)	11 (6.6%)
	2	0	5 (3.0%)
Dysuria	- Any Grade -	2 (2.3%)	7 (4.2%)
	Grade 1-2	2 (2.3%)	7 (4.2%)
	1	2 (2.3%)	6 (3.6%)
	2	0	1 (0.6%)
Haematuria	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Proteinuria	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	0
	2	0	1 (0.6%)
Anuria	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Haemoglobinuria	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Oliguria	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Renal failure	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Renal impairment	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Strangury	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Tubulointerstitial nephritis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Urinary incontinence	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Urinary retention	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Urine flow decreased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Reproductive system and breast disorders			
- Overall -	- Any Grade -	4 (4.6%)	14 (8.4%)
	Grade 1-2	4 (4.6%)	13 (7.8%)
	1	3 (3.4%)	7 (4.2%)
	2	1 (1.1%)	6 (3.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Breast pain	- Any Grade -	3 (3.4%)	9 (5.4%)
	Grade 1-2	3 (3.4%)	9 (5.4%)
	1	2 (2.3%)	4 (2.4%)
	2	1 (1.1%)	5 (3.0%)
Amenorrhoea	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Breast discomfort	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Menopausal symptoms	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Pelvic pain	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Vaginal discharge	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Vulvovaginal burning sensation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Ear and labyrinth disorders			
- Overall -	- Any Grade -	2 (2.3%)	13 (7.8%)
	Grade 1-2	2 (2.3%)	13 (7.8%)
	1	2 (2.3%)	10 (6.0%)
	2	0	3 (1.8%)
Vertigo	- Any Grade -	1 (1.1%)	9 (5.4%)
	Grade 1-2	1 (1.1%)	9 (5.4%)
	1	1 (1.1%)	7 (4.2%)
	2	0	2 (1.2%)
Ear pain	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	1 (1.1%)	2 (1.2%)
Tinnitus	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Cerumen impaction	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hypoacusis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Cardiac disorders			
- Overall -	- Any Grade -	6 (6.9%)	5 (3.0%)
	Grade 1-2	4 (4.6%)	4 (2.4%)
	1	1 (1.1%)	3 (1.8%)
	2	3 (3.4%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	0
	3	2 (2.3%)	0
	Grade 5	0	1 (0.6%)
Sinus tachycardia	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	1 (1.1%)	2 (1.2%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Tachycardia	- Any Grade -	3 (3.4%)	0
	Grade 1-2	3 (3.4%)	0
	2	3 (3.4%)	0
Atrial fibrillation	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Bradycardia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Cardiopulmonary failure	- Any Grade -	0	1 (0.6%)
	Grade 5	0	1 (0.6%)
Extrasystoles	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Immune system disorders			
- Overall -	- Any Grade -	6 (6.9%)	5 (3.0%)
	Grade 1-2	5 (5.7%)	5 (3.0%)
	1	5 (5.7%)	2 (1.2%)
	2	0	3 (1.8%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hypersensitivity	- Any Grade -	5 (5.7%)	5 (3.0%)
	Grade 1-2	4 (4.6%)	5 (3.0%)
	1	4 (4.6%)	2 (1.2%)
	2	0	3 (1.8%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Anaphylactic shock	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Drug hypersensitivity	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Seasonal allergy	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
- Overall -	- Any Grade -	4 (4.6%)	7 (4.2%)
	Grade 1-2	2 (2.3%)	4 (2.4%)
	1	1 (1.1%)	0
	2	1 (1.1%)	4 (2.4%)
	Grade 3-4	1 (1.1%)	3 (1.8%)
	3	0	2 (1.2%)
	4	1 (1.1%)	1 (0.6%)
	Grade 5	1 (1.1%)	0
Cancer pain	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
Infected neoplasm	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
Gastric cancer	- Any Grade -	1 (1.1%)	0
	Grade 5	1 (1.1%)	0
Lymphangiosis carcinomatosa	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	4	1 (1.1%)	0
Schwannoma	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Tumour haemorrhage	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Tumour necrosis	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Tumour pain	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_A_SE.out

Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Tumour ulceration	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hepatobiliary disorders			
- Overall -	- Any Grade -	3 (3.4%)	1 (0.6%)
	Grade 1-2	3 (3.4%)	1 (0.6%)
	1	1 (1.1%)	0
	2	2 (2.3%)	1 (0.6%)
Hyperbilirubinaemia	- Any Grade -	3 (3.4%)	0
	Grade 1-2	3 (3.4%)	0
	1	1 (1.1%)	0
	2	2 (2.3%)	0
Cholecystitis acute	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
No Coding available			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
No Coding available	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
Product issues			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Device occlusion	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_A_SE.out
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Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	74 (98.7%)	144 (99.3%)
	Grade 1-2	37 (49.3%)	61 (42.1%)
	1	5 (6.7%)	3 (2.1%)
	2	32 (42.7%)	58 (40.0%)
	Grade 3-4	36 (48.0%)	78 (53.8%)
	3	33 (44.0%)	70 (48.3%)
	4	3 (4.0%)	8 (5.5%)
	Grade 5	1 (1.3%)	5 (3.4%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	56 (74.7%)	139 (95.9%)
	Grade 1-2	53 (70.7%)	116 (80.0%)
	1	33 (44.0%)	37 (25.5%)
	2	20 (26.7%)	79 (54.5%)
	Grade 3-4	3 (4.0%)	23 (15.9%)
	3	3 (4.0%)	21 (14.5%)
	4	0	2 (1.4%)
Diarrhoea	- Any Grade -	30 (40.0%)	126 (86.9%)
	Grade 1-2	29 (38.7%)	109 (75.2%)
	1	22 (29.3%)	47 (32.4%)
	2	7 (9.3%)	62 (42.8%)
	Grade 3-4	1 (1.3%)	17 (11.7%)
	3	1 (1.3%)	17 (11.7%)
Nausea	- Any Grade -	17 (22.7%)	60 (41.4%)
	Grade 1-2	17 (22.7%)	58 (40.0%)
	1	14 (18.7%)	41 (28.3%)
	2	3 (4.0%)	17 (11.7%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Constipation	- Any Grade -	26 (34.7%)	42 (29.0%)
	Grade 1-2	26 (34.7%)	42 (29.0%)
	1	20 (26.7%)	38 (26.2%)
	2	6 (8.0%)	4 (2.8%)
Vomiting	- Any Grade -	6 (8.0%)	45 (31.0%)
	Grade 1-2	6 (8.0%)	42 (29.0%)
	1	6 (8.0%)	30 (20.7%)
	2	0	12 (8.3%)
	Grade 3-4	0	3 (2.1%)
	3	0	2 (1.4%)
	4	0	1 (0.7%)
Stomatitis	- Any Grade -	6 (8.0%)	16 (11.0%)
	Grade 1-2	6 (8.0%)	16 (11.0%)
	1	5 (6.7%)	13 (9.0%)
	2	1 (1.3%)	3 (2.1%)
Abdominal pain upper	- Any Grade -	5 (6.7%)	15 (10.3%)
	Grade 1-2	5 (6.7%)	15 (10.3%)
	1	3 (4.0%)	10 (6.9%)
	2	2 (2.7%)	5 (3.4%)

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Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Abdominal pain	- Any Grade -	7 (9.3%)	12 (8.3%)
	Grade 1-2	6 (8.0%)	11 (7.6%)
	1	4 (5.3%)	4 (2.8%)
	2	2 (2.7%)	7 (4.8%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Dyspepsia	- Any Grade -	4 (5.3%)	9 (6.2%)
	Grade 1-2	4 (5.3%)	9 (6.2%)
	1	3 (4.0%)	5 (3.4%)
	2	1 (1.3%)	4 (2.8%)
Flatulence	- Any Grade -	4 (5.3%)	7 (4.8%)
	Grade 1-2	4 (5.3%)	7 (4.8%)
	1	3 (4.0%)	6 (4.1%)
	2	1 (1.3%)	1 (0.7%)
Gastrooesophageal reflux disease	- Any Grade -	4 (5.3%)	4 (2.8%)
	Grade 1-2	4 (5.3%)	4 (2.8%)
	1	2 (2.7%)	3 (2.1%)
	2	2 (2.7%)	1 (0.7%)
Mouth ulceration	- Any Grade -	1 (1.3%)	5 (3.4%)
	Grade 1-2	1 (1.3%)	5 (3.4%)
	1	1 (1.3%)	4 (2.8%)
	2	0	1 (0.7%)
Abdominal distension	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	1 (1.3%)	3 (2.1%)
	2	0	1 (0.7%)
Gastritis	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	1 (0.7%)
Toothache	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	1 (1.3%)	3 (2.1%)
	2	1 (1.3%)	0
Abdominal discomfort	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	1 (1.3%)	2 (1.4%)
	2	0	1 (0.7%)
Aphthous ulcer	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	3 (2.1%)
	1	0	2 (1.4%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Haemorrhoids	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	3 (2.1%)
	2	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Haematochezia	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
Oral pain	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	3 (2.1%)
Ascites	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Chronic gastritis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dry mouth	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Enterocolitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Paraesthesia oral	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Abdominal hernia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Abdominal pain lower	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Anal haemorrhage	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Angular cheilitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Dental caries	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Dental discomfort	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Dental necrosis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Eructation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Faeces discoloured	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Faeces soft	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Food poisoning	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperchlorhydria	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hypoaesthesia oral	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Intestinal obstruction	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	4	0	1 (0.7%)
Lip dry	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Odynophagia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Periodontal disease	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Proctalgia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Tongue erythema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Tongue exfoliation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Tongue ulceration	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Nervous system disorders			
- Overall -	- Any Grade -	54 (72.0%)	110 (75.9%)
	Grade 1-2	46 (61.3%)	95 (65.5%)
	1	22 (29.3%)	45 (31.0%)
	2	24 (32.0%)	50 (34.5%)
	Grade 3-4	8 (10.7%)	15 (10.3%)
	3	8 (10.7%)	15 (10.3%)
Neuropathy peripheral	- Any Grade -	12 (16.0%)	46 (31.7%)
	Grade 1-2	9 (12.0%)	36 (24.8%)
	1	2 (2.7%)	19 (13.1%)
	2	7 (9.3%)	17 (11.7%)
	Grade 3-4	3 (4.0%)	10 (6.9%)
	3	3 (4.0%)	10 (6.9%)
Peripheral sensory neuropathy	- Any Grade -	23 (30.7%)	23 (15.9%)
	Grade 1-2	19 (25.3%)	19 (13.1%)
	1	10 (13.3%)	8 (5.5%)
	2	9 (12.0%)	11 (7.6%)
	Grade 3-4	4 (5.3%)	4 (2.8%)
	3	4 (5.3%)	4 (2.8%)
Headache	- Any Grade -	8 (10.7%)	24 (16.6%)
	Grade 1-2	8 (10.7%)	24 (16.6%)
	1	5 (6.7%)	20 (13.8%)
	2	3 (4.0%)	4 (2.8%)
Paraesthesia	- Any Grade -	6 (8.0%)	13 (9.0%)
	Grade 1-2	6 (8.0%)	13 (9.0%)
	1	5 (6.7%)	10 (6.9%)
	2	1 (1.3%)	3 (2.1%)
Polyneuropathy	- Any Grade -	6 (8.0%)	12 (8.3%)
	Grade 1-2	6 (8.0%)	11 (7.6%)
	1	5 (6.7%)	8 (5.5%)
	2	1 (1.3%)	3 (2.1%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dysgeusia	- Any Grade -	4 (5.3%)	11 (7.6%)
	Grade 1-2	4 (5.3%)	11 (7.6%)
	1	3 (4.0%)	10 (6.9%)
	2	1 (1.3%)	1 (0.7%)
Dizziness	- Any Grade -	3 (4.0%)	10 (6.9%)
	Grade 1-2	2 (2.7%)	10 (6.9%)
	1	0	7 (4.8%)
	2	2 (2.7%)	3 (2.1%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Neurotoxicity	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	1 (1.3%)	0
	2	1 (1.3%)	3 (2.1%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hypoaesthesia	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	0
Peripheral motor neuropathy	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	2 (1.4%)
	2	0	2 (1.4%)
Amnesia	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Disturbance in attention	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
Lethargy	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	0	1 (0.7%)
	2	1 (1.3%)	0
Post herpetic neuralgia	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
Radiculopathy	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Sciatica	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
Taste disorder	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Anosmia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Ataxia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Cerebral ischaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Cerebrovascular accident	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Cognitive disorder	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Dysaesthesia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Epilepsy	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Facial paralysis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Head discomfort	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hypertonia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hypotonia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Memory impairment	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Muscle spasticity	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Muscle tone disorder	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Neuritis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Radicular pain	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Somnolence	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Tension headache	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	53 (70.7%)	106 (73.1%)
	Grade 1-2	51 (68.0%)	99 (68.3%)
	1	14 (18.7%)	30 (20.7%)
	2	37 (49.3%)	69 (47.6%)
	Grade 3-4	2 (2.7%)	7 (4.8%)
	3	2 (2.7%)	7 (4.8%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Alopecia	- Any Grade -	44 (58.7%)	75 (51.7%)
	Grade 1-2	44 (58.7%)	75 (51.7%)
	1	9 (12.0%)	20 (13.8%)
	2	35 (46.7%)	55 (37.9%)
Rash	- Any Grade -	9 (12.0%)	31 (21.4%)
	Grade 1-2	9 (12.0%)	29 (20.0%)
	1	9 (12.0%)	21 (14.5%)
	2	0	8 (5.5%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Pruritus	- Any Grade -	3 (4.0%)	15 (10.3%)
	Grade 1-2	3 (4.0%)	15 (10.3%)
	1	2 (2.7%)	11 (7.6%)
	2	1 (1.3%)	4 (2.8%)
Nail discolouration	- Any Grade -	8 (10.7%)	9 (6.2%)
	Grade 1-2	8 (10.7%)	9 (6.2%)
	1	8 (10.7%)	8 (5.5%)
	2	0	1 (0.7%)
Rash maculo-papular	- Any Grade -	4 (5.3%)	7 (4.8%)
	Grade 1-2	4 (5.3%)	5 (3.4%)
	1	3 (4.0%)	3 (2.1%)
	2	1 (1.3%)	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Dry skin	- Any Grade -	5 (6.7%)	5 (3.4%)
	Grade 1-2	5 (6.7%)	5 (3.4%)
	1	5 (6.7%)	5 (3.4%)
Erythema	- Any Grade -	3 (4.0%)	5 (3.4%)
	Grade 1-2	3 (4.0%)	5 (3.4%)
	1	2 (2.7%)	3 (2.1%)
	2	1 (1.3%)	2 (1.4%)
Nail disorder	- Any Grade -	3 (4.0%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	2 (1.4%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Onycholysis	- Any Grade -	1 (1.3%)	5 (3.4%)
	Grade 1-2	1 (1.3%)	5 (3.4%)
	1	1 (1.3%)	5 (3.4%)
Dermatitis acneiform	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	2 (2.7%)	3 (2.1%)
Dermatitis	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	1 (1.3%)	3 (2.1%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Dermatitis contact	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	0	1 (0.7%)
	2	1 (1.3%)	2 (1.4%)
Nail dystrophy	- Any Grade -	3 (4.0%)	1 (0.7%)
	Grade 1-2	3 (4.0%)	1 (0.7%)
	1	0	1 (0.7%)
	2	3 (4.0%)	0
Onychomadesis	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	3 (2.1%)
	2	0	1 (0.7%)
Dermatitis allergic	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	2	2 (2.7%)	1 (0.7%)
Dermatitis bullous	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Drug eruption	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Eczema	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	2 (1.4%)
	2	0	1 (0.7%)
Palmar-plantar erythrodysaesthesia syndrome	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Urticaria	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	1 (0.7%)
	2	0	2 (1.4%)
Eczema asteatotic	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Nail ridging	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
Onychoclasis	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Photosensitivity reaction	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Skin disorder	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Skin hyperpigmentation	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Skin lesion	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Skin ulcer	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	1	2 (2.7%)	0
Blister	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Butterfly rash	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Dermal cyst	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Erythema multiforme	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperhidrosis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Ingrowing nail	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nail bed inflammation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nail toxicity	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Onychalgia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Pain of skin	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Papule	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Periarticular thenar erythema with onycholysis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Polymorphic light eruption	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Rash erythematous	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash papular	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Rash pruritic	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Sclerema	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Skin discolouration	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Skin exfoliation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Skin reaction	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Stasis dermatitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Urticaria contact	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
General disorders and administration site conditions			
- Overall -	- Any Grade -	47 (62.7%)	91 (62.8%)
	Grade 1-2	43 (57.3%)	86 (59.3%)
	1	20 (26.7%)	46 (31.7%)
	2	23 (30.7%)	40 (27.6%)
	Grade 3-4	4 (5.3%)	3 (2.1%)
	3	4 (5.3%)	3 (2.1%)
	Grade 5	0	2 (1.4%)

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Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Fatigue	- Any Grade -	19 (25.3%)	29 (20.0%)
	Grade 1-2	16 (21.3%)	29 (20.0%)
	1	10 (13.3%)	18 (12.4%)
	2	6 (8.0%)	11 (7.6%)
	Grade 3-4	3 (4.0%)	0
	3	3 (4.0%)	0
Asthenia	- Any Grade -	13 (17.3%)	27 (18.6%)
	Grade 1-2	11 (14.7%)	25 (17.2%)
	1	6 (8.0%)	13 (9.0%)
	2	5 (6.7%)	12 (8.3%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	2 (2.7%)	2 (1.4%)
Oedema peripheral	- Any Grade -	14 (18.7%)	21 (14.5%)
	Grade 1-2	14 (18.7%)	21 (14.5%)
	1	6 (8.0%)	14 (9.7%)
	2	8 (10.7%)	7 (4.8%)
Pyrexia	- Any Grade -	4 (5.3%)	23 (15.9%)
	Grade 1-2	4 (5.3%)	23 (15.9%)
	1	3 (4.0%)	18 (12.4%)
	2	1 (1.3%)	5 (3.4%)
Oedema	- Any Grade -	4 (5.3%)	9 (6.2%)
	Grade 1-2	4 (5.3%)	9 (6.2%)
	1	3 (4.0%)	9 (6.2%)
	2	1 (1.3%)	0
Mucosal inflammation	- Any Grade -	3 (4.0%)	8 (5.5%)
	Grade 1-2	3 (4.0%)	8 (5.5%)
	1	2 (2.7%)	6 (4.1%)
	2	1 (1.3%)	2 (1.4%)
Chest pain	- Any Grade -	2 (2.7%)	6 (4.1%)
	Grade 1-2	2 (2.7%)	6 (4.1%)
	1	2 (2.7%)	4 (2.8%)
	2	0	2 (1.4%)
Influenza like illness	- Any Grade -	1 (1.3%)	7 (4.8%)
	Grade 1-2	1 (1.3%)	7 (4.8%)
	1	0	6 (4.1%)
	2	1 (1.3%)	1 (0.7%)
Malaise	- Any Grade -	3 (4.0%)	5 (3.4%)
	Grade 1-2	3 (4.0%)	5 (3.4%)
	1	2 (2.7%)	2 (1.4%)
	2	1 (1.3%)	3 (2.1%)
Chest discomfort	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	1 (1.3%)	3 (2.1%)
	2	0	1 (0.7%)
Pain	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	0	1 (0.7%)
	2	1 (1.3%)	3 (2.1%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Peripheral swelling	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Chills	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Face oedema	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Generalised oedema	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Infusion site extravasation	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Catheter site erythema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Death	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Extravasation	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Feeling drunk	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Gait disturbance	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
General physical health deterioration	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Hyperthermia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Hypothermia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Localised oedema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Non-cardiac chest pain	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Swelling face	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Thirst	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Infections and infestations			
- Overall -	- Any Grade -	42 (56.0%)	76 (52.4%)
	Grade 1-2	39 (52.0%)	71 (49.0%)
	1	11 (14.7%)	20 (13.8%)
	2	28 (37.3%)	51 (35.2%)
	Grade 3-4	2 (2.7%)	4 (2.8%)
	3	2 (2.7%)	4 (2.8%)
	Grade 5	1 (1.3%)	1 (0.7%)
Nasopharyngitis	- Any Grade -	7 (9.3%)	19 (13.1%)
	Grade 1-2	7 (9.3%)	19 (13.1%)
	1	3 (4.0%)	10 (6.9%)
	2	4 (5.3%)	9 (6.2%)
Upper respiratory tract infection	- Any Grade -	7 (9.3%)	14 (9.7%)
	Grade 1-2	7 (9.3%)	14 (9.7%)
	1	2 (2.7%)	1 (0.7%)
	2	5 (6.7%)	13 (9.0%)
Urinary tract infection	- Any Grade -	5 (6.7%)	16 (11.0%)
	Grade 1-2	4 (5.3%)	15 (10.3%)
	1	2 (2.7%)	2 (1.4%)
	2	2 (2.7%)	13 (9.0%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Cystitis	- Any Grade -	6 (8.0%)	7 (4.8%)
	Grade 1-2	6 (8.0%)	7 (4.8%)
	1	1 (1.3%)	1 (0.7%)
	2	5 (6.7%)	6 (4.1%)
Pneumonia	- Any Grade -	4 (5.3%)	6 (4.1%)
	Grade 1-2	3 (4.0%)	5 (3.4%)
	1	0	1 (0.7%)
	2	3 (4.0%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
	Grade 5	0	1 (0.7%)
Influenza	- Any Grade -	2 (2.7%)	6 (4.1%)
	Grade 1-2	2 (2.7%)	6 (4.1%)
	1	1 (1.3%)	3 (2.1%)
	2	1 (1.3%)	3 (2.1%)
Paronychia	- Any Grade -	1 (1.3%)	7 (4.8%)
	Grade 1-2	1 (1.3%)	7 (4.8%)
	1	0	3 (2.1%)
	2	1 (1.3%)	4 (2.8%)
Pharyngitis	- Any Grade -	2 (2.7%)	5 (3.4%)
	Grade 1-2	2 (2.7%)	5 (3.4%)
	2	2 (2.7%)	5 (3.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Bronchitis	- Any Grade -	2 (2.7%)	4 (2.8%)
	Grade 1-2	2 (2.7%)	4 (2.8%)
	1	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	3 (2.1%)
Herpes zoster	- Any Grade -	1 (1.3%)	5 (3.4%)
	Grade 1-2	1 (1.3%)	5 (3.4%)
	1	0	1 (0.7%)
	2	1 (1.3%)	4 (2.8%)
Rhinitis	- Any Grade -	0	6 (4.1%)
	Grade 1-2	0	6 (4.1%)
	1	0	5 (3.4%)
	2	0	1 (0.7%)
Cellulitis	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	0	1 (0.7%)
	2	2 (2.7%)	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Folliculitis	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	0	3 (2.1%)
	2	1 (1.3%)	1 (0.7%)
Conjunctivitis	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	0
Gingivitis	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	0
	2	0	2 (1.4%)
Lower respiratory tract infection	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	2	0	3 (2.1%)
Oral herpes	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	2 (1.4%)
	2	0	1 (0.7%)
Sinusitis	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	1 (0.7%)
	2	0	2 (1.4%)
Vaginal infection	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
COVID-19	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)

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Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Erysipelas	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Escherichia urinary tract infection	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Furuncle	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Respiratory tract infection	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Respiratory tract infection viral	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	2	2 (2.7%)	0
Skin infection	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	0	1 (0.7%)
	2	1 (1.3%)	0
Tonsillitis	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
Tooth abscess	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	2	2 (2.7%)	0
Tracheitis	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	2	2 (2.7%)	0
Wound infection	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Abdominal abscess	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Appendicitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Candida infection	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Colonic abscess	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Diarrhoea infectious	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Enterovirus infection	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Fungal skin infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Herpes ophthalmic	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Herpes simplex	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Herpes virus infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hordeolum	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Laryngitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Laryngitis fungal	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Lymphangitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Nail infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Nasal vestibulitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Onychomycosis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Oral infection	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Otitis externa	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Otitis media acute	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Periodontitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pharyngotonsillitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Pulpitis dental	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Sepsis	- Any Grade -	1 (1.3%)	0
	Grade 5	1 (1.3%)	0
Tinea infection	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Tinea pedis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Tracheobronchitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Vascular access site infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Viral infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Musculoskeletal and connective tissue disorders			
- Overall -	- Any Grade -	39 (52.0%)	69 (47.6%)
	Grade 1-2	37 (49.3%)	66 (45.5%)
	1	21 (28.0%)	41 (28.3%)
	2	16 (21.3%)	25 (17.2%)
	Grade 3-4	2 (2.7%)	3 (2.1%)
	3	2 (2.7%)	3 (2.1%)
Arthralgia	- Any Grade -	10 (13.3%)	26 (17.9%)
	Grade 1-2	9 (12.0%)	26 (17.9%)
	1	4 (5.3%)	16 (11.0%)
	2	5 (6.7%)	10 (6.9%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Back pain	- Any Grade -	7 (9.3%)	21 (14.5%)
	Grade 1-2	6 (8.0%)	21 (14.5%)
	1	3 (4.0%)	14 (9.7%)
	2	3 (4.0%)	7 (4.8%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Myalgia	- Any Grade -	9 (12.0%)	15 (10.3%)
	Grade 1-2	9 (12.0%)	15 (10.3%)
	1	8 (10.7%)	13 (9.0%)
	2	1 (1.3%)	2 (1.4%)
Pain in extremity	- Any Grade -	6 (8.0%)	13 (9.0%)
	Grade 1-2	6 (8.0%)	13 (9.0%)
	1	5 (6.7%)	9 (6.2%)
	2	1 (1.3%)	4 (2.8%)
Bone pain	- Any Grade -	4 (5.3%)	9 (6.2%)
	Grade 1-2	4 (5.3%)	9 (6.2%)
	1	3 (4.0%)	4 (2.8%)
	2	1 (1.3%)	5 (3.4%)
Muscle spasms	- Any Grade -	5 (6.7%)	3 (2.1%)
	Grade 1-2	5 (6.7%)	3 (2.1%)
	1	5 (6.7%)	1 (0.7%)
	2	0	2 (1.4%)
Arthritis	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	0	2 (1.4%)
	2	2 (2.7%)	1 (0.7%)
Muscular weakness	- Any Grade -	3 (4.0%)	2 (1.4%)
	Grade 1-2	3 (4.0%)	2 (1.4%)
	1	3 (4.0%)	2 (1.4%)
Neck pain	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	1 (1.3%)	4 (2.8%)
Musculoskeletal chest pain	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	0	3 (2.1%)
	2	1 (1.3%)	0
Spinal pain	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	0	2 (1.4%)
	2	1 (1.3%)	0
Musculoskeletal pain	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
Osteonecrosis of jaw	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Pain in jaw	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Pathological fracture	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Bone swelling	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Costochondritis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Flank pain	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Fracture pain	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Joint swelling	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Musculoskeletal stiffness	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Osteoarthritis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Rhabdomyolysis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Scleroderma	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Spinal osteoarthritis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Synovitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Investigations			
- Overall -	- Any Grade -	42 (56.0%)	62 (42.8%)
	Grade 1-2	30 (40.0%)	37 (25.5%)
	1	13 (17.3%)	15 (10.3%)
	2	17 (22.7%)	22 (15.2%)
	Grade 3-4	12 (16.0%)	25 (17.2%)
	3	10 (13.3%)	20 (13.8%)
	4	2 (2.7%)	5 (3.4%)
Neutrophil count decreased	- Any Grade -	18 (24.0%)	23 (15.9%)
	Grade 1-2	12 (16.0%)	10 (6.9%)
	1	2 (2.7%)	1 (0.7%)
	2	10 (13.3%)	9 (6.2%)
	Grade 3-4	6 (8.0%)	13 (9.0%)
	3	4 (5.3%)	10 (6.9%)
	4	2 (2.7%)	3 (2.1%)
Alanine aminotransferase increased	- Any Grade -	15 (20.0%)	19 (13.1%)
	Grade 1-2	12 (16.0%)	12 (8.3%)
	1	8 (10.7%)	9 (6.2%)
	2	4 (5.3%)	3 (2.1%)
	Grade 3-4	3 (4.0%)	7 (4.8%)
	3	3 (4.0%)	7 (4.8%)
Aspartate aminotransferase increased	- Any Grade -	10 (13.3%)	13 (9.0%)
	Grade 1-2	9 (12.0%)	11 (7.6%)
	1	8 (10.7%)	8 (5.5%)
	2	1 (1.3%)	3 (2.1%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
White blood cell count decreased	- Any Grade -	5 (6.7%)	10 (6.9%)
	Grade 1-2	4 (5.3%)	5 (3.4%)
	1	0	1 (0.7%)
	2	4 (5.3%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	5 (3.4%)
	3	1 (1.3%)	5 (3.4%)
Blood lactate dehydrogenase increased	- Any Grade -	8 (10.7%)	5 (3.4%)
	Grade 1-2	8 (10.7%)	5 (3.4%)
	1	8 (10.7%)	5 (3.4%)
Blood alkaline phosphatase increased	- Any Grade -	7 (9.3%)	3 (2.1%)
	Grade 1-2	7 (9.3%)	3 (2.1%)
	1	2 (2.7%)	3 (2.1%)
	2	5 (6.7%)	0
Blood cholesterol increased	- Any Grade -	3 (4.0%)	6 (4.1%)
	Grade 1-2	3 (4.0%)	6 (4.1%)
	1	2 (2.7%)	5 (3.4%)
	2	1 (1.3%)	1 (0.7%)
Weight decreased	- Any Grade -	2 (2.7%)	7 (4.8%)
	Grade 1-2	2 (2.7%)	7 (4.8%)
	1	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	5 (3.4%)

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Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Lipase increased	- Any Grade -	3 (4.0%)	5 (3.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	0	2 (1.4%)
	2	1 (1.3%)	0
	Grade 3-4	2 (2.7%)	3 (2.1%)
	3	2 (2.7%)	2 (1.4%)
	4	0	1 (0.7%)
Amylase increased	- Any Grade -	1 (1.3%)	5 (3.4%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	1 (1.3%)	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	4	0	1 (0.7%)
Blood creatinine increased	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Gamma-glutamyltransferase increased	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	2 (2.7%)	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Blood triglycerides increased	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	1 (0.7%)
	2	0	3 (2.1%)
Blood albumin decreased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
Blood urea increased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
Haemoglobin decreased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Low density lipoprotein increased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Weight increased	- Any Grade -	3 (4.0%)	0
	Grade 1-2	3 (4.0%)	0
	1	1 (1.3%)	0
	2	2 (2.7%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Blood bilirubin increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Blood glucose increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Blood bicarbonate increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Blood creatine phosphokinase increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Blood fibrinogen increased	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Blood thyroid stimulating hormone increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
C-reactive protein increased	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Eastern Cooperative Oncology Group performance status worsened	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Glycosylated haemoglobin increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Haematocrit decreased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Heart rate increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Lymphocyte count decreased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Platelet count decreased	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
SARS-CoV-2 test positive	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Very low density lipoprotein increased	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	28 (37.3%)	68 (46.9%)
	Grade 1-2	19 (25.3%)	53 (36.6%)
	1	6 (8.0%)	17 (11.7%)
	2	13 (17.3%)	36 (24.8%)
	Grade 3-4	9 (12.0%)	14 (9.7%)
	3	8 (10.7%)	13 (9.0%)
	4	1 (1.3%)	1 (0.7%)
	Grade 5	0	1 (0.7%)
Anaemia	- Any Grade -	15 (20.0%)	45 (31.0%)
	Grade 1-2	15 (20.0%)	43 (29.7%)
	1	8 (10.7%)	18 (12.4%)
	2	7 (9.3%)	25 (17.2%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Neutropenia	- Any Grade -	18 (24.0%)	38 (26.2%)
	Grade 1-2	11 (14.7%)	26 (17.9%)
	1	1 (1.3%)	7 (4.8%)
	2	10 (13.3%)	19 (13.1%)
	Grade 3-4	7 (9.3%)	12 (8.3%)
	3	7 (9.3%)	10 (6.9%)
	4	0	2 (1.4%)
Leukopenia	- Any Grade -	8 (10.7%)	8 (5.5%)
	Grade 1-2	6 (8.0%)	7 (4.8%)
	1	0	2 (1.4%)
	2	6 (8.0%)	5 (3.4%)
	Grade 3-4	2 (2.7%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
	4	1 (1.3%)	0
Febrile neutropenia	- Any Grade -	0	3 (2.1%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
	Grade 5	0	1 (0.7%)
Thrombocytopenia	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Haemolysis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Lymphadenitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Lymphadenopathy	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Lymphopenia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	18 (24.0%)	57 (39.3%)
	Grade 1-2	16 (21.3%)	53 (36.6%)
	1	11 (14.7%)	33 (22.8%)
	2	5 (6.7%)	20 (13.8%)
	Grade 3-4	2 (2.7%)	3 (2.1%)
	3	2 (2.7%)	3 (2.1%)
	Grade 5	0	1 (0.7%)
Cough	- Any Grade -	6 (8.0%)	23 (15.9%)
	Grade 1-2	6 (8.0%)	23 (15.9%)
	1	4 (5.3%)	16 (11.0%)
	2	2 (2.7%)	7 (4.8%)
Epistaxis	- Any Grade -	4 (5.3%)	15 (10.3%)
	Grade 1-2	4 (5.3%)	15 (10.3%)
	1	4 (5.3%)	14 (9.7%)
	2	0	1 (0.7%)
Oropharyngeal pain	- Any Grade -	2 (2.7%)	11 (7.6%)
	Grade 1-2	2 (2.7%)	11 (7.6%)
	1	2 (2.7%)	9 (6.2%)
	2	0	2 (1.4%)
Dyspnoea	- Any Grade -	2 (2.7%)	10 (6.9%)
	Grade 1-2	2 (2.7%)	8 (5.5%)
	1	1 (1.3%)	5 (3.4%)
	2	1 (1.3%)	3 (2.1%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Pneumonitis	- Any Grade -	0	6 (4.1%)
	Grade 1-2	0	5 (3.4%)
	1	0	4 (2.8%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rhinorrhoea	- Any Grade -	0	6 (4.1%)
	Grade 1-2	0	6 (4.1%)
	1	0	5 (3.4%)
	2	0	1 (0.7%)
Haemoptysis	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Nasal congestion	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	2	0	3 (2.1%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Productive cough	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Pulmonary embolism	- Any Grade -	3 (4.0%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
	Grade 3-4	2 (2.7%)	0
	3	2 (2.7%)	0
Upper respiratory tract inflammation	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	0
	2	0	2 (1.4%)
Catarrh	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Dysphonia	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Oropharyngeal discomfort	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
Pleural effusion	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Rhinitis allergic	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Asthma	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Bronchitis chronic	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Chronic obstructive pulmonary disease	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Diaphragmatic disorder	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Nasal dryness	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Nasal septum ulceration	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Paranasal sinus discomfort	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pleuritic pain	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pulmonary hypertension	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Respiratory disorder	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Respiratory distress	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Sinus pain	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Upper-airway cough syndrome	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vasomotor rhinitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	24 (32.0%)	49 (33.8%)
	Grade 1-2	21 (28.0%)	40 (27.6%)
	1	13 (17.3%)	26 (17.9%)
	2	8 (10.7%)	14 (9.7%)
	Grade 3-4	3 (4.0%)	9 (6.2%)
	3	2 (2.7%)	9 (6.2%)
	4	1 (1.3%)	0
Decreased appetite	- Any Grade -	7 (9.3%)	22 (15.2%)
	Grade 1-2	7 (9.3%)	20 (13.8%)
	1	4 (5.3%)	16 (11.0%)
	2	3 (4.0%)	4 (2.8%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Hyperglycaemia	- Any Grade -	10 (13.3%)	19 (13.1%)
	Grade 1-2	10 (13.3%)	16 (11.0%)
	1	8 (10.7%)	6 (4.1%)
	2	2 (2.7%)	10 (6.9%)
	Grade 3-4	0	3 (2.1%)
	3	0	3 (2.1%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hypertriglyceridaemia	- Any Grade -	5 (6.7%)	7 (4.8%)
	Grade 1-2	4 (5.3%)	6 (4.1%)
	1	3 (4.0%)	2 (1.4%)
	2	1 (1.3%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	0	1 (0.7%)
	4	1 (1.3%)	0
Hypokalaemia	- Any Grade -	2 (2.7%)	6 (4.1%)
	Grade 1-2	2 (2.7%)	4 (2.8%)
	1	2 (2.7%)	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Hypercholesterolaemia	- Any Grade -	2 (2.7%)	4 (2.8%)
	Grade 1-2	2 (2.7%)	4 (2.8%)
	1	0	4 (2.8%)
	2	2 (2.7%)	0
Dehydration	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	3 (2.1%)
	1	0	1 (0.7%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hypocalcaemia	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	1 (1.3%)	2 (1.4%)
	2	0	1 (0.7%)
Hypophosphataemia	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Hypercalcaemia	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Hypercreatininaemia	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	0
Hyperuricaemia	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hypoglycaemia	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
Hypomagnesaemia	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Hyponatraemia	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Calcium deficiency	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Diabetes mellitus	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Dyslipidaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Fluid retention	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hyperlipidaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hypernatraemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hypoalbuminaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Type 2 diabetes mellitus	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vitamin D deficiency	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Vascular disorders			
- Overall -	- Any Grade -	15 (20.0%)	30 (20.7%)
	Grade 1-2	11 (14.7%)	27 (18.6%)
	1	7 (9.3%)	14 (9.7%)
	2	4 (5.3%)	13 (9.0%)
	Grade 3-4	4 (5.3%)	3 (2.1%)
	3	3 (4.0%)	3 (2.1%)
	4	1 (1.3%)	0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hypertension	- Any Grade -	4 (5.3%)	8 (5.5%)
	Grade 1-2	0	6 (4.1%)
	1	0	1 (0.7%)
	2	0	5 (3.4%)
	Grade 3-4	4 (5.3%)	2 (1.4%)
	3	4 (5.3%)	2 (1.4%)
Lymphoedema	- Any Grade -	5 (6.7%)	6 (4.1%)
	Grade 1-2	5 (6.7%)	6 (4.1%)
	1	3 (4.0%)	4 (2.8%)
	2	2 (2.7%)	2 (1.4%)
Flushing	- Any Grade -	2 (2.7%)	4 (2.8%)
	Grade 1-2	2 (2.7%)	4 (2.8%)
	1	2 (2.7%)	3 (2.1%)
	2	0	1 (0.7%)
Hot flush	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	1 (1.3%)	4 (2.8%)
Phlebitis	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	0	1 (0.7%)
	2	1 (1.3%)	2 (1.4%)
Lymphostasis	- Any Grade -	3 (4.0%)	0
	Grade 1-2	3 (4.0%)	0
	1	2 (2.7%)	0
	2	1 (1.3%)	0
Hypotension	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Orthostatic hypotension	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Thrombosis	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
Venous thrombosis limb	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Deep vein thrombosis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Embolism	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Haemorrhage	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hypertensive crisis	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	4	1 (1.3%)	0
Peripheral venous disease	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Injury, poisoning and procedural complications			
- Overall -	- Any Grade -	9 (12.0%)	22 (15.2%)
	Grade 1-2	8 (10.7%)	21 (14.5%)
	1	3 (4.0%)	16 (11.0%)
	2	5 (6.7%)	5 (3.4%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
	Grade 5	0	1 (0.7%)
Accidental overdose	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	4 (2.8%)
Fall	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	2	2 (2.7%)	2 (1.4%)
Vascular access site pain	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	3 (2.1%)
	2	0	1 (0.7%)
Contusion	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Incorrect dose administered	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Poisoning	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	2	2 (2.7%)	0
Thermal burn	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Arthropod bite	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Breast injury	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Femoral neck fracture	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Femur fracture	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Foot fracture	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Fracture	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Limb injury	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Medication error	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Product dose omission issue	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Radiation skin injury	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Road traffic accident	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Spinal fracture	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Traumatic haematoma	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vascular access site discharge	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vascular access site erythema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vascular access site swelling	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Wrist fracture	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Eye disorders			
- Overall -	- Any Grade -	8 (10.7%)	18 (12.4%)
	Grade 1-2	8 (10.7%)	18 (12.4%)
	1	7 (9.3%)	10 (6.9%)
	2	1 (1.3%)	8 (5.5%)

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Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Dry eye	- Any Grade -	1 (1.3%)	6 (4.1%)
	Grade 1-2	1 (1.3%)	6 (4.1%)
	1	1 (1.3%)	6 (4.1%)
Lacrimation increased	- Any Grade -	3 (4.0%)	3 (2.1%)
	Grade 1-2	3 (4.0%)	3 (2.1%)
	1	3 (4.0%)	1 (0.7%)
	2	0	2 (1.4%)
Cataract	- Any Grade -	3 (4.0%)	2 (1.4%)
	Grade 1-2	3 (4.0%)	2 (1.4%)
	1	3 (4.0%)	0
	2	0	2 (1.4%)
Conjunctival haemorrhage	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
Visual acuity reduced	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Visual impairment	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Chalazion	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Diplopia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Eye discharge	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Eye pruritus	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Eyelid oedema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hypermetropia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Keratitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Macular degeneration	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Ocular hypertension	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Retinal oedema	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Vision blurred	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Vitreous degeneration	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vitreous floaters	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Psychiatric disorders			
- Overall -	- Any Grade -	12 (16.0%)	12 (8.3%)
	Grade 1-2	9 (12.0%)	11 (7.6%)
	1	5 (6.7%)	8 (5.5%)
	2	4 (5.3%)	3 (2.1%)
	Grade 3-4	3 (4.0%)	1 (0.7%)
	3	3 (4.0%)	1 (0.7%)
Insomnia	- Any Grade -	6 (8.0%)	6 (4.1%)
	Grade 1-2	5 (6.7%)	6 (4.1%)
	1	3 (4.0%)	5 (3.4%)
	2	2 (2.7%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Anxiety	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	0	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Depression	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	0	2 (1.4%)
	2	1 (1.3%)	1 (0.7%)
Affect lability	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Anxiety disorder	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Confusional state	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Imperception	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Irritability	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Sleep disorder	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Renal and urinary disorders			
- Overall -	- Any Grade -	5 (6.7%)	12 (8.3%)
	Grade 1-2	4 (5.3%)	9 (6.2%)
	1	1 (1.3%)	7 (4.8%)
	2	3 (4.0%)	2 (1.4%)
	Grade 3-4	1 (1.3%)	3 (2.1%)
	3	1 (1.3%)	3 (2.1%)
Pollakiuria	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	1 (1.3%)	4 (2.8%)
Dysuria	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	1 (1.3%)	3 (2.1%)
Hydronephrosis	- Any Grade -	2 (2.7%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Urinary retention	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Acute kidney injury	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Chromaturia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Haematuria	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Oliguria	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Renal failure	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Renal impairment	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Ureterolithiasis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Hepatobiliary disorders			
- Overall -	- Any Grade -	6 (8.0%)	10 (6.9%)
	Grade 1-2	5 (6.7%)	7 (4.8%)
	1	5 (6.7%)	4 (2.8%)
	2	0	3 (2.1%)
	Grade 3-4	1 (1.3%)	3 (2.1%)
	3	1 (1.3%)	3 (2.1%)
Hyperbilirubinaemia	- Any Grade -	4 (5.3%)	6 (4.1%)
	Grade 1-2	4 (5.3%)	6 (4.1%)
	1	3 (4.0%)	4 (2.8%)
	2	1 (1.3%)	2 (1.4%)
Hypertransaminasaemia	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Cholecystitis acute	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Cholestasis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Hepatic cytolysis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Hepatic function abnormal	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Hepatic pain	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hepatic vein thrombosis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Cardiac disorders			
- Overall -	- Any Grade -	4 (5.3%)	11 (7.6%)
	Grade 1-2	4 (5.3%)	10 (6.9%)
	1	2 (2.7%)	4 (2.8%)
	2	2 (2.7%)	6 (4.1%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Palpitations	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	1 (1.3%)	3 (2.1%)
	2	0	1 (0.7%)
Sinus tachycardia	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	1 (1.3%)	1 (0.7%)
	2	0	2 (1.4%)
Angina unstable	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Cardiac failure	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Coronary artery disease	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Extrasystoles	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Left ventricular hypertrophy	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Metabolic cardiomyopathy	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Supraventricular extrasystoles	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Supraventricular tachycardia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Ventricular arrhythmia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Reproductive system and breast disorders			
- Overall -	- Any Grade -	3 (4.0%)	7 (4.8%)
	Grade 1-2	3 (4.0%)	7 (4.8%)
	1	1 (1.3%)	4 (2.8%)
	2	2 (2.7%)	3 (2.1%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Breast pain	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	2 (1.4%)
	2	0	1 (0.7%)
Breast discharge	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Breast ulceration	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Erectile dysfunction	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Menstruation irregular	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Pelvic pain	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Postmenopausal haemorrhage	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Vulvovaginal pruritus	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Ear and labyrinth disorders			
- Overall -	- Any Grade -	3 (4.0%)	6 (4.1%)
	Grade 1-2	3 (4.0%)	6 (4.1%)
	1	3 (4.0%)	6 (4.1%)
Vertigo	- Any Grade -	2 (2.7%)	4 (2.8%)
	Grade 1-2	2 (2.7%)	4 (2.8%)
	1	2 (2.7%)	4 (2.8%)
Deafness	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Ear pain	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Tinnitus	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Immune system disorders			
- Overall -	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	3 (2.1%)
	2	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Allergic oedema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Contrast media allergy	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Drug hypersensitivity	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hypersensitivity	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
- Overall -	- Any Grade -	3 (4.0%)	0
	Grade 1-2	2 (2.7%)	0
	1	2 (2.7%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Ear neoplasm	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Tumour necrosis	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Tumour pain	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Tumour ulceration	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
No Coding available			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
No Coding available	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_B_SE.out
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Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	102 (100%)
	Grade 1-2	40 (39.2%)
	1	4 (3.9%)
	2	36 (35.3%)
	Grade 3-4	58 (56.9%)
	3	52 (51.0%)
	4	6 (5.9%)
	Grade 5	4 (3.9%)
Gastrointestinal disorders		
- Overall -	- Any Grade -	93 (91.2%)
	Grade 1-2	73 (71.6%)
	1	27 (26.5%)
	2	46 (45.1%)
	Grade 3-4	20 (19.6%)
	3	20 (19.6%)
Diarrhoea	- Any Grade -	86 (84.3%)
	Grade 1-2	69 (67.6%)
	1	28 (27.5%)
	2	41 (40.2%)
	Grade 3-4	17 (16.7%)
	3	17 (16.7%)
Nausea	- Any Grade -	42 (41.2%)
	Grade 1-2	40 (39.2%)
	1	29 (28.4%)
	2	11 (10.8%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Vomiting	- Any Grade -	29 (28.4%)
	Grade 1-2	27 (26.5%)
	1	22 (21.6%)
	2	5 (4.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Constipation	- Any Grade -	13 (12.7%)
	Grade 1-2	13 (12.7%)
	1	12 (11.8%)
	2	1 (1.0%)
Abdominal pain	- Any Grade -	12 (11.8%)
	Grade 1-2	11 (10.8%)
	1	6 (5.9%)
	2	5 (4.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Stomatitis	- Any Grade -	7 (6.9%)
	Grade 1-2	7 (6.9%)
	1	6 (5.9%)
	2	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_C_SE.out
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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Abdominal pain upper	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	6 (5.9%)
Dyspepsia	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	5 (4.9%)
	2	1 (1.0%)
Dry mouth	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
Gastrooesophageal reflux disease	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
Toothache	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
Abdominal discomfort	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Flatulence	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Haemorrhoids	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Mouth ulceration	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Abdominal distension	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Breath odour	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Dental caries	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Dental discomfort	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Dysphagia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Epigastric discomfort	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Gastrointestinal disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Gastrooesophageal sphincter insufficiency	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Gingival pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Intestinal mucosal atrophy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Large intestine perforation	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Oesophagitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oral discomfort	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oral pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Paraesthesia oral	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Proctalgia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Retching	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Skin and subcutaneous tissue disorders		
- Overall -	- Any Grade -	78 (76.5%)
	Grade 1-2	72 (70.6%)
	1	35 (34.3%)
	2	37 (36.3%)
	Grade 3-4	6 (5.9%)
	3	6 (5.9%)
Alopecia	- Any Grade -	42 (41.2%)
	Grade 1-2	42 (41.2%)
	1	16 (15.7%)
	2	26 (25.5%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Rash	- Any Grade -	31 (30.4%)
	Grade 1-2	29 (28.4%)
	1	20 (19.6%)
	2	9 (8.8%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Pruritus	- Any Grade -	17 (16.7%)
	Grade 1-2	15 (14.7%)
	1	12 (11.8%)
	2	3 (2.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Rash maculo-papular	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dermatitis acneiform	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Erythema	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
Hand dermatitis	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Acne	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Dermatitis allergic	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Hyperhidrosis	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Nail disorder	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Nail dystrophy	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Rash erythematous	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Rash papular	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Skin hyperpigmentation	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Dermatitis contact	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Dry skin	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Eczema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Madarosis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Miliaria	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nail bed tenderness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nail discolouration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nail ridging	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Night sweats	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Onychalgia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Onychoclasis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Onycholysis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Onychomadesis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Perioral dermatitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Rash pruritic	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Scar pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Seborrhoeic dermatitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Skin exfoliation	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Skin lesion	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Urticaria	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nervous system disorders		
- Overall -	- Any Grade -	68 (66.7%)
	Grade 1-2	58 (56.9%)
	1	35 (34.3%)
	2	23 (22.5%)
	Grade 3-4	10 (9.8%)
	3	10 (9.8%)
Neuropathy peripheral	- Any Grade -	30 (29.4%)
	Grade 1-2	23 (22.5%)
	1	14 (13.7%)
	2	9 (8.8%)
	Grade 3-4	7 (6.9%)
	3	7 (6.9%)
Headache	- Any Grade -	21 (20.6%)
	Grade 1-2	21 (20.6%)
	1	17 (16.7%)
	2	4 (3.9%)
Dizziness	- Any Grade -	10 (9.8%)
	Grade 1-2	10 (9.8%)
	1	7 (6.9%)
	2	3 (2.9%)
Peripheral sensory neuropathy	- Any Grade -	8 (7.8%)
	Grade 1-2	7 (6.9%)
	1	6 (5.9%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Polyneuropathy	- Any Grade -	8 (7.8%)
	Grade 1-2	8 (7.8%)
	1	4 (3.9%)
	2	4 (3.9%)
Dysgeusia	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	4 (3.9%)
	2	2 (2.0%)
Hypoaesthesia	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	4 (3.9%)
	2	1 (1.0%)
Paraesthesia	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
Tremor	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Balance disorder	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Cognitive disorder	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Encephalopathy	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Lethargy	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Peripheral motor neuropathy	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Amnesia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Burning sensation mucosal	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Cerebrovascular insufficiency	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Dystonia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypersomnia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Memory impairment	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Migraine	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Neurotoxicity	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Posterior reversible encephalopathy syndrome	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Somnolence	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Taste disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Thoracic radiculopathy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Transient ischaemic attack	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
General disorders and administration site conditions		
- Overall -	- Any Grade -	62 (60.8%)
	Grade 1-2	56 (54.9%)
	1	30 (29.4%)
	2	26 (25.5%)
	Grade 3-4	6 (5.9%)
	3	6 (5.9%)
Fatigue	- Any Grade -	23 (22.5%)
	Grade 1-2	20 (19.6%)
	1	11 (10.8%)
	2	9 (8.8%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Asthenia	- Any Grade -	19 (18.6%)
	Grade 1-2	18 (17.6%)
	1	12 (11.8%)
	2	6 (5.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Mucosal inflammation	- Any Grade -	12 (11.8%)
	Grade 1-2	12 (11.8%)
	1	10 (9.8%)
	2	2 (2.0%)
Pyrexia	- Any Grade -	12 (11.8%)
	Grade 1-2	12 (11.8%)
	1	8 (7.8%)
	2	4 (3.9%)
Oedema peripheral	- Any Grade -	7 (6.9%)
	Grade 1-2	7 (6.9%)
	1	6 (5.9%)
	2	1 (1.0%)
Chills	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	4 (3.9%)
	2	1 (1.0%)
Pain	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
Chest pain	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
Influenza like illness	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Oedema	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Non-cardiac chest pain	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Thirst	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Axillary pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Chest discomfort	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Facial pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
General physical health deterioration	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Generalised oedema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hyperthermia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Mass	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Peripheral swelling	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Sensation of foreign body	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Vascular device occlusion	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Blood and lymphatic system disorders		
- Overall -	- Any Grade -	53 (52.0%)
	Grade 1-2	41 (40.2%)
	1	15 (14.7%)
	2	26 (25.5%)
	Grade 3-4	12 (11.8%)
	3	10 (9.8%)
	4	2 (2.0%)
Anaemia	- Any Grade -	34 (33.3%)
	Grade 1-2	32 (31.4%)
	1	15 (14.7%)
	2	17 (16.7%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Neutropenia	- Any Grade -	25 (24.5%)
	Grade 1-2	19 (18.6%)
	1	4 (3.9%)
	2	15 (14.7%)
	Grade 3-4	6 (5.9%)
	3	5 (4.9%)
	4	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Leukopenia	- Any Grade -	11 (10.8%)
	Grade 1-2	11 (10.8%)
	1	6 (5.9%)
	2	5 (4.9%)
Lymphopenia	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Febrile neutropenia	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Eosinophilia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Lymphadenopathy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Thrombocytopenia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Thrombocytosis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Investigations		
- Overall -	- Any Grade -	52 (51.0%)
	Grade 1-2	30 (29.4%)
	1	16 (15.7%)
	2	14 (13.7%)
	Grade 3-4	22 (21.6%)
	3	19 (18.6%)
	4	3 (2.9%)
Alanine aminotransferase increased	- Any Grade -	26 (25.5%)
	Grade 1-2	18 (17.6%)
	1	14 (13.7%)
	2	4 (3.9%)
	Grade 3-4	8 (7.8%)
	3	8 (7.8%)
Aspartate aminotransferase increased	- Any Grade -	22 (21.6%)
	Grade 1-2	14 (13.7%)
	1	8 (7.8%)
	2	6 (5.9%)
	Grade 3-4	8 (7.8%)
	3	8 (7.8%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Blood alkaline phosphatase increased	- Any Grade -	12 (11.8%)
	Grade 1-2	9 (8.8%)
	1	8 (7.8%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Neutrophil count decreased	- Any Grade -	8 (7.8%)
	Grade 1-2	4 (3.9%)
	2	4 (3.9%)
	Grade 3-4	4 (3.9%)
	3	3 (2.9%)
	4	1 (1.0%)
Blood lactate dehydrogenase increased	- Any Grade -	7 (6.9%)
	Grade 1-2	7 (6.9%)
	1	6 (5.9%)
	2	1 (1.0%)
Weight decreased	- Any Grade -	7 (6.9%)
	Grade 1-2	7 (6.9%)
	1	5 (4.9%)
	2	2 (2.0%)
Weight increased	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	5 (4.9%)
	2	1 (1.0%)
Blood cholesterol increased	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
White blood cell count decreased	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	2 (2.0%)
	2	3 (2.9%)
Blood bilirubin increased	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
Blood triglycerides increased	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Lipase increased	- Any Grade -	4 (3.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	2 (2.0%)
	4	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Low density lipoprotein increased	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Blood glucose increased	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Blood thyroid stimulating hormone increased	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
High density lipoprotein increased	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Platelet count decreased	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Amylase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Anti-GAD antibody positive	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Anti-islet cell antibody positive	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Basophil percentage increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Blood chloride decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Blood lactate dehydrogenase decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Blood pressure increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Carbon dioxide decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Eosinophil percentage increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Faecal volume increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Gamma-glutamyltransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Glomerular filtration rate decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Glycosylated haemoglobin increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Haematocrit decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Immature granulocyte count increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Immature granulocyte percentage increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Lymphocyte count decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Mean cell volume decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Metamyelocyte percentage increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Monocyte percentage decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oxygen saturation decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Prothrombin time prolonged	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Red blood cell count decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Tri-iodothyronine increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
White blood cell count increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Infections and infestations		
- Overall -	- Any Grade -	50 (49.0%)
	Grade 1-2	39 (38.2%)
	1	15 (14.7%)
	2	24 (23.5%)
	Grade 3-4	9 (8.8%)
	3	9 (8.8%)
	Grade 5	2 (2.0%)
Urinary tract infection	- Any Grade -	10 (9.8%)
	Grade 1-2	7 (6.9%)
	2	7 (6.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Upper respiratory tract infection	- Any Grade -	8 (7.8%)
	Grade 1-2	8 (7.8%)
	1	2 (2.0%)
	2	6 (5.9%)
Pneumonia	- Any Grade -	6 (5.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
	Grade 5	1 (1.0%)
Nasopharyngitis	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	4 (3.9%)
	2	1 (1.0%)
COVID-19	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Herpes zoster	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
Influenza	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	1 (1.0%)
	2	3 (2.9%)
Rhinitis	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
Conjunctivitis	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	2	3 (2.9%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Oral candidiasis	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Cystitis	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Mastitis	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Paronychia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Respiratory tract infection viral	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Skin infection	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Tooth infection	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Bronchitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Cellulitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Emphysematous cystitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Fungal skin infection	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Furuncle	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Gastroenteritis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Gastroenteritis norovirus	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Gingivitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hordeolum	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nail infection	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Oral herpes	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pharyngitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Pneumonia viral	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Postoperative wound infection	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash pustular	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Suspected COVID-19	- Any Grade -	1 (1.0%)
	Grade 5	1 (1.0%)
Tonsillitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Tooth abscess	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Urethritis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Urogenital infection fungal	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Wound infection	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Metabolism and nutrition disorders		
- Overall -	- Any Grade -	50 (49.0%)
	Grade 1-2	42 (41.2%)
	1	24 (23.5%)
	2	18 (17.6%)
	Grade 3-4	8 (7.8%)
	3	7 (6.9%)
	4	1 (1.0%)
Hyperglycaemia	- Any Grade -	22 (21.6%)
	Grade 1-2	18 (17.6%)
	1	9 (8.8%)
	2	9 (8.8%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Decreased appetite	- Any Grade -	14 (13.7%)
	Grade 1-2	13 (12.7%)
	1	11 (10.8%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypokalaemia	- Any Grade -	8 (7.8%)
	Grade 1-2	6 (5.9%)
	1	5 (4.9%)
	2	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Hypoalbuminaemia	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	4 (3.9%)
	2	1 (1.0%)
Hypercholesterolaemia	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
Hypertriglyceridaemia	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
Hyponatraemia	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dehydration	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Dyslipidaemia	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
Hypercalcaemia	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Hyperkalaemia	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
Hypercreatininaemia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Hypomagnesaemia	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alkalosis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Diabetes mellitus	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Fluid retention	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hyperphosphataemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypocalcaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypophosphataemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Increased appetite	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Polydipsia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Type 1 diabetes mellitus	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Respiratory, thoracic and mediastinal disorders		
- Overall -	- Any Grade -	48 (47.1%)
	Grade 1-2	42 (41.2%)
	1	26 (25.5%)
	2	16 (15.7%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
	Grade 5	1 (1.0%)
Cough	- Any Grade -	16 (15.7%)
	Grade 1-2	15 (14.7%)
	1	12 (11.8%)
	2	3 (2.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dyspnoea	- Any Grade -	9 (8.8%)
	Grade 1-2	8 (7.8%)
	1	5 (4.9%)
	2	3 (2.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Epistaxis	- Any Grade -	8 (7.8%)
	Grade 1-2	8 (7.8%)
	1	8 (7.8%)
Pneumonitis	- Any Grade -	7 (6.9%)
	Grade 1-2	6 (5.9%)
	1	4 (3.9%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Oropharyngeal pain	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	4 (3.9%)
	2	2 (2.0%)
Dysphonia	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Pulmonary embolism	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 5	1 (1.0%)

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Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Respiratory disorder	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	2	3 (2.9%)
Rhinorrhoea	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Dyspnoea exertional	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Nasal congestion	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Pleural effusion	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Productive cough	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Rhinitis allergic	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Bronchospasm	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Lung infiltration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nasal crusting	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pleuritic pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pneumothorax	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Wheezing	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Musculoskeletal and connective tissue disorders		
- Overall -	- Any Grade -	37 (36.3%)
	Grade 1-2	35 (34.3%)
	1	24 (23.5%)
	2	11 (10.8%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Arthralgia	- Any Grade -	13 (12.7%)
	Grade 1-2	12 (11.8%)
	1	8 (7.8%)
	2	4 (3.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Back pain	- Any Grade -	10 (9.8%)
	Grade 1-2	10 (9.8%)
	1	5 (4.9%)
	2	5 (4.9%)
Myalgia	- Any Grade -	10 (9.8%)
	Grade 1-2	10 (9.8%)
	1	9 (8.8%)
	2	1 (1.0%)
Muscle spasms	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
Pain in extremity	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
Musculoskeletal chest pain	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Bone pain	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Spinal pain	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Joint swelling	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Mixed connective tissue disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Musculoskeletal pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Musculoskeletal stiffness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Myositis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Vascular disorders		
- Overall -	- Any Grade -	24 (23.5%)
	Grade 1-2	20 (19.6%)
	1	12 (11.8%)
	2	8 (7.8%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Flushing	- Any Grade -	8 (7.8%)
	Grade 1-2	7 (6.9%)
	1	5 (4.9%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypertension	- Any Grade -	8 (7.8%)
	Grade 1-2	6 (5.9%)
	1	2 (2.0%)
	2	4 (3.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Hot flush	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
Lymphoedema	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Embolism	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Jugular vein thrombosis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Phlebitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Psychiatric disorders		
- Overall -	- Any Grade -	20 (19.6%)
	Grade 1-2	19 (18.6%)
	1	13 (12.7%)
	2	6 (5.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Insomnia	- Any Grade -	10 (9.8%)
	Grade 1-2	10 (9.8%)
	1	6 (5.9%)
	2	4 (3.9%)
Anxiety	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Depression	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
Depressed mood	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Irritability	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Sleep disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Stress	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Injury, poisoning and procedural complications		
- Overall -	- Any Grade -	19 (18.6%)
	Grade 1-2	19 (18.6%)
	1	11 (10.8%)
	2	8 (7.8%)
Accidental overdose	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
Fall	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Infusion related reaction	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Procedural pain	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Contusion	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Injury	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Intentional overdose	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Ligament sprain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rib fracture	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Vascular access site inflammation	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Vascular access site pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Wound	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Wound secretion	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Eye disorders		
- Overall -	- Any Grade -	18 (17.6%)
	Grade 1-2	18 (17.6%)
	1	12 (11.8%)
	2	6 (5.9%)
Dry eye	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	4 (3.9%)
	2	1 (1.0%)
Vision blurred	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
Periorbital oedema	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Abnormal sensation in eye	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Eye disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Eye irritation	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Eyelid function disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Foreign body sensation in eyes	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Lacrimation increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Retinal tear	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Visual impairment	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Vitreous detachment	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hepatobiliary disorders		
- Overall -	- Any Grade -	13 (12.7%)
	Grade 1-2	6 (5.9%)
	1	6 (5.9%)
	Grade 3-4	7 (6.9%)
	3	7 (6.9%)
Hyperbilirubinaemia	- Any Grade -	6 (5.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Autoimmune hepatitis	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Cholecystitis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Cholestasis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hypertransaminasaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Reproductive system and breast disorders		
- Overall -	- Any Grade -	11 (10.8%)
	Grade 1-2	11 (10.8%)
	1	5 (4.9%)
	2	6 (5.9%)
Breast pain	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	1 (1.0%)
	2	3 (2.9%)
Vulvovaginal dryness	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Amenorrhoea	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Artificial menopause	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Breast discharge	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Vaginal discharge	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Vulvovaginal discomfort	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Vulvovaginal pruritus	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Endocrine disorders		
- Overall -	- Any Grade -	8 (7.8%)
	Grade 1-2	8 (7.8%)
	1	5 (4.9%)
	2	3 (2.9%)
Hypothyroidism	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	3 (2.9%)
	2	3 (2.9%)
Autoimmune hypothyroidism	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_C_SE.out

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hyperthyroidism	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
- Overall -	- Any Grade -	8 (7.8%)
	Grade 1-2	5 (4.9%)
	1	4 (3.9%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Tumour necrosis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Tumour pain	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Infected neoplasm	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Paraneoplastic syndrome	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Tumour fistulisation	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Tumour inflammation	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Ear and labyrinth disorders		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	3 (2.9%)
	2	3 (2.9%)
Hypoacusis	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Tinnitus	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Vertigo	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Ear pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Immune system disorders		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	5 (4.9%)
	1	3 (2.9%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypersensitivity	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Seasonal allergy	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Contrast media allergy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Contrast media reaction	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Cardiac disorders		
- Overall -	- Any Grade -	5 (4.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
	Grade 5	1 (1.0%)
Cardiac arrest	- Any Grade -	1 (1.0%)
	Grade 5	1 (1.0%)
Myocarditis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Sinus tachycardia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Tachycardia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Ventricular extrasystoles	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Renal and urinary disorders		
- Overall -	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Acute kidney injury	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Urge incontinence	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Urinary incontinence	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Leading to Atezolizumab Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	14 (13.7%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	10 (9.8%)
	3	10 (9.8%)
	Grade 5	2 (2.0%)
Hepatobiliary disorders		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Autoimmune hepatitis	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Investigations		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Alanine aminotransferase increased	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Aspartate aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Blood alkaline phosphatase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Gastrointestinal disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Diarrhoea	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Large intestine perforation	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Infections and infestations		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 5	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Leading to Atezolizumab Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Pneumonia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Suspected COVID-19	- Any Grade -	1 (1.0%)
	Grade 5	1 (1.0%)
Respiratory, thoracic and mediastinal disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
	Grade 5	1 (1.0%)
Pneumonitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pulmonary embolism	- Any Grade -	1 (1.0%)
	Grade 5	1 (1.0%)
Immune system disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypersensitivity	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Musculoskeletal and connective tissue disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Mixed connective tissue disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Nervous system disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dystonia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Adverse Events Leading to Ipatasertib/Placebo Discontinuation by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	6 (6.9%)	17 (10.2%)
	Grade 1-2	1 (1.1%)	4 (2.4%)
	2	1 (1.1%)	4 (2.4%)
	Grade 3-4	4 (4.6%)	12 (7.2%)
	3	4 (4.6%)	10 (6.0%)
	4	0	2 (1.2%)
	Grade 5	1 (1.1%)	1 (0.6%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	0	7 (4.2%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	0	4 (2.4%)
	3	0	3 (1.8%)
	4	0	1 (0.6%)
Diarrhoea	- Any Grade -	0	6 (3.6%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Large intestine perforation	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
	Grade 5	0	1 (0.6%)
Pulmonary embolism	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
	Grade 5	0	1 (0.6%)
Dyspnoea	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Pneumothorax	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
	Grade 5	1 (1.1%)	0

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Adverse Events Leading to Ipatasertib/Placebo Discontinuation by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hyperglycaemia	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Tumour lysis syndrome	- Any Grade -	1 (1.1%)	0
	Grade 5	1 (1.1%)	0
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	1 (1.1%)	2 (1.2%)
Erythema	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Erythema multiforme	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Rash	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Infections and infestations			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Peritonitis	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Investigations			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Aspartate aminotransferase increased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Neutrophil count decreased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)

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Adverse Events Leading to Ipatasertib/Placebo Discontinuation by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Nervous system disorders			
- Overall -	- Any Grade -	2 (2.3%)	0
	Grade 3-4	2 (2.3%)	0
	3	2 (2.3%)	0
Neuropathy peripheral	- Any Grade -	2 (2.3%)	0
	Grade 3-4	2 (2.3%)	0
	3	2 (2.3%)	0
Cardiac disorders			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Atrial fibrillation	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Eye disorders			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Ocular hyperaemia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
General disorders and administration site conditions			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Fatigue	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Immune system disorders			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Anaphylactic shock	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Hypersensitivity	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Renal and urinary disorders			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Leading to Ipatasertib/Placebo Discontinuation by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Haematuria	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Vascular disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hypotension	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Leading to Ipatasertib/Placebo Discontinuation by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	3 (4.0%)	17 (11.7%)
	Grade 1-2	1 (1.3%)	7 (4.8%)
	1	0	1 (0.7%)
	2	1 (1.3%)	6 (4.1%)
	Grade 3-4	2 (2.7%)	7 (4.8%)
	3	2 (2.7%)	7 (4.8%)
	Grade 5	0	3 (2.1%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	1 (1.3%)	5 (3.4%)
	Grade 1-2	0	4 (2.8%)
	2	0	4 (2.8%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Diarrhoea	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	0	3 (2.1%)
	2	0	3 (2.1%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Abdominal discomfort	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Stomatitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vomiting	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	0	3 (2.1%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
	Grade 5	0	1 (0.7%)
Febrile neutropenia	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Neutropenia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
General disorders and administration site conditions			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
	Grade 5	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_DSCIPAT_B_SE.out
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Adverse Events Leading to Ipatasertib/Placebo Discontinuation by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Death	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Fatigue	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Infections and infestations			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
COVID-19	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pneumonia	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperglycaemia	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Nervous system disorders			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Cerebrovascular accident	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Peripheral sensory neuropathy	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Adverse Events Leading to Ipatasertib/Placebo Discontinuation by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Dyspnoea	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hepatobiliary disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hypertransaminasaemia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Investigations			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Alanine aminotransferase increased	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Vascular disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Flushing	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Adverse Events Leading to Ipatasertib Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	11 (10.8%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	8 (7.8%)
	3	7 (6.9%)
	4	1 (1.0%)
	Grade 5	2 (2.0%)
Investigations		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Aspartate aminotransferase increased	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Alanine aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Blood alkaline phosphatase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hepatobiliary disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Autoimmune hepatitis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Respiratory, thoracic and mediastinal disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
	Grade 5	1 (1.0%)
Pneumonitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pulmonary embolism	- Any Grade -	1 (1.0%)
	Grade 5	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Leading to Ipatasertib Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Gastrointestinal disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Large intestine perforation	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune system disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypersensitivity	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Infections and infestations		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 5	1 (1.0%)
Suspected COVID-19	- Any Grade -	1 (1.0%)
	Grade 5	1 (1.0%)
Metabolism and nutrition disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Hyperglycaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Adverse Events Leading to Paclitaxel Discontinuation by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	14 (16.1%)	25 (15.1%)
	Grade 1-2	7 (8.0%)	6 (3.6%)
	1	1 (1.1%)	0
	2	6 (6.9%)	6 (3.6%)
	Grade 3-4	6 (6.9%)	18 (10.8%)
	3	6 (6.9%)	15 (9.0%)
	4	0	3 (1.8%)
	Grade 5	1 (1.1%)	1 (0.6%)
Nervous system disorders			
- Overall -	- Any Grade -	9 (10.3%)	13 (7.8%)
	Grade 1-2	5 (5.7%)	3 (1.8%)
	1	1 (1.1%)	0
	2	4 (4.6%)	3 (1.8%)
	Grade 3-4	4 (4.6%)	10 (6.0%)
	3	4 (4.6%)	10 (6.0%)
Neuropathy peripheral	- Any Grade -	4 (4.6%)	8 (4.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	2	1 (1.1%)	3 (1.8%)
	Grade 3-4	3 (3.4%)	5 (3.0%)
	3	3 (3.4%)	5 (3.0%)
Peripheral sensory neuropathy	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	3 (1.8%)
	3	1 (1.1%)	3 (1.8%)
Polyneuropathy	- Any Grade -	3 (3.4%)	1 (0.6%)
	Grade 1-2	3 (3.4%)	0
	1	1 (1.1%)	0
	2	2 (2.3%)	0
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Peripheral motor neuropathy	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Toxic neuropathy	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	0	4 (2.4%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	3 (1.8%)
	3	0	2 (1.2%)
	4	0	1 (0.6%)

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Adverse Events Leading to Paclitaxel Discontinuation by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Diarrhoea	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Large intestine perforation	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
	Grade 5	0	1 (0.6%)
Pulmonary embolism	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
	Grade 5	0	1 (0.6%)
Dyspnoea	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Pneumothorax	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Erythema	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Onycholysis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Rash	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
General disorders and administration site conditions			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)

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Adverse Events Leading to Paclitaxel Discontinuation by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Fatigue	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Oedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Immune system disorders			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Hypersensitivity	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Anaphylactic shock	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Infections and infestations			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Paronychia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Neutropenia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Cardiac disorders			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0

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Adverse Events Leading to Paclitaxel Discontinuation by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Atrial fibrillation	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Eye disorders			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Ocular hyperaemia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Investigations			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Neutrophil count decreased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 5	1 (1.1%)	0
Tumour lysis syndrome	- Any Grade -	1 (1.1%)	0
	Grade 5	1 (1.1%)	0
Renal and urinary disorders			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Haematuria	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0

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Adverse Events Leading to Paclitaxel Discontinuation by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	12 (16.0%)	42 (29.0%)
	Grade 1-2	5 (6.7%)	20 (13.8%)
	1	2 (2.7%)	1 (0.7%)
	2	3 (4.0%)	19 (13.1%)
	Grade 3-4	6 (8.0%)	19 (13.1%)
	3	5 (6.7%)	19 (13.1%)
	4	1 (1.3%)	0
	Grade 5	1 (1.3%)	3 (2.1%)
Nervous system disorders			
- Overall -	- Any Grade -	7 (9.3%)	24 (16.6%)
	Grade 1-2	3 (4.0%)	14 (9.7%)
	1	1 (1.3%)	0
	2	2 (2.7%)	14 (9.7%)
	Grade 3-4	4 (5.3%)	10 (6.9%)
	3	4 (5.3%)	10 (6.9%)
Peripheral sensory neuropathy	- Any Grade -	5 (6.7%)	7 (4.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	2	1 (1.3%)	4 (2.8%)
	Grade 3-4	4 (5.3%)	3 (2.1%)
	3	4 (5.3%)	3 (2.1%)
Neuropathy peripheral	- Any Grade -	1 (1.3%)	10 (6.9%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	2	1 (1.3%)	4 (2.8%)
	Grade 3-4	0	6 (4.1%)
	3	0	6 (4.1%)
Neurotoxicity	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
Paraesthesia	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
Polyneuropathy	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Cerebrovascular accident	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Dizziness	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Adverse Events Leading to Paclitaxel Discontinuation by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	0	6 (4.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	3 (2.1%)
	3	0	3 (2.1%)
	Grade 5	0	1 (0.7%)
Febrile neutropenia	- Any Grade -	0	3 (2.1%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
	Grade 5	0	1 (0.7%)
Neutropenia	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Anaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Leukopenia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
General disorders and administration site conditions			
- Overall -	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	1	1 (1.3%)	0
	2	1 (1.3%)	1 (0.7%)
	Grade 5	0	1 (0.7%)
Fatigue	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Asthenia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Death	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Oedema	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Investigations			
- Overall -	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
	4	1 (1.3%)	0

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Adverse Events Leading to Paclitaxel Discontinuation by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Neutrophil count decreased	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
	4	1 (1.3%)	0
Gastrointestinal disorders			
- Overall -	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	2	0	3 (2.1%)
Abdominal discomfort	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Diarrhoea	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nausea	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Infections and infestations			
- Overall -	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 5	1 (1.3%)	1 (0.7%)
COVID-19	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pneumonia	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Sepsis	- Any Grade -	1 (1.3%)	0
	Grade 5	1 (1.3%)	0
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dyspnoea	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Adverse Events Leading to Paclitaxel Discontinuation by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hepatobiliary disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hypertransaminasaemia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperglycaemia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Musculoskeletal and connective tissue disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Scleroderma	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Vascular disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Flushing	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Leading to Paclitaxel Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	23 (22.5%)
	Grade 1-2	12 (11.8%)
	1	2 (2.0%)
	2	10 (9.8%)
	Grade 3-4	9 (8.8%)
	3	9 (8.8%)
	Grade 5	2 (2.0%)
Nervous system disorders		
- Overall -	- Any Grade -	12 (11.8%)
	Grade 1-2	8 (7.8%)
	1	2 (2.0%)
	2	6 (5.9%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Neuropathy peripheral	- Any Grade -	7 (6.9%)
	Grade 1-2	4 (3.9%)
	2	4 (3.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Polyneuropathy	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Encephalopathy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Peripheral motor neuropathy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Peripheral sensory neuropathy	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Respiratory, thoracic and mediastinal disorders		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
	Grade 5	1 (1.0%)
Dyspnoea	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Pneumonitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Adverse Events Leading to Paclitaxel Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Pulmonary embolism	- Any Grade -	1 (1.0%)
	Grade 5	1 (1.0%)
Infections and infestations		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 5	1 (1.0%)
Pneumonia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Suspected COVID-19	- Any Grade -	1 (1.0%)
	Grade 5	1 (1.0%)
Investigations		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Neutrophil count decreased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Gastrointestinal disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Large intestine perforation	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
General disorders and administration site conditions		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Fatigue	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hepatobiliary disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Adverse Events Leading to Paclitaxel Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Autoimmune hepatitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune system disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypersensitivity	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Vascular disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Flushing	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Leading to Dose Interruption of Atezolizumab by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	53 (52.0%)
	Grade 1-2	26 (25.5%)
	1	4 (3.9%)
	2	22 (21.6%)
	Grade 3-4	27 (26.5%)
	3	23 (22.5%)
	4	4 (3.9%)
Infections and infestations		
- Overall -	- Any Grade -	15 (14.7%)
	Grade 1-2	11 (10.8%)
	1	3 (2.9%)
	2	8 (7.8%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
COVID-19	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Upper respiratory tract infection	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	1 (1.0%)
	2	3 (2.9%)
Influenza	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Urinary tract infection	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Bronchitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Gastroenteritis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Herpes zoster	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Respiratory tract infection viral	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rhinitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Atezolizumab by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Skin and subcutaneous tissue disorders		
- Overall -	- Any Grade -	12 (11.8%)
	Grade 1-2	7 (6.9%)
	1	4 (3.9%)
	2	3 (2.9%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Rash	- Any Grade -	6 (5.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Pruritus	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Onycholysis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Rash erythematous	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash maculo-papular	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash papular	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash pruritic	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
General disorders and administration site conditions		
- Overall -	- Any Grade -	11 (10.8%)
	Grade 1-2	9 (8.8%)
	1	4 (3.9%)
	2	5 (4.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Pyrexia	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	3 (2.9%)
	2	3 (2.9%)

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Adverse Events Leading to Dose Interruption of Atezolizumab by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Fatigue	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
General physical health deterioration	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Influenza like illness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Investigations		
- Overall -	- Any Grade -	11 (10.8%)
	Grade 1-2	5 (4.9%)
	1	1 (1.0%)
	2	4 (3.9%)
	Grade 3-4	6 (5.9%)
	3	5 (4.9%)
	4	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	7 (6.9%)
	Grade 1-2	5 (4.9%)
	1	3 (2.9%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Alanine aminotransferase increased	- Any Grade -	5 (4.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Blood alkaline phosphatase increased	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Amylase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Blood bilirubin increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Blood lactate dehydrogenase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Atezolizumab by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Lipase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neutrophil count decreased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Weight decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Respiratory, thoracic and mediastinal disorders		
- Overall -	- Any Grade -	10 (9.8%)
	Grade 1-2	10 (9.8%)
	1	3 (2.9%)
	2	7 (6.9%)
Pneumonitis	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
Respiratory disorder	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Dyspnoea	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Lung infiltration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pulmonary embolism	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Blood and lymphatic system disorders		
- Overall -	- Any Grade -	9 (8.8%)
	Grade 1-2	5 (4.9%)
	2	5 (4.9%)
	Grade 3-4	4 (3.9%)
	3	3 (2.9%)
	4	1 (1.0%)
Neutropenia	- Any Grade -	7 (6.9%)
	Grade 1-2	5 (4.9%)
	2	5 (4.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)

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Adverse Events Leading to Dose Interruption of Atezolizumab by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Febrile neutropenia	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Gastrointestinal disorders		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Diarrhoea	- Any Grade -	5 (4.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Nausea	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Metabolism and nutrition disorders		
- Overall -	- Any Grade -	5 (4.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	4 (3.9%)
	3	3 (2.9%)
	4	1 (1.0%)
Hyperglycaemia	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Dehydration	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Atezolizumab by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Injury, poisoning and procedural complications		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
Infusion related reaction	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Procedural pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Vascular access site inflammation	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hepatobiliary disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Cholecystitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypertransaminasaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Musculoskeletal and connective tissue disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Back pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Myositis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)

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Adverse Events Leading to Dose Interruption of Atezolizumab by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Tumour necrosis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Renal and urinary disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Acute kidney injury	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Cardiac disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Myocarditis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Endocrine disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hypothyroidism	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Nervous system disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Cerebrovascular insufficiency	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	26 (29.9%)	73 (44.0%)
	Grade 1-2	6 (6.9%)	41 (24.7%)
	1	0	11 (6.6%)
	2	6 (6.9%)	30 (18.1%)
	Grade 3-4	20 (23.0%)	32 (19.3%)
	3	16 (18.4%)	28 (16.9%)
	4	4 (4.6%)	4 (2.4%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	3 (3.4%)	23 (13.9%)
	Grade 1-2	0	15 (9.0%)
	1	0	2 (1.2%)
	2	0	13 (7.8%)
	Grade 3-4	3 (3.4%)	8 (4.8%)
	3	3 (3.4%)	7 (4.2%)
	4	0	1 (0.6%)
Diarrhoea	- Any Grade -	0	14 (8.4%)
	Grade 1-2	0	8 (4.8%)
	1	0	1 (0.6%)
	2	0	7 (4.2%)
	Grade 3-4	0	6 (3.6%)
	3	0	6 (3.6%)
Nausea	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	2	1 (1.1%)	3 (1.8%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Vomiting	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	1 (1.1%)	1 (0.6%)
	4	0	1 (0.6%)
Abdominal discomfort	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Abdominal pain	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Colitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Dyspepsia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Enteritis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Pancreatitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Upper gastrointestinal haemorrhage	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Infections and infestations			
- Overall -	- Any Grade -	7 (8.0%)	18 (10.8%)
	Grade 1-2	3 (3.4%)	15 (9.0%)
	1	0	8 (4.8%)
	2	3 (3.4%)	7 (4.2%)
	Grade 3-4	4 (4.6%)	3 (1.8%)
	3	4 (4.6%)	3 (1.8%)
COVID-19	- Any Grade -	0	6 (3.6%)
	Grade 1-2	0	6 (3.6%)
	1	0	6 (3.6%)
Pneumonia	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
Herpes zoster	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
Upper respiratory tract infection	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Abscess jaw	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Bronchiolitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Bronchitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Cellulitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Conjunctivitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Erysipelas	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Respiratory tract infection viral	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Skin infection	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Tooth abscess	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Tooth infection	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Urinary tract infection	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Viral infection	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	4 (4.6%)	12 (7.2%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	2	1 (1.1%)	3 (1.8%)
	Grade 3-4	3 (3.4%)	9 (5.4%)
	3	2 (2.3%)	9 (5.4%)
	4	1 (1.1%)	0
Neutropenia	- Any Grade -	4 (4.6%)	10 (6.0%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	2	1 (1.1%)	3 (1.8%)
	Grade 3-4	3 (3.4%)	7 (4.2%)
	3	2 (2.3%)	7 (4.2%)
	4	1 (1.1%)	0
Anaemia	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	0	2 (1.2%)
	4	1 (1.1%)	0
Leukopenia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	3 (3.4%)	13 (7.8%)
	Grade 1-2	2 (2.3%)	11 (6.6%)
	1	0	2 (1.2%)
	2	2 (2.3%)	9 (5.4%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	0	1 (0.6%)
	4	1 (1.1%)	1 (0.6%)
Hyperglycaemia	- Any Grade -	2 (2.3%)	8 (4.8%)
	Grade 1-2	2 (2.3%)	7 (4.2%)
	2	2 (2.3%)	7 (4.2%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Hypertriglyceridaemia	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Decreased appetite	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Electrolyte imbalance	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hyperamylasaemia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Hyperlipasaemia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	4	1 (1.1%)	0
Hypokalaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Investigations			
- Overall -	- Any Grade -	5 (5.7%)	7 (4.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
	Grade 3-4	4 (4.6%)	5 (3.0%)
	3	4 (4.6%)	5 (3.0%)
Neutrophil count decreased	- Any Grade -	4 (4.6%)	5 (3.0%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	3 (3.4%)	4 (2.4%)
	3	3 (3.4%)	4 (2.4%)
Alanine aminotransferase increased	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Aspartate aminotransferase increased	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Influenza A virus test positive	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
White blood cell count decreased	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
General disorders and administration site conditions			
- Overall -	- Any Grade -	2 (2.3%)	9 (5.4%)
	Grade 1-2	2 (2.3%)	5 (3.0%)
	1	1 (1.1%)	3 (1.8%)
	2	1 (1.1%)	2 (1.2%)
	Grade 3-4	0	4 (2.4%)
	3	0	4 (2.4%)
Asthenia	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Pyrexia	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	1 (1.1%)	2 (1.2%)
Mucosal inflammation	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Face oedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Fatigue	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Influenza like illness	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Localised oedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Malaise	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Swelling face	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	1 (1.1%)	8 (4.8%)
	Grade 1-2	1 (1.1%)	8 (4.8%)
	1	0	2 (1.2%)
	2	1 (1.1%)	6 (3.6%)
Rash	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	4 (2.4%)
	1	0	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
Pruritus	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Dermatitis allergic	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Rash maculo-papular	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	3 (3.4%)	5 (3.0%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	0	2 (1.2%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	1 (0.6%)
	4	0	1 (0.6%)
Pleural effusion	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
Cough	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Dyspnoea	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Haemoptysis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Oropharyngeal pain	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Pneumonitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Nervous system disorders			
- Overall -	- Any Grade -	2 (2.3%)	5 (3.0%)
	Grade 1-2	1 (1.1%)	5 (3.0%)
	1	0	3 (1.8%)
	2	1 (1.1%)	2 (1.2%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Headache	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Neuropathy peripheral	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Ataxia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Dizziness	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Peripheral sensory neuropathy	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
- Overall -	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	0	1 (0.6%)
	4	1 (1.1%)	1 (0.6%)
Infected neoplasm	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Lymphangiosis carcinomatosa	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	4	1 (1.1%)	0
Schwannoma	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Tumour haemorrhage	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Tumour necrosis	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Renal and urinary disorders			
- Overall -	- Any Grade -	0	4 (2.4%)
	Grade 1-2	0	4 (2.4%)
	1	0	1 (0.6%)
	2	0	3 (1.8%)
Anuria	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Dysuria	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Proteinuria	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Renal failure	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Injury, poisoning and procedural complications			
- Overall -	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
	4	1 (1.1%)	0
Spinal fracture	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	0	1 (0.6%)
	4	1 (1.1%)	0
Skin laceration	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Cardiac disorders			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	0	1 (0.6%)
	2	1 (1.1%)	0
Atrial fibrillation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Tachycardia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Eye disorders			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Cystoid macular oedema	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Glaucoma	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Musculoskeletal and connective tissue disorders			
- Overall -	- Any Grade -	2 (2.3%)	0
	Grade 3-4	2 (2.3%)	0
	3	1 (1.1%)	0
	4	1 (1.1%)	0
Arthralgia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Intervertebral disc compression	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	4	1 (1.1%)	0
Hepatobiliary disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Cholecystitis acute	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Immune system disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hypersensitivity	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Psychiatric disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Anxiety	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Reproductive system and breast disorders			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Breast pain	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Vascular disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Lymphoedema	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	32 (42.7%)	67 (46.2%)
	Grade 1-2	13 (17.3%)	31 (21.4%)
	1	2 (2.7%)	5 (3.4%)
	2	11 (14.7%)	26 (17.9%)
	Grade 3-4	19 (25.3%)	36 (24.8%)
	3	18 (24.0%)	31 (21.4%)
	4	1 (1.3%)	5 (3.4%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	3 (4.0%)	29 (20.0%)
	Grade 1-2	3 (4.0%)	19 (13.1%)
	1	1 (1.3%)	5 (3.4%)
	2	2 (2.7%)	14 (9.7%)
	Grade 3-4	0	10 (6.9%)
	3	0	8 (5.5%)
	4	0	2 (1.4%)
Diarrhoea	- Any Grade -	0	14 (9.7%)
	Grade 1-2	0	7 (4.8%)
	1	0	1 (0.7%)
	2	0	6 (4.1%)
	Grade 3-4	0	7 (4.8%)
	3	0	7 (4.8%)
Vomiting	- Any Grade -	0	7 (4.8%)
	Grade 1-2	0	5 (3.4%)
	1	0	1 (0.7%)
	2	0	4 (2.8%)
	Grade 3-4	0	2 (1.4%)
	3	0	1 (0.7%)
	4	0	1 (0.7%)
Abdominal pain	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Abdominal pain upper	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Nausea	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Enterocolitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Stomatitis	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Abdominal hernia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Intestinal obstruction	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	4	0	1 (0.7%)
Odynophagia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Paraesthesia oral	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Investigations			
- Overall -	- Any Grade -	8 (10.7%)	18 (12.4%)
	Grade 1-2	1 (1.3%)	6 (4.1%)
	2	1 (1.3%)	6 (4.1%)
	Grade 3-4	7 (9.3%)	12 (8.3%)
	3	7 (9.3%)	11 (7.6%)
	4	0	1 (0.7%)
Neutrophil count decreased	- Any Grade -	6 (8.0%)	11 (7.6%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	2	2 (2.7%)	3 (2.1%)
	Grade 3-4	4 (5.3%)	8 (5.5%)
	3	4 (5.3%)	8 (5.5%)
Alanine aminotransferase increased	- Any Grade -	2 (2.7%)	4 (2.8%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	2 (2.7%)	2 (1.4%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Amylase increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	4	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Blood creatinine increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
C-reactive protein increased	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Glycosylated haemoglobin increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Lipase increased	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
White blood cell count decreased	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Infections and infestations			
- Overall -	- Any Grade -	7 (9.3%)	14 (9.7%)
	Grade 1-2	6 (8.0%)	12 (8.3%)
	1	1 (1.3%)	1 (0.7%)
	2	5 (6.7%)	11 (7.6%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
Upper respiratory tract infection	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	2	2 (2.7%)	3 (2.1%)
Herpes zoster	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	2	1 (1.3%)	3 (2.1%)
Cellulitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Influenza	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Abdominal abscess	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Appendicitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Bronchitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
COVID-19	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Diarrhoea infectious	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Lower respiratory tract infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nasopharyngitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Pharyngitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Pneumonia	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Respiratory tract infection viral	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Wound infection	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
General disorders and administration site conditions			
- Overall -	- Any Grade -	7 (9.3%)	7 (4.8%)
	Grade 1-2	4 (5.3%)	6 (4.1%)
	1	1 (1.3%)	3 (2.1%)
	2	3 (4.0%)	3 (2.1%)
	Grade 3-4	3 (4.0%)	1 (0.7%)
	3	3 (4.0%)	1 (0.7%)
Asthenia	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Fatigue	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	2 (2.7%)	0
	3	2 (2.7%)	0

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Malaise	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Pyrexia	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
Mucosal inflammation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Oedema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Oedema peripheral	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Peripheral swelling	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	6 (8.0%)	7 (4.8%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
	Grade 3-4	5 (6.7%)	5 (3.4%)
	3	5 (6.7%)	3 (2.1%)
	4	0	2 (1.4%)
Neutropenia	- Any Grade -	6 (8.0%)	7 (4.8%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
	Grade 3-4	5 (6.7%)	5 (3.4%)
	3	5 (6.7%)	3 (2.1%)
	4	0	2 (1.4%)
Anaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Leukopenia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	2 (2.7%)	9 (6.2%)
	Grade 1-2	2 (2.7%)	7 (4.8%)
	2	2 (2.7%)	7 (4.8%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Drug eruption	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Pruritus	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Rash maculo-papular	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Alopecia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Dermatitis bullous	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Erythema	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	3 (4.0%)	5 (3.4%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	2	2 (2.7%)	2 (1.4%)
	Grade 3-4	1 (1.3%)	3 (2.1%)
	3	0	3 (2.1%)
	4	1 (1.3%)	0
Hyperglycaemia	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	2	1 (1.3%)	3 (2.1%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Decreased appetite	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dehydration	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hypertriglyceridaemia	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	4	1 (1.3%)	0
Hypoglycaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nervous system disorders			
- Overall -	- Any Grade -	4 (5.3%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	0	1 (0.7%)
	2	2 (2.7%)	2 (1.4%)
	Grade 3-4	2 (2.7%)	0
	3	2 (2.7%)	0
Dizziness	- Any Grade -	2 (2.7%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Neuropathy peripheral	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Paraesthesia	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Peripheral sensory neuropathy	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Hepatobiliary disorders			
- Overall -	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
Cholecystitis acute	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Hyperbilirubinaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hypertransaminasaemia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Musculoskeletal and connective tissue disorders			
- Overall -	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	3 (2.1%)
	1	0	3 (2.1%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Myalgia	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Arthritis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pathological fracture	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Cough	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Oropharyngeal pain	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pulmonary embolism	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Cardiac disorders			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Sinus tachycardia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Supraventricular tachycardia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Injury, poisoning and procedural complications			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Femoral neck fracture	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Femur fracture	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Psychiatric disorders			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Anxiety	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Imperception	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vascular disorders			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
Thrombosis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Venous thrombosis limb	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Ear and labyrinth disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vertigo	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Eye disorders			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Vitreous floaters	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Immune system disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hypersensitivity	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Tumour necrosis	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0

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Adverse Events Leading to Dose Interruption of Ipatasertib by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	59 (57.8%)
	Grade 1-2	27 (26.5%)
	1	5 (4.9%)
	2	22 (21.6%)
	Grade 3-4	32 (31.4%)
	3	28 (27.5%)
	4	4 (3.9%)
Gastrointestinal disorders		
- Overall -	- Any Grade -	21 (20.6%)
	Grade 1-2	15 (14.7%)
	1	5 (4.9%)
	2	10 (9.8%)
	Grade 3-4	6 (5.9%)
	3	6 (5.9%)
Diarrhoea	- Any Grade -	15 (14.7%)
	Grade 1-2	9 (8.8%)
	2	9 (8.8%)
	Grade 3-4	6 (5.9%)
	3	6 (5.9%)
Nausea	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Vomiting	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Gastrooesophageal reflux disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Toothache	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Investigations		
- Overall -	- Any Grade -	15 (14.7%)
	Grade 1-2	4 (3.9%)
	1	1 (1.0%)
	2	3 (2.9%)
	Grade 3-4	11 (10.8%)
	3	10 (9.8%)
	4	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Dose Interruption of Ipatasertib by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Alanine aminotransferase increased	- Any Grade -	6 (5.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Aspartate aminotransferase increased	- Any Grade -	6 (5.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Neutrophil count decreased	- Any Grade -	4 (3.9%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Amylase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Blood alkaline phosphatase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Blood bilirubin increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Blood glucose increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Blood lactate dehydrogenase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Lipase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Weight decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Infections and infestations		
- Overall -	- Any Grade -	13 (12.7%)
	Grade 1-2	9 (8.8%)
	1	2 (2.0%)
	2	7 (6.9%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
COVID-19	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Dose Interruption of Ipatasertib by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Upper respiratory tract infection	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	2	3 (2.9%)
Influenza	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Urinary tract infection	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Bronchitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Gastroenteritis norovirus	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Herpes zoster	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Pneumonia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rhinitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Skin and subcutaneous tissue disorders		
- Overall -	- Any Grade -	12 (11.8%)
	Grade 1-2	8 (7.8%)
	1	4 (3.9%)
	2	4 (3.9%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Rash	- Any Grade -	6 (5.9%)
	Grade 1-2	4 (3.9%)
	1	1 (1.0%)
	2	3 (2.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Pruritus	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash maculo-papular	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Leading to Dose Interruption of Ipatasertib by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Onycholysis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Rash erythematous	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash pruritic	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Blood and lymphatic system disorders		
- Overall -	- Any Grade -	11 (10.8%)
	Grade 1-2	7 (6.9%)
	2	7 (6.9%)
	Grade 3-4	4 (3.9%)
	3	2 (2.0%)
	4	2 (2.0%)
Neutropenia	- Any Grade -	10 (9.8%)
	Grade 1-2	7 (6.9%)
	2	7 (6.9%)
	Grade 3-4	3 (2.9%)
	3	2 (2.0%)
	4	1 (1.0%)
Febrile neutropenia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
General disorders and administration site conditions		
- Overall -	- Any Grade -	9 (8.8%)
	Grade 1-2	8 (7.8%)
	1	2 (2.0%)
	2	6 (5.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pyrexia	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	2 (2.0%)
	2	4 (3.9%)
Asthenia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Fatigue	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
General physical health deterioration	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Ipatasertib by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Influenza like illness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Metabolism and nutrition disorders		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	4 (3.9%)
	1	1 (1.0%)
	2	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Hyperglycaemia	- Any Grade -	5 (4.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Dehydration	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Respiratory, thoracic and mediastinal disorders		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	2 (2.0%)
	2	4 (3.9%)
Pneumonitis	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Dyspnoea	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Lung infiltration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Respiratory disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Ipatasertib by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hepatobiliary disorders		
- Overall -	- Any Grade -	4 (3.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Autoimmune hepatitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Cholecystitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hyperbilirubinaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypertransaminasaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Tumour necrosis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Infected neoplasm	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Injury, poisoning and procedural complications		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Accidental overdose	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Procedural pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Ipatasertib by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Renal and urinary disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Acute kidney injury	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Cardiac disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Myocarditis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Endocrine disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hypothyroidism	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Musculoskeletal and connective tissue disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Myositis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nervous system disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dystonia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	41 (47.1%)	85 (51.2%)
	Grade 1-2	18 (20.7%)	49 (29.5%)
	1	4 (4.6%)	14 (8.4%)
	2	14 (16.1%)	35 (21.1%)
	Grade 3-4	23 (26.4%)	36 (21.7%)
	3	19 (21.8%)	32 (19.3%)
	4	4 (4.6%)	4 (2.4%)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	14 (16.1%)	24 (14.5%)
	Grade 1-2	10 (11.5%)	9 (5.4%)
	1	1 (1.1%)	1 (0.6%)
	2	9 (10.3%)	8 (4.8%)
	Grade 3-4	4 (4.6%)	15 (9.0%)
	3	3 (3.4%)	14 (8.4%)
	4	1 (1.1%)	1 (0.6%)
Neutropenia	- Any Grade -	13 (14.9%)	20 (12.0%)
	Grade 1-2	10 (11.5%)	8 (4.8%)
	1	1 (1.1%)	0
	2	9 (10.3%)	8 (4.8%)
	Grade 3-4	3 (3.4%)	12 (7.2%)
	3	2 (2.3%)	11 (6.6%)
	4	1 (1.1%)	1 (0.6%)
Anaemia	- Any Grade -	1 (1.1%)	7 (4.2%)
	Grade 1-2	0	5 (3.0%)
	1	0	1 (0.6%)
	2	0	4 (2.4%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	0	2 (1.2%)
	4	1 (1.1%)	0
Leukopenia	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
Febrile neutropenia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Lymphopenia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Thrombocytopenia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Infections and infestations			
- Overall -	- Any Grade -	10 (11.5%)	25 (15.1%)
	Grade 1-2	6 (6.9%)	22 (13.3%)
	1	2 (2.3%)	9 (5.4%)
	2	4 (4.6%)	13 (7.8%)
	Grade 3-4	4 (4.6%)	3 (1.8%)
	3	4 (4.6%)	3 (1.8%)
COVID-19	- Any Grade -	0	6 (3.6%)
	Grade 1-2	0	6 (3.6%)
	1	0	6 (3.6%)
Upper respiratory tract infection	- Any Grade -	1 (1.1%)	5 (3.0%)
	Grade 1-2	1 (1.1%)	5 (3.0%)
	1	1 (1.1%)	2 (1.2%)
	2	0	3 (1.8%)
Pneumonia	- Any Grade -	3 (3.4%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
Bronchitis	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Herpes zoster	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Respiratory tract infection viral	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Abscess jaw	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Bronchiolitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Cellulitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Cystitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Device related infection	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Erysipelas	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Furuncle	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Influenza	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Laryngitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Nail infection	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Nasopharyngitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Periodontitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Skin infection	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Tooth abscess	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Tooth infection	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Urinary tract infection	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Viral infection	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Investigations			
- Overall -	- Any Grade -	10 (11.5%)	18 (10.8%)
	Grade 1-2	4 (4.6%)	12 (7.2%)
	2	4 (4.6%)	12 (7.2%)
	Grade 3-4	6 (6.9%)	6 (3.6%)
	3	6 (6.9%)	6 (3.6%)
Neutrophil count decreased	- Any Grade -	8 (9.2%)	15 (9.0%)
	Grade 1-2	4 (4.6%)	11 (6.6%)
	2	4 (4.6%)	11 (6.6%)
	Grade 3-4	4 (4.6%)	4 (2.4%)
	3	4 (4.6%)	4 (2.4%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Alanine aminotransferase increased	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	2 (1.2%)
Aspartate aminotransferase increased	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
White blood cell count decreased	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 1-2	2 (2.3%)	1 (0.6%)
	2	2 (2.3%)	1 (0.6%)
Eastern Cooperative Oncology Group performance status worsened	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	2 (2.3%)	17 (10.2%)
	Grade 1-2	0	10 (6.0%)
	1	0	2 (1.2%)
	2	0	8 (4.8%)
	Grade 3-4	2 (2.3%)	7 (4.2%)
	3	2 (2.3%)	7 (4.2%)
Nausea	- Any Grade -	0	8 (4.8%)
	Grade 1-2	0	4 (2.4%)
	1	0	1 (0.6%)
	2	0	3 (1.8%)
	Grade 3-4	0	4 (2.4%)
	3	0	4 (2.4%)
Diarrhoea	- Any Grade -	0	7 (4.2%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	0	4 (2.4%)
	3	0	4 (2.4%)
Vomiting	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Abdominal pain	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Colitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Enteritis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Pancreatitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Stomatitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Upper gastrointestinal haemorrhage	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
General disorders and administration site conditions			
- Overall -	- Any Grade -	5 (5.7%)	12 (7.2%)
	Grade 1-2	5 (5.7%)	8 (4.8%)
	1	3 (3.4%)	4 (2.4%)
	2	2 (2.3%)	4 (2.4%)
	Grade 3-4	0	4 (2.4%)
	3	0	4 (2.4%)
Asthenia	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	2	2 (2.3%)	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Pyrexia	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	1	2 (2.3%)	2 (1.2%)
	2	0	1 (0.6%)
Fatigue	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Influenza like illness	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Chest pain	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Face oedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Localised oedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Mucosal inflammation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Non-cardiac chest pain	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	6 (6.9%)	6 (3.6%)
	Grade 1-2	2 (2.3%)	4 (2.4%)
	1	0	3 (1.8%)
	2	2 (2.3%)	1 (0.6%)
	Grade 3-4	4 (4.6%)	2 (1.2%)
	3	4 (4.6%)	1 (0.6%)
	4	0	1 (0.6%)
Dyspnoea	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	0
	4	0	1 (0.6%)
Pleural effusion	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
Cough	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Haemoptysis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Hypoxia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Oropharyngeal pain	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Respiratory disorder	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Tachypnoea	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Nervous system disorders			
- Overall -	- Any Grade -	3 (3.4%)	8 (4.8%)
	Grade 1-2	2 (2.3%)	5 (3.0%)
	1	0	2 (1.2%)
	2	2 (2.3%)	3 (1.8%)
	Grade 3-4	1 (1.1%)	3 (1.8%)
	3	1 (1.1%)	3 (1.8%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Neuropathy peripheral	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Peripheral sensory neuropathy	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Altered state of consciousness	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Ataxia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Dizziness	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Dysgeusia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Headache	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Paraesthesia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Seizure	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	2 (2.3%)	8 (4.8%)
	Grade 1-2	2 (2.3%)	7 (4.2%)
	1	1 (1.1%)	2 (1.2%)
	2	1 (1.1%)	5 (3.0%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Rash	- Any Grade -	0	4 (2.4%)
	Grade 1-2	0	3 (1.8%)
	1	0	1 (0.6%)
	2	0	2 (1.2%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Dermatitis allergic	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Erythema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Hyperhidrosis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Onycholysis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Pruritus	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Rash maculo-papular	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	3 (3.4%)	6 (3.6%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	1	0	1 (0.6%)
	2	2 (2.3%)	2 (1.2%)
	Grade 3-4	1 (1.1%)	3 (1.8%)
	3	0	2 (1.2%)
	4	1 (1.1%)	1 (0.6%)
Hyperglycaemia	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	0
	2	2 (2.3%)	0
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
Decreased appetite	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Electrolyte imbalance	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hyperamylasaemia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Hyperlipasaemia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	4	1 (1.1%)	0
Hypertriglyceridaemia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hypokalaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Injury, poisoning and procedural complications			
- Overall -	- Any Grade -	1 (1.1%)	6 (3.6%)
	Grade 1-2	0	4 (2.4%)
	2	0	4 (2.4%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	0	2 (1.2%)
	4	1 (1.1%)	0
Spinal fracture	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	0	1 (0.6%)
	4	1 (1.1%)	0
Wound	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Fall	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Fracture	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Infusion related reaction	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Musculoskeletal and connective tissue disorders			
- Overall -	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
	4	1 (1.1%)	0
Bone pain	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Arthralgia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Back pain	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Intervertebral disc compression	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	4	1 (1.1%)	0
Pathological fracture	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
- Overall -	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	0	1 (0.6%)
	4	1 (1.1%)	1 (0.6%)
Infected neoplasm	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Lymphangiosis carcinomatosa	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	4	1 (1.1%)	0
Schwannoma	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Tumour haemorrhage	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Tumour necrosis	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Vascular disorders			
- Overall -	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	0	1 (0.6%)
	2	1 (1.1%)	2 (1.2%)
Flushing	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Embolism	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hypertension	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hypertensive crisis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hypotension	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Hepatobiliary disorders			
- Overall -	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 1-2	2 (2.3%)	1 (0.6%)
	2	2 (2.3%)	1 (0.6%)
Hyperbilirubinaemia	- Any Grade -	2 (2.3%)	0
	Grade 1-2	2 (2.3%)	0
	2	2 (2.3%)	0
Cholecystitis acute	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Renal and urinary disorders			
- Overall -	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	1 (0.6%)
	2	0	2 (1.2%)
Dysuria	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Proteinuria	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Renal failure	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Immune system disorders			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Hypersensitivity	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Cardiac disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Atrial fibrillation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Ear and labyrinth disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Vertigo	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Eye disorders			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Cystoid macular oedema	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
No Coding available			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
No Coding available	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Psychiatric disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Anxiety	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Reproductive system and breast disorders			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Breast pain	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	40 (53.3%)	77 (53.1%)
	Grade 1-2	19 (25.3%)	32 (22.1%)
	1	1 (1.3%)	3 (2.1%)
	2	18 (24.0%)	29 (20.0%)
	Grade 3-4	21 (28.0%)	45 (31.0%)
	3	20 (26.7%)	42 (29.0%)
	4	1 (1.3%)	3 (2.1%)
Investigations			
- Overall -	- Any Grade -	15 (20.0%)	24 (16.6%)
	Grade 1-2	6 (8.0%)	10 (6.9%)
	1	0	1 (0.7%)
	2	6 (8.0%)	9 (6.2%)
	Grade 3-4	9 (12.0%)	14 (9.7%)
	3	9 (12.0%)	13 (9.0%)
	4	0	1 (0.7%)
Neutrophil count decreased	- Any Grade -	13 (17.3%)	17 (11.7%)
	Grade 1-2	7 (9.3%)	8 (5.5%)
	2	7 (9.3%)	8 (5.5%)
	Grade 3-4	6 (8.0%)	9 (6.2%)
	3	6 (8.0%)	9 (6.2%)
Alanine aminotransferase increased	- Any Grade -	2 (2.7%)	5 (3.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	2 (2.7%)	4 (2.8%)
	3	2 (2.7%)	4 (2.8%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
White blood cell count decreased	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Amylase increased	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	4	0	1 (0.7%)
Blood alkaline phosphatase increased	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Blood creatine phosphokinase increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Blood creatinine increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Glycosylated haemoglobin increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Lipase increased	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
SARS-CoV-2 test positive	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Infections and infestations			
- Overall -	- Any Grade -	14 (18.7%)	21 (14.5%)
	Grade 1-2	13 (17.3%)	17 (11.7%)
	1	2 (2.7%)	1 (0.7%)
	2	11 (14.7%)	16 (11.0%)
	Grade 3-4	1 (1.3%)	4 (2.8%)
	3	1 (1.3%)	4 (2.8%)
Herpes zoster	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	2	1 (1.3%)	4 (2.8%)
Upper respiratory tract infection	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	2	2 (2.7%)	2 (1.4%)
Nasopharyngitis	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
Pneumonia	- Any Grade -	3 (4.0%)	0
	Grade 1-2	2 (2.7%)	0
	2	2 (2.7%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Bronchitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Cystitis	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Influenza	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
Respiratory tract infection viral	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	2	2 (2.7%)	0

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Urinary tract infection	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Wound infection	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Abdominal abscess	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Appendicitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
COVID-19	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Cellulitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erysipelas	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Laryngitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Lower respiratory tract infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Skin infection	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Tonsillitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Tracheobronchitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Vascular access site infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Viral infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	11 (14.7%)	19 (13.1%)
	Grade 1-2	4 (5.3%)	10 (6.9%)
	2	4 (5.3%)	10 (6.9%)
	Grade 3-4	7 (9.3%)	9 (6.2%)
	3	7 (9.3%)	8 (5.5%)
	4	0	1 (0.7%)
Neutropenia	- Any Grade -	10 (13.3%)	19 (13.1%)
	Grade 1-2	4 (5.3%)	10 (6.9%)
	2	4 (5.3%)	10 (6.9%)
	Grade 3-4	6 (8.0%)	9 (6.2%)
	3	6 (8.0%)	8 (5.5%)
	4	0	1 (0.7%)
Leukopenia	- Any Grade -	3 (4.0%)	1 (0.7%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	2	2 (2.7%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Thrombocytopenia	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Anaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	2 (2.7%)	24 (16.6%)
	Grade 1-2	2 (2.7%)	16 (11.0%)
	1	0	3 (2.1%)
	2	2 (2.7%)	13 (9.0%)
	Grade 3-4	0	8 (5.5%)
	3	0	7 (4.8%)
	4	0	1 (0.7%)
Diarrhoea	- Any Grade -	0	10 (6.9%)
	Grade 1-2	0	6 (4.1%)
	2	0	6 (4.1%)
	Grade 3-4	0	4 (2.8%)
	3	0	4 (2.8%)
Abdominal pain	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Vomiting	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	1 (0.7%)
	2	0	3 (2.1%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Enterocolitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Nausea	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Abdominal hernia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Abdominal pain upper	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Aphthous ulcer	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Ascites	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dyspepsia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hypoaesthesia oral	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Intestinal obstruction	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	4	0	1 (0.7%)
Odynophagia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Paraesthesia oral	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Stomatitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
General disorders and administration site conditions			
- Overall -	- Any Grade -	11 (14.7%)	15 (10.3%)
	Grade 1-2	7 (9.3%)	13 (9.0%)
	1	3 (4.0%)	5 (3.4%)
	2	4 (5.3%)	8 (5.5%)
	Grade 3-4	4 (5.3%)	2 (1.4%)
	3	4 (5.3%)	2 (1.4%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Asthenia	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
Pyrexia	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	2 (2.7%)	1 (0.7%)
	2	0	2 (1.4%)
Fatigue	- Any Grade -	3 (4.0%)	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	3 (4.0%)	0
	3	3 (4.0%)	0
Malaise	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Oedema peripheral	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Catheter site erythema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Chest discomfort	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Chest pain	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Hyperthermia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Influenza like illness	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Infusion site extravasation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Oedema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Peripheral swelling	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	3 (4.0%)	10 (6.9%)
	Grade 1-2	3 (4.0%)	8 (5.5%)
	1	1 (1.3%)	2 (1.4%)
	2	2 (2.7%)	6 (4.1%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Rash	- Any Grade -	0	5 (3.4%)
	Grade 1-2	0	4 (2.8%)
	2	0	4 (2.8%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erythema	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	1	1 (1.3%)	0
	2	1 (1.3%)	0
Pruritus	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Dermatitis allergic	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Drug eruption	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nail discolouration	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Nail disorder	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nail ridging	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Rash maculo-papular	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Nervous system disorders			
- Overall -	- Any Grade -	5 (6.7%)	7 (4.8%)
	Grade 1-2	5 (6.7%)	4 (2.8%)
	1	1 (1.3%)	1 (0.7%)
	2	4 (5.3%)	3 (2.1%)
	Grade 3-4	0	3 (2.1%)
	3	0	3 (2.1%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Neuropathy peripheral	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Paraesthesia	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Dizziness	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Headache	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Muscle tone disorder	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Peripheral sensory neuropathy	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Radiculopathy	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Musculoskeletal and connective tissue disorders			
- Overall -	- Any Grade -	2 (2.7%)	6 (4.1%)
	Grade 1-2	2 (2.7%)	5 (3.4%)
	1	0	4 (2.8%)
	2	2 (2.7%)	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Myalgia	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	3 (2.1%)
Arthritis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Flank pain	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Pathological fracture	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Spinal pain	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hepatobiliary disorders			
- Overall -	- Any Grade -	1 (1.3%)	5 (3.4%)
	Grade 1-2	0	3 (2.1%)
	1	0	1 (0.7%)
	2	0	2 (1.4%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
Hyperbilirubinaemia	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	0	1 (0.7%)
	2	1 (1.3%)	2 (1.4%)
Cholecystitis acute	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Hypertransaminasaemia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	3 (4.0%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	1 (1.3%)	3 (2.1%)
	2	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Dyspnoea	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
Pulmonary embolism	- Any Grade -	2 (2.7%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Cough	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Oropharyngeal pain	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Respiratory disorder	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	0	2 (1.4%)
	4	1 (1.3%)	0
Decreased appetite	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dehydration	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperglycaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hypertriglyceridaemia	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	4	1 (1.3%)	0
Vascular disorders			
- Overall -	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	2 (2.7%)	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Flushing	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Haemorrhage	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hypertension	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Thrombosis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Venous thrombosis limb	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Cardiac disorders			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Supraventricular tachycardia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Ventricular arrhythmia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Immune system disorders			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Drug hypersensitivity	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hypersensitivity	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Injury, poisoning and procedural complications			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Femoral neck fracture	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Poisoning	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Psychiatric disorders			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Anxiety	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Imperception	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Eye disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Visual impairment	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Tumour necrosis	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	67 (65.7%)
	Grade 1-2	31 (30.4%)
	1	9 (8.8%)
	2	22 (21.6%)
	Grade 3-4	36 (35.3%)
	3	32 (31.4%)
	4	4 (3.9%)
Blood and lymphatic system disorders		
- Overall -	- Any Grade -	20 (19.6%)
	Grade 1-2	15 (14.7%)
	1	1 (1.0%)
	2	14 (13.7%)
	Grade 3-4	5 (4.9%)
	3	3 (2.9%)
	4	2 (2.0%)
Neutropenia	- Any Grade -	16 (15.7%)
	Grade 1-2	12 (11.8%)
	2	12 (11.8%)
	Grade 3-4	4 (3.9%)
	3	3 (2.9%)
	4	1 (1.0%)
Anaemia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Leukopenia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Febrile neutropenia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Thrombocytopenia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Infections and infestations		
- Overall -	- Any Grade -	20 (19.6%)
	Grade 1-2	15 (14.7%)
	1	5 (4.9%)
	2	10 (9.8%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
COVID-19	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Upper respiratory tract infection	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	1 (1.0%)
	2	3 (2.9%)
Pneumonia	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Urinary tract infection	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Herpes zoster	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Influenza	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Bronchitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Gastroenteritis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nasopharyngitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oral candidiasis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rhinitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Skin infection	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Gastrointestinal disorders		
- Overall -	- Any Grade -	15 (14.7%)
	Grade 1-2	8 (7.8%)
	1	4 (3.9%)
	2	4 (3.9%)
	Grade 3-4	7 (6.9%)
	3	7 (6.9%)
Diarrhoea	- Any Grade -	9 (8.8%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	6 (5.9%)
	3	6 (5.9%)
Nausea	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Abdominal pain	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Abdominal pain upper	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Gastrooesophageal reflux disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Paraesthesia oral	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Stomatitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Vomiting	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
General disorders and administration site conditions		
- Overall -	- Any Grade -	15 (14.7%)
	Grade 1-2	12 (11.8%)
	1	4 (3.9%)
	2	8 (7.8%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Pyrexia	- Any Grade -	7 (6.9%)
	Grade 1-2	7 (6.9%)
	1	3 (2.9%)
	2	4 (3.9%)
Fatigue	- Any Grade -	4 (3.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Asthenia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
General physical health deterioration	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Influenza like illness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Non-cardiac chest pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Sensation of foreign body	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Investigations		
- Overall -	- Any Grade -	15 (14.7%)
	Grade 1-2	6 (5.9%)
	1	1 (1.0%)
	2	5 (4.9%)
	Grade 3-4	9 (8.8%)
	3	9 (8.8%)
Alanine aminotransferase increased	- Any Grade -	8 (7.8%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Aspartate aminotransferase increased	- Any Grade -	7 (6.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Neutrophil count decreased	- Any Grade -	6 (5.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Amylase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Blood alkaline phosphatase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Lipase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Weight decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
White blood cell count decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Skin and subcutaneous tissue disorders		
- Overall -	- Any Grade -	11 (10.8%)
	Grade 1-2	8 (7.8%)
	1	5 (4.9%)
	2	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Rash	- Any Grade -	4 (3.9%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Pruritus	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Erythema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hyperhidrosis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Onycholysis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Rash erythematous	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash pruritic	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Scar pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Respiratory, thoracic and mediastinal disorders		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	6 (5.9%)
	1	3 (2.9%)
	2	3 (2.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dyspnoea	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Lung infiltration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pneumonitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Respiratory disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hepatobiliary disorders		
- Overall -	- Any Grade -	5 (4.9%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Autoimmune hepatitis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Cholecystitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hyperbilirubinaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypertransaminasaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nervous system disorders		
- Overall -	- Any Grade -	5 (4.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Cognitive disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Dizziness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Dystonia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypoaesthesia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Neuropathy peripheral	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Tremor	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Injury, poisoning and procedural complications		
- Overall -	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	1 (1.0%)
	2	3 (2.9%)
Infusion related reaction	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Procedural pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Vascular access site inflammation	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Metabolism and nutrition disorders		
- Overall -	- Any Grade -	4 (3.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	2 (2.0%)
	4	1 (1.0%)
Dehydration	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hyperglycaemia	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Musculoskeletal and connective tissue disorders		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Back pain	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Myositis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Tumour necrosis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Infected neoplasm	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Paclitaxel by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Vascular disorders		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Flushing	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Phlebitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Cardiac disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Myocarditis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Endocrine disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hypothyroidism	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Renal and urinary disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Acute kidney injury	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

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Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	7 (8.0%)	46 (27.7%)
	Grade 1-2	3 (3.4%)	21 (12.7%)
	2	3 (3.4%)	21 (12.7%)
	Grade 3-4	4 (4.6%)	25 (15.1%)
	3	4 (4.6%)	21 (12.7%)
	4	0	4 (2.4%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	2 (2.3%)	28 (16.9%)
	Grade 1-2	1 (1.1%)	18 (10.8%)
	2	1 (1.1%)	18 (10.8%)
	Grade 3-4	1 (1.1%)	10 (6.0%)
	3	1 (1.1%)	10 (6.0%)
Diarrhoea	- Any Grade -	2 (2.3%)	23 (13.9%)
	Grade 1-2	1 (1.1%)	16 (9.6%)
	2	1 (1.1%)	16 (9.6%)
	Grade 3-4	1 (1.1%)	7 (4.2%)
	3	1 (1.1%)	7 (4.2%)
Nausea	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Abdominal pain	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Colitis	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Stomatitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Investigations			
- Overall -	- Any Grade -	3 (3.4%)	8 (4.8%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	3 (3.4%)	6 (3.6%)
	3	3 (3.4%)	5 (3.0%)
	4	0	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 3-4	1 (1.1%)	4 (2.4%)
	3	1 (1.1%)	4 (2.4%)

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Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Aspartate aminotransferase increased	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	3 (1.8%)
	3	1 (1.1%)	3 (1.8%)
Neutrophil count decreased	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	1 (0.6%)
	4	0	1 (0.6%)
Weight decreased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
White blood cell count decreased	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	2 (2.3%)	6 (3.6%)
	Grade 1-2	2 (2.3%)	5 (3.0%)
	2	2 (2.3%)	5 (3.0%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hyperglycaemia	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	2	2 (2.3%)	3 (1.8%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Decreased appetite	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	0	7 (4.2%)
	Grade 3-4	0	7 (4.2%)
	3	0	4 (2.4%)
	4	0	3 (1.8%)
Neutropenia	- Any Grade -	0	4 (2.4%)
	Grade 3-4	0	4 (2.4%)
	3	0	2 (1.2%)
	4	0	2 (1.2%)
Febrile neutropenia	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	2 (1.2%)
	4	0	1 (0.6%)

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Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Rash	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
General disorders and administration site conditions			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Fatigue	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Injury, poisoning and procedural complications			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Eschar	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Nervous system disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Neuropathy peripheral	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_DSRIPAT_A_SE.out
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Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	6 (8.0%)	50 (34.5%)
	Grade 1-2	1 (1.3%)	24 (16.6%)
	2	1 (1.3%)	24 (16.6%)
	Grade 3-4	5 (6.7%)	26 (17.9%)
	3	3 (4.0%)	23 (15.9%)
	4	2 (2.7%)	3 (2.1%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	1 (1.3%)	35 (24.1%)
	Grade 1-2	1 (1.3%)	23 (15.9%)
	2	1 (1.3%)	23 (15.9%)
	Grade 3-4	0	12 (8.3%)
	3	0	12 (8.3%)
Diarrhoea	- Any Grade -	0	33 (22.8%)
	Grade 1-2	0	23 (15.9%)
	2	0	23 (15.9%)
	Grade 3-4	0	10 (6.9%)
	3	0	10 (6.9%)
Nausea	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	0	1 (0.7%)
	2	1 (1.3%)	0
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Aphthous ulcer	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Vomiting	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Investigations			
- Overall -	- Any Grade -	3 (4.0%)	9 (6.2%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	3 (4.0%)	7 (4.8%)
	3	1 (1.3%)	4 (2.8%)
	4	2 (2.7%)	3 (2.1%)
Neutrophil count decreased	- Any Grade -	3 (4.0%)	6 (4.1%)
	Grade 3-4	3 (4.0%)	6 (4.1%)
	3	1 (1.3%)	3 (2.1%)
	4	2 (2.7%)	3 (2.1%)
Alanine aminotransferase increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_DSRIPAT_B_SE.out
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Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Aspartate aminotransferase increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Blood creatine phosphokinase increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Gamma-glutamyltransferase increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
White blood cell count decreased	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	2 (2.7%)	4 (2.8%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	2 (2.7%)	2 (1.4%)
Neutropenia	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	2 (2.7%)	1 (0.7%)
	3	2 (2.7%)	1 (0.7%)
Leukopenia	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Febrile neutropenia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	0	6 (4.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	4 (2.8%)
	3	0	4 (2.8%)
Rash	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
Rash maculo-papular	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Erythema multiforme	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Rash erythematous	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	0	5 (3.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	3 (2.1%)
	3	0	3 (2.1%)
Hyperglycaemia	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Decreased appetite	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
General disorders and administration site conditions			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Asthenia	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Fatigue	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Oedema peripheral	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nervous system disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Peripheral sensory neuropathy	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Leading to Dose Reduction of Ipatasertib by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	37 (36.3%)
	Grade 1-2	15 (14.7%)
	1	3 (2.9%)
	2	12 (11.8%)
	Grade 3-4	22 (21.6%)
	3	20 (19.6%)
	4	2 (2.0%)
Gastrointestinal disorders		
- Overall -	- Any Grade -	25 (24.5%)
	Grade 1-2	15 (14.7%)
	1	4 (3.9%)
	2	11 (10.8%)
	Grade 3-4	10 (9.8%)
	3	10 (9.8%)
Diarrhoea	- Any Grade -	21 (20.6%)
	Grade 1-2	13 (12.7%)
	1	3 (2.9%)
	2	10 (9.8%)
	Grade 3-4	8 (7.8%)
	3	8 (7.8%)
Nausea	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Vomiting	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Investigations		
- Overall -	- Any Grade -	5 (4.9%)
	Grade 3-4	5 (4.9%)
	3	3 (2.9%)
	4	2 (2.0%)
Neutrophil count decreased	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	2 (2.0%)
	4	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_ctc.sas
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Adverse Events Leading to Dose Reduction of Ipatasertib by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Blood triglycerides increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Lipase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Metabolism and nutrition disorders		
- Overall -	- Any Grade -	5 (4.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Hyperglycaemia	- Any Grade -	5 (4.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Blood and lymphatic system disorders		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Neutropenia	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Febrile neutropenia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Eye disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Visual impairment	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hepatobiliary disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Adverse Events Leading to Dose Reduction of Ipatasertib by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hyperbilirubinaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Infections and infestations		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Gastroenteritis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nervous system disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Dizziness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Skin and subcutaneous tissue disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Leading to Dose Reduction of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	9 (10.3%)	34 (20.5%)
	Grade 1-2	6 (6.9%)	18 (10.8%)
	1	0	3 (1.8%)
	2	6 (6.9%)	15 (9.0%)
	Grade 3-4	3 (3.4%)	16 (9.6%)
	3	3 (3.4%)	14 (8.4%)
	4	0	2 (1.2%)
Nervous system disorders			
- Overall -	- Any Grade -	3 (3.4%)	13 (7.8%)
	Grade 1-2	3 (3.4%)	11 (6.6%)
	1	0	4 (2.4%)
	2	3 (3.4%)	7 (4.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Peripheral sensory neuropathy	- Any Grade -	2 (2.3%)	5 (3.0%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	1	0	1 (0.6%)
	2	2 (2.3%)	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Neuropathy peripheral	- Any Grade -	1 (1.1%)	5 (3.0%)
	Grade 1-2	1 (1.1%)	5 (3.0%)
	1	0	2 (1.2%)
	2	1 (1.1%)	3 (1.8%)
Neurotoxicity	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Paraesthesia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Peripheral motor neuropathy	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	0	8 (4.8%)
	Grade 1-2	0	4 (2.4%)
	2	0	4 (2.4%)
	Grade 3-4	0	4 (2.4%)
	3	0	3 (1.8%)
	4	0	1 (0.6%)
Neutropenia	- Any Grade -	0	5 (3.0%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)

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Adverse Events Leading to Dose Reduction of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Febrile neutropenia	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
Anaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Investigations			
- Overall -	- Any Grade -	2 (2.3%)	6 (3.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	2 (2.3%)	5 (3.0%)
	3	2 (2.3%)	4 (2.4%)
	4	0	1 (0.6%)
Neutrophil count decreased	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	1 (0.6%)
	4	0	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Aspartate aminotransferase increased	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
White blood cell count decreased	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
General disorders and administration site conditions			
- Overall -	- Any Grade -	3 (3.4%)	3 (1.8%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	2	2 (2.3%)	2 (1.2%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Fatigue	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Asthenia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Ill-defined disorder	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_DSRPAC_A_SE.out
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Adverse Events Leading to Dose Reduction of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Oedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Oedema peripheral	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Gastrointestinal disorders			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Diarrhoea	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Injury, poisoning and procedural complications			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Eschar	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Toxicity to various agents	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Decreased appetite	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hyperglycaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Renal and urinary disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Oliguria	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Dose Reduction of Paclitaxel by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Vascular disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hypotension	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Adverse Events Leading to Dose Reduction of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	19 (25.3%)	39 (26.9%)
	Grade 1-2	13 (17.3%)	23 (15.9%)
	1	1 (1.3%)	1 (0.7%)
	2	12 (16.0%)	22 (15.2%)
	Grade 3-4	6 (8.0%)	16 (11.0%)
	3	5 (6.7%)	12 (8.3%)
	4	1 (1.3%)	4 (2.8%)
Nervous system disorders			
- Overall -	- Any Grade -	6 (8.0%)	19 (13.1%)
	Grade 1-2	5 (6.7%)	18 (12.4%)
	1	0	1 (0.7%)
	2	5 (6.7%)	17 (11.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Neuropathy peripheral	- Any Grade -	2 (2.7%)	9 (6.2%)
	Grade 1-2	1 (1.3%)	8 (5.5%)
	2	1 (1.3%)	8 (5.5%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Peripheral sensory neuropathy	- Any Grade -	2 (2.7%)	5 (3.4%)
	Grade 1-2	2 (2.7%)	5 (3.4%)
	2	2 (2.7%)	5 (3.4%)
Polyneuropathy	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	0	1 (0.7%)
	2	1 (1.3%)	2 (1.4%)
Neurotoxicity	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Peripheral motor neuropathy	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Investigations			
- Overall -	- Any Grade -	4 (5.3%)	8 (5.5%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
	Grade 3-4	3 (4.0%)	7 (4.8%)
	3	2 (2.7%)	4 (2.8%)
	4	1 (1.3%)	3 (2.1%)
Neutrophil count decreased	- Any Grade -	3 (4.0%)	8 (5.5%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
	Grade 3-4	2 (2.7%)	7 (4.8%)
	3	1 (1.3%)	4 (2.8%)
	4	1 (1.3%)	3 (2.1%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Leading to Dose Reduction of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Alanine aminotransferase increased	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
White blood cell count decreased	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	4 (5.3%)	6 (4.1%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	1 (1.3%)	0
	2	1 (1.3%)	2 (1.4%)
	Grade 3-4	2 (2.7%)	4 (2.8%)
	3	2 (2.7%)	3 (2.1%)
	4	0	1 (0.7%)
Neutropenia	- Any Grade -	3 (4.0%)	5 (3.4%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
	Grade 3-4	2 (2.7%)	4 (2.8%)
	3	2 (2.7%)	3 (2.1%)
	4	0	1 (0.7%)
Anaemia	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
General disorders and administration site conditions			
- Overall -	- Any Grade -	4 (5.3%)	2 (1.4%)
	Grade 1-2	4 (5.3%)	2 (1.4%)
	1	1 (1.3%)	0
	2	3 (4.0%)	2 (1.4%)
Oedema peripheral	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
Asthenia	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	1	1 (1.3%)	0
	2	1 (1.3%)	0
Gait disturbance	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Oedema	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0

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Adverse Events Leading to Dose Reduction of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Gastrointestinal disorders			
- Overall -	- Any Grade -	0	5 (3.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	4 (2.8%)
	3	0	4 (2.8%)
Diarrhoea	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	3 (2.1%)
	3	0	3 (2.1%)
Nausea	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Infections and infestations			
- Overall -	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	2	2 (2.7%)	1 (0.7%)
Cystitis	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	2	2 (2.7%)	0
Paronychia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Injury, poisoning and procedural complications			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Poisoning	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Decreased appetite	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Adverse Events Leading to Dose Reduction of Paclitaxel by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Dose Reduction of Paclitaxel by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	25 (24.5%)
	Grade 1-2	17 (16.7%)
	1	4 (3.9%)
	2	13 (12.7%)
	Grade 3-4	8 (7.8%)
	3	7 (6.9%)
	4	1 (1.0%)
Nervous system disorders		
- Overall -	- Any Grade -	12 (11.8%)
	Grade 1-2	10 (9.8%)
	1	3 (2.9%)
	2	7 (6.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Neuropathy peripheral	- Any Grade -	8 (7.8%)
	Grade 1-2	6 (5.9%)
	1	2 (2.0%)
	2	4 (3.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Polyneuropathy	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
Dizziness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Investigations		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	3 (2.9%)
	3	2 (2.0%)
	4	1 (1.0%)
Neutrophil count decreased	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_DSRPAC_C_SE.out
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Adverse Events Leading to Dose Reduction of Paclitaxel by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Weight decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Blood and lymphatic system disorders		
- Overall -	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	2	3 (2.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neutropenia	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Anaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Gastrointestinal disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Diarrhoea	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Eye disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Visual impairment	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
General disorders and administration site conditions		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oedema peripheral	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_DSRPAC_C_SE.out
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Adverse Events Leading to Dose Reduction of Paclitaxel by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Skin and subcutaneous tissue disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Nail disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_DSRPAC_C_SE.out
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Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	75 (73.5%)
	Grade 1-2	38 (37.3%)
	1	16 (15.7%)
	2	22 (21.6%)
	Grade 3-4	36 (35.3%)
	3	33 (32.4%)
	4	3 (2.9%)
	Grade 5	1 (1.0%)
Gastrointestinal disorders		
- Overall -	- Any Grade -	44 (43.1%)
	Grade 1-2	31 (30.4%)
	1	19 (18.6%)
	2	12 (11.8%)
	Grade 3-4	13 (12.7%)
	3	13 (12.7%)
Diarrhoea	- Any Grade -	34 (33.3%)
	Grade 1-2	24 (23.5%)
	1	12 (11.8%)
	2	12 (11.8%)
	Grade 3-4	10 (9.8%)
	3	10 (9.8%)
Nausea	- Any Grade -	15 (14.7%)
	Grade 1-2	14 (13.7%)
	1	14 (13.7%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Vomiting	- Any Grade -	10 (9.8%)
	Grade 1-2	10 (9.8%)
	1	7 (6.9%)
	2	3 (2.9%)
Abdominal pain	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Abdominal pain upper	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Gastrooesophageal reflux disease	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Abdominal discomfort	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_RELATZ_C_SE.out
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Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Constipation	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Flatulence	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Stomatitis	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Dental discomfort	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Dry mouth	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Dyspepsia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Gingival pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Large intestine perforation	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Mouth ulceration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oesophagitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oral discomfort	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Skin and subcutaneous tissue disorders		
- Overall -	- Any Grade -	32 (31.4%)
	Grade 1-2	27 (26.5%)
	1	15 (14.7%)
	2	12 (11.8%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Rash	- Any Grade -	20 (19.6%)
	Grade 1-2	18 (17.6%)
	1	10 (9.8%)
	2	8 (7.8%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)

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Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Pruritus	- Any Grade -	7 (6.9%)
	Grade 1-2	6 (5.9%)
	1	5 (4.9%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alopecia	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Erythema	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Hand dermatitis	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Rash maculo-papular	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dermatitis allergic	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Eczema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nail bed tenderness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nail disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash erythematous	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Rash papular	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash pruritic	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Seborrhoeic dermatitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Skin lesion	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Investigations		
- Overall -	- Any Grade -	26 (25.5%)
	Grade 1-2	16 (15.7%)
	1	11 (10.8%)
	2	5 (4.9%)
	Grade 3-4	10 (9.8%)
	3	9 (8.8%)
	4	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	15 (14.7%)
	Grade 1-2	9 (8.8%)
	1	7 (6.9%)
	2	2 (2.0%)
	Grade 3-4	6 (5.9%)
	3	6 (5.9%)
Aspartate aminotransferase increased	- Any Grade -	13 (12.7%)
	Grade 1-2	10 (9.8%)
	1	6 (5.9%)
	2	4 (3.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Blood alkaline phosphatase increased	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Lipase increased	- Any Grade -	4 (3.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	2 (2.0%)
	4	1 (1.0%)
Blood lactate dehydrogenase increased	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Blood bilirubin increased	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Blood thyroid stimulating hormone increased	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Blood triglycerides increased	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)

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Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Amylase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Blood chloride decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
High density lipoprotein increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Neutrophil count decreased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Weight decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
White blood cell count decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
General disorders and administration site conditions		
- Overall -	- Any Grade -	25 (24.5%)
	Grade 1-2	24 (23.5%)
	1	11 (10.8%)
	2	13 (12.7%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Asthenia	- Any Grade -	11 (10.8%)
	Grade 1-2	11 (10.8%)
	1	7 (6.9%)
	2	4 (3.9%)
Fatigue	- Any Grade -	9 (8.8%)
	Grade 1-2	8 (7.8%)
	1	2 (2.0%)
	2	6 (5.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Mucosal inflammation	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	5 (4.9%)
	2	1 (1.0%)
Pyrexia	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)

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Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Oedema peripheral	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Generalised oedema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oedema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Thirst	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nervous system disorders		
- Overall -	- Any Grade -	17 (16.7%)
	Grade 1-2	15 (14.7%)
	1	10 (9.8%)
	2	5 (4.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Neuropathy peripheral	- Any Grade -	8 (7.8%)
	Grade 1-2	8 (7.8%)
	1	6 (5.9%)
	2	2 (2.0%)
Headache	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Polyneuropathy	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Balance disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Cognitive disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Dizziness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Dysgeusia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Dystonia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypersomnia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypoaesthesia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Lethargy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Paraesthesia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Peripheral sensory neuropathy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Posterior reversible encephalopathy syndrome	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Metabolism and nutrition disorders		
- Overall -	- Any Grade -	16 (15.7%)
	Grade 1-2	12 (11.8%)
	1	10 (9.8%)
	2	2 (2.0%)
	Grade 3-4	4 (3.9%)
	3	3 (2.9%)
	4	1 (1.0%)
Hyperglycaemia	- Any Grade -	8 (7.8%)
	Grade 1-2	5 (4.9%)
	1	4 (3.9%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Decreased appetite	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Dehydration	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypercreatininaemia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)

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Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hypokalaemia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Alkalosis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Dyslipidaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypercalcaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hyperkalaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypertriglyceridaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypoalbuminaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypomagnesaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hyponatraemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypophosphataemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Type 1 diabetes mellitus	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Blood and lymphatic system disorders		
- Overall -	- Any Grade -	15 (14.7%)
	Grade 1-2	13 (12.7%)
	1	4 (3.9%)
	2	9 (8.8%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)

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Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Neutropenia	- Any Grade -	8 (7.8%)
	Grade 1-2	6 (5.9%)
	1	1 (1.0%)
	2	5 (4.9%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Anaemia	- Any Grade -	7 (6.9%)
	Grade 1-2	7 (6.9%)
	1	3 (2.9%)
	2	4 (3.9%)
Leukopenia	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Eosinophilia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Lymphadenopathy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Lymphopenia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Thrombocytosis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Respiratory, thoracic and mediastinal disorders		
- Overall -	- Any Grade -	13 (12.7%)
	Grade 1-2	11 (10.8%)
	1	8 (7.8%)
	2	3 (2.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
	Grade 5	1 (1.0%)
Pneumonitis	- Any Grade -	7 (6.9%)
	Grade 1-2	6 (5.9%)
	1	4 (3.9%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Epistaxis	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Cough	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Lung infiltration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Productive cough	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pulmonary embolism	- Any Grade -	1 (1.0%)
	Grade 5	1 (1.0%)
Musculoskeletal and connective tissue disorders		
- Overall -	- Any Grade -	12 (11.8%)
	Grade 1-2	11 (10.8%)
	1	9 (8.8%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Arthralgia	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
Muscle spasms	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Myalgia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Mixed connective tissue disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Musculoskeletal stiffness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Myositis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pain in extremity	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hepatobiliary disorders		
- Overall -	- Any Grade -	9 (8.8%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Hyperbilirubinaemia	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Autoimmune hepatitis	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Hypertransaminasaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Endocrine disorders		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	4 (3.9%)
	2	2 (2.0%)
Hypothyroidism	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
Autoimmune hypothyroidism	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hyperthyroidism	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Infections and infestations		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	5 (4.9%)
	1	2 (2.0%)
	2	3 (2.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Urinary tract infection	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_RELATZ_C_SE.out

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Furuncle	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pneumonia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pneumonia viral	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Eye disorders		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Dry eye	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Eyelid function disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Vision blurred	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Tumour necrosis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Tumour inflammation	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Ear and labyrinth disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Hypoacusis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Tinnitus	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Vertigo	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Immune system disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypersensitivity	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Psychiatric disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Insomnia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Vascular disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Flushing	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypertension	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Cardiac disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Myocarditis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)

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Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Renal and urinary disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Acute kidney injury	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	55 (63.2%)	152 (91.6%)
	Grade 1-2	44 (50.6%)	96 (57.8%)
	1	24 (27.6%)	28 (16.9%)
	2	20 (23.0%)	68 (41.0%)
	Grade 3-4	10 (11.5%)	56 (33.7%)
	3	10 (11.5%)	50 (30.1%)
	4	0	6 (3.6%)
	Grade 5	1 (1.1%)	0
Gastrointestinal disorders			
- Overall -	- Any Grade -	35 (40.2%)	142 (85.5%)
	Grade 1-2	32 (36.8%)	122 (73.5%)
	1	22 (25.3%)	59 (35.5%)
	2	10 (11.5%)	63 (38.0%)
	Grade 3-4	3 (3.4%)	20 (12.0%)
	3	3 (3.4%)	19 (11.4%)
	4	0	1 (0.6%)
Diarrhoea	- Any Grade -	24 (27.6%)	135 (81.3%)
	Grade 1-2	23 (26.4%)	120 (72.3%)
	1	16 (18.4%)	65 (39.2%)
	2	7 (8.0%)	55 (33.1%)
	Grade 3-4	1 (1.1%)	15 (9.0%)
	3	1 (1.1%)	15 (9.0%)
Nausea	- Any Grade -	9 (10.3%)	49 (29.5%)
	Grade 1-2	9 (10.3%)	45 (27.1%)
	1	7 (8.0%)	36 (21.7%)
	2	2 (2.3%)	9 (5.4%)
	Grade 3-4	0	4 (2.4%)
	3	0	4 (2.4%)
Vomiting	- Any Grade -	5 (5.7%)	40 (24.1%)
	Grade 1-2	4 (4.6%)	38 (22.9%)
	1	3 (3.4%)	33 (19.9%)
	2	1 (1.1%)	5 (3.0%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	1 (1.1%)	2 (1.2%)
Stomatitis	- Any Grade -	4 (4.6%)	12 (7.2%)
	Grade 1-2	4 (4.6%)	12 (7.2%)
	1	3 (3.4%)	7 (4.2%)
	2	1 (1.1%)	5 (3.0%)
Dyspepsia	- Any Grade -	1 (1.1%)	12 (7.2%)
	Grade 1-2	1 (1.1%)	12 (7.2%)
	1	1 (1.1%)	9 (5.4%)
	2	0	3 (1.8%)
Abdominal pain upper	- Any Grade -	4 (4.6%)	7 (4.2%)
	Grade 1-2	4 (4.6%)	7 (4.2%)
	1	4 (4.6%)	6 (3.6%)
	2	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Abdominal pain	- Any Grade -	0	10 (6.0%)
	Grade 1-2	0	9 (5.4%)
	1	0	5 (3.0%)
	2	0	4 (2.4%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Constipation	- Any Grade -	2 (2.3%)	7 (4.2%)
	Grade 1-2	2 (2.3%)	7 (4.2%)
	1	2 (2.3%)	7 (4.2%)
Abdominal discomfort	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	2 (2.3%)	2 (1.2%)
Abdominal distension	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Flatulence	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Cheilitis	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Colitis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Dry mouth	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Gastrooesophageal reflux disease	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Enteritis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Gastrointestinal pain	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Large intestine perforation	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Mouth ulceration	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Proctalgia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
General disorders and administration site conditions			
- Overall -	- Any Grade -	14 (16.1%)	56 (33.7%)
	Grade 1-2	13 (14.9%)	44 (26.5%)
	1	12 (13.8%)	26 (15.7%)
	2	1 (1.1%)	18 (10.8%)
	Grade 3-4	1 (1.1%)	12 (7.2%)
	3	1 (1.1%)	12 (7.2%)
Asthenia	- Any Grade -	5 (5.7%)	27 (16.3%)
	Grade 1-2	5 (5.7%)	21 (12.7%)
	1	4 (4.6%)	12 (7.2%)
	2	1 (1.1%)	9 (5.4%)
	Grade 3-4	0	6 (3.6%)
	3	0	6 (3.6%)
Fatigue	- Any Grade -	6 (6.9%)	20 (12.0%)
	Grade 1-2	5 (5.7%)	15 (9.0%)
	1	5 (5.7%)	11 (6.6%)
	2	0	4 (2.4%)
	Grade 3-4	1 (1.1%)	5 (3.0%)
	3	1 (1.1%)	5 (3.0%)
Mucosal inflammation	- Any Grade -	2 (2.3%)	6 (3.6%)
	Grade 1-2	2 (2.3%)	5 (3.0%)
	1	2 (2.3%)	3 (1.8%)
	2	0	2 (1.2%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Pyrexia	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	2 (2.3%)	4 (2.4%)
	1	2 (2.3%)	3 (1.8%)
	2	0	1 (0.6%)
Oedema peripheral	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	4 (2.4%)
	1	1 (1.1%)	2 (1.2%)
	2	0	2 (1.2%)
Influenza like illness	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Malaise	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Pain	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Face oedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hyperthermia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	12 (13.8%)	56 (33.7%)
	Grade 1-2	11 (12.6%)	49 (29.5%)
	1	7 (8.0%)	25 (15.1%)
	2	4 (4.6%)	24 (14.5%)
	Grade 3-4	0	7 (4.2%)
	3	0	6 (3.6%)
	4	0	1 (0.6%)
	Grade 5	1 (1.1%)	0
Hyperglycaemia	- Any Grade -	7 (8.0%)	27 (16.3%)
	Grade 1-2	7 (8.0%)	25 (15.1%)
	1	4 (4.6%)	13 (7.8%)
	2	3 (3.4%)	12 (7.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
Decreased appetite	- Any Grade -	2 (2.3%)	23 (13.9%)
	Grade 1-2	2 (2.3%)	22 (13.3%)
	1	2 (2.3%)	14 (8.4%)
	2	0	8 (4.8%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hypertriglyceridaemia	- Any Grade -	1 (1.1%)	8 (4.8%)
	Grade 1-2	1 (1.1%)	5 (3.0%)
	1	1 (1.1%)	0
	2	0	5 (3.0%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Hypophosphataemia	- Any Grade -	3 (3.4%)	1 (0.6%)
	Grade 1-2	3 (3.4%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
	2	2 (2.3%)	0
Hypoalbuminaemia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Hypomagnesaemia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Dehydration	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Dyslipidaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Electrolyte imbalance	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hyperamylasaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hypercreatininaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Hyperkalaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Hypokalaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Increased appetite	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Tumour lysis syndrome	- Any Grade -	1 (1.1%)	0
	Grade 5	1 (1.1%)	0
Investigations			
- Overall -	- Any Grade -	13 (14.9%)	50 (30.1%)
	Grade 1-2	10 (11.5%)	35 (21.1%)
	1	7 (8.0%)	20 (12.0%)
	2	3 (3.4%)	15 (9.0%)
	Grade 3-4	3 (3.4%)	15 (9.0%)
	3	3 (3.4%)	14 (8.4%)
	4	0	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	5 (5.7%)	18 (10.8%)
	Grade 1-2	4 (4.6%)	11 (6.6%)
	1	4 (4.6%)	7 (4.2%)
	2	0	4 (2.4%)
	Grade 3-4	1 (1.1%)	7 (4.2%)
	3	1 (1.1%)	7 (4.2%)
Aspartate aminotransferase increased	- Any Grade -	3 (3.4%)	12 (7.2%)
	Grade 1-2	2 (2.3%)	9 (5.4%)
	1	1 (1.1%)	5 (3.0%)
	2	1 (1.1%)	4 (2.4%)
	Grade 3-4	1 (1.1%)	3 (1.8%)
	3	1 (1.1%)	3 (1.8%)
Neutrophil count decreased	- Any Grade -	4 (4.6%)	11 (6.6%)
	Grade 1-2	2 (2.3%)	7 (4.2%)
	1	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	6 (3.6%)
	Grade 3-4	2 (2.3%)	4 (2.4%)
	3	2 (2.3%)	3 (1.8%)
	4	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
White blood cell count decreased	- Any Grade -	5 (5.7%)	6 (3.6%)
	Grade 1-2	4 (4.6%)	4 (2.4%)
	1	2 (2.3%)	2 (1.2%)
	2	2 (2.3%)	2 (1.2%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	1 (1.1%)	2 (1.2%)
Blood cholesterol increased	- Any Grade -	2 (2.3%)	6 (3.6%)
	Grade 1-2	2 (2.3%)	6 (3.6%)
	1	2 (2.3%)	5 (3.0%)
	2	0	1 (0.6%)
Weight decreased	- Any Grade -	1 (1.1%)	6 (3.6%)
	Grade 1-2	1 (1.1%)	6 (3.6%)
	1	1 (1.1%)	4 (2.4%)
	2	0	2 (1.2%)
Blood alkaline phosphatase increased	- Any Grade -	0	5 (3.0%)
	Grade 1-2	0	5 (3.0%)
	1	0	5 (3.0%)
Blood urea increased	- Any Grade -	3 (3.4%)	2 (1.2%)
	Grade 1-2	3 (3.4%)	2 (1.2%)
	1	3 (3.4%)	2 (1.2%)
Blood lactate dehydrogenase increased	- Any Grade -	0	4 (2.4%)
	Grade 1-2	0	4 (2.4%)
	1	0	3 (1.8%)
	2	0	1 (0.6%)
Lipase increased	- Any Grade -	0	4 (2.4%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Blood creatinine increased	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Gamma-glutamyltransferase increased	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Low density lipoprotein increased	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Lymphocyte count decreased	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Blood bilirubin increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Blood glucose increased	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Blood phosphorus increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Blood triglycerides increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Body temperature increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Eastern Cooperative Oncology Group performance status worsened	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Glycosylated haemoglobin abnormal	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Haematocrit decreased	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	14 (16.1%)	47 (28.3%)
	Grade 1-2	14 (16.1%)	44 (26.5%)
	1	9 (10.3%)	24 (14.5%)
	2	5 (5.7%)	20 (12.0%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Rash	- Any Grade -	6 (6.9%)	19 (11.4%)
	Grade 1-2	6 (6.9%)	17 (10.2%)
	1	4 (4.6%)	13 (7.8%)
	2	2 (2.3%)	4 (2.4%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Alopecia	- Any Grade -	4 (4.6%)	12 (7.2%)
	Grade 1-2	4 (4.6%)	12 (7.2%)
	1	0	1 (0.6%)
	2	4 (4.6%)	11 (6.6%)
Pruritus	- Any Grade -	4 (4.6%)	7 (4.2%)
	Grade 1-2	4 (4.6%)	7 (4.2%)
	1	3 (3.4%)	5 (3.0%)
	2	1 (1.1%)	2 (1.2%)
Dermatitis acneiform	- Any Grade -	0	7 (4.2%)
	Grade 1-2	0	7 (4.2%)
	1	0	7 (4.2%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Rash maculo-papular	- Any Grade -	0	4 (2.4%)
	Grade 1-2	0	4 (2.4%)
	1	0	3 (1.8%)
	2	0	1 (0.6%)
Dermatitis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	0
	2	0	1 (0.6%)
Nail discolouration	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Onychoclasis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Dermatitis contact	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Dry skin	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Erythema multiforme	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hand dermatitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Hyperhidrosis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Nail disorder	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Nail dystrophy	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Onycholysis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Skin exfoliation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Skin hyperpigmentation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Urticaria	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	14 (16.1%)	25 (15.1%)
	Grade 1-2	11 (12.6%)	20 (12.0%)
	1	5 (5.7%)	8 (4.8%)
	2	6 (6.9%)	12 (7.2%)
	Grade 3-4	3 (3.4%)	5 (3.0%)
	3	3 (3.4%)	3 (1.8%)
	4	0	2 (1.2%)
Anaemia	- Any Grade -	6 (6.9%)	14 (8.4%)
	Grade 1-2	5 (5.7%)	14 (8.4%)
	1	3 (3.4%)	9 (5.4%)
	2	2 (2.3%)	5 (3.0%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Neutropenia	- Any Grade -	7 (8.0%)	10 (6.0%)
	Grade 1-2	6 (6.9%)	6 (3.6%)
	1	2 (2.3%)	0
	2	4 (4.6%)	6 (3.6%)
	Grade 3-4	1 (1.1%)	4 (2.4%)
	3	1 (1.1%)	2 (1.2%)
	4	0	2 (1.2%)
Leukopenia	- Any Grade -	2 (2.3%)	7 (4.2%)
	Grade 1-2	2 (2.3%)	7 (4.2%)
	1	2 (2.3%)	5 (3.0%)
	2	0	2 (1.2%)
Thrombocytopenia	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Lymphopenia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	0
	2	0	1 (0.6%)
Anaemia macrocytic	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Febrile neutropenia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Leukocytosis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Thrombocytosis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Nervous system disorders			
- Overall -	- Any Grade -	8 (9.2%)	19 (11.4%)
	Grade 1-2	8 (9.2%)	18 (10.8%)
	1	7 (8.0%)	14 (8.4%)
	2	1 (1.1%)	4 (2.4%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Headache	- Any Grade -	1 (1.1%)	6 (3.6%)
	Grade 1-2	1 (1.1%)	6 (3.6%)
	1	1 (1.1%)	4 (2.4%)
	2	0	2 (1.2%)
Dysgeusia	- Any Grade -	3 (3.4%)	3 (1.8%)
	Grade 1-2	3 (3.4%)	3 (1.8%)
	1	2 (2.3%)	3 (1.8%)
	2	1 (1.1%)	0
Peripheral sensory neuropathy	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	1 (1.1%)	3 (1.8%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Dizziness	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	1 (1.1%)	2 (1.2%)
	2	0	1 (0.6%)
Neuropathy peripheral	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	1 (1.1%)	3 (1.8%)
Paraesthesia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Polyneuropathy	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Altered state of consciousness	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Anosmia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Encephalopathy	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Neurotoxicity	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Taste disorder	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Tremor	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	5 (5.7%)	17 (10.2%)
	Grade 1-2	5 (5.7%)	16 (9.6%)
	1	4 (4.6%)	13 (7.8%)
	2	1 (1.1%)	3 (1.8%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Epistaxis	- Any Grade -	1 (1.1%)	6 (3.6%)
	Grade 1-2	1 (1.1%)	6 (3.6%)
	1	1 (1.1%)	5 (3.0%)
	2	0	1 (0.6%)
Cough	- Any Grade -	3 (3.4%)	2 (1.2%)
	Grade 1-2	3 (3.4%)	2 (1.2%)
	1	2 (2.3%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
Oropharyngeal pain	- Any Grade -	0	5 (3.0%)
	Grade 1-2	0	5 (3.0%)
	1	0	5 (3.0%)
Productive cough	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	3 (1.8%)
Dysphonia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Dyspnoea	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Nasal congestion	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Pneumonitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Pulmonary embolism	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Pulmonary hypertension	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Rhinitis allergic	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Rhinorrhoea	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Musculoskeletal and connective tissue disorders			
- Overall -	- Any Grade -	2 (2.3%)	16 (9.6%)
	Grade 1-2	2 (2.3%)	15 (9.0%)
	1	0	10 (6.0%)
	2	2 (2.3%)	5 (3.0%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Myalgia	- Any Grade -	0	8 (4.8%)
	Grade 1-2	0	8 (4.8%)
	1	0	8 (4.8%)
Arthralgia	- Any Grade -	1 (1.1%)	6 (3.6%)
	Grade 1-2	1 (1.1%)	6 (3.6%)
	1	0	3 (1.8%)
	2	1 (1.1%)	3 (1.8%)
Pain in extremity	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	0	2 (1.2%)
	2	1 (1.1%)	1 (0.6%)
Bone pain	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Muscle spasms	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Back pain	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Infections and infestations			
- Overall -	- Any Grade -	6 (6.9%)	11 (6.6%)
	Grade 1-2	5 (5.7%)	11 (6.6%)
	1	2 (2.3%)	5 (3.0%)
	2	3 (3.4%)	6 (3.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Fungal skin infection	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	0	1 (0.6%)
	2	1 (1.1%)	0
Rash pustular	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Conjunctivitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Cystitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Fungal infection	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Herpes simplex	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Influenza	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Mucosal infection	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Oral candidiasis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Oral herpes	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Paronychia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Periodontitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Pharyngitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Pneumonia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Upper respiratory tract infection	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Urinary tract infection	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Vulvitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_RELIPAT_A_SE.out
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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Eye disorders			
- Overall -	- Any Grade -	2 (2.3%)	8 (4.8%)
	Grade 1-2	1 (1.1%)	8 (4.8%)
	1	1 (1.1%)	5 (3.0%)
	2	0	3 (1.8%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Vision blurred	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Visual acuity reduced	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Visual impairment	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	0
	2	0	1 (0.6%)
Blepharitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Conjunctival irritation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Cystoid macular oedema	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Lacrimation increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Renal and urinary disorders			
- Overall -	- Any Grade -	2 (2.3%)	5 (3.0%)
	Grade 1-2	2 (2.3%)	5 (3.0%)
	1	2 (2.3%)	3 (1.8%)
	2	0	2 (1.2%)
Dysuria	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Haematuria	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Oliguria	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Renal failure	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Renal impairment	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Tubulointerstitial nephritis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Psychiatric disorders			
- Overall -	- Any Grade -	1 (1.1%)	5 (3.0%)
	Grade 1-2	1 (1.1%)	5 (3.0%)
	1	0	1 (0.6%)
	2	1 (1.1%)	4 (2.4%)
Insomnia	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
Anxiety	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Depression	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Dyssomnia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Vascular disorders			
- Overall -	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	1	2 (2.3%)	1 (0.6%)
	2	0	2 (1.2%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hypertension	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Hypotension	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Venous thrombosis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Venous thrombosis limb	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Cardiac disorders			
- Overall -	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	1 (1.1%)	2 (1.2%)
	2	1 (1.1%)	0
Sinus tachycardia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Atrial fibrillation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Bradycardia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Tachycardia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Ear and labyrinth disorders			
- Overall -	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Vertigo	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Hepatobiliary disorders			
- Overall -	- Any Grade -	3 (3.4%)	0
	Grade 1-2	3 (3.4%)	0
	1	1 (1.1%)	0
	2	2 (2.3%)	0
Hyperbilirubinaemia	- Any Grade -	3 (3.4%)	0
	Grade 1-2	3 (3.4%)	0
	1	1 (1.1%)	0
	2	2 (2.3%)	0
Reproductive system and breast disorders			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Breast pain	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Vulvovaginal burning sensation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Immune system disorders			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Hypersensitivity	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Tumour necrosis	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	54 (72.0%)	134 (92.4%)
	Grade 1-2	35 (46.7%)	90 (62.1%)
	1	16 (21.3%)	25 (17.2%)
	2	19 (25.3%)	65 (44.8%)
	Grade 3-4	19 (25.3%)	43 (29.7%)
	3	17 (22.7%)	40 (27.6%)
	4	2 (2.7%)	3 (2.1%)
	Grade 5	0	1 (0.7%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	36 (48.0%)	130 (89.7%)
	Grade 1-2	35 (46.7%)	111 (76.6%)
	1	26 (34.7%)	40 (27.6%)
	2	9 (12.0%)	71 (49.0%)
	Grade 3-4	1 (1.3%)	19 (13.1%)
	3	1 (1.3%)	18 (12.4%)
	4	0	1 (0.7%)
Diarrhoea	- Any Grade -	24 (32.0%)	121 (83.4%)
	Grade 1-2	23 (30.7%)	105 (72.4%)
	1	18 (24.0%)	42 (29.0%)
	2	5 (6.7%)	63 (43.4%)
	Grade 3-4	1 (1.3%)	16 (11.0%)
	3	1 (1.3%)	16 (11.0%)
Nausea	- Any Grade -	9 (12.0%)	43 (29.7%)
	Grade 1-2	9 (12.0%)	42 (29.0%)
	1	7 (9.3%)	29 (20.0%)
	2	2 (2.7%)	13 (9.0%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Vomiting	- Any Grade -	4 (5.3%)	30 (20.7%)
	Grade 1-2	4 (5.3%)	28 (19.3%)
	1	4 (5.3%)	20 (13.8%)
	2	0	8 (5.5%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Stomatitis	- Any Grade -	5 (6.7%)	11 (7.6%)
	Grade 1-2	5 (6.7%)	11 (7.6%)
	1	4 (5.3%)	10 (6.9%)
	2	1 (1.3%)	1 (0.7%)
Abdominal pain upper	- Any Grade -	3 (4.0%)	4 (2.8%)
	Grade 1-2	3 (4.0%)	4 (2.8%)
	1	3 (4.0%)	4 (2.8%)
Constipation	- Any Grade -	6 (8.0%)	1 (0.7%)
	Grade 1-2	6 (8.0%)	1 (0.7%)
	1	5 (6.7%)	1 (0.7%)
	2	1 (1.3%)	0

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Abdominal pain	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	1 (1.3%)	1 (0.7%)
	2	0	2 (1.4%)
Dyspepsia	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	1 (1.3%)	1 (0.7%)
	2	0	2 (1.4%)
Flatulence	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	0
Abdominal discomfort	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
Abdominal distension	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	2 (1.4%)
	2	0	1 (0.7%)
Gastrooesophageal reflux disease	- Any Grade -	3 (4.0%)	0
	Grade 1-2	3 (4.0%)	0
	1	1 (1.3%)	0
	2	2 (2.7%)	0
Aphthous ulcer	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dry mouth	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Enterocolitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Gastritis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Mouth ulceration	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Oral pain	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Anal haemorrhage	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Angular cheilitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Eructation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Faeces discoloured	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Faeces soft	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hyperchlorhydria	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Intestinal obstruction	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	4	0	1 (0.7%)
Lip dry	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Odynophagia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Tongue ulceration	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	25 (33.3%)	45 (31.0%)
	Grade 1-2	25 (33.3%)	39 (26.9%)
	1	12 (16.0%)	22 (15.2%)
	2	13 (17.3%)	17 (11.7%)
	Grade 3-4	0	6 (4.1%)
	3	0	6 (4.1%)
Alopecia	- Any Grade -	14 (18.7%)	9 (6.2%)
	Grade 1-2	14 (18.7%)	9 (6.2%)
	1	3 (4.0%)	6 (4.1%)
	2	11 (14.7%)	3 (2.1%)
Rash	- Any Grade -	5 (6.7%)	17 (11.7%)
	Grade 1-2	5 (6.7%)	16 (11.0%)
	1	5 (6.7%)	11 (7.6%)
	2	0	5 (3.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Pruritus	- Any Grade -	1 (1.3%)	6 (4.1%)
	Grade 1-2	1 (1.3%)	6 (4.1%)
	1	1 (1.3%)	4 (2.8%)
	2	0	2 (1.4%)
Rash maculo-papular	- Any Grade -	3 (4.0%)	4 (2.8%)
	Grade 1-2	3 (4.0%)	2 (1.4%)
	1	2 (2.7%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Dry skin	- Any Grade -	3 (4.0%)	3 (2.1%)
	Grade 1-2	3 (4.0%)	3 (2.1%)
	1	3 (4.0%)	3 (2.1%)
Dermatitis acneiform	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	2 (2.7%)	2 (1.4%)
Nail discolouration	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Nail dystrophy	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	1	0	1 (0.7%)
	2	2 (2.7%)	0
Dermatitis allergic	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Drug eruption	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Onychoclasis	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Onychomadesis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Palmar-plantar erythrodysaesthesia syndrome	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Dermal cyst	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Dermatitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Dermatitis bullous	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Eczema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Eczema asteatotic	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Erythema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Erythema multiforme	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperhidrosis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Nail disorder	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nail ridging	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Onychalgia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Papule	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Photosensitivity reaction	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Polymorphic light eruption	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Rash erythematous	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash papular	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Skin exfoliation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Skin hyperpigmentation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Stasis dermatitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
General disorders and administration site conditions			
- Overall -	- Any Grade -	19 (25.3%)	38 (26.2%)
	Grade 1-2	16 (21.3%)	37 (25.5%)
	1	8 (10.7%)	25 (17.2%)
	2	8 (10.7%)	12 (8.3%)
	Grade 3-4	3 (4.0%)	1 (0.7%)
	3	3 (4.0%)	1 (0.7%)
Fatigue	- Any Grade -	8 (10.7%)	12 (8.3%)
	Grade 1-2	5 (6.7%)	12 (8.3%)
	1	2 (2.7%)	9 (6.2%)
	2	3 (4.0%)	3 (2.1%)
	Grade 3-4	3 (4.0%)	0
	3	3 (4.0%)	0
Asthenia	- Any Grade -	7 (9.3%)	9 (6.2%)
	Grade 1-2	6 (8.0%)	8 (5.5%)
	1	4 (5.3%)	4 (2.8%)
	2	2 (2.7%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Oedema peripheral	- Any Grade -	3 (4.0%)	4 (2.8%)
	Grade 1-2	3 (4.0%)	4 (2.8%)
	1	1 (1.3%)	3 (2.1%)
	2	2 (2.7%)	1 (0.7%)
Pyrexia	- Any Grade -	0	7 (4.8%)
	Grade 1-2	0	7 (4.8%)
	1	0	5 (3.4%)
	2	0	2 (1.4%)
Malaise	- Any Grade -	3 (4.0%)	3 (2.1%)
	Grade 1-2	3 (4.0%)	3 (2.1%)
	1	2 (2.7%)	2 (1.4%)
	2	1 (1.3%)	1 (0.7%)
Mucosal inflammation	- Any Grade -	0	5 (3.4%)
	Grade 1-2	0	5 (3.4%)
	1	0	3 (2.1%)
	2	0	2 (1.4%)
Oedema	- Any Grade -	0	5 (3.4%)
	Grade 1-2	0	5 (3.4%)
	1	0	5 (3.4%)
Chest pain	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hypothermia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Pain	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Thirst	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Investigations			
- Overall -	- Any Grade -	21 (28.0%)	33 (22.8%)
	Grade 1-2	14 (18.7%)	22 (15.2%)
	1	5 (6.7%)	11 (7.6%)
	2	9 (12.0%)	11 (7.6%)
	Grade 3-4	7 (9.3%)	11 (7.6%)
	3	6 (8.0%)	9 (6.2%)
	4	1 (1.3%)	2 (1.4%)
Alanine aminotransferase increased	- Any Grade -	9 (12.0%)	11 (7.6%)
	Grade 1-2	7 (9.3%)	7 (4.8%)
	1	3 (4.0%)	6 (4.1%)
	2	4 (5.3%)	1 (0.7%)
	Grade 3-4	2 (2.7%)	4 (2.8%)
	3	2 (2.7%)	4 (2.8%)
Neutrophil count decreased	- Any Grade -	8 (10.7%)	12 (8.3%)
	Grade 1-2	5 (6.7%)	6 (4.1%)
	1	1 (1.3%)	1 (0.7%)
	2	4 (5.3%)	5 (3.4%)
	Grade 3-4	3 (4.0%)	6 (4.1%)
	3	2 (2.7%)	5 (3.4%)
	4	1 (1.3%)	1 (0.7%)
Aspartate aminotransferase increased	- Any Grade -	6 (8.0%)	7 (4.8%)
	Grade 1-2	5 (6.7%)	6 (4.1%)
	1	4 (5.3%)	4 (2.8%)
	2	1 (1.3%)	2 (1.4%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Blood lactate dehydrogenase increased	- Any Grade -	6 (8.0%)	3 (2.1%)
	Grade 1-2	6 (8.0%)	3 (2.1%)
	1	6 (8.0%)	3 (2.1%)
Blood alkaline phosphatase increased	- Any Grade -	3 (4.0%)	2 (1.4%)
	Grade 1-2	3 (4.0%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
	2	2 (2.7%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Lipase increased	- Any Grade -	3 (4.0%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	0	1 (0.7%)
	2	1 (1.3%)	0
	Grade 3-4	2 (2.7%)	1 (0.7%)
	3	2 (2.7%)	0
	4	0	1 (0.7%)
White blood cell count decreased	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	1	0	1 (0.7%)
	2	2 (2.7%)	0
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Blood cholesterol increased	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	3 (2.1%)
	2	0	1 (0.7%)
Amylase increased	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	2 (1.4%)
	2	0	1 (0.7%)
Blood triglycerides increased	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	1 (0.7%)
	2	0	2 (1.4%)
Blood urea increased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
Haemoglobin decreased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Weight decreased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
Blood creatinine increased	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Blood glucose increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Gamma-glutamyltransferase increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Blood albumin decreased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Blood thyroid stimulating hormone increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Glycosylated haemoglobin increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Haematocrit decreased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Low density lipoprotein increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	13 (17.3%)	32 (22.1%)
	Grade 1-2	12 (16.0%)	27 (18.6%)
	1	8 (10.7%)	18 (12.4%)
	2	4 (5.3%)	9 (6.2%)
	Grade 3-4	1 (1.3%)	5 (3.4%)
	3	0	5 (3.4%)
	4	1 (1.3%)	0
Hyperglycaemia	- Any Grade -	7 (9.3%)	16 (11.0%)
	Grade 1-2	7 (9.3%)	13 (9.0%)
	1	6 (8.0%)	6 (4.1%)
	2	1 (1.3%)	7 (4.8%)
	Grade 3-4	0	3 (2.1%)
	3	0	3 (2.1%)
Decreased appetite	- Any Grade -	5 (6.7%)	10 (6.9%)
	Grade 1-2	5 (6.7%)	8 (5.5%)
	1	3 (4.0%)	7 (4.8%)
	2	2 (2.7%)	1 (0.7%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Hypertriglyceridaemia	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	1 (1.3%)	0
	4	1 (1.3%)	0
Hypercholesterolaemia	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	0	2 (1.4%)
	2	1 (1.3%)	0

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hypercreatininaemia	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	0
Hypokalaemia	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
Dehydration	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hypercalcaemia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Hypernatraemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hyperuricaemia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Hypocalcaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hypoglycaemia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Hypomagnesaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hyponatraemia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Type 2 diabetes mellitus	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	14 (18.7%)	25 (17.2%)
	Grade 1-2	10 (13.3%)	21 (14.5%)
	1	2 (2.7%)	7 (4.8%)
	2	8 (10.7%)	14 (9.7%)
	Grade 3-4	4 (5.3%)	3 (2.1%)
	3	4 (5.3%)	3 (2.1%)
	Grade 5	0	1 (0.7%)

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Neutropenia	- Any Grade -	12 (16.0%)	11 (7.6%)
	Grade 1-2	8 (10.7%)	8 (5.5%)
	1	1 (1.3%)	3 (2.1%)
	2	7 (9.3%)	5 (3.4%)
	Grade 3-4	4 (5.3%)	3 (2.1%)
	3	4 (5.3%)	2 (1.4%)
	4	0	1 (0.7%)
Anaemia	- Any Grade -	3 (4.0%)	18 (12.4%)
	Grade 1-2	3 (4.0%)	17 (11.7%)
	1	2 (2.7%)	9 (6.2%)
	2	1 (1.3%)	8 (5.5%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Leukopenia	- Any Grade -	5 (6.7%)	6 (4.1%)
	Grade 1-2	5 (6.7%)	6 (4.1%)
	1	0	2 (1.4%)
	2	5 (6.7%)	4 (2.8%)
Febrile neutropenia	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Lymphadenopathy	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Lymphopenia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Thrombocytopenia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Nervous system disorders			
- Overall -	- Any Grade -	12 (16.0%)	19 (13.1%)
	Grade 1-2	11 (14.7%)	19 (13.1%)
	1	6 (8.0%)	14 (9.7%)
	2	5 (6.7%)	5 (3.4%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Polyneuropathy	- Any Grade -	3 (4.0%)	3 (2.1%)
	Grade 1-2	3 (4.0%)	3 (2.1%)
	1	3 (4.0%)	3 (2.1%)
Dizziness	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	0	2 (1.4%)
	2	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Headache	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	1 (0.7%)
Dysgeusia	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	0	3 (2.1%)
	2	1 (1.3%)	0
Neuropathy peripheral	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	0	3 (2.1%)
	2	1 (1.3%)	0
Paraesthesia	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Peripheral sensory neuropathy	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	1 (0.7%)
	2	0	2 (1.4%)
Anosmia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Cognitive disorder	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Disturbance in attention	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Dysaesthesia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Lethargy	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Memory impairment	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Peripheral motor neuropathy	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Taste disorder	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_RELIPAT_B_SE.out
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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Infections and infestations			
- Overall -	- Any Grade -	11 (14.7%)	16 (11.0%)
	Grade 1-2	11 (14.7%)	16 (11.0%)
	1	1 (1.3%)	3 (2.1%)
	2	10 (13.3%)	13 (9.0%)
Upper respiratory tract infection	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	2	2 (2.7%)	3 (2.1%)
Paronychia	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	1 (0.7%)
	2	0	3 (2.1%)
Cystitis	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	2	2 (2.7%)	1 (0.7%)
Nasopharyngitis	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
Folliculitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Gingivitis	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
Bronchitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Conjunctivitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Erysipelas	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Herpes zoster	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Lower respiratory tract infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Pharyngitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_RELIPAT_B_SE.out
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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Pneumonia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Tooth abscess	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Tracheitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	6 (8.0%)	18 (12.4%)
	Grade 1-2	5 (6.7%)	17 (11.7%)
	1	3 (4.0%)	13 (9.0%)
	2	2 (2.7%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Epistaxis	- Any Grade -	3 (4.0%)	6 (4.1%)
	Grade 1-2	3 (4.0%)	6 (4.1%)
	1	3 (4.0%)	5 (3.4%)
	2	0	1 (0.7%)
Oropharyngeal pain	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	3 (2.1%)
	2	0	1 (0.7%)
Cough	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	2 (1.4%)
	2	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Productive cough	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Nasal septum ulceration	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Oropharyngeal discomfort	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Pulmonary embolism	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Pulmonary hypertension	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Rhinitis allergic	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vasomotor rhinitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Musculoskeletal and connective tissue disorders			
- Overall -	- Any Grade -	5 (6.7%)	13 (9.0%)
	Grade 1-2	4 (5.3%)	12 (8.3%)
	1	2 (2.7%)	6 (4.1%)
	2	2 (2.7%)	6 (4.1%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Arthralgia	- Any Grade -	1 (1.3%)	5 (3.4%)
	Grade 1-2	1 (1.3%)	5 (3.4%)
	1	0	2 (1.4%)
	2	1 (1.3%)	3 (2.1%)
Muscle spasms	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	2 (2.7%)	1 (0.7%)
	2	0	1 (0.7%)
Back pain	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
Pain in extremity	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	1 (0.7%)
	2	0	2 (1.4%)
Muscular weakness	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
Myalgia	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Bone pain	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Flank pain	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Pain in jaw	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Rhabdomyolysis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hepatobiliary disorders			
- Overall -	- Any Grade -	6 (8.0%)	6 (4.1%)
	Grade 1-2	5 (6.7%)	3 (2.1%)
	1	5 (6.7%)	1 (0.7%)
	2	0	2 (1.4%)
	Grade 3-4	1 (1.3%)	3 (2.1%)
	3	1 (1.3%)	3 (2.1%)
Hyperbilirubinaemia	- Any Grade -	4 (5.3%)	4 (2.8%)
	Grade 1-2	4 (5.3%)	4 (2.8%)
	1	3 (4.0%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
Cholecystitis acute	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Hypertransaminasaemia	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Cholestasis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Hepatic cytolysis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Hepatic function abnormal	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Eye disorders			
- Overall -	- Any Grade -	3 (4.0%)	4 (2.8%)
	Grade 1-2	3 (4.0%)	4 (2.8%)
	1	2 (2.7%)	3 (2.1%)
	2	1 (1.3%)	1 (0.7%)
Lacrimation increased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Dry eye	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
Visual acuity reduced	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Cataract	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Eye discharge	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vitreous floaters	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Injury, poisoning and procedural complications			
- Overall -	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	0	2 (1.4%)
	2	2 (2.7%)	0
Poisoning	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	2	2 (2.7%)	0
Accidental overdose	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Incorrect dose administered	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vascular disorders			
- Overall -	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	2 (2.7%)	0
	3	2 (2.7%)	0
Hypertension	- Any Grade -	2 (2.7%)	0
	Grade 3-4	2 (2.7%)	0
	3	2 (2.7%)	0
Embolism	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hot flush	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Cardiac disorders			
- Overall -	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	0
	2	0	2 (1.4%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Extrasystoles	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Supraventricular extrasystoles	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Ventricular arrhythmia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Ear and labyrinth disorders			
- Overall -	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
Vertigo	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
Renal and urinary disorders			
- Overall -	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Hydronephrosis	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Pollakiuria	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Renal failure	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Psychiatric disorders			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
Insomnia	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)

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Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Reproductive system and breast disorders			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
Breast ulceration	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Menstruation irregular	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Ear neoplasm	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
No Coding available			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
No Coding available	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	98 (96.1%)
	Grade 1-2	54 (52.9%)
	1	15 (14.7%)
	2	39 (38.2%)
	Grade 3-4	44 (43.1%)
	3	41 (40.2%)
	4	3 (2.9%)
Gastrointestinal disorders		
- Overall -	- Any Grade -	89 (87.3%)
	Grade 1-2	69 (67.6%)
	1	27 (26.5%)
	2	42 (41.2%)
	Grade 3-4	20 (19.6%)
	3	20 (19.6%)
Diarrhoea	- Any Grade -	85 (83.3%)
	Grade 1-2	68 (66.7%)
	1	28 (27.5%)
	2	40 (39.2%)
	Grade 3-4	17 (16.7%)
	3	17 (16.7%)
Nausea	- Any Grade -	31 (30.4%)
	Grade 1-2	29 (28.4%)
	1	20 (19.6%)
	2	9 (8.8%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Vomiting	- Any Grade -	18 (17.6%)
	Grade 1-2	17 (16.7%)
	1	13 (12.7%)
	2	4 (3.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Abdominal pain	- Any Grade -	7 (6.9%)
	Grade 1-2	6 (5.9%)
	1	4 (3.9%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Constipation	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Dyspepsia	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Abdominal discomfort	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Abdominal pain upper	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Flatulence	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Gastrooesophageal reflux disease	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Stomatitis	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Dental discomfort	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Dry mouth	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Gastrooesophageal sphincter insufficiency	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Intestinal mucosal atrophy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Large intestine perforation	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Mouth ulceration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oesophagitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oral discomfort	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Skin and subcutaneous tissue disorders		
- Overall -	- Any Grade -	38 (37.3%)
	Grade 1-2	34 (33.3%)
	1	20 (19.6%)
	2	14 (13.7%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Rash	- Any Grade -	23 (22.5%)
	Grade 1-2	21 (20.6%)
	1	15 (14.7%)
	2	6 (5.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Pruritus	- Any Grade -	9 (8.8%)
	Grade 1-2	8 (7.8%)
	1	8 (7.8%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alopecia	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	1 (1.0%)
	2	4 (3.9%)
Rash maculo-papular	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Acne	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Dermatitis allergic	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Eczema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Erythema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hand dermatitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nail bed tenderness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nail disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash erythematous	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash papular	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Rash pruritic	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Seborrhoeic dermatitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
General disorders and administration site conditions		
- Overall -	- Any Grade -	36 (35.3%)
	Grade 1-2	35 (34.3%)
	1	20 (19.6%)
	2	15 (14.7%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Fatigue	- Any Grade -	18 (17.6%)
	Grade 1-2	17 (16.7%)
	1	9 (8.8%)
	2	8 (7.8%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Asthenia	- Any Grade -	14 (13.7%)
	Grade 1-2	14 (13.7%)
	1	9 (8.8%)
	2	5 (4.9%)
Mucosal inflammation	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	4 (3.9%)
	2	1 (1.0%)
Oedema peripheral	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Pyrexia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Generalised oedema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oedema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Thirst	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Investigations		
- Overall -	- Any Grade -	31 (30.4%)
	Grade 1-2	20 (19.6%)
	1	10 (9.8%)
	2	10 (9.8%)
	Grade 3-4	11 (10.8%)
	3	10 (9.8%)
	4	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	16 (15.7%)
	Grade 1-2	11 (10.8%)
	1	8 (7.8%)
	2	3 (2.9%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Aspartate aminotransferase increased	- Any Grade -	13 (12.7%)
	Grade 1-2	11 (10.8%)
	1	7 (6.9%)
	2	4 (3.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Blood alkaline phosphatase increased	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Blood cholesterol increased	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neutrophil count decreased	- Any Grade -	4 (3.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Blood lactate dehydrogenase increased	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Lipase increased	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)

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Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Low density lipoprotein increased	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
White blood cell count decreased	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
Blood bilirubin increased	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Blood triglycerides increased	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Amylase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Basophil percentage increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Blood chloride decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Blood glucose increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Eosinophil percentage increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Faecal volume increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Gamma-glutamyltransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Haematocrit decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Immature granulocyte count increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Lymphocyte count decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

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Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Monocyte percentage decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Platelet count decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Red blood cell count decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Weight decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Weight increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
White blood cell count increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Metabolism and nutrition disorders		
- Overall -	- Any Grade -	30 (29.4%)
	Grade 1-2	24 (23.5%)
	1	12 (11.8%)
	2	12 (11.8%)
	Grade 3-4	6 (5.9%)
	3	5 (4.9%)
	4	1 (1.0%)
Hyperglycaemia	- Any Grade -	18 (17.6%)
	Grade 1-2	14 (13.7%)
	1	7 (6.9%)
	2	7 (6.9%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Decreased appetite	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	4 (3.9%)
	2	2 (2.0%)
Hyperkalaemia	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
Hypertriglyceridaemia	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)

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Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hypokalaemia	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dehydration	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypercholesterolaemia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Hypercreatininaemia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Hypoalbuminaemia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Hyponatraemia	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alkalosis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Dyslipidaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypercalcaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypomagnesaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypophosphataemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Type 1 diabetes mellitus	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

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Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Blood and lymphatic system disorders		
- Overall -	- Any Grade -	24 (23.5%)
	Grade 1-2	17 (16.7%)
	1	5 (4.9%)
	2	12 (11.8%)
	Grade 3-4	7 (6.9%)
	3	6 (5.9%)
	4	1 (1.0%)
Neutropenia	- Any Grade -	12 (11.8%)
	Grade 1-2	8 (7.8%)
	2	8 (7.8%)
	Grade 3-4	4 (3.9%)
	3	3 (2.9%)
	4	1 (1.0%)
Anaemia	- Any Grade -	9 (8.8%)
	Grade 1-2	9 (8.8%)
	1	4 (3.9%)
	2	5 (4.9%)
Leukopenia	- Any Grade -	7 (6.9%)
	Grade 1-2	7 (6.9%)
	1	5 (4.9%)
	2	2 (2.0%)
Lymphopenia	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Eosinophilia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Febrile neutropenia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Lymphadenopathy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Thrombocytosis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nervous system disorders		
- Overall -	- Any Grade -	18 (17.6%)
	Grade 1-2	15 (14.7%)
	1	10 (9.8%)
	2	5 (4.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Neuropathy peripheral	- Any Grade -	8 (7.8%)
	Grade 1-2	7 (6.9%)
	1	5 (4.9%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Headache	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
Dizziness	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Dysgeusia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Paraesthesia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Balance disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Cognitive disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hypersomnia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypoaesthesia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Lethargy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Peripheral sensory neuropathy	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Posterior reversible encephalopathy syndrome	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Musculoskeletal and connective tissue disorders		
- Overall -	- Any Grade -	10 (9.8%)
	Grade 1-2	10 (9.8%)
	1	9 (8.8%)
	2	1 (1.0%)
Arthralgia	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Myalgia	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Muscle spasms	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Back pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pain in extremity	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Respiratory, thoracic and mediastinal disorders		
- Overall -	- Any Grade -	8 (7.8%)
	Grade 1-2	8 (7.8%)
	1	7 (6.9%)
	2	1 (1.0%)
Epistaxis	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Pneumonitis	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Dyspnoea	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Lung infiltration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Productive cough	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_RELIPAT_C_SE.out
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Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Infections and infestations		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	5 (4.9%)
	1	3 (2.9%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Gastroenteritis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Gingivitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oral herpes	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Paronychia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Pneumonia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pneumonia viral	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Urinary tract infection	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Eye disorders		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	5 (4.9%)
	2	1 (1.0%)
Vision blurred	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Dry eye	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Eyelid function disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Periorbital oedema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Visual impairment	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hepatobiliary disorders		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hyperbilirubinaemia	- Any Grade -	6 (5.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Injury, poisoning and procedural complications		
- Overall -	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
Accidental overdose	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
Intentional overdose	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Tumour necrosis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Tumour inflammation	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Ear and labyrinth disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)

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Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hypoacusis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Tinnitus	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Vertigo	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Vascular disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Flushing	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypertension	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Endocrine disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hypothyroidism	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Immune system disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hypersensitivity	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Psychiatric disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Insomnia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	81 (93.1%)	152 (91.6%)
	Grade 1-2	55 (63.2%)	94 (56.6%)
	1	17 (19.5%)	24 (14.5%)
	2	38 (43.7%)	70 (42.2%)
	Grade 3-4	25 (28.7%)	58 (34.9%)
	3	24 (27.6%)	50 (30.1%)
	4	1 (1.1%)	8 (4.8%)
	Grade 5	1 (1.1%)	0
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	49 (56.3%)	93 (56.0%)
	Grade 1-2	47 (54.0%)	92 (55.4%)
	1	16 (18.4%)	29 (17.5%)
	2	31 (35.6%)	63 (38.0%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
Alopecia	- Any Grade -	38 (43.7%)	78 (47.0%)
	Grade 1-2	38 (43.7%)	78 (47.0%)
	1	8 (9.2%)	19 (11.4%)
	2	30 (34.5%)	59 (35.5%)
Rash	- Any Grade -	6 (6.9%)	18 (10.8%)
	Grade 1-2	6 (6.9%)	17 (10.2%)
	1	5 (5.7%)	14 (8.4%)
	2	1 (1.1%)	3 (1.8%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Pruritus	- Any Grade -	3 (3.4%)	9 (5.4%)
	Grade 1-2	3 (3.4%)	9 (5.4%)
	1	2 (2.3%)	7 (4.2%)
	2	1 (1.1%)	2 (1.2%)
Nail discolouration	- Any Grade -	4 (4.6%)	6 (3.6%)
	Grade 1-2	4 (4.6%)	6 (3.6%)
	1	4 (4.6%)	6 (3.6%)
Dermatitis acneiform	- Any Grade -	1 (1.1%)	5 (3.0%)
	Grade 1-2	1 (1.1%)	5 (3.0%)
	1	1 (1.1%)	5 (3.0%)
Onychoclasis	- Any Grade -	3 (3.4%)	2 (1.2%)
	Grade 1-2	3 (3.4%)	2 (1.2%)
	1	3 (3.4%)	2 (1.2%)
Onycholysis	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	4 (2.4%)
	1	0	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
Dermatitis	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	2 (2.3%)	1 (0.6%)
	2	0	1 (0.6%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Dermatitis allergic	- Any Grade -	0	4 (2.4%)
	Grade 1-2	0	4 (2.4%)
	1	0	2 (1.2%)
	2	0	2 (1.2%)
Dry skin	- Any Grade -	4 (4.6%)	0
	Grade 1-2	4 (4.6%)	0
	1	4 (4.6%)	0
Nail disorder	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	2 (2.3%)	1 (0.6%)
	2	0	1 (0.6%)
Erythema	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Nail dystrophy	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	0	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
Rash maculo-papular	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	3 (1.8%)
Eczema	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Hyperhidrosis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	0
	2	0	1 (0.6%)
Nail toxicity	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Onychomadesis	- Any Grade -	2 (2.3%)	0
	Grade 1-2	2 (2.3%)	0
	1	2 (2.3%)	0
Skin hyperpigmentation	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Dermatitis contact	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Hand dermatitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Nail ridging	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Onychalgia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Onychomalacia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Pain of skin	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Palmar-plantar erythrodysaesthesia syndrome	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Rash papular	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Gastrointestinal disorders			
- Overall -	- Any Grade -	32 (36.8%)	108 (65.1%)
	Grade 1-2	29 (33.3%)	99 (59.6%)
	1	21 (24.1%)	55 (33.1%)
	2	8 (9.2%)	44 (26.5%)
	Grade 3-4	3 (3.4%)	9 (5.4%)
	3	3 (3.4%)	7 (4.2%)
	4	0	2 (1.2%)
Diarrhoea	- Any Grade -	11 (12.6%)	75 (45.2%)
	Grade 1-2	11 (12.6%)	71 (42.8%)
	1	8 (9.2%)	46 (27.7%)
	2	3 (3.4%)	25 (15.1%)
	Grade 3-4	0	4 (2.4%)
	3	0	4 (2.4%)
Nausea	- Any Grade -	15 (17.2%)	55 (33.1%)
	Grade 1-2	15 (17.2%)	50 (30.1%)
	1	12 (13.8%)	38 (22.9%)
	2	3 (3.4%)	12 (7.2%)
	Grade 3-4	0	5 (3.0%)
	3	0	5 (3.0%)
Vomiting	- Any Grade -	4 (4.6%)	41 (24.7%)
	Grade 1-2	3 (3.4%)	38 (22.9%)
	1	2 (2.3%)	31 (18.7%)
	2	1 (1.1%)	7 (4.2%)
	Grade 3-4	1 (1.1%)	3 (1.8%)
	3	1 (1.1%)	2 (1.2%)
	4	0	1 (0.6%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Stomatitis	- Any Grade -	5 (5.7%)	18 (10.8%)
	Grade 1-2	5 (5.7%)	18 (10.8%)
	1	4 (4.6%)	10 (6.0%)
	2	1 (1.1%)	8 (4.8%)
Dyspepsia	- Any Grade -	3 (3.4%)	12 (7.2%)
	Grade 1-2	3 (3.4%)	12 (7.2%)
	1	3 (3.4%)	9 (5.4%)
	2	0	3 (1.8%)
Constipation	- Any Grade -	4 (4.6%)	10 (6.0%)
	Grade 1-2	4 (4.6%)	10 (6.0%)
	1	4 (4.6%)	9 (5.4%)
	2	0	1 (0.6%)
Abdominal pain upper	- Any Grade -	3 (3.4%)	7 (4.2%)
	Grade 1-2	3 (3.4%)	7 (4.2%)
	1	3 (3.4%)	5 (3.0%)
	2	0	2 (1.2%)
Abdominal pain	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	2 (2.3%)	4 (2.4%)
	1	1 (1.1%)	3 (1.8%)
	2	1 (1.1%)	1 (0.6%)
Abdominal discomfort	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	1	2 (2.3%)	3 (1.8%)
Flatulence	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Abdominal distension	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Cheilitis	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Dry mouth	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Colitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Gastrooesophageal reflux disease	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Haemorrhoids	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Large intestine perforation	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Oesophagitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Periodontal disease	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Proctalgia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Upper gastrointestinal haemorrhage	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Nervous system disorders			
- Overall -	- Any Grade -	52 (59.8%)	87 (52.4%)
	Grade 1-2	47 (54.0%)	72 (43.4%)
	1	35 (40.2%)	44 (26.5%)
	2	12 (13.8%)	28 (16.9%)
	Grade 3-4	5 (5.7%)	15 (9.0%)
	3	5 (5.7%)	15 (9.0%)
Neuropathy peripheral	- Any Grade -	19 (21.8%)	38 (22.9%)
	Grade 1-2	16 (18.4%)	30 (18.1%)
	1	12 (13.8%)	18 (10.8%)
	2	4 (4.6%)	12 (7.2%)
	Grade 3-4	3 (3.4%)	8 (4.8%)
	3	3 (3.4%)	8 (4.8%)
Peripheral sensory neuropathy	- Any Grade -	19 (21.8%)	31 (18.7%)
	Grade 1-2	17 (19.5%)	27 (16.3%)
	1	13 (14.9%)	18 (10.8%)
	2	4 (4.6%)	9 (5.4%)
	Grade 3-4	2 (2.3%)	4 (2.4%)
	3	2 (2.3%)	4 (2.4%)
Dysgeusia	- Any Grade -	6 (6.9%)	8 (4.8%)
	Grade 1-2	6 (6.9%)	8 (4.8%)
	1	5 (5.7%)	8 (4.8%)
	2	1 (1.1%)	0
Polyneuropathy	- Any Grade -	7 (8.0%)	4 (2.4%)
	Grade 1-2	7 (8.0%)	3 (1.8%)
	1	4 (4.6%)	3 (1.8%)
	2	3 (3.4%)	0
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_RELPAC_A_SE.out
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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Headache	- Any Grade -	2 (2.3%)	6 (3.6%)
	Grade 1-2	2 (2.3%)	6 (3.6%)
	1	2 (2.3%)	4 (2.4%)
	2	0	2 (1.2%)
Paraesthesia	- Any Grade -	2 (2.3%)	6 (3.6%)
	Grade 1-2	2 (2.3%)	5 (3.0%)
	1	2 (2.3%)	2 (1.2%)
	2	0	3 (1.8%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Dizziness	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	4 (2.4%)
	1	1 (1.1%)	3 (1.8%)
	2	0	1 (0.6%)
Neurotoxicity	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	0
	2	0	1 (0.6%)
Peripheral motor neuropathy	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Taste disorder	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Ageusia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Altered state of consciousness	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Anosmia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Ataxia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Cranial nerve disorder	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Dysaesthesia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Encephalopathy	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Head discomfort	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Hypersomnia	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Memory impairment	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Seizure	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Toxic neuropathy	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Tremor	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
General disorders and administration site conditions			
- Overall -	- Any Grade -	32 (36.8%)	71 (42.8%)
	Grade 1-2	30 (34.5%)	61 (36.7%)
	1	23 (26.4%)	38 (22.9%)
	2	7 (8.0%)	23 (13.9%)
	Grade 3-4	2 (2.3%)	10 (6.0%)
	3	2 (2.3%)	10 (6.0%)
Fatigue	- Any Grade -	15 (17.2%)	23 (13.9%)
	Grade 1-2	13 (14.9%)	19 (11.4%)
	1	11 (12.6%)	15 (9.0%)
	2	2 (2.3%)	4 (2.4%)
	Grade 3-4	2 (2.3%)	4 (2.4%)
	3	2 (2.3%)	4 (2.4%)
Asthenia	- Any Grade -	8 (9.2%)	29 (17.5%)
	Grade 1-2	8 (9.2%)	23 (13.9%)
	1	5 (5.7%)	14 (8.4%)
	2	3 (3.4%)	9 (5.4%)
	Grade 3-4	0	6 (3.6%)
	3	0	6 (3.6%)
Oedema peripheral	- Any Grade -	3 (3.4%)	11 (6.6%)
	Grade 1-2	3 (3.4%)	11 (6.6%)
	1	2 (2.3%)	6 (3.6%)
	2	1 (1.1%)	5 (3.0%)
Mucosal inflammation	- Any Grade -	2 (2.3%)	7 (4.2%)
	Grade 1-2	2 (2.3%)	7 (4.2%)
	1	2 (2.3%)	5 (3.0%)
	2	0	2 (1.2%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Oedema	- Any Grade -	1 (1.1%)	5 (3.0%)
	Grade 1-2	1 (1.1%)	5 (3.0%)
	1	1 (1.1%)	3 (1.8%)
	2	0	2 (1.2%)
Pyrexia	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	2 (2.3%)	4 (2.4%)
	1	2 (2.3%)	3 (1.8%)
	2	0	1 (0.6%)
Pain	- Any Grade -	0	4 (2.4%)
	Grade 1-2	0	4 (2.4%)
	1	0	4 (2.4%)
Influenza like illness	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Malaise	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	1 (1.1%)	2 (1.2%)
Chest pain	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Chest discomfort	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Chills	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Face oedema	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Generalised oedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Hyperthermia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Ill-defined disorder	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Infusion site extravasation	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Mucosal dryness	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Non-cardiac chest pain	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Peripheral swelling	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	38 (43.7%)	63 (38.0%)
	Grade 1-2	32 (36.8%)	46 (27.7%)
	1	9 (10.3%)	21 (12.7%)
	2	23 (26.4%)	25 (15.1%)
	Grade 3-4	6 (6.9%)	17 (10.2%)
	3	5 (5.7%)	14 (8.4%)
	4	1 (1.1%)	3 (1.8%)
Anaemia	- Any Grade -	19 (21.8%)	37 (22.3%)
	Grade 1-2	16 (18.4%)	35 (21.1%)
	1	7 (8.0%)	19 (11.4%)
	2	9 (10.3%)	16 (9.6%)
	Grade 3-4	3 (3.4%)	2 (1.2%)
	3	2 (2.3%)	2 (1.2%)
	4	1 (1.1%)	0
Neutropenia	- Any Grade -	20 (23.0%)	27 (16.3%)
	Grade 1-2	17 (19.5%)	15 (9.0%)
	1	4 (4.6%)	3 (1.8%)
	2	13 (14.9%)	12 (7.2%)
	Grade 3-4	3 (3.4%)	12 (7.2%)
	3	2 (2.3%)	10 (6.0%)
	4	1 (1.1%)	2 (1.2%)
Leukopenia	- Any Grade -	4 (4.6%)	7 (4.2%)
	Grade 1-2	3 (3.4%)	7 (4.2%)
	1	2 (2.3%)	3 (1.8%)
	2	1 (1.1%)	4 (2.4%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Lymphopenia	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Thrombocytopenia	- Any Grade -	4 (4.6%)	1 (0.6%)
	Grade 1-2	3 (3.4%)	1 (0.6%)
	1	1 (1.1%)	0
	2	2 (2.3%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Febrile neutropenia	- Any Grade -	0	4 (2.4%)
	Grade 3-4	0	4 (2.4%)
	3	0	3 (1.8%)
	4	0	1 (0.6%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Anaemia macrocytic	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Eosinophilia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Leukocytosis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Thrombocytosis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Investigations			
- Overall -	- Any Grade -	21 (24.1%)	51 (30.7%)
	Grade 1-2	13 (14.9%)	35 (21.1%)
	1	7 (8.0%)	17 (10.2%)
	2	6 (6.9%)	18 (10.8%)
	Grade 3-4	8 (9.2%)	16 (9.6%)
	3	8 (9.2%)	14 (8.4%)
	4	0	2 (1.2%)
Neutrophil count decreased	- Any Grade -	10 (11.5%)	21 (12.7%)
	Grade 1-2	5 (5.7%)	14 (8.4%)
	1	1 (1.1%)	2 (1.2%)
	2	4 (4.6%)	12 (7.2%)
	Grade 3-4	5 (5.7%)	7 (4.2%)
	3	5 (5.7%)	6 (3.6%)
	4	0	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	7 (8.0%)	16 (9.6%)
	Grade 1-2	5 (5.7%)	11 (6.6%)
	1	5 (5.7%)	7 (4.2%)
	2	0	4 (2.4%)
	Grade 3-4	2 (2.3%)	5 (3.0%)
	3	2 (2.3%)	5 (3.0%)
White blood cell count decreased	- Any Grade -	7 (8.0%)	11 (6.6%)
	Grade 1-2	5 (5.7%)	9 (5.4%)
	1	2 (2.3%)	3 (1.8%)
	2	3 (3.4%)	6 (3.6%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	2 (1.2%)
Aspartate aminotransferase increased	- Any Grade -	5 (5.7%)	11 (6.6%)
	Grade 1-2	3 (3.4%)	8 (4.8%)
	1	2 (2.3%)	5 (3.0%)
	2	1 (1.1%)	3 (1.8%)
	Grade 3-4	2 (2.3%)	3 (1.8%)
	3	2 (2.3%)	3 (1.8%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Weight decreased	- Any Grade -	2 (2.3%)	6 (3.6%)
	Grade 1-2	2 (2.3%)	6 (3.6%)
	1	1 (1.1%)	4 (2.4%)
	2	1 (1.1%)	2 (1.2%)
Blood alkaline phosphatase increased	- Any Grade -	0	7 (4.2%)
	Grade 1-2	0	7 (4.2%)
	1	0	6 (3.6%)
	2	0	1 (0.6%)
Blood lactate dehydrogenase increased	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	2 (2.3%)	4 (2.4%)
	1	2 (2.3%)	3 (1.8%)
	2	0	1 (0.6%)
Blood urea increased	- Any Grade -	3 (3.4%)	3 (1.8%)
	Grade 1-2	3 (3.4%)	3 (1.8%)
	1	3 (3.4%)	3 (1.8%)
Lymphocyte count decreased	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	0
	4	0	1 (0.6%)
Blood creatinine increased	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Weight increased	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
Blood bilirubin increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Body temperature increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Eastern Cooperative Oncology Group performance status worsened	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Gamma-glutamyltransferase increased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Glycosylated haemoglobin abnormal	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Haematocrit decreased	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Lipase increased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Low density lipoprotein increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	12 (13.8%)	33 (19.9%)
	Grade 1-2	10 (11.5%)	31 (18.7%)
	1	6 (6.9%)	22 (13.3%)
	2	4 (4.6%)	9 (5.4%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	1 (1.1%)	2 (1.2%)
	Grade 5	1 (1.1%)	0
Decreased appetite	- Any Grade -	7 (8.0%)	23 (13.9%)
	Grade 1-2	7 (8.0%)	22 (13.3%)
	1	5 (5.7%)	14 (8.4%)
	2	2 (2.3%)	8 (4.8%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hyperglycaemia	- Any Grade -	3 (3.4%)	6 (3.6%)
	Grade 1-2	3 (3.4%)	5 (3.0%)
	1	1 (1.1%)	5 (3.0%)
	2	2 (2.3%)	0
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hypomagnesaemia	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	1 (1.1%)	3 (1.8%)
Hypophosphataemia	- Any Grade -	3 (3.4%)	1 (0.6%)
	Grade 1-2	3 (3.4%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
	2	2 (2.3%)	0
Hyperkalaemia	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Hypoalbuminaemia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Hypokalaemia	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Electrolyte imbalance	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hypercreatininaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Hyponatraemia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Increased appetite	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Tumour lysis syndrome	- Any Grade -	1 (1.1%)	0
	Grade 5	1 (1.1%)	0
Musculoskeletal and connective tissue disorders			
- Overall -	- Any Grade -	12 (13.8%)	30 (18.1%)
	Grade 1-2	12 (13.8%)	29 (17.5%)
	1	9 (10.3%)	22 (13.3%)
	2	3 (3.4%)	7 (4.2%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Myalgia	- Any Grade -	3 (3.4%)	14 (8.4%)
	Grade 1-2	3 (3.4%)	14 (8.4%)
	1	3 (3.4%)	13 (7.8%)
	2	0	1 (0.6%)
Arthralgia	- Any Grade -	5 (5.7%)	9 (5.4%)
	Grade 1-2	5 (5.7%)	9 (5.4%)
	1	5 (5.7%)	5 (3.0%)
	2	0	4 (2.4%)
Pain in extremity	- Any Grade -	1 (1.1%)	7 (4.2%)
	Grade 1-2	1 (1.1%)	7 (4.2%)
	1	0	4 (2.4%)
	2	1 (1.1%)	3 (1.8%)
Back pain	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	1	2 (2.3%)	1 (0.6%)
	2	0	2 (1.2%)
Bone pain	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Muscle spasms	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	3 (1.8%)
Musculoskeletal pain	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	0	1 (0.6%)
	2	1 (1.1%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Myosclerosis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	12 (13.8%)	23 (13.9%)
	Grade 1-2	9 (10.3%)	22 (13.3%)
	1	7 (8.0%)	18 (10.8%)
	2	2 (2.3%)	4 (2.4%)
	Grade 3-4	3 (3.4%)	1 (0.6%)
	3	3 (3.4%)	1 (0.6%)
Epistaxis	- Any Grade -	2 (2.3%)	10 (6.0%)
	Grade 1-2	2 (2.3%)	10 (6.0%)
	1	2 (2.3%)	9 (5.4%)
	2	0	1 (0.6%)
Oropharyngeal pain	- Any Grade -	0	7 (4.2%)
	Grade 1-2	0	7 (4.2%)
	1	0	7 (4.2%)
Cough	- Any Grade -	3 (3.4%)	2 (1.2%)
	Grade 1-2	3 (3.4%)	2 (1.2%)
	1	2 (2.3%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
Dyspnoea	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	0	4 (2.4%)
	1	0	3 (1.8%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Dysphonia	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	1 (1.1%)	2 (1.2%)
Productive cough	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	3 (1.8%)
Rhinitis allergic	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 1-2	2 (2.3%)	1 (0.6%)
	1	2 (2.3%)	1 (0.6%)
Nasal congestion	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Rhinorrhoea	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Hypoxia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Nasal dryness	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Nasal inflammation	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Nasal mucosa atrophy	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Pleural effusion	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Pulmonary embolism	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Pulmonary hypertension	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Rhinalgia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Tachypnoea	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Throat tightness	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Infections and infestations			
- Overall -	- Any Grade -	10 (11.5%)	19 (11.4%)
	Grade 1-2	8 (9.2%)	18 (10.8%)
	1	1 (1.1%)	8 (4.8%)
	2	7 (8.0%)	10 (6.0%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
Cystitis	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	0	2 (1.2%)
	2	2 (2.3%)	0
Fungal skin infection	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	0	2 (1.2%)
	2	1 (1.1%)	0
Nail infection	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Oral candidiasis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	0	1 (0.6%)
	2	1 (1.1%)	0
Paronychia	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Pharyngitis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	0	1 (0.6%)
	2	1 (1.1%)	0
Pneumonia	- Any Grade -	2 (2.3%)	0
	Grade 3-4	2 (2.3%)	0
	3	2 (2.3%)	0
Rash pustular	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Upper respiratory tract infection	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Conjunctivitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Erythrasma	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Folliculitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Fungal infection	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Fungal oesophagitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Herpes zoster	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Influenza	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Mucosal infection	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Nasopharyngitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Oral herpes	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Periodontitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Rhinitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Urinary tract infection	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Vulvitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Eye disorders			
- Overall -	- Any Grade -	6 (6.9%)	12 (7.2%)
	Grade 1-2	4 (4.6%)	12 (7.2%)
	1	4 (4.6%)	8 (4.8%)
	2	0	4 (2.4%)
	Grade 3-4	2 (2.3%)	0
	3	2 (2.3%)	0
Lacrimation increased	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Ocular hyperaemia	- Any Grade -	2 (2.3%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Vision blurred	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Visual acuity reduced	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Visual impairment	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	0
	2	0	1 (0.6%)
Blepharitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Conjunctival irritation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Cystoid macular oedema	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Eye pain	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Eye pruritus	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Periorbital swelling	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Retinal vascular disorder	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Strabismus	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Vascular disorders			
- Overall -	- Any Grade -	2 (2.3%)	14 (8.4%)
	Grade 1-2	2 (2.3%)	12 (7.2%)
	1	1 (1.1%)	6 (3.6%)
	2	1 (1.1%)	6 (3.6%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Flushing	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	0	1 (0.6%)
	2	1 (1.1%)	2 (1.2%)
Hypertension	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hypotension	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hot flush	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hyperaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Lymphoedema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Phlebitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Thrombophlebitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Venous thrombosis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Venous thrombosis limb	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Immune system disorders			
- Overall -	- Any Grade -	3 (3.4%)	4 (2.4%)
	Grade 1-2	2 (2.3%)	4 (2.4%)
	1	2 (2.3%)	2 (1.2%)
	2	0	2 (1.2%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Hypersensitivity	- Any Grade -	3 (3.4%)	4 (2.4%)
	Grade 1-2	2 (2.3%)	4 (2.4%)
	1	2 (2.3%)	2 (1.2%)
	2	0	2 (1.2%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Anaphylactic shock	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Ear and labyrinth disorders			
- Overall -	- Any Grade -	0	6 (3.6%)
	Grade 1-2	0	6 (3.6%)
	1	0	5 (3.0%)
	2	0	1 (0.6%)
Vertigo	- Any Grade -	0	5 (3.0%)
	Grade 1-2	0	5 (3.0%)
	1	0	4 (2.4%)
	2	0	1 (0.6%)
Ear pain	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Psychiatric disorders			
- Overall -	- Any Grade -	1 (1.1%)	5 (3.0%)
	Grade 1-2	1 (1.1%)	5 (3.0%)
	1	0	1 (0.6%)
	2	1 (1.1%)	4 (2.4%)
Insomnia	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
Anxiety	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Depression	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Dyssomnia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Injury, poisoning and procedural complications			
- Overall -	- Any Grade -	3 (3.4%)	1 (0.6%)
	Grade 1-2	3 (3.4%)	1 (0.6%)
	1	2 (2.3%)	0
	2	1 (1.1%)	1 (0.6%)
Infusion related reaction	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	0
	2	0	1 (0.6%)
Recall phenomenon	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Toxicity to various agents	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Renal and urinary disorders			
- Overall -	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	2 (2.3%)	1 (0.6%)
	2	0	1 (0.6%)
Dysuria	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Haemoglobinuria	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Proteinuria	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Renal failure	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hepatobiliary disorders			
- Overall -	- Any Grade -	3 (3.4%)	0
	Grade 1-2	3 (3.4%)	0
	1	1 (1.1%)	0
	2	2 (2.3%)	0
Hyperbilirubinaemia	- Any Grade -	3 (3.4%)	0
	Grade 1-2	3 (3.4%)	0
	1	1 (1.1%)	0
	2	2 (2.3%)	0
Reproductive system and breast disorders			
- Overall -	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Amenorrhoea	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Breast pain	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Vulvovaginal burning sensation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Cardiac disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Sinus tachycardia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Tumour necrosis	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
No Coding available			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
No Coding available	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/ HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	70 (93.3%)	138 (95.2%)
	Grade 1-2	43 (57.3%)	82 (56.6%)
	1	7 (9.3%)	14 (9.7%)
	2	36 (48.0%)	68 (46.9%)
	Grade 3-4	26 (34.7%)	55 (37.9%)
	3	24 (32.0%)	49 (33.8%)
	4	2 (2.7%)	6 (4.1%)
	Grade 5	1 (1.3%)	1 (0.7%)
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	51 (68.0%)	98 (67.6%)
	Grade 1-2	50 (66.7%)	96 (66.2%)
	1	14 (18.7%)	32 (22.1%)
	2	36 (48.0%)	64 (44.1%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
Alopecia	- Any Grade -	43 (57.3%)	75 (51.7%)
	Grade 1-2	43 (57.3%)	75 (51.7%)
	1	9 (12.0%)	20 (13.8%)
	2	34 (45.3%)	55 (37.9%)
Rash	- Any Grade -	3 (4.0%)	21 (14.5%)
	Grade 1-2	3 (4.0%)	20 (13.8%)
	1	3 (4.0%)	17 (11.7%)
	2	0	3 (2.1%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Nail discolouration	- Any Grade -	8 (10.7%)	9 (6.2%)
	Grade 1-2	8 (10.7%)	9 (6.2%)
	1	8 (10.7%)	8 (5.5%)
	2	0	1 (0.7%)
Pruritus	- Any Grade -	2 (2.7%)	9 (6.2%)
	Grade 1-2	2 (2.7%)	9 (6.2%)
	1	2 (2.7%)	7 (4.8%)
	2	0	2 (1.4%)
Onycholysis	- Any Grade -	1 (1.3%)	5 (3.4%)
	Grade 1-2	1 (1.3%)	5 (3.4%)
	1	1 (1.3%)	5 (3.4%)
Dry skin	- Any Grade -	4 (5.3%)	1 (0.7%)
	Grade 1-2	4 (5.3%)	1 (0.7%)
	1	4 (5.3%)	1 (0.7%)
Erythema	- Any Grade -	3 (4.0%)	2 (1.4%)
	Grade 1-2	3 (4.0%)	2 (1.4%)
	1	2 (2.7%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Nail disorder	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	2 (1.4%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Nail dystrophy	- Any Grade -	3 (4.0%)	1 (0.7%)
	Grade 1-2	3 (4.0%)	1 (0.7%)
	1	0	1 (0.7%)
	2	3 (4.0%)	0
Onychomadesis	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	3 (2.1%)
	2	0	1 (0.7%)
Rash maculo-papular	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	3 (2.1%)
	1	0	2 (1.4%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dermatitis acneiform	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	1	2 (2.7%)	1 (0.7%)
Dermatitis allergic	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Nail ridging	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
Onychoclasis	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Palmar-plantar erythrodysaesthesia syndrome	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Skin hyperpigmentation	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Urticaria	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Butterfly rash	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Dermal cyst	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Dermatitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Dermatitis bullous	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Drug eruption	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Eczema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Eczema asteatotic	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hyperhidrosis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Nail bed inflammation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nail toxicity	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Onychalgia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Pain of skin	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Periarticular thenar erythema with onycholysis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Photosensitivity reaction	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Polymorphic light eruption	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Skin discolouration	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Skin exfoliation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Skin reaction	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/ HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Stasis dermatitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nervous system disorders			
- Overall -	- Any Grade -	49 (65.3%)	98 (67.6%)
	Grade 1-2	43 (57.3%)	83 (57.2%)
	1	21 (28.0%)	44 (30.3%)
	2	22 (29.3%)	39 (26.9%)
	Grade 3-4	6 (8.0%)	15 (10.3%)
	3	6 (8.0%)	15 (10.3%)
Neuropathy peripheral	- Any Grade -	10 (13.3%)	46 (31.7%)
	Grade 1-2	8 (10.7%)	36 (24.8%)
	1	2 (2.7%)	19 (13.1%)
	2	6 (8.0%)	17 (11.7%)
	Grade 3-4	2 (2.7%)	10 (6.9%)
	3	2 (2.7%)	10 (6.9%)
Peripheral sensory neuropathy	- Any Grade -	23 (30.7%)	22 (15.2%)
	Grade 1-2	19 (25.3%)	18 (12.4%)
	1	10 (13.3%)	7 (4.8%)
	2	9 (12.0%)	11 (7.6%)
	Grade 3-4	4 (5.3%)	4 (2.8%)
	3	4 (5.3%)	4 (2.8%)
Polyneuropathy	- Any Grade -	6 (8.0%)	12 (8.3%)
	Grade 1-2	6 (8.0%)	11 (7.6%)
	1	5 (6.7%)	8 (5.5%)
	2	1 (1.3%)	3 (2.1%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Paraesthesia	- Any Grade -	6 (8.0%)	10 (6.9%)
	Grade 1-2	6 (8.0%)	10 (6.9%)
	1	5 (6.7%)	8 (5.5%)
	2	1 (1.3%)	2 (1.4%)
Dysgeusia	- Any Grade -	4 (5.3%)	9 (6.2%)
	Grade 1-2	4 (5.3%)	9 (6.2%)
	1	3 (4.0%)	8 (5.5%)
	2	1 (1.3%)	1 (0.7%)
Headache	- Any Grade -	4 (5.3%)	6 (4.1%)
	Grade 1-2	4 (5.3%)	6 (4.1%)
	1	2 (2.7%)	4 (2.8%)
	2	2 (2.7%)	2 (1.4%)
Dizziness	- Any Grade -	2 (2.7%)	5 (3.4%)
	Grade 1-2	2 (2.7%)	5 (3.4%)
	1	1 (1.3%)	3 (2.1%)
	2	1 (1.3%)	2 (1.4%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/ HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Neurotoxicity	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	1 (1.3%)	0
	2	1 (1.3%)	3 (2.1%)
Peripheral motor neuropathy	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	2 (1.4%)
	2	0	2 (1.4%)
Hypoaesthesia	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
Disturbance in attention	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
Taste disorder	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Anosmia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Cognitive disorder	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Dysaesthesia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Lethargy	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Memory impairment	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Neuritis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Radicular pain	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Somnolence	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/ HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Gastrointestinal disorders			
- Overall -	- Any Grade -	33 (44.0%)	88 (60.7%)
	Grade 1-2	33 (44.0%)	78 (53.8%)
	1	25 (33.3%)	45 (31.0%)
	2	8 (10.7%)	33 (22.8%)
	Grade 3-4	0	10 (6.9%)
	3	0	9 (6.2%)
	4	0	1 (0.7%)
Diarrhoea	- Any Grade -	13 (17.3%)	51 (35.2%)
	Grade 1-2	13 (17.3%)	44 (30.3%)
	1	11 (14.7%)	26 (17.9%)
	2	2 (2.7%)	18 (12.4%)
	Grade 3-4	0	7 (4.8%)
	3	0	7 (4.8%)
Nausea	- Any Grade -	16 (21.3%)	39 (26.9%)
	Grade 1-2	16 (21.3%)	38 (26.2%)
	1	13 (17.3%)	27 (18.6%)
	2	3 (4.0%)	11 (7.6%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Vomiting	- Any Grade -	4 (5.3%)	25 (17.2%)
	Grade 1-2	4 (5.3%)	23 (15.9%)
	1	4 (5.3%)	18 (12.4%)
	2	0	5 (3.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Stomatitis	- Any Grade -	6 (8.0%)	14 (9.7%)
	Grade 1-2	6 (8.0%)	14 (9.7%)
	1	5 (6.7%)	12 (8.3%)
	2	1 (1.3%)	2 (1.4%)
Constipation	- Any Grade -	6 (8.0%)	5 (3.4%)
	Grade 1-2	6 (8.0%)	5 (3.4%)
	1	5 (6.7%)	4 (2.8%)
	2	1 (1.3%)	1 (0.7%)
Dyspepsia	- Any Grade -	2 (2.7%)	5 (3.4%)
	Grade 1-2	2 (2.7%)	5 (3.4%)
	1	2 (2.7%)	3 (2.1%)
	2	0	2 (1.4%)
Abdominal pain	- Any Grade -	1 (1.3%)	5 (3.4%)
	Grade 1-2	1 (1.3%)	5 (3.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	4 (2.8%)
Abdominal pain upper	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	2 (2.7%)	3 (2.1%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Abdominal discomfort	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Flatulence	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	0
Aphthous ulcer	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Enterocolitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Gastrooesophageal reflux disease	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	2	2 (2.7%)	0
Mouth ulceration	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
Oral pain	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Abdominal distension	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Abdominal pain lower	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Angular cheilitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Eructation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Gastritis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Haematochezia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Haemorrhoids	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/ HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hypoaesthesia oral	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Intestinal obstruction	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	4	0	1 (0.7%)
Lip dry	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Odynophagia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Paraesthesia oral	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Tongue exfoliation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Tongue ulceration	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
General disorders and administration site conditions			
- Overall -	- Any Grade -	41 (54.7%)	64 (44.1%)
	Grade 1-2	39 (52.0%)	61 (42.1%)
	1	21 (28.0%)	41 (28.3%)
	2	18 (24.0%)	20 (13.8%)
	Grade 3-4	2 (2.7%)	3 (2.1%)
	3	2 (2.7%)	3 (2.1%)
Fatigue	- Any Grade -	16 (21.3%)	21 (14.5%)
	Grade 1-2	14 (18.7%)	21 (14.5%)
	1	8 (10.7%)	14 (9.7%)
	2	6 (8.0%)	7 (4.8%)
	Grade 3-4	2 (2.7%)	0
	3	2 (2.7%)	0
Asthenia	- Any Grade -	11 (14.7%)	21 (14.5%)
	Grade 1-2	11 (14.7%)	19 (13.1%)
	1	7 (9.3%)	12 (8.3%)
	2	4 (5.3%)	7 (4.8%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Oedema peripheral	- Any Grade -	11 (14.7%)	13 (9.0%)
	Grade 1-2	11 (14.7%)	13 (9.0%)
	1	4 (5.3%)	9 (6.2%)
	2	7 (9.3%)	4 (2.8%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Oedema	- Any Grade -	4 (5.3%)	8 (5.5%)
	Grade 1-2	4 (5.3%)	8 (5.5%)
	1	3 (4.0%)	8 (5.5%)
	2	1 (1.3%)	0
Pyrexia	- Any Grade -	1 (1.3%)	10 (6.9%)
	Grade 1-2	1 (1.3%)	10 (6.9%)
	1	1 (1.3%)	8 (5.5%)
	2	0	2 (1.4%)
Mucosal inflammation	- Any Grade -	2 (2.7%)	6 (4.1%)
	Grade 1-2	2 (2.7%)	6 (4.1%)
	1	2 (2.7%)	5 (3.4%)
	2	0	1 (0.7%)
Malaise	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	1 (0.7%)
Chest discomfort	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
Chest pain	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	1	2 (2.7%)	0
	2	0	1 (0.7%)
Chills	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Pain	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
Peripheral swelling	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Extravasation	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Feeling drunk	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Gait disturbance	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Hypothermia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Infusion site extravasation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Localised oedema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Thirst	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	23 (30.7%)	64 (44.1%)
	Grade 1-2	15 (20.0%)	50 (34.5%)
	1	4 (5.3%)	18 (12.4%)
	2	11 (14.7%)	32 (22.1%)
	Grade 3-4	8 (10.7%)	13 (9.0%)
	3	8 (10.7%)	12 (8.3%)
	4	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Neutropenia	- Any Grade -	17 (22.7%)	36 (24.8%)
	Grade 1-2	10 (13.3%)	24 (16.6%)
	1	1 (1.3%)	7 (4.8%)
	2	9 (12.0%)	17 (11.7%)
	Grade 3-4	7 (9.3%)	12 (8.3%)
	3	7 (9.3%)	10 (6.9%)
	4	0	2 (1.4%)
Anaemia	- Any Grade -	11 (14.7%)	40 (27.6%)
	Grade 1-2	11 (14.7%)	39 (26.9%)
	1	6 (8.0%)	17 (11.7%)
	2	5 (6.7%)	22 (15.2%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Leukopenia	- Any Grade -	6 (8.0%)	8 (5.5%)
	Grade 1-2	5 (6.7%)	7 (4.8%)
	1	0	3 (2.1%)
	2	5 (6.7%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Febrile neutropenia	- Any Grade -	0	3 (2.1%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
	Grade 5	0	1 (0.7%)
Thrombocytopenia	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Lymphopenia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/ HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Investigations			
- Overall -	- Any Grade -	35 (46.7%)	43 (29.7%)
	Grade 1-2	23 (30.7%)	25 (17.2%)
	1	7 (9.3%)	9 (6.2%)
	2	16 (21.3%)	16 (11.0%)
	Grade 3-4	12 (16.0%)	18 (12.4%)
	3	10 (13.3%)	14 (9.7%)
	4	2 (2.7%)	4 (2.8%)
Neutrophil count decreased	- Any Grade -	18 (24.0%)	23 (15.9%)
	Grade 1-2	12 (16.0%)	11 (7.6%)
	1	2 (2.7%)	1 (0.7%)
	2	10 (13.3%)	10 (6.9%)
	Grade 3-4	6 (8.0%)	12 (8.3%)
	3	4 (5.3%)	9 (6.2%)
	4	2 (2.7%)	3 (2.1%)
Alanine aminotransferase increased	- Any Grade -	10 (13.3%)	13 (9.0%)
	Grade 1-2	7 (9.3%)	10 (6.9%)
	1	3 (4.0%)	8 (5.5%)
	2	4 (5.3%)	2 (1.4%)
	Grade 3-4	3 (4.0%)	3 (2.1%)
	3	3 (4.0%)	3 (2.1%)
Aspartate aminotransferase increased	- Any Grade -	8 (10.7%)	10 (6.9%)
	Grade 1-2	7 (9.3%)	8 (5.5%)
	1	6 (8.0%)	7 (4.8%)
	2	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
White blood cell count decreased	- Any Grade -	5 (6.7%)	10 (6.9%)
	Grade 1-2	4 (5.3%)	5 (3.4%)
	1	0	1 (0.7%)
	2	4 (5.3%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	5 (3.4%)
	3	1 (1.3%)	5 (3.4%)
Blood alkaline phosphatase increased	- Any Grade -	6 (8.0%)	3 (2.1%)
	Grade 1-2	6 (8.0%)	3 (2.1%)
	1	1 (1.3%)	3 (2.1%)
	2	5 (6.7%)	0
Blood lactate dehydrogenase increased	- Any Grade -	6 (8.0%)	3 (2.1%)
	Grade 1-2	6 (8.0%)	3 (2.1%)
	1	6 (8.0%)	3 (2.1%)
Lipase increased	- Any Grade -	3 (4.0%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	0	1 (0.7%)
	2	1 (1.3%)	0
	Grade 3-4	2 (2.7%)	1 (0.7%)
	3	2 (2.7%)	0
	4	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Amylase increased	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	2 (1.4%)
	2	0	1 (0.7%)
Blood urea increased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
Haemoglobin decreased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Weight decreased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
Blood cholesterol increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Blood creatinine increased	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Blood triglycerides increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Gamma-glutamyltransferase increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Blood albumin decreased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Blood thyroid stimulating hormone increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Glycosylated haemoglobin increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Haematocrit decreased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Lymphocyte count decreased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Platelet count decreased	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/ HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Weight increased	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Musculoskeletal and connective tissue disorders			
- Overall -	- Any Grade -	19 (25.3%)	33 (22.8%)
	Grade 1-2	18 (24.0%)	33 (22.8%)
	1	12 (16.0%)	21 (14.5%)
	2	6 (8.0%)	12 (8.3%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Arthralgia	- Any Grade -	6 (8.0%)	12 (8.3%)
	Grade 1-2	6 (8.0%)	12 (8.3%)
	1	2 (2.7%)	6 (4.1%)
	2	4 (5.3%)	6 (4.1%)
Myalgia	- Any Grade -	6 (8.0%)	9 (6.2%)
	Grade 1-2	6 (8.0%)	9 (6.2%)
	1	5 (6.7%)	7 (4.8%)
	2	1 (1.3%)	2 (1.4%)
Pain in extremity	- Any Grade -	2 (2.7%)	7 (4.8%)
	Grade 1-2	2 (2.7%)	7 (4.8%)
	1	2 (2.7%)	5 (3.4%)
	2	0	2 (1.4%)
Back pain	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	1 (1.3%)	4 (2.8%)
Bone pain	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	1 (1.3%)	1 (0.7%)
	2	0	3 (2.1%)
Muscle spasms	- Any Grade -	3 (4.0%)	2 (1.4%)
	Grade 1-2	3 (4.0%)	2 (1.4%)
	1	3 (4.0%)	1 (0.7%)
	2	0	1 (0.7%)
Muscular weakness	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	1	2 (2.7%)	1 (0.7%)
Arthritis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Flank pain	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Musculoskeletal chest pain	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/ HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Pain in jaw	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Scleroderma	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	13 (17.3%)	26 (17.9%)
	Grade 1-2	13 (17.3%)	23 (15.9%)
	1	9 (12.0%)	16 (11.0%)
	2	4 (5.3%)	7 (4.8%)
	Grade 3-4	0	3 (2.1%)
	3	0	3 (2.1%)
Decreased appetite	- Any Grade -	6 (8.0%)	15 (10.3%)
	Grade 1-2	6 (8.0%)	13 (9.0%)
	1	4 (5.3%)	11 (7.6%)
	2	2 (2.7%)	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Hyperglycaemia	- Any Grade -	5 (6.7%)	6 (4.1%)
	Grade 1-2	5 (6.7%)	5 (3.4%)
	1	4 (5.3%)	2 (1.4%)
	2	1 (1.3%)	3 (2.1%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hypercreatininaemia	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	0
Hypercholesterolaemia	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	0	1 (0.7%)
	2	1 (1.3%)	0
Calcium deficiency	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Dehydration	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Fluid retention	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hypercalcaemia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hypernatraemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hyperuricaemia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Hypocalcaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hypokalaemia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Hypomagnesaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hypophosphataemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Infections and infestations			
- Overall -	- Any Grade -	16 (21.3%)	22 (15.2%)
	Grade 1-2	15 (20.0%)	22 (15.2%)
	1	4 (5.3%)	7 (4.8%)
	2	11 (14.7%)	15 (10.3%)
	Grade 5	1 (1.3%)	0
Paronychia	- Any Grade -	1 (1.3%)	6 (4.1%)
	Grade 1-2	1 (1.3%)	6 (4.1%)
	1	0	3 (2.1%)
	2	1 (1.3%)	3 (2.1%)
Cystitis	- Any Grade -	3 (4.0%)	3 (2.1%)
	Grade 1-2	3 (4.0%)	3 (2.1%)
	2	3 (4.0%)	3 (2.1%)
Upper respiratory tract infection	- Any Grade -	2 (2.7%)	4 (2.8%)
	Grade 1-2	2 (2.7%)	4 (2.8%)
	2	2 (2.7%)	4 (2.8%)
Nasopharyngitis	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
Conjunctivitis	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	0	1 (0.7%)
	2	1 (1.3%)	0
Gingivitis	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/ HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Herpes zoster	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Pharyngitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
Rhinitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Sinusitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Tooth abscess	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	2	2 (2.7%)	0
Urinary tract infection	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
Bronchitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Cellulitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Erysipelas	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Laryngitis fungal	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Lower respiratory tract infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nail infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Nasal vestibulitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Oral herpes	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/ HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Oral infection	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Sepsis	- Any Grade -	1 (1.3%)	0
	Grade 5	1 (1.3%)	0
Tracheitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Vaginal infection	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	10 (13.3%)	22 (15.2%)
	Grade 1-2	9 (12.0%)	22 (15.2%)
	1	6 (8.0%)	14 (9.7%)
	2	3 (4.0%)	8 (5.5%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Epistaxis	- Any Grade -	3 (4.0%)	9 (6.2%)
	Grade 1-2	3 (4.0%)	9 (6.2%)
	1	3 (4.0%)	8 (5.5%)
	2	0	1 (0.7%)
Cough	- Any Grade -	1 (1.3%)	5 (3.4%)
	Grade 1-2	1 (1.3%)	5 (3.4%)
	1	1 (1.3%)	3 (2.1%)
	2	0	2 (1.4%)
Dyspnoea	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	2 (1.4%)
Oropharyngeal pain	- Any Grade -	0	5 (3.4%)
	Grade 1-2	0	5 (3.4%)
	1	0	3 (2.1%)
	2	0	2 (1.4%)
Pneumonitis	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	3 (2.1%)
	1	0	2 (1.4%)
	2	0	1 (0.7%)
Productive cough	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Diaphragmatic disorder	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Dysphonia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Nasal congestion	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nasal dryness	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Nasal septum ulceration	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Oropharyngeal discomfort	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Pulmonary embolism	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Rhinitis allergic	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vasomotor rhinitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Vascular disorders			
- Overall -	- Any Grade -	8 (10.7%)	10 (6.9%)
	Grade 1-2	6 (8.0%)	9 (6.2%)
	1	2 (2.7%)	4 (2.8%)
	2	4 (5.3%)	5 (3.4%)
	Grade 3-4	2 (2.7%)	1 (0.7%)
	3	2 (2.7%)	1 (0.7%)
Flushing	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	1 (1.3%)	3 (2.1%)
	2	0	1 (0.7%)
Hypertension	- Any Grade -	3 (4.0%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
	Grade 3-4	2 (2.7%)	1 (0.7%)
	3	2 (2.7%)	1 (0.7%)
Hot flush	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
Lymphoedema	- Any Grade -	3 (4.0%)	0
	Grade 1-2	3 (4.0%)	0
	1	1 (1.3%)	0
	2	2 (2.7%)	0

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Phlebitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
Embolism	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Venous thrombosis limb	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Hepatobiliary disorders			
- Overall -	- Any Grade -	6 (8.0%)	6 (4.1%)
	Grade 1-2	6 (8.0%)	4 (2.8%)
	1	5 (6.7%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Hyperbilirubinaemia	- Any Grade -	4 (5.3%)	4 (2.8%)
	Grade 1-2	4 (5.3%)	4 (2.8%)
	1	3 (4.0%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
Hypertransaminasaemia	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Cholecystitis acute	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Cholestasis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Hepatic cytolysis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Hepatic function abnormal	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Eye disorders			
- Overall -	- Any Grade -	4 (5.3%)	7 (4.8%)
	Grade 1-2	4 (5.3%)	7 (4.8%)
	1	4 (5.3%)	4 (2.8%)
	2	0	3 (2.1%)
Lacrimation increased	- Any Grade -	3 (4.0%)	3 (2.1%)
	Grade 1-2	3 (4.0%)	3 (2.1%)
	1	3 (4.0%)	1 (0.7%)
	2	0	2 (1.4%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Dry eye	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
Visual acuity reduced	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Cataract	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Eye discharge	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Eyelid oedema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Retinal oedema	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Cardiac disorders			
- Overall -	- Any Grade -	3 (4.0%)	4 (2.8%)
	Grade 1-2	3 (4.0%)	4 (2.8%)
	1	1 (1.3%)	2 (1.4%)
	2	2 (2.7%)	2 (1.4%)
Palpitations	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Cardiac failure	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Coronary artery disease	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Extrasystoles	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Metabolic cardiomyopathy	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Supraventricular extrasystoles	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Ventricular arrhythmia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/ HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Injury, poisoning and procedural complications			
- Overall -	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	0	2 (1.4%)
	2	2 (2.7%)	0
Poisoning	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	2	2 (2.7%)	0
Traumatic haematoma	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vascular access site swelling	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Psychiatric disorders			
- Overall -	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Insomnia	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Depression	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Reproductive system and breast disorders			
- Overall -	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Breast ulceration	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Menstruation irregular	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Vulvovaginal pruritus	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/ HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Ear and labyrinth disorders			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Vertigo	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Immune system disorders			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Drug hypersensitivity	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hypersensitivity	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
No Coding available			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
No Coding available	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Renal and urinary disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pollakiuria	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	96 (94.1%)
	Grade 1-2	53 (52.0%)
	1	9 (8.8%)
	2	44 (43.1%)
	Grade 3-4	43 (42.2%)
	3	40 (39.2%)
	4	3 (2.9%)
Gastrointestinal disorders		
- Overall -	- Any Grade -	65 (63.7%)
	Grade 1-2	53 (52.0%)
	1	30 (29.4%)
	2	23 (22.5%)
	Grade 3-4	12 (11.8%)
	3	12 (11.8%)
Diarrhoea	- Any Grade -	46 (45.1%)
	Grade 1-2	36 (35.3%)
	1	17 (16.7%)
	2	19 (18.6%)
	Grade 3-4	10 (9.8%)
	3	10 (9.8%)
Nausea	- Any Grade -	32 (31.4%)
	Grade 1-2	31 (30.4%)
	1	23 (22.5%)
	2	8 (7.8%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Vomiting	- Any Grade -	19 (18.6%)
	Grade 1-2	19 (18.6%)
	1	15 (14.7%)
	2	4 (3.9%)
Stomatitis	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	5 (4.9%)
	2	1 (1.0%)
Abdominal pain	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dyspepsia	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
Gastrooesophageal reflux disease	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Abdominal pain upper	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Constipation	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Abdominal discomfort	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Dry mouth	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Flatulence	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Mouth ulceration	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Gingival pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oesophagitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oral discomfort	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Paraesthesia oral	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Skin and subcutaneous tissue disorders		
- Overall -	- Any Grade -	62 (60.8%)
	Grade 1-2	61 (59.8%)
	1	30 (29.4%)
	2	31 (30.4%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alopecia	- Any Grade -	41 (40.2%)
	Grade 1-2	41 (40.2%)
	1	15 (14.7%)
	2	26 (25.5%)
Rash	- Any Grade -	10 (9.8%)
	Grade 1-2	10 (9.8%)
	1	8 (7.8%)
	2	2 (2.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Pruritus	- Any Grade -	8 (7.8%)
	Grade 1-2	7 (6.9%)
	1	7 (6.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hand dermatitis	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Nail disorder	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Nail dystrophy	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Dermatitis acneiform	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Dermatitis allergic	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Eczema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Erythema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hyperhidrosis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Madarosis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Nail bed tenderness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nail discolouration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nail ridging	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Onychalgia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Onychoclasis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Onycholysis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Onychomadesis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash maculo-papular	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Skin exfoliation	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Skin hyperpigmentation	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Urticaria	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nervous system disorders		
- Overall -	- Any Grade -	53 (52.0%)
	Grade 1-2	46 (45.1%)
	1	25 (24.5%)
	2	21 (20.6%)
	Grade 3-4	7 (6.9%)
	3	7 (6.9%)
Neuropathy peripheral	- Any Grade -	28 (27.5%)
	Grade 1-2	21 (20.6%)
	1	12 (11.8%)
	2	9 (8.8%)
	Grade 3-4	7 (6.9%)
	3	7 (6.9%)
Polyneuropathy	- Any Grade -	8 (7.8%)
	Grade 1-2	8 (7.8%)
	1	4 (3.9%)
	2	4 (3.9%)
Dysgeusia	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	4 (3.9%)
	2	2 (2.0%)
Peripheral sensory neuropathy	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	5 (4.9%)
	2	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hypoaesthesia	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
Paraesthesia	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
Headache	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
Cognitive disorder	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Dizziness	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Lethargy	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Balance disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Burning sensation mucosal	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Cerebrovascular insufficiency	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Encephalopathy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hypersomnia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Memory impairment	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Neurotoxicity	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Peripheral motor neuropathy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Taste disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Tremor	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Blood and lymphatic system disorders		
- Overall -	- Any Grade -	50 (49.0%)
	Grade 1-2	40 (39.2%)
	1	14 (13.7%)
	2	26 (25.5%)
	Grade 3-4	10 (9.8%)
	3	8 (7.8%)
	4	2 (2.0%)
Anaemia	- Any Grade -	31 (30.4%)
	Grade 1-2	30 (29.4%)
	1	14 (13.7%)
	2	16 (15.7%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neutropenia	- Any Grade -	25 (24.5%)
	Grade 1-2	19 (18.6%)
	1	4 (3.9%)
	2	15 (14.7%)
	Grade 3-4	6 (5.9%)
	3	5 (4.9%)
	4	1 (1.0%)
Leukopenia	- Any Grade -	11 (10.8%)
	Grade 1-2	11 (10.8%)
	1	6 (5.9%)
	2	5 (4.9%)
Febrile neutropenia	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Lymphopenia	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Eosinophilia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Lymphadenopathy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Thrombocytopenia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Thrombocytosis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
General disorders and administration site conditions		
- Overall -	- Any Grade -	48 (47.1%)
	Grade 1-2	44 (43.1%)
	1	23 (22.5%)
	2	21 (20.6%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Fatigue	- Any Grade -	20 (19.6%)
	Grade 1-2	18 (17.6%)
	1	8 (7.8%)
	2	10 (9.8%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Asthenia	- Any Grade -	18 (17.6%)
	Grade 1-2	17 (16.7%)
	1	12 (11.8%)
	2	5 (4.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Mucosal inflammation	- Any Grade -	10 (9.8%)
	Grade 1-2	10 (9.8%)
	1	8 (7.8%)
	2	2 (2.0%)
Oedema	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Oedema peripheral	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Pyrexia	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Chills	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Pain	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Thirst	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Chest discomfort	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Generalised oedema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Influenza like illness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Non-cardiac chest pain	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Peripheral swelling	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Sensation of foreign body	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Investigations		
- Overall -	- Any Grade -	36 (35.3%)
	Grade 1-2	24 (23.5%)
	1	12 (11.8%)
	2	12 (11.8%)
	Grade 3-4	12 (11.8%)
	3	11 (10.8%)
	4	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	18 (17.6%)
	Grade 1-2	13 (12.7%)
	1	11 (10.8%)
	2	2 (2.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Aspartate aminotransferase increased	- Any Grade -	13 (12.7%)
	Grade 1-2	12 (11.8%)
	1	6 (5.9%)
	2	6 (5.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Blood alkaline phosphatase increased	- Any Grade -	9 (8.8%)
	Grade 1-2	8 (7.8%)
	1	7 (6.9%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Neutrophil count decreased	- Any Grade -	8 (7.8%)
	Grade 1-2	4 (3.9%)
	2	4 (3.9%)
	Grade 3-4	4 (3.9%)
	3	3 (2.9%)
	4	1 (1.0%)
White blood cell count decreased	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	2 (2.0%)
	2	3 (2.9%)
Blood bilirubin increased	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Blood lactate dehydrogenase increased	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Lipase increased	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Weight decreased	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Platelet count decreased	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Amylase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Basophil percentage increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Eosinophil percentage increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Haematocrit decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
High density lipoprotein increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Immature granulocyte count increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Lymphocyte count decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Monocyte percentage decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Oxygen saturation decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Red blood cell count decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
White blood cell count increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Metabolism and nutrition disorders		
- Overall -	- Any Grade -	20 (19.6%)
	Grade 1-2	17 (16.7%)
	1	9 (8.8%)
	2	8 (7.8%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Decreased appetite	- Any Grade -	7 (6.9%)
	Grade 1-2	7 (6.9%)
	1	5 (4.9%)
	2	2 (2.0%)
Hyperglycaemia	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dehydration	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Hyperkalaemia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Alkalosis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Dyslipidaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Fluid retention	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hypercalcaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypercreatininaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hypoalbuminaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Musculoskeletal and connective tissue disorders		
- Overall -	- Any Grade -	19 (18.6%)
	Grade 1-2	18 (17.6%)
	1	17 (16.7%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Myalgia	- Any Grade -	8 (7.8%)
	Grade 1-2	8 (7.8%)
	1	7 (6.9%)
	2	1 (1.0%)
Arthralgia	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Back pain	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Muscle spasms	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Musculoskeletal stiffness	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pain in extremity	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Respiratory, thoracic and mediastinal disorders		
- Overall -	- Any Grade -	19 (18.6%)
	Grade 1-2	16 (15.7%)
	1	15 (14.7%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Epistaxis	- Any Grade -	7 (6.9%)
	Grade 1-2	7 (6.9%)
	1	7 (6.9%)
Dyspnoea	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Cough	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rhinorrhoea	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Bronchospasm	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nasal crusting	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pneumonitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Productive cough	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Infections and infestations		
- Overall -	- Any Grade -	13 (12.7%)
	Grade 1-2	11 (10.8%)
	1	4 (3.9%)
	2	7 (6.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Oral candidiasis	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Urinary tract infection	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Bronchitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Conjunctivitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Gingivitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Nail infection	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Oral herpes	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Paronychia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pneumonia viral	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Skin infection	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Upper respiratory tract infection	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Vascular disorders		
- Overall -	- Any Grade -	11 (10.8%)
	Grade 1-2	10 (9.8%)
	1	6 (5.9%)
	2	4 (3.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Flushing	- Any Grade -	6 (5.9%)
	Grade 1-2	5 (4.9%)
	1	3 (2.9%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hot flush	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Hypertension	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Jugular vein thrombosis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Lymphoedema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Eye disorders		
- Overall -	- Any Grade -	10 (9.8%)
	Grade 1-2	10 (9.8%)
	1	7 (6.9%)
	2	3 (2.9%)
Dry eye	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Vision blurred	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Abnormal sensation in eye	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Eye disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Eye irritation	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Eyelid function disorder	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Foreign body sensation in eyes	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Lacrimation increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hepatobiliary disorders		
- Overall -	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hyperbilirubinaemia	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Reproductive system and breast disorders		
- Overall -	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
Vulvovaginal dryness	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Amenorrhoea	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Artificial menopause	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Ear and labyrinth disorders		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Vertigo	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Hypoacusis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Tinnitus	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Tumour necrosis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Tumour inflammation	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Injury, poisoning and procedural complications		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Infusion related reaction	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Psychiatric disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
Insomnia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Irritability	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Immune system disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hypersensitivity	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

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Serious Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	20 (23.0%)	34 (20.5%)
	Grade 1-2	4 (4.6%)	4 (2.4%)
	1	1 (1.1%)	1 (0.6%)
	2	3 (3.4%)	3 (1.8%)
	Grade 3-4	14 (16.1%)	28 (16.9%)
	3	10 (11.5%)	19 (11.4%)
	4	4 (4.6%)	9 (5.4%)
	Grade 5	2 (2.3%)	2 (1.2%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	2 (2.3%)	10 (6.0%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	2 (2.3%)	7 (4.2%)
	3	2 (2.3%)	5 (3.0%)
	4	0	2 (1.2%)
Diarrhoea	- Any Grade -	0	6 (3.6%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Nausea	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Vomiting	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
Abdominal pain	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Colitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Large intestine perforation	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Upper gastrointestinal haemorrhage	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Infections and infestations			
- Overall -	- Any Grade -	6 (6.9%)	6 (3.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	6 (6.9%)	5 (3.0%)
	3	5 (5.7%)	5 (3.0%)
	4	1 (1.1%)	0

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Serious Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Pneumonia	- Any Grade -	4 (4.6%)	2 (1.2%)
	Grade 3-4	4 (4.6%)	2 (1.2%)
	3	3 (3.4%)	2 (1.2%)
	4	1 (1.1%)	0
Abscess jaw	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
COVID-19	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Cellulitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Peritonitis	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Urinary tract infection	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Viral infection	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	5 (5.7%)	5 (3.0%)
	Grade 1-2	2 (2.3%)	0
	2	2 (2.3%)	0
	Grade 3-4	3 (3.4%)	4 (2.4%)
	3	3 (3.4%)	2 (1.2%)
	4	0	2 (1.2%)
	Grade 5	0	1 (0.6%)
Pleural effusion	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
Pulmonary embolism	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
	Grade 5	0	1 (0.6%)
Dyspnoea	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	0
	4	0	1 (0.6%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Haemoptysis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Pneumothorax	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 3-4	2 (2.3%)	4 (2.4%)
	3	1 (1.1%)	2 (1.2%)
	4	1 (1.1%)	2 (1.2%)
Febrile neutropenia	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	2 (1.2%)
	4	0	1 (0.6%)
Anaemia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	0	1 (0.6%)
	4	1 (1.1%)	0
Neutropenia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	4	1 (1.1%)	1 (0.6%)
Thrombocytopenia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
- Overall -	- Any Grade -	3 (3.4%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	3 (1.8%)
	3	0	2 (1.2%)
	4	1 (1.1%)	1 (0.6%)
	Grade 5	1 (1.1%)	0
Gastric cancer	- Any Grade -	1 (1.1%)	0
	Grade 5	1 (1.1%)	0
Infected neoplasm	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Lymphangiosis carcinomatosa	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	4	1 (1.1%)	0
Schwannoma	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Serious Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Tumour haemorrhage	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Tumour necrosis	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Injury, poisoning and procedural complications			
- Overall -	- Any Grade -	3 (3.4%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	1 (1.1%)	2 (1.2%)
	4	1 (1.1%)	0
Spinal fracture	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	0	1 (0.6%)
	4	1 (1.1%)	0
Fracture	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Procedural pain	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Skin laceration	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Cardiac disorders			
- Overall -	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
	Grade 5	0	1 (0.6%)
Atrial fibrillation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Cardiopulmonary failure	- Any Grade -	0	1 (0.6%)
	Grade 5	0	1 (0.6%)
Sinus tachycardia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Eye disorders			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Serious Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Epiretinal membrane	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Glaucoma	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Macular oedema	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
General disorders and administration site conditions			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Fatigue	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hyperthermia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
	Grade 5	1 (1.1%)	0
Hyperglycaemia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Tumour lysis syndrome	- Any Grade -	1 (1.1%)	0
	Grade 5	1 (1.1%)	0
Immune system disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hypersensitivity	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Investigations			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Serious Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Lymphocyte count decreased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Musculoskeletal and connective tissue disorders			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	4	1 (1.1%)	0
Intervertebral disc compression	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	4	1 (1.1%)	0
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Erythema multiforme	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Serious Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	11 (14.7%)	30 (20.7%)
	Grade 1-2	2 (2.7%)	6 (4.1%)
	1	0	1 (0.7%)
	2	2 (2.7%)	5 (3.4%)
	Grade 3-4	8 (10.7%)	19 (13.1%)
	3	8 (10.7%)	18 (12.4%)
	4	0	1 (0.7%)
	Grade 5	1 (1.3%)	5 (3.4%)
Infections and infestations			
- Overall -	- Any Grade -	5 (6.7%)	5 (3.4%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	1	0	1 (0.7%)
	2	2 (2.7%)	0
	Grade 3-4	2 (2.7%)	3 (2.1%)
	3	2 (2.7%)	3 (2.1%)
	Grade 5	1 (1.3%)	1 (0.7%)
Pneumonia	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
	Grade 5	0	1 (0.7%)
Abdominal abscess	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
COVID-19	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Cellulitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erysipelas	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Lower respiratory tract infection	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Sepsis	- Any Grade -	1 (1.3%)	0
	Grade 5	1 (1.3%)	0
Upper respiratory tract infection	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Urinary tract infection	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0

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Serious Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Wound infection	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Gastrointestinal disorders			
- Overall -	- Any Grade -	1 (1.3%)	7 (4.8%)
	Grade 3-4	1 (1.3%)	7 (4.8%)
	3	1 (1.3%)	6 (4.1%)
	4	0	1 (0.7%)
Diarrhoea	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	4 (2.8%)
	3	1 (1.3%)	4 (2.8%)
Abdominal hernia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Abdominal pain	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Chronic gastritis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Enterocolitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Intestinal obstruction	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	4	0	1 (0.7%)
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	1 (1.3%)	5 (3.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
	Grade 5	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dyspnoea	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Pleural effusion	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Pulmonary embolism	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Respiratory distress	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	0	2 (1.4%)
	4	1 (1.3%)	0
	Grade 5	0	1 (0.7%)
Febrile neutropenia	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Neutropenia	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	1 (0.7%)
	4	0	1 (0.7%)
Leukopenia	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	4	1 (1.3%)	0
General disorders and administration site conditions			
- Overall -	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
	Grade 5	0	2 (1.4%)
Death	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Extravasation	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Fatigue	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
General physical health deterioration	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Renal and urinary disorders			
- Overall -	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Serious Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Acute kidney injury	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Hydronephrosis	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Renal impairment	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hepatobiliary disorders			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Cholecystitis acute	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Injury, poisoning and procedural complications			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
	Grade 5	0	1 (0.7%)
Femur fracture	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Road traffic accident	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Decreased appetite	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dehydration	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperglycaemia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hypoglycaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Serious Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Eye disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Eyelid oedema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Immune system disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hypersensitivity	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Investigations			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Blood creatine phosphokinase increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Musculoskeletal and connective tissue disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Pathological fracture	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Tumour necrosis	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Nervous system disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Cerebrovascular accident	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Serious Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Psychiatric disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Anxiety	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erythema multiforme	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Vascular disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Deep vein thrombosis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Serious Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	29 (28.4%)
	Grade 1-2	5 (4.9%)
	2	5 (4.9%)
	Grade 3-4	20 (19.6%)
	3	18 (17.6%)
	4	2 (2.0%)
	Grade 5	4 (3.9%)
Infections and infestations		
- Overall -	- Any Grade -	12 (11.8%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	8 (7.8%)
	3	8 (7.8%)
	Grade 5	2 (2.0%)
Pneumonia	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
	Grade 5	1 (1.0%)
Urinary tract infection	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
COVID-19	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Emphysematous cystitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Gastroenteritis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Gastroenteritis norovirus	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Influenza	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Skin infection	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Suspected COVID-19	- Any Grade -	1 (1.0%)
	Grade 5	1 (1.0%)

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Serious Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Gastrointestinal disorders		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Diarrhoea	- Any Grade -	4 (3.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Vomiting	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Large intestine perforation	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nausea	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
General disorders and administration site conditions		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	4 (3.9%)
	2	4 (3.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Pyrexia	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	2	4 (3.9%)
Fatigue	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
General physical health deterioration	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Serious Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Respiratory, thoracic and mediastinal disorders		
- Overall -	- Any Grade -	5 (4.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
	Grade 5	1 (1.0%)
Pneumonitis	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Pleural effusion	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pulmonary embolism	- Any Grade -	1 (1.0%)
	Grade 5	1 (1.0%)
Hepatobiliary disorders		
- Overall -	- Any Grade -	4 (3.9%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Cholecystitis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Autoimmune hepatitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypertransaminasaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Metabolism and nutrition disorders		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Dehydration	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Serious Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Tumour necrosis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Tumour fistulisation	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Blood and lymphatic system disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Febrile neutropenia	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Cardiac disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
	Grade 5	1 (1.0%)
Cardiac arrest	- Any Grade -	1 (1.0%)
	Grade 5	1 (1.0%)
Myocarditis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Musculoskeletal and connective tissue disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Musculoskeletal chest pain	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Myositis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Serious Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Nervous system disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Dystonia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Posterior reversible encephalopathy syndrome	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Skin and subcutaneous tissue disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune system disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypersensitivity	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Investigations		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Renal and urinary disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Serious Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Acute kidney injury	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Vascular disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Lymphoedema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Serious Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	18 (17.6%)
	Grade 1-2	4 (3.9%)
	2	4 (3.9%)
	Grade 3-4	13 (12.7%)
	3	12 (11.8%)
	4	1 (1.0%)
	Grade 5	1 (1.0%)
Gastrointestinal disorders		
- Overall -	- Any Grade -	4 (3.9%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Diarrhoea	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Large intestine perforation	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nausea	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Respiratory, thoracic and mediastinal disorders		
- Overall -	- Any Grade -	4 (3.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
	Grade 5	1 (1.0%)
Pneumonitis	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Pulmonary embolism	- Any Grade -	1 (1.0%)
	Grade 5	1 (1.0%)
Metabolism and nutrition disorders		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Serious Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Dehydration	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
General disorders and administration site conditions		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Fatigue	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Pyrexia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hepatobiliary disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Autoimmune hepatitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypertransaminasaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Tumour necrosis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Nervous system disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Dystonia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Serious Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Posterior reversible encephalopathy syndrome	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Skin and subcutaneous tissue disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Cardiac disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Myocarditis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Immune system disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypersensitivity	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Infections and infestations		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Urinary tract infection	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Musculoskeletal and connective tissue disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Serious Adverse Events Related to Atezolizumab Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Myositis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Renal and urinary disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Acute kidney injury	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Serious Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	3 (3.4%)	15 (9.0%)
	Grade 1-2	0	4 (2.4%)
	2	0	4 (2.4%)
	Grade 3-4	2 (2.3%)	11 (6.6%)
	3	2 (2.3%)	7 (4.2%)
	4	0	4 (2.4%)
	Grade 5	1 (1.1%)	0
Gastrointestinal disorders			
- Overall -	- Any Grade -	1 (1.1%)	9 (5.4%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	1 (1.1%)	6 (3.6%)
	3	1 (1.1%)	5 (3.0%)
	4	0	1 (0.6%)
Diarrhoea	- Any Grade -	0	6 (3.6%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Abdominal pain	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Colitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Large intestine perforation	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Nausea	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	0
	4	0	1 (0.6%)
Neutropenia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Thrombocytopenia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_ctc.sas
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Serious Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
General disorders and administration site conditions			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Fatigue	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hyperthermia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
	Grade 5	1 (1.1%)	0
Hyperglycaemia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Tumour lysis syndrome	- Any Grade -	1 (1.1%)	0
	Grade 5	1 (1.1%)	0
Cardiac disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Atrial fibrillation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Infections and infestations			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Pneumonia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Serious Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Tumour necrosis	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Pulmonary embolism	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Erythema multiforme	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Serious Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	4 (5.3%)	9 (6.2%)
	Grade 3-4	4 (5.3%)	8 (5.5%)
	3	4 (5.3%)	7 (4.8%)
	4	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	4 (2.8%)
	3	1 (1.3%)	3 (2.1%)
	4	0	1 (0.7%)
Diarrhoea	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	4 (2.8%)
	3	1 (1.3%)	4 (2.8%)
Enterocolitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Intestinal obstruction	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	4	0	1 (0.7%)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Febrile neutropenia	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Neutropenia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	4	0	1 (0.7%)
Hepatobiliary disorders			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Cholecystitis acute	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Serious Adverse Events Related to Ipatasertib/Placebo Treatment by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Decreased appetite	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperglycaemia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
General disorders and administration site conditions			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Fatigue	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Renal and urinary disorders			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Hydronephrosis	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Skin and subcutaneous tissue disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erythema multiforme	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Serious Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	12 (11.8%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	11 (10.8%)
	3	10 (9.8%)
	4	1 (1.0%)
Gastrointestinal disorders		
- Overall -	- Any Grade -	5 (4.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Diarrhoea	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Large intestine perforation	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nausea	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Vomiting	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Metabolism and nutrition disorders		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Dehydration	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Infections and infestations		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_ctc.sas
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Serious Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Gastroenteritis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Urinary tract infection	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Tumour necrosis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Blood and lymphatic system disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Febrile neutropenia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
General disorders and administration site conditions		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Fatigue	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Nervous system disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Posterior reversible encephalopathy syndrome	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Skin and subcutaneous tissue disorders		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Serious Adverse Events Related to Ipatasertib Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Rash	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Serious Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	7 (8.0%)	15 (9.0%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	6 (6.9%)	12 (7.2%)
	3	5 (5.7%)	6 (3.6%)
	4	1 (1.1%)	6 (3.6%)
	Grade 5	1 (1.1%)	0
Gastrointestinal disorders			
- Overall -	- Any Grade -	2 (2.3%)	5 (3.0%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	2 (2.3%)	4 (2.4%)
	3	2 (2.3%)	2 (1.2%)
	4	0	2 (1.2%)
Nausea	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Vomiting	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
Colitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Diarrhoea	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Large intestine perforation	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Upper gastrointestinal haemorrhage	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 3-4	2 (2.3%)	4 (2.4%)
	3	1 (1.1%)	2 (1.2%)
	4	1 (1.1%)	2 (1.2%)
Febrile neutropenia	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	2 (1.2%)
	4	0	1 (0.6%)
Anaemia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	0	1 (0.6%)
	4	1 (1.1%)	0

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_SER_RELPAC_A_SE.out
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Serious Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Neutropenia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	4	1 (1.1%)	1 (0.6%)
Thrombocytopenia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Infections and infestations			
- Overall -	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
Pneumonia	- Any Grade -	2 (2.3%)	0
	Grade 3-4	2 (2.3%)	0
	3	2 (2.3%)	0
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
General disorders and administration site conditions			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Fatigue	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hyperthermia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Pleural effusion	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Pulmonary embolism	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Immune system disorders			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
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Serious Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hypersensitivity	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Investigations			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Lymphocyte count decreased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 5	1 (1.1%)	0
Tumour lysis syndrome	- Any Grade -	1 (1.1%)	0
	Grade 5	1 (1.1%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Tumour necrosis	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_SER_RELPAC_A_SE.out
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Serious Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	2 (2.7%)	10 (6.9%)
	Grade 1-2	0	3 (2.1%)
	2	0	3 (2.1%)
	Grade 3-4	1 (1.3%)	6 (4.1%)
	3	1 (1.3%)	5 (3.4%)
	4	0	1 (0.7%)
	Grade 5	1 (1.3%)	1 (0.7%)
Blood and lymphatic system disorders			
- Overall -	- Any Grade -	0	3 (2.1%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
	Grade 5	0	1 (0.7%)
Febrile neutropenia	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Neutropenia	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	1 (0.7%)
	4	0	1 (0.7%)
General disorders and administration site conditions			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Extravasation	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Fatigue	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Eye disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Eyelid oedema	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Gastrointestinal disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	4	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_SER_RELPAC_B_SE.out
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Serious Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Diarrhoea	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Enterocolitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Intestinal obstruction	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	4	0	1 (0.7%)
Hepatobiliary disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Cholecystitis acute	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Immune system disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hypersensitivity	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Infections and infestations			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 5	1 (1.3%)	0
Sepsis	- Any Grade -	1 (1.3%)	0
	Grade 5	1 (1.3%)	0
Metabolism and nutrition disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Decreased appetite	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Respiratory, thoracic and mediastinal disorders			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_SER_RELPAC_B_SE.out
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Serious Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	9 (8.8%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	7 (6.9%)
	3	6 (5.9%)
	4	1 (1.0%)
Gastrointestinal disorders		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Diarrhoea	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nausea	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Vomiting	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Blood and lymphatic system disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Febrile neutropenia	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
General disorders and administration site conditions		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Fatigue	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Pyrexia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_ctc_SER_RELPAC_C_SE.out
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Serious Adverse Events Related to Paclitaxel Treatment by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Infections and infestations		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Urinary tract infection	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Metabolism and nutrition disorders		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dehydration	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Tumour necrosis	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)

Investigator text for AEs encoded using MedDRA version 25.1. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_ctc.sas
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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one such adverse event	40 (46.0%)	84 (50.6%)
Overall total number of events	85	178
Investigations		
Total number of patients with at least one such adverse event	9 (10.3%)	22 (13.3%)
Total number of events	18	33
Neutrophil count decreased	5 (5.7%)	8 (4.8%)
Alanine aminotransferase increased	3 (3.4%)	8 (4.8%)
Aspartate aminotransferase increased	3 (3.4%)	5 (3.0%)
White blood cell count decreased	2 (2.3%)	3 (1.8%)
Lipase increased	0	3 (1.8%)
Gamma-glutamyltransferase increased	0	2 (1.2%)
Lymphocyte count decreased	1 (1.1%)	1 (0.6%)
Electrocardiogram QT prolonged	1 (1.1%)	0
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	7 (8.0%)	21 (12.7%)
Total number of events	7	30
Diarrhoea	2 (2.3%)	15 (9.0%)
Nausea	0	5 (3.0%)
Vomiting	1 (1.1%)	4 (2.4%)
Abdominal pain	1 (1.1%)	2 (1.2%)
Colitis	1 (1.1%)	1 (0.6%)
Constipation	1 (1.1%)	0
Large intestine perforation	0	1 (0.6%)
Upper gastrointestinal haemorrhage	1 (1.1%)	0
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	7 (8.0%)	19 (11.4%)
Total number of events	11	31
Neutropenia	4 (4.6%)	12 (7.2%)
Anaemia	3 (3.4%)	4 (2.4%)
Febrile neutropenia	0	4 (2.4%)
Leukopenia	1 (1.1%)	0
Lymphopenia	0	1 (0.6%)
Thrombocytopenia	1 (1.1%)	0
Nervous system disorders		
Total number of patients with at least one such adverse event	5 (5.7%)	18 (10.8%)
Total number of events	5	22
Neuropathy peripheral	3 (3.4%)	8 (4.8%)
Peripheral sensory neuropathy	2 (2.3%)	5 (3.0%)
Syncope	0	3 (1.8%)
Loss of consciousness	0	1 (0.6%)
Paraesthesia	0	1 (0.6%)
Peripheral motor neuropathy	0	1 (0.6%)
Polyneuropathy	0	1 (0.6%)
Toxic neuropathy	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_CTC35_A_SE.out
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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	3 (3.4%)	15 (9.0%)
Total number of events	3	16
Fatigue	2 (2.3%)	6 (3.6%)
Asthenia	1 (1.1%)	6 (3.6%)
Mucosal inflammation	0	1 (0.6%)
Non-cardiac chest pain	0	1 (0.6%)
Oedema peripheral	0	1 (0.6%)
Swelling face	0	1 (0.6%)
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	5 (5.7%)	11 (6.6%)
Total number of events	10	14
Hyperglycaemia	0	3 (1.8%)
Hypertriglyceridaemia	0	3 (1.8%)
Hyponatraemia	2 (2.3%)	1 (0.6%)
Decreased appetite	0	1 (0.6%)
Dehydration	0	1 (0.6%)
Glucose tolerance impaired	0	1 (0.6%)
Hyperamylasaemia	1 (1.1%)	0
Hypercholesterolaemia	0	1 (0.6%)
Hyperkalaemia	0	1 (0.6%)
Hyperlipasaemia	1 (1.1%)	0
Hypocalcaemia	1 (1.1%)	0
Hypokalaemia	1 (1.1%)	0
Tumour lysis syndrome	1 (1.1%)	0
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	7 (8.0%)	5 (3.0%)
Total number of events	9	5
Dyspnoea	3 (3.4%)	1 (0.6%)
Pleural effusion	2 (2.3%)	1 (0.6%)
Pulmonary embolism	0	3 (1.8%)
Dyspnoea exertional	1 (1.1%)	0
Hypoxia	1 (1.1%)	0
Infections and infestations		
Total number of patients with at least one such adverse event	6 (6.9%)	5 (3.0%)
Total number of events	7	6
Pneumonia	4 (4.6%)	2 (1.2%)
Abscess jaw	0	1 (0.6%)
COVID-19 pneumonia	0	1 (0.6%)
Cellulitis	1 (1.1%)	0
Peritonitis	0	1 (0.6%)
Urinary tract infection	0	1 (0.6%)
Viral infection	1 (1.1%)	0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Vascular disorders		
Total number of patients with at least one such adverse event	0	6 (3.6%)
Total number of events	0	6
Hypertension	0	2 (1.2%)
Hypotension	0	2 (1.2%)
Hypertensive urgency	0	1 (0.6%)
Lymphoedema	0	1 (0.6%)
Injury, poisoning and procedural complications		
Total number of patients with at least one such adverse event	2 (2.3%)	3 (1.8%)
Total number of events	2	3
Spinal fracture	1 (1.1%)	1 (0.6%)
Eschar	0	1 (0.6%)
Fracture	0	1 (0.6%)
Skin laceration	1 (1.1%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Total number of patients with at least one such adverse event	2 (2.3%)	3 (1.8%)
Total number of events	2	3
Gastric cancer	1 (1.1%)	0
Lymphangiosis carcinomatosa	1 (1.1%)	0
Schwannoma	0	1 (0.6%)
Tumour haemorrhage	0	1 (0.6%)
Tumour necrosis	0	1 (0.6%)
Skin and subcutaneous tissue disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	3 (1.8%)
Total number of events	2	3
Rash	0	2 (1.2%)
Erythema	1 (1.1%)	0
Erythema multiforme	0	1 (0.6%)
Nail toxicity	1 (1.1%)	0
Eye disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	2 (1.2%)
Total number of events	2	3
Cystoid macular oedema	1 (1.1%)	0
Epiretinal membrane	0	1 (0.6%)
Glaucoma	0	1 (0.6%)
Macular oedema	0	1 (0.6%)
Ocular hyperaemia	1 (1.1%)	0
Cardiac disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	1 (0.6%)
Total number of events	2	1
Atrial fibrillation	1 (1.1%)	0
Cardiopulmonary failure	0	1 (0.6%)
Sinus tachycardia	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grade 3-5 Adverse Events, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Musculoskeletal and connective tissue disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	1 (0.6%)
Total number of events	2	1
Arthralgia	1 (1.1%)	0
Bone pain	0	1 (0.6%)
Intervertebral disc compression	1 (1.1%)	0
Immune system disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	2	0
Anaphylactic shock	1 (1.1%)	0
Hypersensitivity	1 (1.1%)	0
Psychiatric disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Depression	1 (1.1%)	0
Reproductive system and breast disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Pelvic pain	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one such adverse event	37 (49.3%)	83 (57.2%)
Overall total number of events	87	182
Investigations		
Total number of patients with at least one such adverse event	12 (16.0%)	25 (17.2%)
Total number of events	26	49
Neutrophil count decreased	6 (8.0%)	13 (9.0%)
Alanine aminotransferase increased	3 (4.0%)	7 (4.8%)
White blood cell count decreased	1 (1.3%)	5 (3.4%)
Lipase increased	2 (2.7%)	3 (2.1%)
Aspartate aminotransferase increased	1 (1.3%)	2 (1.4%)
Amylase increased	0	1 (0.7%)
Blood creatinine increased	0	1 (0.7%)
C-reactive protein increased	0	1 (0.7%)
Gamma-glutamyltransferase increased	0	1 (0.7%)
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	3 (4.0%)	23 (15.9%)
Total number of events	5	37
Diarrhoea	1 (1.3%)	17 (11.7%)
Vomiting	0	3 (2.1%)
Abdominal pain	1 (1.3%)	1 (0.7%)
Ascites	1 (1.3%)	1 (0.7%)
Nausea	0	2 (1.4%)
Abdominal hernia	0	1 (0.7%)
Aphthous ulcer	0	1 (0.7%)
Chronic gastritis	0	1 (0.7%)
Dental caries	1 (1.3%)	0
Enterocolitis	0	1 (0.7%)
Food poisoning	0	1 (0.7%)
Intestinal obstruction	0	1 (0.7%)
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	9 (12.0%)	15 (10.3%)
Total number of events	16	26
Neutropenia	7 (9.3%)	12 (8.3%)
Febrile neutropenia	0	3 (2.1%)
Leukopenia	2 (2.7%)	1 (0.7%)
Anaemia	0	2 (1.4%)
Thrombocytopenia	0	1 (0.7%)
Nervous system disorders		
Total number of patients with at least one such adverse event	8 (10.7%)	15 (10.3%)
Total number of events	8	15
Neuropathy peripheral	3 (4.0%)	10 (6.9%)
Peripheral sensory neuropathy	4 (5.3%)	4 (2.8%)
Dizziness	1 (1.3%)	0
Polyneuropathy	0	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	3 (4.0%)	9 (6.2%)
Total number of events	3	15
Hyperglycaemia	0	3 (2.1%)
Decreased appetite	0	2 (1.4%)
Hypertriglyceridaemia	1 (1.3%)	1 (0.7%)
Hypokalaemia	0	2 (1.4%)
Hyponatraemia	0	2 (1.4%)
Hypophosphataemia	1 (1.3%)	1 (0.7%)
Dehydration	0	1 (0.7%)
Hypercalcaemia	1 (1.3%)	0
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	4 (5.3%)	5 (3.4%)
Total number of events	6	6
Asthenia	2 (2.7%)	2 (1.4%)
Fatigue	3 (4.0%)	0
Death	0	1 (0.7%)
Extravasation	0	1 (0.7%)
General physical health deterioration	0	1 (0.7%)
Skin and subcutaneous tissue disorders		
Total number of patients with at least one such adverse event	2 (2.7%)	7 (4.8%)
Total number of events	2	7
Rash	0	2 (1.4%)
Rash maculo-papular	0	2 (1.4%)
Drug eruption	0	1 (0.7%)
Erythema multiforme	0	1 (0.7%)
Nail disorder	1 (1.3%)	0
Palmar-plantar erythrodysaesthesia syndrome	1 (1.3%)	0
Rash erythematous	0	1 (0.7%)
Infections and infestations		
Total number of patients with at least one such adverse event	3 (4.0%)	5 (3.4%)
Total number of events	3	6
Pneumonia	1 (1.3%)	1 (0.7%)
Urinary tract infection	1 (1.3%)	1 (0.7%)
Abdominal abscess	0	1 (0.7%)
Appendicitis	0	1 (0.7%)
Cellulitis	0	1 (0.7%)
Erysipelas	0	1 (0.7%)
Sepsis	1 (1.3%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Vascular disorders		
Total number of patients with at least one such adverse event	4 (5.3%)	3 (2.1%)
Total number of events	6	3
Hypertension	4 (5.3%)	2 (1.4%)
Deep vein thrombosis	0	1 (0.7%)
Hypertensive crisis	1 (1.3%)	0
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	2 (2.7%)	4 (2.8%)
Total number of events	2	4
Dyspnoea	0	2 (1.4%)
Pulmonary embolism	2 (2.7%)	0
Pneumonitis	0	1 (0.7%)
Respiratory distress	0	1 (0.7%)
Musculoskeletal and connective tissue disorders		
Total number of patients with at least one such adverse event	2 (2.7%)	3 (2.1%)
Total number of events	3	3
Arthralgia	1 (1.3%)	0
Back pain	1 (1.3%)	0
Osteonecrosis of jaw	0	1 (0.7%)
Pain in jaw	1 (1.3%)	0
Pathological fracture	0	1 (0.7%)
Rhabdomyolysis	0	1 (0.7%)
Hepatobiliary disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	3 (2.1%)
Total number of events	1	3
Cholecystitis acute	1 (1.3%)	1 (0.7%)
Hypertransaminasaemia	0	2 (1.4%)
Psychiatric disorders		
Total number of patients with at least one such adverse event	3 (4.0%)	1 (0.7%)
Total number of events	3	1
Anxiety	1 (1.3%)	1 (0.7%)
Confusional state	1 (1.3%)	0
Insomnia	1 (1.3%)	0
Renal and urinary disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	3 (2.1%)
Total number of events	1	3
Haematuria	0	1 (0.7%)
Hydronephrosis	1 (1.3%)	0
Oliguria	0	1 (0.7%)
Renal impairment	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Injury, poisoning and procedural complications		
Total number of patients with at least one such adverse event	1 (1.3%)	1 (0.7%)
Total number of events	1	1
Femur fracture	1 (1.3%)	0
Road traffic accident	0	1 (0.7%)
Cardiac disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	3
Supraventricular tachycardia	0	1 (0.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Total number of patients with at least one such adverse event	1 (1.3%)	0
Total number of events	1	0
Tumour necrosis	1 (1.3%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grade 3-5 Adverse Events, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	62 (60.8%)
Overall total number of events	176
Investigations	
Total number of patients with at least one such adverse event	22 (21.6%)
Total number of events	43
Alanine aminotransferase increased	8 (7.8%)
Aspartate aminotransferase increased	8 (7.8%)
Neutrophil count decreased	4 (3.9%)
Blood alkaline phosphatase increased	3 (2.9%)
Lipase increased	3 (2.9%)
Blood cholesterol increased	1 (1.0%)
Blood glucose increased	1 (1.0%)
Blood triglycerides increased	1 (1.0%)
Gamma-glutamyltransferase increased	1 (1.0%)
Low density lipoprotein increased	1 (1.0%)
Platelet count decreased	1 (1.0%)
Gastrointestinal disorders	
Total number of patients with at least one such adverse event	20 (19.6%)
Total number of events	29
Diarrhoea	17 (16.7%)
Nausea	2 (2.0%)
Vomiting	2 (2.0%)
Abdominal pain	1 (1.0%)
Large intestine perforation	1 (1.0%)
Blood and lymphatic system disorders	
Total number of patients with at least one such adverse event	12 (11.8%)
Total number of events	18
Neutropenia	6 (5.9%)
Lymphopenia	3 (2.9%)
Anaemia	2 (2.0%)
Febrile neutropenia	2 (2.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_CTC35_C_SE.out
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MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Infections and infestations	
Total number of patients with at least one such adverse event	11 (10.8%)
Total number of events	12
Urinary tract infection	3 (2.9%)
Pneumonia	2 (2.0%)
COVID-19	1 (1.0%)
Emphysematous cystitis	1 (1.0%)
Gastroenteritis	1 (1.0%)
Gastroenteritis norovirus	1 (1.0%)
Skin infection	1 (1.0%)
Suspected COVID-19	1 (1.0%)
Tooth abscess	1 (1.0%)
Nervous system disorders	
Total number of patients with at least one such adverse event	10 (9.8%)
Total number of events	12
Neuropathy peripheral	7 (6.9%)
Cerebrovascular insufficiency	1 (1.0%)
Dystonia	1 (1.0%)
Peripheral motor neuropathy	1 (1.0%)
Peripheral sensory neuropathy	1 (1.0%)
Posterior reversible encephalopathy syndrome	1 (1.0%)
Metabolism and nutrition disorders	
Total number of patients with at least one such adverse event	8 (7.8%)
Total number of events	18
Hyperglycaemia	4 (3.9%)
Dehydration	2 (2.0%)
Hypokalaemia	2 (2.0%)
Decreased appetite	1 (1.0%)
Diabetes mellitus	1 (1.0%)
Diabetic ketoacidosis	1 (1.0%)
Hypomagnesaemia	1 (1.0%)
Hyponatraemia	1 (1.0%)
Hypophosphataemia	1 (1.0%)
Hepatobiliary disorders	
Total number of patients with at least one such adverse event	7 (6.9%)
Total number of events	7
Autoimmune hepatitis	3 (2.9%)
Cholecystitis	2 (2.0%)
Hyperbilirubinaemia	1 (1.0%)
Hypertransaminasaemia	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
General disorders and administration site conditions	
Total number of patients with at least one such adverse event	6 (5.9%)
Total number of events	7
Fatigue	3 (2.9%)
Asthenia	1 (1.0%)
Chest discomfort	1 (1.0%)
General physical health deterioration	1 (1.0%)
Respiratory, thoracic and mediastinal disorders	
Total number of patients with at least one such adverse event	6 (5.9%)
Total number of events	7
Bronchospasm	1 (1.0%)
Cough	1 (1.0%)
Dyspnoea	1 (1.0%)
Pleural effusion	1 (1.0%)
Pneumonitis	1 (1.0%)
Pulmonary embolism	1 (1.0%)
Skin and subcutaneous tissue disorders	
Total number of patients with at least one such adverse event	6 (5.9%)
Total number of events	8
Pruritus	2 (2.0%)
Rash	2 (2.0%)
Rash maculo-papular	1 (1.0%)
Rash papular	1 (1.0%)
Rash pruritic	1 (1.0%)
Vascular disorders	
Total number of patients with at least one such adverse event	4 (3.9%)
Total number of events	4
Hypertension	2 (2.0%)
Flushing	1 (1.0%)
Phlebitis	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Tumour necrosis	2 (2.0%)
Tumour fistulisation	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cardiac disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Cardiac arrest	1 (1.0%)
Myocarditis	1 (1.0%)
Musculoskeletal and connective tissue disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	3
Arthralgia	1 (1.0%)
Musculoskeletal chest pain	1 (1.0%)
Myositis	1 (1.0%)
Immune system disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Hypersensitivity	1 (1.0%)
Psychiatric disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Anxiety	1 (1.0%)
Renal and urinary disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Acute kidney injury	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Adverse Events Leading to Atezolizumab Discontinuation, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	14 (13.7%)
Overall total number of events	18
Hepatobiliary disorders	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Autoimmune hepatitis	3 (2.9%)
Investigations	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	6
Alanine aminotransferase increased	3 (2.9%)
Aspartate aminotransferase increased	2 (2.0%)
Blood alkaline phosphatase increased	1 (1.0%)
Gastrointestinal disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Diarrhoea	1 (1.0%)
Large intestine perforation	1 (1.0%)
Infections and infestations	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Pneumonia	1 (1.0%)
Suspected COVID-19	1 (1.0%)
Respiratory, thoracic and mediastinal disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Pneumonitis	1 (1.0%)
Pulmonary embolism	1 (1.0%)
Immune system disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Hypersensitivity	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Atezolizumab Discontinuation, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Musculoskeletal and connective tissue disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Mixed connective tissue disease	1 (1.0%)
Nervous system disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Dystonia	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Ipatasertib/Placebo Discontinuation, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one such adverse event	6 (6.9%)	17 (10.2%)
Overall total number of events	11	20
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	0	7 (4.2%)
Total number of events	0	7
Diarrhoea	0	6 (3.6%)
Large intestine perforation	0	1 (0.6%)
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	2 (1.2%)
Total number of events	2	2
Pulmonary embolism	0	2 (1.2%)
Dyspnoea	1 (1.1%)	0
Pneumothorax	1 (1.1%)	0
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	2 (1.2%)
Total number of events	1	2
Hyperglycaemia	0	2 (1.2%)
Tumour lysis syndrome	1 (1.1%)	0
Skin and subcutaneous tissue disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	2 (1.2%)
Total number of events	1	2
Erythema	1 (1.1%)	0
Erythema multiforme	0	1 (0.6%)
Rash	0	1 (0.6%)
Infections and infestations		
Total number of patients with at least one such adverse event	0	2 (1.2%)
Total number of events	0	2
Peritonitis	0	1 (0.6%)
Pneumonia	0	1 (0.6%)
Investigations		
Total number of patients with at least one such adverse event	0	2 (1.2%)
Total number of events	0	3
Alanine aminotransferase increased	0	1 (0.6%)
Aspartate aminotransferase increased	0	1 (0.6%)
Neutrophil count decreased	0	1 (0.6%)
Nervous system disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	0
Total number of events	2	0
Neuropathy peripheral	2 (2.3%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_DSCIPAT_A_SE.out
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Adverse Events Leading to Ipatasertib/Placebo Discontinuation, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Cardiac disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Atrial fibrillation	1 (1.1%)	0
Eye disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Ocular hyperaemia	1 (1.1%)	0
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Fatigue	0	1 (0.6%)
Immune system disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	2	0
Anaphylactic shock	1 (1.1%)	0
Hypersensitivity	1 (1.1%)	0
Renal and urinary disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Haematuria	1 (1.1%)	0
Vascular disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Hypotension	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Ipatasertib/Placebo Discontinuation, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one such adverse event	3 (4.0%)	17 (11.7%)
Overall total number of events	3	21
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	5 (3.4%)
Total number of events	1	7
Diarrhoea	1 (1.3%)	4 (2.8%)
Abdominal discomfort	0	1 (0.7%)
Stomatitis	0	1 (0.7%)
Vomiting	0	1 (0.7%)
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	0	3 (2.1%)
Total number of events	0	3
Febrile neutropenia	0	2 (1.4%)
Neutropenia	0	1 (0.7%)
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	1 (1.3%)	1 (0.7%)
Total number of events	1	1
Death	0	1 (0.7%)
Fatigue	1 (1.3%)	0
Infections and infestations		
Total number of patients with at least one such adverse event	0	2 (1.4%)
Total number of events	0	2
COVID-19	0	1 (0.7%)
Pneumonia	0	1 (0.7%)
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	0	2 (1.4%)
Total number of events	0	2
Hyperglycaemia	0	2 (1.4%)
Nervous system disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	1 (0.7%)
Total number of events	1	1
Cerebrovascular accident	0	1 (0.7%)
Peripheral sensory neuropathy	1 (1.3%)	0
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	0	2 (1.4%)
Total number of events	0	2
Dyspnoea	0	1 (0.7%)
Pneumonitis	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
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Adverse Events Leading to Ipatasertib/Placebo Discontinuation, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hepatobiliary disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Hypertransaminasaemia	0	1 (0.7%)
Investigations		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Alanine aminotransferase increased	0	1 (0.7%)
Vascular disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Flushing	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
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Adverse Events Leading to Ipatasertib Discontinuation, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	11 (10.8%)
Overall total number of events	16
Investigations	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	6
Aspartate aminotransferase increased	3 (2.9%)
Alanine aminotransferase increased	2 (2.0%)
Blood alkaline phosphatase increased	1 (1.0%)
Hepatobiliary disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Autoimmune hepatitis	2 (2.0%)
Respiratory, thoracic and mediastinal disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Pneumonitis	1 (1.0%)
Pulmonary embolism	1 (1.0%)
Gastrointestinal disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Large intestine perforation	1 (1.0%)
Immune system disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Hypersensitivity	1 (1.0%)
Infections and infestations	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Suspected COVID-19	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_DSCIPAT_C_SE.out
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Adverse Events Leading to Ipatasertib Discontinuation, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Metabolism and nutrition disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	3
Diabetic ketoacidosis	1 (1.0%)
Hyperglycaemia	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_DSCIPAT_C_SE.out
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Adverse Events Leading to Paclitaxel Discontinuation, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one such adverse event	14 (16.1%)	25 (15.1%)
Overall total number of events	19	29
Nervous system disorders		
Total number of patients with at least one such adverse event	9 (10.3%)	13 (7.8%)
Total number of events	9	15
Neuropathy peripheral	4 (4.6%)	8 (4.8%)
Peripheral sensory neuropathy	2 (2.3%)	4 (2.4%)
Polyneuropathy	3 (3.4%)	1 (0.6%)
Peripheral motor neuropathy	0	1 (0.6%)
Toxic neuropathy	0	1 (0.6%)
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	0	4 (2.4%)
Total number of events	0	4
Diarrhoea	0	3 (1.8%)
Large intestine perforation	0	1 (0.6%)
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	2 (1.2%)
Total number of events	2	2
Pulmonary embolism	0	2 (1.2%)
Dyspnoea	1 (1.1%)	0
Pneumothorax	1 (1.1%)	0
Skin and subcutaneous tissue disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	2 (1.2%)
Total number of events	1	2
Erythema	1 (1.1%)	0
Onycholysis	0	1 (0.6%)
Rash	0	1 (0.6%)
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	1 (1.1%)	1 (0.6%)
Total number of events	1	1
Fatigue	1 (1.1%)	0
Oedema	0	1 (0.6%)
Immune system disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	1 (0.6%)
Total number of events	2	1
Hypersensitivity	1 (1.1%)	1 (0.6%)
Anaphylactic shock	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_DSCPAC_A_SE.out
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Adverse Events Leading to Paclitaxel Discontinuation, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Infections and infestations		
Total number of patients with at least one such adverse event	0	2 (1.2%)
Total number of events	0	2
Paronychia	0	1 (0.6%)
Pneumonia	0	1 (0.6%)
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Neutropenia	0	1 (0.6%)
Cardiac disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Atrial fibrillation	1 (1.1%)	0
Eye disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Ocular hyperaemia	1 (1.1%)	0
Investigations		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Neutrophil count decreased	0	1 (0.6%)
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Tumour lysis syndrome	1 (1.1%)	0
Renal and urinary disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Haematuria	1 (1.1%)	0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Paclitaxel Discontinuation, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one such adverse event	12 (16.0%)	42 (29.0%)
Overall total number of events	12	49
Nervous system disorders		
Total number of patients with at least one such adverse event	7 (9.3%)	24 (16.6%)
Total number of events	7	24
Peripheral sensory neuropathy	5 (6.7%)	7 (4.8%)
Neuropathy peripheral	1 (1.3%)	10 (6.9%)
Neurotoxicity	0	2 (1.4%)
Paraesthesia	1 (1.3%)	1 (0.7%)
Polyneuropathy	0	2 (1.4%)
Cerebrovascular accident	0	1 (0.7%)
Dizziness	0	1 (0.7%)
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	0	6 (4.1%)
Total number of events	0	8
Febrile neutropenia	0	3 (2.1%)
Neutropenia	0	3 (2.1%)
Anaemia	0	1 (0.7%)
Leukopenia	0	1 (0.7%)
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	2 (2.7%)	2 (1.4%)
Total number of events	2	3
Fatigue	1 (1.3%)	1 (0.7%)
Asthenia	0	1 (0.7%)
Death	0	1 (0.7%)
Oedema	1 (1.3%)	0
Investigations		
Total number of patients with at least one such adverse event	2 (2.7%)	2 (1.4%)
Total number of events	2	2
Neutrophil count decreased	2 (2.7%)	2 (1.4%)
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	0	3 (2.1%)
Total number of events	0	3
Abdominal discomfort	0	1 (0.7%)
Diarrhoea	0	1 (0.7%)
Nausea	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Paclitaxel Discontinuation, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Infections and infestations		
Total number of patients with at least one such adverse event	1 (1.3%)	2 (1.4%)
Total number of events	1	2
COVID-19	0	1 (0.7%)
Pneumonia	0	1 (0.7%)
Sepsis	1 (1.3%)	0
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	0	2 (1.4%)
Total number of events	0	2
Dyspnoea	0	1 (0.7%)
Pneumonitis	0	1 (0.7%)
Hepatobiliary disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Hypertransaminasaemia	0	1 (0.7%)
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Hyperglycaemia	0	1 (0.7%)
Musculoskeletal and connective tissue disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Scleroderma	0	1 (0.7%)
Skin and subcutaneous tissue disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Rash	0	1 (0.7%)
Vascular disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Flushing	0	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Paclitaxel Discontinuation, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	23 (22.5%)
Overall total number of events	25
Nervous system disorders	
Total number of patients with at least one such adverse event	12 (11.8%)
Total number of events	13
Neuropathy peripheral	7 (6.9%)
Polyneuropathy	2 (2.0%)
Encephalopathy	1 (1.0%)
Peripheral motor neuropathy	1 (1.0%)
Peripheral sensory neuropathy	1 (1.0%)
Respiratory, thoracic and mediastinal disorders	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Dyspnoea	1 (1.0%)
Pneumonitis	1 (1.0%)
Pulmonary embolism	1 (1.0%)
Infections and infestations	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Pneumonia	1 (1.0%)
Suspected COVID-19	1 (1.0%)
Investigations	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Aspartate aminotransferase increased	1 (1.0%)
Neutrophil count decreased	1 (1.0%)
Gastrointestinal disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Large intestine perforation	1 (1.0%)
General disorders and administration site conditions	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Fatigue	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Paclitaxel Discontinuation, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hepatobiliary disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Autoimmune hepatitis	1 (1.0%)
Immune system disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Hypersensitivity	1 (1.0%)
Vascular disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Flushing	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_DSCPAC_C_SE.out
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Adverse Events Leading to Dose Interruption of Atezolizumab, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	53 (52.0%)
Overall total number of events	124
Infections and infestations	
Total number of patients with at least one such adverse event	15 (14.7%)
Total number of events	17
COVID-19	4 (3.9%)
Upper respiratory tract infection	4 (3.9%)
Influenza	2 (2.0%)
Urinary tract infection	2 (2.0%)
Bronchitis	1 (1.0%)
Gastroenteritis	1 (1.0%)
Herpes zoster	1 (1.0%)
Respiratory tract infection viral	1 (1.0%)
Rhinitis	1 (1.0%)
Skin and subcutaneous tissue disorders	
Total number of patients with at least one such adverse event	12 (11.8%)
Total number of events	14
Rash	6 (5.9%)
Pruritus	2 (2.0%)
Onycholysis	1 (1.0%)
Rash erythematous	1 (1.0%)
Rash maculo-papular	1 (1.0%)
Rash papular	1 (1.0%)
Rash pruritic	1 (1.0%)
General disorders and administration site conditions	
Total number of patients with at least one such adverse event	11 (10.8%)
Total number of events	11
Pyrexia	6 (5.9%)
Fatigue	3 (2.9%)
General physical health deterioration	1 (1.0%)
Influenza like illness	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_DSIATZ_C_SE.out
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Adverse Events Leading to Dose Interruption of Atezolizumab, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Investigations	
Total number of patients with at least one such adverse event	11 (10.8%)
Total number of events	25
Aspartate aminotransferase increased	7 (6.9%)
Alanine aminotransferase increased	5 (4.9%)
Blood alkaline phosphatase increased	2 (2.0%)
Amylase increased	1 (1.0%)
Blood bilirubin increased	1 (1.0%)
Blood lactate dehydrogenase increased	1 (1.0%)
Lipase increased	1 (1.0%)
Neutrophil count decreased	1 (1.0%)
Weight decreased	1 (1.0%)
Respiratory, thoracic and mediastinal disorders	
Total number of patients with at least one such adverse event	10 (9.8%)
Total number of events	10
Pneumonitis	4 (3.9%)
Respiratory disorder	2 (2.0%)
Dyspnoea	1 (1.0%)
Immune-mediated lung disease	1 (1.0%)
Lung infiltration	1 (1.0%)
Pulmonary embolism	1 (1.0%)
Blood and lymphatic system disorders	
Total number of patients with at least one such adverse event	9 (8.8%)
Total number of events	13
Neutropenia	7 (6.9%)
Febrile neutropenia	2 (2.0%)
Gastrointestinal disorders	
Total number of patients with at least one such adverse event	7 (6.9%)
Total number of events	8
Diarrhoea	5 (4.9%)
Nausea	3 (2.9%)
Metabolism and nutrition disorders	
Total number of patients with at least one such adverse event	5 (4.9%)
Total number of events	11
Hyperglycaemia	3 (2.9%)
Dehydration	2 (2.0%)
Diabetic ketoacidosis	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_DSIATZ_C_SE.out

Adverse Events Leading to Dose Interruption of Atezolizumab, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Injury, poisoning and procedural complications	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Infusion related reaction	1 (1.0%)
Procedural pain	1 (1.0%)
Vascular access site inflammation	1 (1.0%)
Hepatobiliary disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Cholecystitis	1 (1.0%)
Hypertransaminasaemia	1 (1.0%)
Musculoskeletal and connective tissue disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Back pain	1 (1.0%)
Myositis	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Tumour necrosis	2 (2.0%)
Renal and urinary disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	3
Acute kidney injury	2 (2.0%)
Cardiac disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Myocarditis	1 (1.0%)
Endocrine disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Hypothyroidism	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
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Adverse Events Leading to Dose Interruption of Atezolizumab, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Nervous system disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Cerebrovascular insufficiency	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one such adverse event	26 (29.9%)	74 (44.6%)
Overall total number of events	54	135
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	3 (3.4%)	23 (13.9%)
Total number of events	4	27
Diarrhoea	0	14 (8.4%)
Nausea	1 (1.1%)	4 (2.4%)
Vomiting	1 (1.1%)	3 (1.8%)
Abdominal discomfort	0	1 (0.6%)
Abdominal pain	0	1 (0.6%)
Colitis	1 (1.1%)	0
Dyspepsia	0	1 (0.6%)
Enteritis	0	1 (0.6%)
Pancreatitis	0	1 (0.6%)
Upper gastrointestinal haemorrhage	1 (1.1%)	0
Infections and infestations		
Total number of patients with at least one such adverse event	7 (8.0%)	18 (10.8%)
Total number of events	8	22
COVID-19	0	6 (3.6%)
Pneumonia	2 (2.3%)	2 (1.2%)
Herpes zoster	1 (1.1%)	2 (1.2%)
Upper respiratory tract infection	0	3 (1.8%)
Abscess jaw	0	1 (0.6%)
Bronchiolitis	0	1 (0.6%)
Bronchitis	0	1 (0.6%)
COVID-19 pneumonia	0	1 (0.6%)
Cellulitis	1 (1.1%)	0
Conjunctivitis	0	1 (0.6%)
Erysipelas	1 (1.1%)	0
Respiratory tract infection viral	0	1 (0.6%)
Skin infection	0	1 (0.6%)
Tooth abscess	1 (1.1%)	0
Tooth infection	0	1 (0.6%)
Urinary tract infection	0	1 (0.6%)
Viral infection	1 (1.1%)	0
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	4 (4.6%)	12 (7.2%)
Total number of events	5	18
Neutropenia	4 (4.6%)	10 (6.0%)
Anaemia	1 (1.1%)	3 (1.8%)
Leukopenia	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	3 (3.4%)	13 (7.8%)
Total number of events	8	14
Hyperglycaemia	2 (2.3%)	8 (4.8%)
Hypertriglyceridaemia	0	2 (1.2%)
Decreased appetite	0	1 (0.6%)
Electrolyte imbalance	0	1 (0.6%)
Hyperamylasaemia	1 (1.1%)	0
Hyperlipasaemia	1 (1.1%)	0
Hypokalaemia	0	1 (0.6%)
Investigations		
Total number of patients with at least one such adverse event	5 (5.7%)	7 (4.2%)
Total number of events	10	9
Neutrophil count decreased	4 (4.6%)	5 (3.0%)
Alanine aminotransferase increased	1 (1.1%)	1 (0.6%)
Aspartate aminotransferase increased	1 (1.1%)	0
Influenza A virus test positive	0	1 (0.6%)
White blood cell count decreased	1 (1.1%)	0
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	2 (2.3%)	9 (5.4%)
Total number of events	2	12
Asthenia	1 (1.1%)	2 (1.2%)
Pyrexia	1 (1.1%)	2 (1.2%)
Mucosal inflammation	0	2 (1.2%)
Face oedema	0	1 (0.6%)
Fatigue	0	1 (0.6%)
Influenza like illness	0	1 (0.6%)
Localised oedema	0	1 (0.6%)
Malaise	0	1 (0.6%)
Swelling face	0	1 (0.6%)
Skin and subcutaneous tissue disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	8 (4.8%)
Total number of events	1	8
Rash	1 (1.1%)	4 (2.4%)
Pruritus	0	2 (1.2%)
Dermatitis allergic	0	1 (0.6%)
Rash maculo-papular	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	3 (3.4%)	5 (3.0%)
Total number of events	4	5
Pleural effusion	2 (2.3%)	1 (0.6%)
Cough	0	1 (0.6%)
Dyspnoea	0	1 (0.6%)
Haemoptysis	1 (1.1%)	0
Oropharyngeal pain	0	1 (0.6%)
Pneumonitis	0	1 (0.6%)
Nervous system disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	5 (3.0%)
Total number of events	2	5
Headache	0	2 (1.2%)
Neuropathy peripheral	1 (1.1%)	1 (0.6%)
Ataxia	0	1 (0.6%)
Dizziness	1 (1.1%)	0
Peripheral sensory neuropathy	0	1 (0.6%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Total number of patients with at least one such adverse event	2 (2.3%)	3 (1.8%)
Total number of events	3	3
Infected neoplasm	1 (1.1%)	0
Lymphangiosis carcinomatosa	1 (1.1%)	0
Schwannoma	0	1 (0.6%)
Tumour haemorrhage	0	1 (0.6%)
Tumour necrosis	0	1 (0.6%)
Injury, poisoning and procedural complications		
Total number of patients with at least one such adverse event	2 (2.3%)	2 (1.2%)
Total number of events	2	2
Spinal fracture	1 (1.1%)	1 (0.6%)
Accidental overdose	0	1 (0.6%)
Skin laceration	1 (1.1%)	0
Renal and urinary disorders		
Total number of patients with at least one such adverse event	0	4 (2.4%)
Total number of events	0	4
Anuria	0	1 (0.6%)
Dysuria	0	1 (0.6%)
Proteinuria	0	1 (0.6%)
Renal failure	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Cardiac disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	1 (0.6%)
Total number of events	1	1
Atrial fibrillation	0	1 (0.6%)
Tachycardia	1 (1.1%)	0
Eye disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	1 (0.6%)
Total number of events	1	1
Cystoid macular oedema	1 (1.1%)	0
Glaucoma	0	1 (0.6%)
Musculoskeletal and connective tissue disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	0
Total number of events	2	0
Arthralgia	1 (1.1%)	0
Intervertebral disc compression	1 (1.1%)	0
Hepatobiliary disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Cholecystitis acute	0	1 (0.6%)
Immune system disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Hypersensitivity	0	1 (0.6%)
Psychiatric disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Anxiety	0	1 (0.6%)
Reproductive system and breast disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Breast pain	1 (1.1%)	0
Vascular disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Lymphoedema	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one such adverse event	32 (42.7%)	67 (46.2%)
Overall total number of events	54	145
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	3 (4.0%)	29 (20.0%)
Total number of events	3	36
Diarrhoea	0	14 (9.7%)
Vomiting	0	7 (4.8%)
Abdominal pain	1 (1.3%)	2 (1.4%)
Abdominal pain upper	1 (1.3%)	2 (1.4%)
Nausea	0	3 (2.1%)
Enterocolitis	0	2 (1.4%)
Stomatitis	1 (1.3%)	1 (0.7%)
Abdominal hernia	0	1 (0.7%)
Intestinal obstruction	0	1 (0.7%)
Odynophagia	0	1 (0.7%)
Paraesthesia oral	0	1 (0.7%)
Investigations		
Total number of patients with at least one such adverse event	8 (10.7%)	18 (12.4%)
Total number of events	13	30
Neutrophil count decreased	6 (8.0%)	11 (7.6%)
Alanine aminotransferase increased	2 (2.7%)	4 (2.8%)
Aspartate aminotransferase increased	1 (1.3%)	2 (1.4%)
Amylase increased	0	2 (1.4%)
Blood creatinine increased	0	1 (0.7%)
C-reactive protein increased	0	1 (0.7%)
Glycosylated haemoglobin increased	0	1 (0.7%)
Lipase increased	0	1 (0.7%)
White blood cell count decreased	1 (1.3%)	0

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Infections and infestations		
Total number of patients with at least one such adverse event	7 (9.3%)	14 (9.7%)
Total number of events	8	21
Upper respiratory tract infection	2 (2.7%)	3 (2.1%)
Herpes zoster	1 (1.3%)	3 (2.1%)
Cellulitis	0	2 (1.4%)
Influenza	0	2 (1.4%)
Abdominal abscess	0	1 (0.7%)
Appendicitis	0	1 (0.7%)
Bronchitis	0	1 (0.7%)
COVID-19	1 (1.3%)	0
Diarrhoea infectious	0	1 (0.7%)
Infection	0	1 (0.7%)
Lower respiratory tract infection	0	1 (0.7%)
Nasopharyngitis	0	1 (0.7%)
Pharyngitis	0	1 (0.7%)
Pneumonia	1 (1.3%)	0
Respiratory tract infection viral	1 (1.3%)	0
Wound infection	1 (1.3%)	0
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	7 (9.3%)	7 (4.8%)
Total number of events	7	7
Asthenia	1 (1.3%)	2 (1.4%)
Fatigue	2 (2.7%)	1 (0.7%)
Malaise	1 (1.3%)	1 (0.7%)
Pyrexia	1 (1.3%)	1 (0.7%)
Mucosal inflammation	0	1 (0.7%)
Oedema	0	1 (0.7%)
Oedema peripheral	1 (1.3%)	0
Peripheral swelling	1 (1.3%)	0
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	6 (8.0%)	7 (4.8%)
Total number of events	8	10
Neutropenia	6 (8.0%)	7 (4.8%)
Anaemia	0	1 (0.7%)
Leukopenia	1 (1.3%)	0

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Skin and subcutaneous tissue disorders		
Total number of patients with at least one such adverse event	2 (2.7%)	9 (6.2%)
Total number of events	2	12
Drug eruption	0	3 (2.1%)
Rash	0	3 (2.1%)
Pruritus	0	2 (1.4%)
Rash maculo-papular	1 (1.3%)	1 (0.7%)
Alopecia	0	1 (0.7%)
Dermatitis bullous	0	1 (0.7%)
Erythema	1 (1.3%)	0
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	3 (4.0%)	5 (3.4%)
Total number of events	3	8
Hyperglycaemia	1 (1.3%)	4 (2.8%)
Decreased appetite	1 (1.3%)	1 (0.7%)
Dehydration	0	1 (0.7%)
Hypertriglyceridaemia	1 (1.3%)	0
Hypoglycaemia	0	1 (0.7%)
Nervous system disorders		
Total number of patients with at least one such adverse event	4 (5.3%)	3 (2.1%)
Total number of events	4	3
Dizziness	2 (2.7%)	0
Neuropathy peripheral	1 (1.3%)	1 (0.7%)
Paraesthesia	0	2 (1.4%)
Peripheral sensory neuropathy	1 (1.3%)	0
Hepatobiliary disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	3 (2.1%)
Total number of events	1	3
Cholecystitis acute	1 (1.3%)	1 (0.7%)
Hyperbilirubinaemia	0	1 (0.7%)
Hypertransaminasaemia	0	1 (0.7%)
Musculoskeletal and connective tissue disorders		
Total number of patients with at least one such adverse event	0	4 (2.8%)
Total number of events	0	4
Myalgia	0	2 (1.4%)
Arthritis	0	1 (0.7%)
Pathological fracture	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	2 (1.4%)
Total number of events	1	3
Cough	0	1 (0.7%)
Oropharyngeal pain	0	1 (0.7%)
Pneumonitis	0	1 (0.7%)
Pulmonary embolism	1 (1.3%)	0
Cardiac disorders		
Total number of patients with at least one such adverse event	0	2 (1.4%)
Total number of events	0	2
Sinus tachycardia	0	1 (0.7%)
Supraventricular tachycardia	0	1 (0.7%)
Injury, poisoning and procedural complications		
Total number of patients with at least one such adverse event	1 (1.3%)	1 (0.7%)
Total number of events	1	1
Femoral neck fracture	0	1 (0.7%)
Femur fracture	1 (1.3%)	0
Psychiatric disorders		
Total number of patients with at least one such adverse event	0	2 (1.4%)
Total number of events	0	2
Anxiety	0	1 (0.7%)
Imperception	0	1 (0.7%)
Vascular disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	1 (0.7%)
Total number of events	1	1
Thrombosis	1 (1.3%)	0
Venous thrombosis limb	0	1 (0.7%)
Ear and labyrinth disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Vertigo	0	1 (0.7%)
Eye disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	0
Total number of events	1	0
Vitreous floaters	1 (1.3%)	0
Immune system disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Hypersensitivity	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Total number of patients with at least one such adverse event	1 (1.3%)	0
Total number of events	1	0
Tumour necrosis	1 (1.3%)	0

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Adverse Events Leading to Dose Interruption of Ipatasertib, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	59 (57.8%)
Overall total number of events	144
Gastrointestinal disorders	
Total number of patients with at least one such adverse event	21 (20.6%)
Total number of events	29
Diarrhoea	15 (14.7%)
Nausea	5 (4.9%)
Vomiting	2 (2.0%)
Gastrooesophageal reflux disease	1 (1.0%)
Toothache	1 (1.0%)
Investigations	
Total number of patients with at least one such adverse event	15 (14.7%)
Total number of events	30
Alanine aminotransferase increased	6 (5.9%)
Aspartate aminotransferase increased	6 (5.9%)
Neutrophil count decreased	4 (3.9%)
Amylase increased	1 (1.0%)
Blood alkaline phosphatase increased	1 (1.0%)
Blood bilirubin increased	1 (1.0%)
Blood glucose increased	1 (1.0%)
Blood lactate dehydrogenase increased	1 (1.0%)
Lipase increased	1 (1.0%)
Weight decreased	1 (1.0%)
Infections and infestations	
Total number of patients with at least one such adverse event	13 (12.7%)
Total number of events	15
COVID-19	3 (2.9%)
Upper respiratory tract infection	3 (2.9%)
Influenza	2 (2.0%)
Urinary tract infection	2 (2.0%)
Bronchitis	1 (1.0%)
Gastroenteritis norovirus	1 (1.0%)
Herpes zoster	1 (1.0%)
Pneumonia	1 (1.0%)
Rhinitis	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Ipatasertib, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Skin and subcutaneous tissue disorders	
Total number of patients with at least one such adverse event	12 (11.8%)
Total number of events	13
Rash	6 (5.9%)
Pruritus	2 (2.0%)
Rash maculo-papular	2 (2.0%)
Onycholysis	1 (1.0%)
Rash erythematous	1 (1.0%)
Rash pruritic	1 (1.0%)
Blood and lymphatic system disorders	
Total number of patients with at least one such adverse event	11 (10.8%)
Total number of events	15
Neutropenia	10 (9.8%)
Febrile neutropenia	1 (1.0%)
General disorders and administration site conditions	
Total number of patients with at least one such adverse event	9 (8.8%)
Total number of events	11
Pyrexia	6 (5.9%)
Asthenia	1 (1.0%)
Fatigue	1 (1.0%)
General physical health deterioration	1 (1.0%)
Influenza like illness	1 (1.0%)
Pain	1 (1.0%)
Metabolism and nutrition disorders	
Total number of patients with at least one such adverse event	7 (6.9%)
Total number of events	9
Hyperglycaemia	5 (4.9%)
Dehydration	2 (2.0%)
Respiratory, thoracic and mediastinal disorders	
Total number of patients with at least one such adverse event	6 (5.9%)
Total number of events	6
Pneumonitis	2 (2.0%)
Dyspnoea	1 (1.0%)
Immune-mediated lung disease	1 (1.0%)
Lung infiltration	1 (1.0%)
Respiratory disorder	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Ipatasertib, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hepatobiliary disorders	
Total number of patients with at least one such adverse event	4 (3.9%)
Total number of events	4
Autoimmune hepatitis	1 (1.0%)
Cholecystitis	1 (1.0%)
Hyperbilirubinaemia	1 (1.0%)
Hypertransaminasaemia	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Tumour necrosis	2 (2.0%)
Infected neoplasm	1 (1.0%)
Injury, poisoning and procedural complications	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Accidental overdose	1 (1.0%)
Procedural pain	1 (1.0%)
Renal and urinary disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	3
Acute kidney injury	2 (2.0%)
Cardiac disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Myocarditis	1 (1.0%)
Endocrine disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Hypothyroidism	1 (1.0%)
Musculoskeletal and connective tissue disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Myositis	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
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Adverse Events Leading to Dose Interruption of Ipatasertib, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Nervous system disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Dystonia	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Dose Interruption of Paclitaxel, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one such adverse event	41 (47.1%)	85 (51.2%)
Overall total number of events	90	214
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	14 (16.1%)	24 (14.5%)
Total number of events	19	53
Neutropenia	13 (14.9%)	20 (12.0%)
Anaemia	1 (1.1%)	7 (4.2%)
Leukopenia	1 (1.1%)	2 (1.2%)
Febrile neutropenia	0	1 (0.6%)
Lymphopenia	0	1 (0.6%)
Thrombocytopenia	1 (1.1%)	0
Infections and infestations		
Total number of patients with at least one such adverse event	10 (11.5%)	25 (15.1%)
Total number of events	12	30
COVID-19	0	6 (3.6%)
Upper respiratory tract infection	1 (1.1%)	5 (3.0%)
Pneumonia	3 (3.4%)	2 (1.2%)
Bronchitis	0	2 (1.2%)
Herpes zoster	0	2 (1.2%)
Respiratory tract infection viral	0	2 (1.2%)
Abscess jaw	0	1 (0.6%)
Bronchiolitis	0	1 (0.6%)
COVID-19 pneumonia	0	1 (0.6%)
Cellulitis	1 (1.1%)	0
Cystitis	1 (1.1%)	0
Device related infection	0	1 (0.6%)
Erysipelas	1 (1.1%)	0
Furuncle	0	1 (0.6%)
Influenza	1 (1.1%)	0
Laryngitis	0	1 (0.6%)
Nail infection	0	1 (0.6%)
Nasopharyngitis	1 (1.1%)	0
Periodontitis	0	1 (0.6%)
Skin infection	0	1 (0.6%)
Tooth abscess	1 (1.1%)	0
Tooth infection	0	1 (0.6%)
Urinary tract infection	0	1 (0.6%)
Viral infection	1 (1.1%)	0

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Adverse Events Leading to Dose Interruption of Paclitaxel, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Investigations		
Total number of patients with at least one such adverse event	10 (11.5%)	18 (10.8%)
Total number of events	18	33
Neutrophil count decreased	8 (9.2%)	15 (9.0%)
Alanine aminotransferase increased	2 (2.3%)	2 (1.2%)
Aspartate aminotransferase increased	2 (2.3%)	1 (0.6%)
White blood cell count decreased	2 (2.3%)	1 (0.6%)
Eastern Cooperative Oncology Group performance status worsened	0	1 (0.6%)
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	17 (10.2%)
Total number of events	2	23
Nausea	0	8 (4.8%)
Diarrhoea	0	7 (4.2%)
Vomiting	0	3 (1.8%)
Abdominal pain	0	1 (0.6%)
Colitis	1 (1.1%)	0
Enteritis	0	1 (0.6%)
Pancreatitis	0	1 (0.6%)
Stomatitis	0	1 (0.6%)
Upper gastrointestinal haemorrhage	1 (1.1%)	0
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	5 (5.7%)	12 (7.2%)
Total number of events	6	15
Asthenia	2 (2.3%)	4 (2.4%)
Pyrexia	2 (2.3%)	3 (1.8%)
Fatigue	0	3 (1.8%)
Influenza like illness	0	2 (1.2%)
Chest pain	1 (1.1%)	0
Face oedema	0	1 (0.6%)
Localised oedema	0	1 (0.6%)
Mucosal inflammation	0	1 (0.6%)
Non-cardiac chest pain	1 (1.1%)	0
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	6 (6.9%)	6 (3.6%)
Total number of events	7	6
Dyspnoea	1 (1.1%)	2 (1.2%)
Pleural effusion	2 (2.3%)	1 (0.6%)
Cough	0	1 (0.6%)
Haemoptysis	1 (1.1%)	0
Hypoxia	1 (1.1%)	0
Oropharyngeal pain	0	1 (0.6%)
Respiratory disorder	1 (1.1%)	0
Tachypnoea	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Paclitaxel, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Nervous system disorders		
Total number of patients with at least one such adverse event	3 (3.4%)	8 (4.8%)
Total number of events	3	9
Neuropathy peripheral	1 (1.1%)	2 (1.2%)
Peripheral sensory neuropathy	1 (1.1%)	1 (0.6%)
Altered state of consciousness	0	1 (0.6%)
Ataxia	0	1 (0.6%)
Dizziness	1 (1.1%)	0
Dysgeusia	0	1 (0.6%)
Headache	0	1 (0.6%)
Paraesthesia	0	1 (0.6%)
Seizure	0	1 (0.6%)
Skin and subcutaneous tissue disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	8 (4.8%)
Total number of events	2	9
Rash	0	4 (2.4%)
Dermatitis allergic	0	2 (1.2%)
Erythema	0	1 (0.6%)
Hyperhidrosis	1 (1.1%)	0
Onycholysis	1 (1.1%)	0
Pruritus	0	1 (0.6%)
Rash maculo-papular	0	1 (0.6%)
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	3 (3.4%)	6 (3.6%)
Total number of events	8	8
Hyperglycaemia	2 (2.3%)	2 (1.2%)
Decreased appetite	0	2 (1.2%)
Electrolyte imbalance	0	1 (0.6%)
Hyperamylasaemia	1 (1.1%)	0
Hyperlipasaemia	1 (1.1%)	0
Hypertriglyceridaemia	0	1 (0.6%)
Hypokalaemia	0	1 (0.6%)
Injury, poisoning and procedural complications		
Total number of patients with at least one such adverse event	1 (1.1%)	6 (3.6%)
Total number of events	1	6
Spinal fracture	1 (1.1%)	1 (0.6%)
Wound	0	2 (1.2%)
Fall	0	1 (0.6%)
Fracture	0	1 (0.6%)
Infusion related reaction	0	1 (0.6%)

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Adverse Events Leading to Dose Interruption of Paclitaxel, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Musculoskeletal and connective tissue disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	4 (2.4%)
Total number of events	2	4
Bone pain	0	2 (1.2%)
Arthralgia	1 (1.1%)	0
Back pain	0	1 (0.6%)
Intervertebral disc compression	1 (1.1%)	0
Pathological fracture	0	1 (0.6%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Total number of patients with at least one such adverse event	2 (2.3%)	3 (1.8%)
Total number of events	2	3
Infected neoplasm	1 (1.1%)	0
Lymphangiosis carcinomatosa	1 (1.1%)	0
Schwannoma	0	1 (0.6%)
Tumour haemorrhage	0	1 (0.6%)
Tumour necrosis	0	1 (0.6%)
Vascular disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	3 (1.8%)
Total number of events	2	5
Flushing	1 (1.1%)	1 (0.6%)
Embolism	0	1 (0.6%)
Hypertension	0	1 (0.6%)
Hypertensive crisis	0	1 (0.6%)
Hypotension	1 (1.1%)	0
Hepatobiliary disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	1 (0.6%)
Total number of events	4	1
Hyperbilirubinaemia	2 (2.3%)	0
Cholecystitis acute	0	1 (0.6%)
Renal and urinary disorders		
Total number of patients with at least one such adverse event	0	3 (1.8%)
Total number of events	0	3
Dysuria	0	1 (0.6%)
Proteinuria	0	1 (0.6%)
Renal failure	0	1 (0.6%)
Immune system disorders		
Total number of patients with at least one such adverse event	0	2 (1.2%)
Total number of events	0	2
Hypersensitivity	0	2 (1.2%)

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Adverse Events Leading to Dose Interruption of Paclitaxel, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Cardiac disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Atrial fibrillation	0	1 (0.6%)
Ear and labyrinth disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Vertigo	0	1 (0.6%)
Eye disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Cystoid macular oedema	1 (1.1%)	0
No Coding available		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
No Coding available	0	1 (0.6%)
Psychiatric disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Anxiety	0	1 (0.6%)
Reproductive system and breast disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Breast pain	1 (1.1%)	0

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Adverse Events Leading to Dose Interruption of Paclitaxel, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one such adverse event	40 (53.3%)	77 (53.1%)
Overall total number of events	114	243
Investigations		
Total number of patients with at least one such adverse event	15 (20.0%)	24 (16.6%)
Total number of events	38	67
Neutrophil count decreased	13 (17.3%)	17 (11.7%)
Alanine aminotransferase increased	2 (2.7%)	5 (3.4%)
Aspartate aminotransferase increased	1 (1.3%)	3 (2.1%)
White blood cell count decreased	1 (1.3%)	1 (0.7%)
Amylase increased	0	1 (0.7%)
Blood alkaline phosphatase increased	1 (1.3%)	0
Blood creatine phosphokinase increased	0	1 (0.7%)
Blood creatinine increased	0	1 (0.7%)
Glycosylated haemoglobin increased	0	1 (0.7%)
Lipase increased	0	1 (0.7%)
SARS-CoV-2 test positive	0	1 (0.7%)
Infections and infestations		
Total number of patients with at least one such adverse event	14 (18.7%)	21 (14.5%)
Total number of events	17	27
Herpes zoster	1 (1.3%)	4 (2.8%)
Upper respiratory tract infection	2 (2.7%)	2 (1.4%)
Nasopharyngitis	1 (1.3%)	2 (1.4%)
Pneumonia	3 (4.0%)	0
Bronchitis	0	2 (1.4%)
Cystitis	1 (1.3%)	1 (0.7%)
Influenza	0	2 (1.4%)
Respiratory tract infection viral	2 (2.7%)	0
Urinary tract infection	0	2 (1.4%)
Wound infection	1 (1.3%)	1 (0.7%)
Abdominal abscess	0	1 (0.7%)
Appendicitis	0	1 (0.7%)
COVID-19	1 (1.3%)	0
Cellulitis	0	1 (0.7%)
Erysipelas	0	1 (0.7%)
Infection	0	1 (0.7%)
Laryngitis	0	1 (0.7%)
Lower respiratory tract infection	0	1 (0.7%)
Skin infection	1 (1.3%)	0
Tonsillitis	1 (1.3%)	0
Tracheobronchitis	1 (1.3%)	0
Vascular access site infection	0	1 (0.7%)
Viral infection	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Paclitaxel, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	11 (14.7%)	19 (13.1%)
Total number of events	18	55
Neutropenia	10 (13.3%)	19 (13.1%)
Leukopenia	3 (4.0%)	1 (0.7%)
Thrombocytopenia	0	2 (1.4%)
Anaemia	0	1 (0.7%)
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	2 (2.7%)	24 (16.6%)
Total number of events	2	31
Diarrhoea	0	10 (6.9%)
Abdominal pain	1 (1.3%)	3 (2.1%)
Vomiting	0	4 (2.8%)
Enterocolitis	0	2 (1.4%)
Nausea	0	2 (1.4%)
Abdominal hernia	0	1 (0.7%)
Abdominal pain upper	0	1 (0.7%)
Aphthous ulcer	0	1 (0.7%)
Ascites	0	1 (0.7%)
Dyspepsia	0	1 (0.7%)
Hypoaesthesia oral	0	1 (0.7%)
Intestinal obstruction	0	1 (0.7%)
Odynophagia	0	1 (0.7%)
Paraesthesia oral	0	1 (0.7%)
Stomatitis	1 (1.3%)	0
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	11 (14.7%)	15 (10.3%)
Total number of events	11	15
Asthenia	1 (1.3%)	4 (2.8%)
Pyrexia	2 (2.7%)	3 (2.1%)
Fatigue	3 (4.0%)	1 (0.7%)
Malaise	1 (1.3%)	1 (0.7%)
Oedema peripheral	1 (1.3%)	1 (0.7%)
Catheter site erythema	0	1 (0.7%)
Chest discomfort	0	1 (0.7%)
Chest pain	1 (1.3%)	0
Hyperthermia	1 (1.3%)	0
Influenza like illness	0	1 (0.7%)
Infusion site extravasation	0	1 (0.7%)
Oedema	0	1 (0.7%)
Peripheral swelling	1 (1.3%)	0

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Adverse Events Leading to Dose Interruption of Paclitaxel, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Skin and subcutaneous tissue disorders		
Total number of patients with at least one such adverse event	3 (4.0%)	10 (6.9%)
Total number of events	3	12
Rash	0	5 (3.4%)
Erythema	2 (2.7%)	0
Pruritus	0	2 (1.4%)
Dermatitis allergic	1 (1.3%)	0
Drug eruption	0	1 (0.7%)
Nail discolouration	0	1 (0.7%)
Nail disorder	0	1 (0.7%)
Nail ridging	0	1 (0.7%)
Rash maculo-papular	0	1 (0.7%)
Nervous system disorders		
Total number of patients with at least one such adverse event	5 (6.7%)	7 (4.8%)
Total number of events	7	7
Neuropathy peripheral	1 (1.3%)	4 (2.8%)
Paraesthesia	2 (2.7%)	2 (1.4%)
Dizziness	1 (1.3%)	0
Headache	1 (1.3%)	0
Muscle tone disorder	1 (1.3%)	0
Peripheral sensory neuropathy	0	1 (0.7%)
Radiculopathy	1 (1.3%)	0
Musculoskeletal and connective tissue disorders		
Total number of patients with at least one such adverse event	2 (2.7%)	6 (4.1%)
Total number of events	2	6
Myalgia	0	3 (2.1%)
Arthritis	0	2 (1.4%)
Flank pain	1 (1.3%)	0
Pathological fracture	0	1 (0.7%)
Spinal pain	1 (1.3%)	0
Hepatobiliary disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	5 (3.4%)
Total number of events	4	5
Hyperbilirubinaemia	1 (1.3%)	3 (2.1%)
Cholecystitis acute	1 (1.3%)	1 (0.7%)
Hypertransaminasaemia	0	1 (0.7%)

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Adverse Events Leading to Dose Interruption of Paclitaxel, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	3 (4.0%)	3 (2.1%)
Total number of events	4	4
Dyspnoea	1 (1.3%)	1 (0.7%)
Pulmonary embolism	2 (2.7%)	0
Cough	0	1 (0.7%)
Oropharyngeal pain	0	1 (0.7%)
Pneumonitis	0	1 (0.7%)
Respiratory disorder	1 (1.3%)	0
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	2 (2.7%)	3 (2.1%)
Total number of events	2	4
Decreased appetite	1 (1.3%)	1 (0.7%)
Dehydration	0	1 (0.7%)
Hyperglycaemia	0	1 (0.7%)
Hypertriglyceridaemia	1 (1.3%)	0
Vascular disorders		
Total number of patients with at least one such adverse event	2 (2.7%)	3 (2.1%)
Total number of events	2	3
Flushing	1 (1.3%)	0
Haemorrhage	0	1 (0.7%)
Hypertension	0	1 (0.7%)
Thrombosis	1 (1.3%)	0
Venous thrombosis limb	0	1 (0.7%)
Cardiac disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	1 (0.7%)
Total number of events	1	2
Supraventricular tachycardia	0	1 (0.7%)
Ventricular arrhythmia	1 (1.3%)	0
Immune system disorders		
Total number of patients with at least one such adverse event	0	2 (1.4%)
Total number of events	0	2
Drug hypersensitivity	0	1 (0.7%)
Hypersensitivity	0	1 (0.7%)
Injury, poisoning and procedural complications		
Total number of patients with at least one such adverse event	1 (1.3%)	1 (0.7%)
Total number of events	1	1
Femoral neck fracture	0	1 (0.7%)
Poisoning	1 (1.3%)	0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Dose Interruption of Paclitaxel, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Psychiatric disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	1 (0.7%)
Total number of events	1	1
Anxiety	1 (1.3%)	0
Imperception	0	1 (0.7%)
Eye disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Visual impairment	0	1 (0.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Total number of patients with at least one such adverse event	1 (1.3%)	0
Total number of events	1	0
Tumour necrosis	1 (1.3%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
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Adverse Events Leading to Dose Interruption of Paclitaxel, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	67 (65.7%)
Overall total number of events	204
Blood and lymphatic system disorders	
Total number of patients with at least one such adverse event	20 (19.6%)
Total number of events	48
Neutropenia	16 (15.7%)
Anaemia	2 (2.0%)
Leukopenia	2 (2.0%)
Febrile neutropenia	1 (1.0%)
Thrombocytopenia	1 (1.0%)
Infections and infestations	
Total number of patients with at least one such adverse event	20 (19.6%)
Total number of events	24
COVID-19	4 (3.9%)
Upper respiratory tract infection	4 (3.9%)
Pneumonia	3 (2.9%)
Urinary tract infection	3 (2.9%)
Herpes zoster	2 (2.0%)
Influenza	2 (2.0%)
Bronchitis	1 (1.0%)
Gastroenteritis	1 (1.0%)
Nasopharyngitis	1 (1.0%)
Oral candidiasis	1 (1.0%)
Rhinitis	1 (1.0%)
Skin infection	1 (1.0%)
Gastrointestinal disorders	
Total number of patients with at least one such adverse event	15 (14.7%)
Total number of events	19
Diarrhoea	9 (8.8%)
Nausea	4 (3.9%)
Abdominal pain	1 (1.0%)
Abdominal pain upper	1 (1.0%)
Gastrooesophageal reflux disease	1 (1.0%)
Paraesthesia oral	1 (1.0%)
Stomatitis	1 (1.0%)
Vomiting	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Paclitaxel, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
General disorders and administration site conditions	
Total number of patients with at least one such adverse event	15 (14.7%)
Total number of events	19
Pyrexia	7 (6.9%)
Fatigue	4 (3.9%)
Asthenia	2 (2.0%)
General physical health deterioration	1 (1.0%)
Influenza like illness	1 (1.0%)
Non-cardiac chest pain	1 (1.0%)
Pain	1 (1.0%)
Sensation of foreign body	1 (1.0%)
Investigations	
Total number of patients with at least one such adverse event	15 (14.7%)
Total number of events	40
Alanine aminotransferase increased	8 (7.8%)
Aspartate aminotransferase increased	7 (6.9%)
Neutrophil count decreased	6 (5.9%)
Amylase increased	1 (1.0%)
Blood alkaline phosphatase increased	1 (1.0%)
Lipase increased	1 (1.0%)
Weight decreased	1 (1.0%)
White blood cell count decreased	1 (1.0%)
Skin and subcutaneous tissue disorders	
Total number of patients with at least one such adverse event	11 (10.8%)
Total number of events	12
Rash	4 (3.9%)
Pruritus	2 (2.0%)
Erythema	1 (1.0%)
Hyperhidrosis	1 (1.0%)
Onycholysis	1 (1.0%)
Rash erythematous	1 (1.0%)
Rash pruritic	1 (1.0%)
Scar pain	1 (1.0%)
Respiratory, thoracic and mediastinal disorders	
Total number of patients with at least one such adverse event	7 (6.9%)
Total number of events	8
Dyspnoea	3 (2.9%)
Immune-mediated lung disease	1 (1.0%)
Lung infiltration	1 (1.0%)
Pneumonitis	1 (1.0%)
Respiratory disorder	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Paclitaxel, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hepatobiliary disorders	
Total number of patients with at least one such adverse event	5 (4.9%)
Total number of events	5
Autoimmune hepatitis	2 (2.0%)
Cholecystitis	1 (1.0%)
Hyperbilirubinaemia	1 (1.0%)
Hypertransaminasaemia	1 (1.0%)
Nervous system disorders	
Total number of patients with at least one such adverse event	5 (4.9%)
Total number of events	7
Cognitive disorder	1 (1.0%)
Dizziness	1 (1.0%)
Dystonia	1 (1.0%)
Hypoaesthesia	1 (1.0%)
Neuropathy peripheral	1 (1.0%)
Tremor	1 (1.0%)
Injury, poisoning and procedural complications	
Total number of patients with at least one such adverse event	4 (3.9%)
Total number of events	4
Infusion related reaction	2 (2.0%)
Procedural pain	1 (1.0%)
Vascular access site inflammation	1 (1.0%)
Metabolism and nutrition disorders	
Total number of patients with at least one such adverse event	4 (3.9%)
Total number of events	6
Dehydration	2 (2.0%)
Hyperglycaemia	2 (2.0%)
Diabetic ketoacidosis	1 (1.0%)
Musculoskeletal and connective tissue disorders	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Back pain	2 (2.0%)
Myositis	1 (1.0%)

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Adverse Events Leading to Dose Interruption of Paclitaxel, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Tumour necrosis	2 (2.0%)
Infected neoplasm	1 (1.0%)
Vascular disorders	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Flushing	2 (2.0%)
Phlebitis	1 (1.0%)
Cardiac disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Myocarditis	1 (1.0%)
Endocrine disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Hypothyroidism	1 (1.0%)
Renal and urinary disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Acute kidney injury	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
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Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one such adverse event	7 (8.0%)	46 (27.7%)
Overall total number of events	10	63
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	28 (16.9%)
Total number of events	2	32
Diarrhoea	2 (2.3%)	23 (13.9%)
Nausea	0	3 (1.8%)
Abdominal pain	0	1 (0.6%)
Colitis	0	1 (0.6%)
Stomatitis	0	1 (0.6%)
Investigations		
Total number of patients with at least one such adverse event	3 (3.4%)	8 (4.8%)
Total number of events	5	11
Alanine aminotransferase increased	1 (1.1%)	4 (2.4%)
Aspartate aminotransferase increased	1 (1.1%)	4 (2.4%)
Neutrophil count decreased	2 (2.3%)	2 (1.2%)
Weight decreased	0	1 (0.6%)
White blood cell count decreased	1 (1.1%)	0
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	6 (3.6%)
Total number of events	3	7
Hyperglycaemia	2 (2.3%)	4 (2.4%)
Decreased appetite	0	2 (1.2%)
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	0	7 (4.2%)
Total number of events	0	8
Neutropenia	0	4 (2.4%)
Febrile neutropenia	0	3 (1.8%)
Skin and subcutaneous tissue disorders		
Total number of patients with at least one such adverse event	0	2 (1.2%)
Total number of events	0	2
Rash	0	2 (1.2%)
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Fatigue	0	1 (0.6%)
Injury, poisoning and procedural complications		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Eschar	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Nervous system disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Neuropathy peripheral	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
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Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one such adverse event	6 (8.0%)	50 (34.5%)
Overall total number of events	10	75
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	35 (24.1%)
Total number of events	1	42
Diarrhoea	0	33 (22.8%)
Nausea	1 (1.3%)	2 (1.4%)
Aphthous ulcer	0	1 (0.7%)
Vomiting	0	1 (0.7%)
Investigations		
Total number of patients with at least one such adverse event	3 (4.0%)	9 (6.2%)
Total number of events	4	14
Neutrophil count decreased	3 (4.0%)	6 (4.1%)
Alanine aminotransferase increased	0	2 (1.4%)
Aspartate aminotransferase increased	0	1 (0.7%)
Blood creatine phosphokinase increased	0	1 (0.7%)
Gamma-glutamyltransferase increased	0	1 (0.7%)
White blood cell count decreased	0	1 (0.7%)
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	2 (2.7%)	4 (2.8%)
Total number of events	3	5
Neutropenia	2 (2.7%)	2 (1.4%)
Leukopenia	0	2 (1.4%)
Febrile neutropenia	0	1 (0.7%)
Skin and subcutaneous tissue disorders		
Total number of patients with at least one such adverse event	0	6 (4.1%)
Total number of events	0	6
Rash	0	2 (1.4%)
Rash maculo-papular	0	2 (1.4%)
Erythema multiforme	0	1 (0.7%)
Rash erythematous	0	1 (0.7%)
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	0	5 (3.4%)
Total number of events	0	5
Hyperglycaemia	0	3 (2.1%)
Decreased appetite	0	2 (1.4%)

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Adverse Events Leading to Dose Reduction of Ipatasertib/Placebo, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	1 (1.3%)	1 (0.7%)
Total number of events	2	1
Asthenia	1 (1.3%)	0
Fatigue	1 (1.3%)	0
Oedema peripheral	0	1 (0.7%)
Nervous system disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Peripheral sensory neuropathy	0	1 (0.7%)
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Pneumonitis	0	1 (0.7%)

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Adverse Events Leading to Dose Reduction of Ipatasertib, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	37 (36.3%)
Overall total number of events	52
Gastrointestinal disorders	
Total number of patients with at least one such adverse event	25 (24.5%)
Total number of events	29
Diarrhoea	21 (20.6%)
Nausea	4 (3.9%)
Vomiting	1 (1.0%)
Investigations	
Total number of patients with at least one such adverse event	5 (4.9%)
Total number of events	9
Neutrophil count decreased	3 (2.9%)
Alanine aminotransferase increased	1 (1.0%)
Aspartate aminotransferase increased	1 (1.0%)
Blood triglycerides increased	1 (1.0%)
Lipase increased	1 (1.0%)
Metabolism and nutrition disorders	
Total number of patients with at least one such adverse event	5 (4.9%)
Total number of events	6
Hyperglycaemia	5 (4.9%)
Blood and lymphatic system disorders	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Neutropenia	2 (2.0%)
Febrile neutropenia	1 (1.0%)
Eye disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Visual impairment	1 (1.0%)
Hepatobiliary disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Hyperbilirubinaemia	1 (1.0%)

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Adverse Events Leading to Dose Reduction of Ipatasertib, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Infections and infestations	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Gastroenteritis	1 (1.0%)
Nervous system disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Dizziness	1 (1.0%)
Skin and subcutaneous tissue disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Rash	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
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Adverse Events Leading to Dose Reduction of Paclitaxel, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one such adverse event	9 (10.3%)	34 (20.5%)
Overall total number of events	10	39
Nervous system disorders		
Total number of patients with at least one such adverse event	3 (3.4%)	13 (7.8%)
Total number of events	3	13
Peripheral sensory neuropathy	2 (2.3%)	5 (3.0%)
Neuropathy peripheral	1 (1.1%)	5 (3.0%)
Neurotoxicity	0	1 (0.6%)
Paraesthesia	0	1 (0.6%)
Peripheral motor neuropathy	0	1 (0.6%)
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	0	8 (4.8%)
Total number of events	0	8
Neutropenia	0	5 (3.0%)
Febrile neutropenia	0	2 (1.2%)
Anaemia	0	1 (0.6%)
Investigations		
Total number of patients with at least one such adverse event	2 (2.3%)	6 (3.6%)
Total number of events	3	8
Neutrophil count decreased	2 (2.3%)	3 (1.8%)
Alanine aminotransferase increased	0	3 (1.8%)
Aspartate aminotransferase increased	0	2 (1.2%)
White blood cell count decreased	1 (1.1%)	0
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	3 (3.4%)	3 (1.8%)
Total number of events	3	3
Fatigue	1 (1.1%)	1 (0.6%)
Asthenia	0	1 (0.6%)
Ill-defined disorder	1 (1.1%)	0
Oedema	0	1 (0.6%)
Oedema peripheral	1 (1.1%)	0
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	0	2 (1.2%)
Total number of events	0	2
Diarrhoea	0	2 (1.2%)
Injury, poisoning and procedural complications		
Total number of patients with at least one such adverse event	1 (1.1%)	1 (0.6%)
Total number of events	1	1
Eschar	0	1 (0.6%)
Toxicity to various agents	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_DSRPAC_A_SE.out
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Adverse Events Leading to Dose Reduction of Paclitaxel, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	0	2 (1.2%)
Total number of events	0	2
Decreased appetite	0	1 (0.6%)
Hyperglycaemia	0	1 (0.6%)
Renal and urinary disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Oliguria	0	1 (0.6%)
Vascular disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Hypotension	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_DSRPAC_A_SE.out
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Adverse Events Leading to Dose Reduction of Paclitaxel, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one such adverse event	19 (25.3%)	39 (26.9%)
Overall total number of events	23	46
Nervous system disorders		
Total number of patients with at least one such adverse event	6 (8.0%)	19 (13.1%)
Total number of events	6	20
Neuropathy peripheral	2 (2.7%)	9 (6.2%)
Peripheral sensory neuropathy	2 (2.7%)	5 (3.4%)
Polyneuropathy	1 (1.3%)	3 (2.1%)
Neurotoxicity	1 (1.3%)	1 (0.7%)
Peripheral motor neuropathy	0	1 (0.7%)
Investigations		
Total number of patients with at least one such adverse event	4 (5.3%)	8 (5.5%)
Total number of events	4	10
Neutrophil count decreased	3 (4.0%)	8 (5.5%)
Alanine aminotransferase increased	1 (1.3%)	0
White blood cell count decreased	0	1 (0.7%)
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	4 (5.3%)	6 (4.1%)
Total number of events	5	6
Neutropenia	3 (4.0%)	5 (3.4%)
Anaemia	1 (1.3%)	1 (0.7%)
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	4 (5.3%)	2 (1.4%)
Total number of events	5	2
Oedema peripheral	1 (1.3%)	2 (1.4%)
Asthenia	2 (2.7%)	0
Gait disturbance	1 (1.3%)	0
Oedema	1 (1.3%)	0
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	0	5 (3.4%)
Total number of events	0	5
Diarrhoea	0	4 (2.8%)
Nausea	0	1 (0.7%)
Infections and infestations		
Total number of patients with at least one such adverse event	2 (2.7%)	1 (0.7%)
Total number of events	2	1
Cystitis	2 (2.7%)	0
Paronychia	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_DSRPAC_B_SE.out
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Adverse Events Leading to Dose Reduction of Paclitaxel, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Injury, poisoning and procedural complications		
Total number of patients with at least one such adverse event	1 (1.3%)	0
Total number of events	1	0
Poisoning	1 (1.3%)	0
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Decreased appetite	0	1 (0.7%)
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Pneumonitis	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_DSRPAC_B_SE.out
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Adverse Events Leading to Dose Reduction of Paclitaxel, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	25 (24.5%)
Overall total number of events	28
Nervous system disorders	
Total number of patients with at least one such adverse event	12 (11.8%)
Total number of events	12
Neuropathy peripheral	8 (7.8%)
Polyneuropathy	3 (2.9%)
Dizziness	1 (1.0%)
Investigations	
Total number of patients with at least one such adverse event	6 (5.9%)
Total number of events	7
Neutrophil count decreased	3 (2.9%)
Alanine aminotransferase increased	2 (2.0%)
Aspartate aminotransferase increased	1 (1.0%)
Weight decreased	1 (1.0%)
Blood and lymphatic system disorders	
Total number of patients with at least one such adverse event	4 (3.9%)
Total number of events	4
Neutropenia	3 (2.9%)
Anaemia	1 (1.0%)
Gastrointestinal disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Diarrhoea	2 (2.0%)
Eye disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Visual impairment	1 (1.0%)
General disorders and administration site conditions	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Oedema peripheral	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_DSRPAC_C_SE.out
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Adverse Events Leading to Dose Reduction of Paclitaxel, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Skin and subcutaneous tissue disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Nail disorder	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_DSRPAC_C_SE.out
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Serious Adverse Events with an Incidence Rate of at Least 1% in Any Treatment Arm by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Diarrhoea	0	6 (3.6%)
Pneumonia	4 (4.6%)	2 (1.2%)
Febrile neutropenia	0	3 (1.8%)
Pleural effusion	2 (2.3%)	1 (0.6%)
Pulmonary embolism	0	3 (1.8%)
Anaemia	1 (1.1%)	1 (0.6%)
Dyspnoea	1 (1.1%)	1 (0.6%)
Nausea	0	2 (1.2%)
Neutropenia	1 (1.1%)	1 (0.6%)
Spinal fracture	1 (1.1%)	1 (0.6%)
Vomiting	0	2 (1.2%)
Cellulitis	1 (1.1%)	0
Colitis	1 (1.1%)	0
Gastric cancer	1 (1.1%)	0
Haemoptysis	1 (1.1%)	0
Infected neoplasm	1 (1.1%)	0
Intervertebral disc compression	1 (1.1%)	0
Lymphangiosis carcinomatosa	1 (1.1%)	0
Pneumothorax	1 (1.1%)	0
Procedural pain	1 (1.1%)	0
Sinus tachycardia	1 (1.1%)	0
Skin laceration	1 (1.1%)	0
Thrombocytopenia	1 (1.1%)	0
Tumour lysis syndrome	1 (1.1%)	0
Upper gastrointestinal haemorrhage	1 (1.1%)	0
Viral infection	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_1P_SER_A_SE.out
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Serious Adverse Events with an Incidence Rate of at Least 1% in Any Treatment Arm by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Diarrhoea	1 (1.3%)	4 (2.8%)
Pneumonia	1 (1.3%)	2 (1.4%)
Cholecystitis acute	1 (1.3%)	1 (0.7%)
Febrile neutropenia	0	2 (1.4%)
Neutropenia	0	2 (1.4%)
Pneumonitis	0	2 (1.4%)
Acute kidney injury	1 (1.3%)	0
Fatigue	1 (1.3%)	0
Femur fracture	1 (1.3%)	0
Hydronephrosis	1 (1.3%)	0
Leukopenia	1 (1.3%)	0
Pulmonary embolism	1 (1.3%)	0
Sepsis	1 (1.3%)	0
Tumour necrosis	1 (1.3%)	0
Upper respiratory tract infection	1 (1.3%)	0
Urinary tract infection	1 (1.3%)	0
Wound infection	1 (1.3%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_1P_SER_B_SE.out
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Serious Adverse Events with an Incidence Rate of at Least 1% by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diarrhoea	4 (3.9%)
Pyrexia	4 (3.9%)
Pneumonia	3 (2.9%)
Urinary tract infection	3 (2.9%)
Cholecystitis	2 (2.0%)
Dehydration	2 (2.0%)
Fatigue	2 (2.0%)
Febrile neutropenia	2 (2.0%)
Pneumonitis	2 (2.0%)
Rash	2 (2.0%)
Tumour necrosis	2 (2.0%)
Vomiting	2 (2.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_1P_SER_C_SE.out
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Adverse Events with a Difference of at Least 2% between Treatment Arms by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Diarrhoea	28 (32.2%)	141 (84.9%)
Alopecia	38 (43.7%)	78 (47.0%)
Nausea	22 (25.3%)	66 (39.8%)
Constipation	31 (35.6%)	49 (29.5%)
Vomiting	8 (9.2%)	54 (32.5%)
Peripheral sensory neuropathy	19 (21.8%)	32 (19.3%)
Neutropenia	21 (24.1%)	28 (16.9%)
Asthenia	10 (11.5%)	35 (21.1%)
Hyperglycaemia	9 (10.3%)	31 (18.7%)
Decreased appetite	10 (11.5%)	29 (17.5%)
Headache	10 (11.5%)	28 (16.9%)
Rash	11 (12.6%)	26 (15.7%)
Alanine aminotransferase increased	7 (8.0%)	23 (13.9%)
Arthralgia	12 (13.8%)	16 (9.6%)
Oedema peripheral	7 (8.0%)	18 (10.8%)
Aspartate aminotransferase increased	6 (6.9%)	18 (10.8%)
Cough	10 (11.5%)	14 (8.4%)
Stomatitis	6 (6.9%)	18 (10.8%)
Pyrexia	6 (6.9%)	16 (9.6%)
Myalgia	5 (5.7%)	16 (9.6%)
Abdominal pain	5 (5.7%)	15 (9.0%)
Dysgeusia	8 (9.2%)	10 (6.0%)
Dyspepsia	4 (4.6%)	14 (8.4%)
Pain in extremity	4 (4.6%)	14 (8.4%)
Dyspnoea	7 (8.0%)	8 (4.8%)
Epistaxis	3 (3.4%)	12 (7.2%)
Upper respiratory tract infection	3 (3.4%)	12 (7.2%)
Urinary tract infection	2 (2.3%)	13 (7.8%)
Weight decreased	3 (3.4%)	12 (7.2%)
Dizziness	8 (9.2%)	6 (3.6%)
Nasopharyngitis	3 (3.4%)	11 (6.6%)
Mucosal inflammation	2 (2.3%)	11 (6.6%)
Oropharyngeal pain	0	13 (7.8%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2D_A_SE.out
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Adverse Events with a Difference of at Least 2% between Treatment Arms by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Polyneuropathy	7 (8.0%)	5 (3.0%)
Hypertriglyceridaemia	2 (2.3%)	9 (5.4%)
Pneumonia	5 (5.7%)	6 (3.6%)
Anxiety	2 (2.3%)	8 (4.8%)
Blood alkaline phosphatase increased	1 (1.1%)	9 (5.4%)
Hypersensitivity	5 (5.7%)	5 (3.0%)
Paraesthesia	2 (2.3%)	8 (4.8%)
Vertigo	1 (1.1%)	9 (5.4%)
Influenza like illness	1 (1.1%)	8 (4.8%)
COVID-19	0	8 (4.8%)
Dermatitis acneiform	1 (1.1%)	7 (4.2%)
Erythema	5 (5.7%)	3 (1.8%)
Bone pain	0	7 (4.2%)
Hypomagnesaemia	1 (1.1%)	6 (3.6%)
Lymphoedema	0	7 (4.2%)
Pain	1 (1.1%)	6 (3.6%)
Blood creatinine increased	0	6 (3.6%)
Dermatitis allergic	0	6 (3.6%)
Abdominal distension	0	5 (3.0%)
Dyspnoea exertional	3 (3.4%)	2 (1.2%)
Lipase increased	0	5 (3.0%)
Musculoskeletal pain	3 (3.4%)	2 (1.2%)
Onychoclasis	3 (3.4%)	2 (1.2%)
Rash maculo-papular	0	5 (3.0%)
Syncope	0	5 (3.0%)
Thrombocytopenia	4 (4.6%)	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2D_A_SE.out
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Adverse Events with a Difference of at Least 2% between Treatment Arms by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Dry skin	4 (4.6%)	0
Febrile neutropenia	0	4 (2.4%)
Gastrooesophageal reflux disease	0	4 (2.4%)
Hypophosphataemia	3 (3.4%)	1 (0.6%)
Muscular weakness	3 (3.4%)	1 (0.6%)
Oral candidiasis	3 (3.4%)	1 (0.6%)
Oral herpes	0	4 (2.4%)
Vascular access site pain	3 (3.4%)	1 (0.6%)
Hyperbilirubinaemia	3 (3.4%)	0
Tachycardia	3 (3.4%)	0
Chest discomfort	2 (2.3%)	0
Infusion site extravasation	2 (2.3%)	0
Ocular hyperaemia	2 (2.3%)	0
Onychomadesis	2 (2.3%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2D_A_SE.out
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Adverse Events with a Difference of at Least 2% between Treatment Arms by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Diarrhoea	30 (40.0%)	126 (86.9%)
Alopecia	44 (58.7%)	75 (51.7%)
Nausea	17 (22.7%)	60 (41.4%)
Constipation	26 (34.7%)	42 (29.0%)
Anaemia	15 (20.0%)	45 (31.0%)
Neuropathy peripheral	12 (16.0%)	46 (31.7%)
Neutropenia	18 (24.0%)	38 (26.2%)
Vomiting	6 (8.0%)	45 (31.0%)
Fatigue	19 (25.3%)	29 (20.0%)
Peripheral sensory neuropathy	23 (30.7%)	23 (15.9%)
Neutrophil count decreased	18 (24.0%)	23 (15.9%)
Rash	9 (12.0%)	31 (21.4%)
Arthralgia	10 (13.3%)	26 (17.9%)
Oedema peripheral	14 (18.7%)	21 (14.5%)
Alanine aminotransferase increased	15 (20.0%)	19 (13.1%)
Headache	8 (10.7%)	24 (16.6%)
Cough	6 (8.0%)	23 (15.9%)
Decreased appetite	7 (9.3%)	22 (15.2%)
Back pain	7 (9.3%)	21 (14.5%)
Pyrexia	4 (5.3%)	23 (15.9%)
Nasopharyngitis	7 (9.3%)	19 (13.1%)
Aspartate aminotransferase increased	10 (13.3%)	13 (9.0%)
Stomatitis	6 (8.0%)	16 (11.0%)
Urinary tract infection	5 (6.7%)	16 (11.0%)
Abdominal pain upper	5 (6.7%)	15 (10.3%)
Epistaxis	4 (5.3%)	15 (10.3%)
Pruritus	3 (4.0%)	15 (10.3%)
Nail discolouration	8 (10.7%)	9 (6.2%)
Leukopenia	8 (10.7%)	8 (5.5%)
Dysgeusia	4 (5.3%)	11 (7.6%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2D_B_SE.out
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Adverse Events with a Difference of at Least 2% between Treatment Arms by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Blood lactate dehydrogenase increased	8 (10.7%)	5 (3.4%)
Cystitis	6 (8.0%)	7 (4.8%)
Dizziness	3 (4.0%)	10 (6.9%)
Oropharyngeal pain	2 (2.7%)	11 (7.6%)
Dyspnoea	2 (2.7%)	10 (6.9%)
Insomnia	6 (8.0%)	6 (4.1%)
Lymphoedema	5 (6.7%)	6 (4.1%)
Blood alkaline phosphatase increased	7 (9.3%)	3 (2.1%)
Dry skin	5 (6.7%)	5 (3.4%)
Weight decreased	2 (2.7%)	7 (4.8%)
Gastrooesophageal reflux disease	4 (5.3%)	4 (2.8%)
Influenza like illness	1 (1.3%)	7 (4.8%)
Muscle spasms	5 (6.7%)	3 (2.1%)
Paronychia	1 (1.3%)	7 (4.8%)
Accidental overdose	1 (1.3%)	6 (4.1%)
Dry eye	1 (1.3%)	6 (4.1%)
Amylase increased	1 (1.3%)	5 (3.4%)
Herpes zoster	1 (1.3%)	5 (3.4%)
Mouth ulceration	1 (1.3%)	5 (3.4%)
Onycholysis	1 (1.3%)	5 (3.4%)
Pneumonitis	0	6 (4.1%)
Rhinitis	0	6 (4.1%)
Rhinorrhoea	0	6 (4.1%)
Cataract	3 (4.0%)	2 (1.4%)
Muscular weakness	3 (4.0%)	2 (1.4%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2D_B_SE.out
08MAY2023 6:26

Adverse Events with a Difference of at Least 2% between Treatment Arms by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Aphthous ulcer	0	4 (2.8%)
Blood triglycerides increased	0	4 (2.8%)
Dehydration	0	4 (2.8%)
Haemorrhoids	0	4 (2.8%)
Nail dystrophy	3 (4.0%)	1 (0.7%)
Onychomadesis	0	4 (2.8%)
Peripheral motor neuropathy	0	4 (2.8%)
Vascular access site pain	0	4 (2.8%)
Breast pain	0	3 (2.1%)
Drug eruption	0	3 (2.1%)
Eczema	0	3 (2.1%)
Febrile neutropenia	0	3 (2.1%)
Hypertransaminasaemia	0	3 (2.1%)
Lower respiratory tract infection	0	3 (2.1%)
Lymphostasis	3 (4.0%)	0
Nasal congestion	0	3 (2.1%)
Oral herpes	0	3 (2.1%)
Oral pain	0	3 (2.1%)
Pulmonary embolism	3 (4.0%)	0
Sinusitis	0	3 (2.1%)
Thrombocytopenia	0	3 (2.1%)
Treatment noncompliance	0	3 (2.1%)
Urticaria	0	3 (2.1%)
Weight increased	3 (4.0%)	0
Hydronephrosis	2 (2.7%)	0
Poisoning	2 (2.7%)	0
Respiratory tract infection viral	2 (2.7%)	0
Skin ulcer	2 (2.7%)	0
Tooth abscess	2 (2.7%)	0
Tracheitis	2 (2.7%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2D_B_SE.out
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Serious Adverse Events with a Difference of at Least 2% between Treatment Arms by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Diarrhoea	0	6 (3.6%)
Pneumonia	4 (4.6%)	2 (1.2%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2D_SER_A_SE.out
08MAY2023 6:35 Page 1 of 1

Serious Adverse Events with a Difference of at Least 2% between Treatment Arms by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Null Report: No results could be derived for this output.

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2D_SER_B_SE.out
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Serious Adverse Events Related to Atezolizumab with an Incidence Rate of at Least 2% by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Null Report: No results could be derived for this output.

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2P_SER_RELATZ_C_SE.out
08MAY2023 6:34 Page 1 of 1

Serious Adverse Events Related to Ipatasertib/Placebo with an Incidence Rate of at Least 2% in Any Treatment Arm by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Diarrhoea	0	6 (3.6%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2P_SER_RELIPAT_A_SE.out
08MAY2023 6:30 Page 1 of 1

Serious Adverse Events Related to Ipatasertib/Placebo with an Incidence Rate of at Least 2% in Any Treatment Arm by Preferred Term,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Diarrhoea	1 (1.3%)	4 (2.8%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2P_SER_RELIPAT_B_SE.out
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Serious Adverse Events Related to Ipatasertib with an Incidence Rate of at Least 2% by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diarrhoea	3 (2.9%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2P_SER_RELIPAT_C_SE.out
08MAY2023 6:31 Page 1 of 1

Serious Adverse Events Related to Paclitaxel with an Incidence Rate of at Least 2% in Any Treatment Arm by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Pneumonia	2 (2.3%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2P_SER_RELPAC_A_SE.out
08MAY2023 6:32 Page 1 of 1

Serious Adverse Events Related to Paclitaxel with an Incidence Rate of at Least 2% in Any Treatment Arm by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Null Report: No results could be derived for this output.

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2P_SER_RELPAC_B_SE.out
08MAY2023 6:33 Page 1 of 1

Serious Adverse Events Related to Paclitaxel with an Incidence Rate of at Least 2% by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Null Report: No results could be derived for this output.

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_2P_SER_RELPAC_C_SE.out
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Adverse Events with an Incidence Rate of at Least 10% in Any Treatment Arm by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Diarrhoea	30 (40.0%)	126 (86.9%)
Alopecia	44 (58.7%)	75 (51.7%)
Nausea	17 (22.7%)	60 (41.4%)
Constipation	26 (34.7%)	42 (29.0%)
Anaemia	15 (20.0%)	45 (31.0%)
Neuropathy peripheral	12 (16.0%)	46 (31.7%)
Neutropenia	18 (24.0%)	38 (26.2%)
Vomiting	6 (8.0%)	45 (31.0%)
Fatigue	19 (25.3%)	29 (20.0%)
Peripheral sensory neuropathy	23 (30.7%)	23 (15.9%)
Neutrophil count decreased	18 (24.0%)	23 (15.9%)
Asthenia	13 (17.3%)	27 (18.6%)
Rash	9 (12.0%)	31 (21.4%)
Arthralgia	10 (13.3%)	26 (17.9%)
Oedema peripheral	14 (18.7%)	21 (14.5%)
Alanine aminotransferase increased	15 (20.0%)	19 (13.1%)
Headache	8 (10.7%)	24 (16.6%)
Cough	6 (8.0%)	23 (15.9%)
Decreased appetite	7 (9.3%)	22 (15.2%)
Hyperglycaemia	10 (13.3%)	19 (13.1%)
Back pain	7 (9.3%)	21 (14.5%)
Pyrexia	4 (5.3%)	23 (15.9%)
Nasopharyngitis	7 (9.3%)	19 (13.1%)
Myalgia	9 (12.0%)	15 (10.3%)
Aspartate aminotransferase increased	10 (13.3%)	13 (9.0%)
Stomatitis	6 (8.0%)	16 (11.0%)
Urinary tract infection	5 (6.7%)	16 (11.0%)
Abdominal pain upper	5 (6.7%)	15 (10.3%)
Epistaxis	4 (5.3%)	15 (10.3%)
Pruritus	3 (4.0%)	15 (10.3%)
Nail discolouration	8 (10.7%)	9 (6.2%)
Leukopenia	8 (10.7%)	8 (5.5%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_10P_B_SE.out
08MAY2023 6:28

Adverse Events with an Incidence Rate of at Least 10% in Any Treatment Arm by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Blood lactate dehydrogenase increased	8 (10.7%)	5 (3.4%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_10P_B_SE.out
08MAY2023 6:28

Adverse Events by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diarrhoea	86 (84.3%)
Alopecia	42 (41.2%)
Nausea	42 (41.2%)
Anaemia	34 (33.3%)
Rash	31 (30.4%)
Neuropathy peripheral	30 (29.4%)
Vomiting	29 (28.4%)
Alanine aminotransferase increased	26 (25.5%)
Neutropenia	25 (24.5%)
Fatigue	23 (22.5%)
Aspartate aminotransferase increased	22 (21.6%)
Hyperglycaemia	22 (21.6%)
Headache	21 (20.6%)
Asthenia	19 (18.6%)
Pruritus	17 (16.7%)
Cough	16 (15.7%)
Decreased appetite	14 (13.7%)
Arthralgia	13 (12.7%)
Constipation	13 (12.7%)
Abdominal pain	12 (11.8%)
Blood alkaline phosphatase increased	12 (11.8%)
Mucosal inflammation	12 (11.8%)
Pyrexia	12 (11.8%)
Leukopenia	11 (10.8%)
Back pain	10 (9.8%)
Dizziness	10 (9.8%)
Insomnia	10 (9.8%)
Myalgia	10 (9.8%)
Urinary tract infection	10 (9.8%)
Dyspnoea	9 (8.8%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_C_SE.out
08MAY2023 6:39

Adverse Events by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Epistaxis	8 (7.8%)
Flushing	8 (7.8%)
Hypertension	8 (7.8%)
Hypokalaemia	8 (7.8%)
Neutrophil count decreased	8 (7.8%)
Peripheral sensory neuropathy	8 (7.8%)
Polyneuropathy	8 (7.8%)
Upper respiratory tract infection	8 (7.8%)
Blood lactate dehydrogenase increased	7 (6.9%)
Oedema peripheral	7 (6.9%)
Pneumonitis	7 (6.9%)
Stomatitis	7 (6.9%)
Weight decreased	7 (6.9%)
Abdominal pain upper	6 (5.9%)
Accidental overdose	6 (5.9%)
Dysgeusia	6 (5.9%)
Dyspepsia	6 (5.9%)
Hyperbilirubinaemia	6 (5.9%)
Hypothyroidism	6 (5.9%)
Oropharyngeal pain	6 (5.9%)
Pneumonia	6 (5.9%)
Weight increased	6 (5.9%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_C_SE.out
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Adverse Events by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Anxiety	5 (4.9%)
Blood cholesterol increased	5 (4.9%)
Chills	5 (4.9%)
Depression	5 (4.9%)
Dry eye	5 (4.9%)
Dry mouth	5 (4.9%)
Gastrooesophageal reflux disease	5 (4.9%)
Hypoaesthesia	5 (4.9%)
Hypoalbuminaemia	5 (4.9%)
Muscle spasms	5 (4.9%)
Nasopharyngitis	5 (4.9%)
Pain	5 (4.9%)
Paraesthesia	5 (4.9%)
Rash maculo-papular	5 (4.9%)
White blood cell count decreased	5 (4.9%)
Blood bilirubin increased	4 (3.9%)
Blood triglycerides increased	4 (3.9%)
Breast pain	4 (3.9%)
COVID-19	4 (3.9%)
Chest pain	4 (3.9%)
Herpes zoster	4 (3.9%)
Hot flush	4 (3.9%)
Hypercholesterolaemia	4 (3.9%)
Hypertriglyceridaemia	4 (3.9%)
Hyponatraemia	4 (3.9%)
Influenza	4 (3.9%)
Lipase increased	4 (3.9%)
Low density lipoprotein increased	4 (3.9%)
Pain in extremity	4 (3.9%)
Rhinitis	4 (3.9%)
Toothache	4 (3.9%)
Vision blurred	4 (3.9%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_C_SE.out
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Adverse Events by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Abdominal discomfort	3 (2.9%)
Acute kidney injury	3 (2.9%)
Autoimmune hepatitis	3 (2.9%)
Conjunctivitis	3 (2.9%)
Dehydration	3 (2.9%)
Dermatitis acneiform	3 (2.9%)
Dyslipidaemia	3 (2.9%)
Dysphonia	3 (2.9%)
Erythema	3 (2.9%)
Flatulence	3 (2.9%)
Hand dermatitis	3 (2.9%)
Hypercalcaemia	3 (2.9%)
Hyperkalaemia	3 (2.9%)
Influenza like illness	3 (2.9%)
Lymphoedema	3 (2.9%)
Lymphopenia	3 (2.9%)
Musculoskeletal chest pain	3 (2.9%)
Oedema	3 (2.9%)
Oral candidiasis	3 (2.9%)
Pulmonary embolism	3 (2.9%)
Respiratory disorder	3 (2.9%)
Rhinorrhoea	3 (2.9%)
Tremor	3 (2.9%)
Acne	2 (2.0%)
Balance disorder	2 (2.0%)
Blood glucose increased	2 (2.0%)
Blood thyroid stimulating hormone increased	2 (2.0%)
Bone pain	2 (2.0%)
Cholecystitis	2 (2.0%)
Cognitive disorder	2 (2.0%)
Cystitis	2 (2.0%)
Dermatitis allergic	2 (2.0%)
Dyspnoea exertional	2 (2.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_C_SE.out
08MAY2023 6:39

Adverse Events by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Encephalopathy	2 (2.0%)
Fall	2 (2.0%)
Febrile neutropenia	2 (2.0%)
Haemorrhoids	2 (2.0%)
High density lipoprotein increased	2 (2.0%)
Hypercreatininaemia	2 (2.0%)
Hyperhidrosis	2 (2.0%)
Hypersensitivity	2 (2.0%)
Hypoacusis	2 (2.0%)
Hypomagnesaemia	2 (2.0%)
Infusion related reaction	2 (2.0%)
Lethargy	2 (2.0%)
Mastitis	2 (2.0%)
Mouth ulceration	2 (2.0%)
Nail disorder	2 (2.0%)
Nail dystrophy	2 (2.0%)
Nasal congestion	2 (2.0%)
Non-cardiac chest pain	2 (2.0%)
Paronychia	2 (2.0%)
Periorbital oedema	2 (2.0%)
Peripheral motor neuropathy	2 (2.0%)
Platelet count decreased	2 (2.0%)
Pleural effusion	2 (2.0%)
Procedural pain	2 (2.0%)
Productive cough	2 (2.0%)
Rash erythematous	2 (2.0%)
Rash papular	2 (2.0%)
Respiratory tract infection viral	2 (2.0%)
Rhinitis allergic	2 (2.0%)
Seasonal allergy	2 (2.0%)
Skin hyperpigmentation	2 (2.0%)
Skin infection	2 (2.0%)
Spinal pain	2 (2.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_C_SE.out
08MAY2023 6:39

Adverse Events by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Thirst	2 (2.0%)
Tinnitus	2 (2.0%)
Tooth infection	2 (2.0%)
Tumour necrosis	2 (2.0%)
Tumour pain	2 (2.0%)
Vertigo	2 (2.0%)
Vulvovaginal dryness	2 (2.0%)
Abdominal distension	1 (1.0%)
Abnormal sensation in eye	1 (1.0%)
Alkalosis	1 (1.0%)
Amenorrhoea	1 (1.0%)
Amnesia	1 (1.0%)
Amylase increased	1 (1.0%)
Anti-GAD antibody positive	1 (1.0%)
Anti-islet cell antibody positive	1 (1.0%)
Artificial menopause	1 (1.0%)
Autoimmune hypothyroidism	1 (1.0%)
Axillary pain	1 (1.0%)
Basophil percentage increased	1 (1.0%)
Blood chloride decreased	1 (1.0%)
Blood lactate dehydrogenase decreased	1 (1.0%)
Blood pressure increased	1 (1.0%)
Breast discharge	1 (1.0%)
Breath odour	1 (1.0%)
Bronchitis	1 (1.0%)
Bronchospasm	1 (1.0%)
Burning sensation mucosal	1 (1.0%)
Carbon dioxide decreased	1 (1.0%)
Cardiac arrest	1 (1.0%)
Cellulitis	1 (1.0%)
Cerebrovascular insufficiency	1 (1.0%)
Chest discomfort	1 (1.0%)
Cholestasis	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_C_SE.out
08MAY2023 6:39

Adverse Events by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Contrast media allergy	1 (1.0%)
Contrast media reaction	1 (1.0%)
Contusion	1 (1.0%)
Dental caries	1 (1.0%)
Dental discomfort	1 (1.0%)
Depressed mood	1 (1.0%)
Dermatitis contact	1 (1.0%)
Diabetes mellitus	1 (1.0%)
Diabetic ketoacidosis	1 (1.0%)
Dry skin	1 (1.0%)
Dysphagia	1 (1.0%)
Dystonia	1 (1.0%)
Ear pain	1 (1.0%)
Eczema	1 (1.0%)
Embolism	1 (1.0%)
Emphysematous cystitis	1 (1.0%)
Eosinophil percentage increased	1 (1.0%)
Eosinophilia	1 (1.0%)
Epigastric discomfort	1 (1.0%)
Eye disorder	1 (1.0%)
Eye irritation	1 (1.0%)
Eyelid function disorder	1 (1.0%)
Facial pain	1 (1.0%)
Faecal volume increased	1 (1.0%)
Fluid retention	1 (1.0%)
Foreign body sensation in eyes	1 (1.0%)
Fungal skin infection	1 (1.0%)
Furuncle	1 (1.0%)
Gamma-glutamyltransferase increased	1 (1.0%)
Gastroenteritis	1 (1.0%)
Gastroenteritis norovirus	1 (1.0%)
Gastrointestinal disorder	1 (1.0%)
Gastrooesophageal sphincter insufficiency	1 (1.0%)

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Adverse Events by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
General physical health deterioration	1 (1.0%)
Generalised oedema	1 (1.0%)
Gingival pain	1 (1.0%)
Gingivitis	1 (1.0%)
Glomerular filtration rate decreased	1 (1.0%)
Glycosylated haemoglobin increased	1 (1.0%)
Haematocrit decreased	1 (1.0%)
Hordeolum	1 (1.0%)
Hyperphosphataemia	1 (1.0%)
Hypersomnia	1 (1.0%)
Hyperthermia	1 (1.0%)
Hyperthyroidism	1 (1.0%)
Hypertransaminasaemia	1 (1.0%)
Hypocalcaemia	1 (1.0%)
Hypophosphataemia	1 (1.0%)
Immature granulocyte count increased	1 (1.0%)
Immature granulocyte percentage increased	1 (1.0%)
Immune-mediated lung disease	1 (1.0%)
Incorrect dose administered	1 (1.0%)
Increased appetite	1 (1.0%)
Infected neoplasm	1 (1.0%)
Injury	1 (1.0%)
Intentional overdose	1 (1.0%)
Intentional product misuse	1 (1.0%)
Intestinal mucosal atrophy	1 (1.0%)
Irritability	1 (1.0%)
Joint swelling	1 (1.0%)
Jugular vein thrombosis	1 (1.0%)
Lacrimation increased	1 (1.0%)
Large intestine perforation	1 (1.0%)
Ligament sprain	1 (1.0%)
Lung infiltration	1 (1.0%)
Lymphadenopathy	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Lymphocyte count decreased	1 (1.0%)
Madarosis	1 (1.0%)
Mass	1 (1.0%)
Mean cell volume decreased	1 (1.0%)
Memory impairment	1 (1.0%)
Metamyelocyte percentage increased	1 (1.0%)
Migraine	1 (1.0%)
Miliaria	1 (1.0%)
Mixed connective tissue disease	1 (1.0%)
Monocyte percentage decreased	1 (1.0%)
Musculoskeletal pain	1 (1.0%)
Musculoskeletal stiffness	1 (1.0%)
Myocarditis	1 (1.0%)
Myositis	1 (1.0%)
Nail bed tenderness	1 (1.0%)
Nail discolouration	1 (1.0%)
Nail infection	1 (1.0%)
Nail ridging	1 (1.0%)
Nasal crusting	1 (1.0%)
Neurotoxicity	1 (1.0%)
Night sweats	1 (1.0%)
Oesophagitis	1 (1.0%)
Onychalgia	1 (1.0%)
Onychoclasis	1 (1.0%)
Onycholysis	1 (1.0%)
Onychomadesis	1 (1.0%)
Oral discomfort	1 (1.0%)
Oral herpes	1 (1.0%)
Oral pain	1 (1.0%)
Overdose	1 (1.0%)
Oxygen saturation decreased	1 (1.0%)
Paraesthesia oral	1 (1.0%)
Paraneoplastic syndrome	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Perioral dermatitis	1 (1.0%)
Peripheral swelling	1 (1.0%)
Pharyngitis	1 (1.0%)
Phlebitis	1 (1.0%)
Pleuritic pain	1 (1.0%)
Pneumonia viral	1 (1.0%)
Pneumothorax	1 (1.0%)
Polydipsia	1 (1.0%)
Posterior reversible encephalopathy syndrome	1 (1.0%)
Postoperative wound infection	1 (1.0%)
Proctalgia	1 (1.0%)
Product dose omission in error	1 (1.0%)
Product dose omission issue	1 (1.0%)
Prothrombin time prolonged	1 (1.0%)
Rash pruritic	1 (1.0%)
Rash pustular	1 (1.0%)
Red blood cell count decreased	1 (1.0%)
Retching	1 (1.0%)
Retinal tear	1 (1.0%)
Rib fracture	1 (1.0%)
Scar pain	1 (1.0%)
Seborrhoeic dermatitis	1 (1.0%)
Sensation of foreign body	1 (1.0%)
Sinus tachycardia	1 (1.0%)
Skin exfoliation	1 (1.0%)
Skin lesion	1 (1.0%)
Sleep disorder	1 (1.0%)
Somnolence	1 (1.0%)
Stress	1 (1.0%)
Suspected COVID-19	1 (1.0%)
Tachycardia	1 (1.0%)
Taste disorder	1 (1.0%)
Thoracic radiculopathy	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
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Adverse Events by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Thrombocytopenia	1 (1.0%)
Thrombocytosis	1 (1.0%)
Tonsillitis	1 (1.0%)
Tooth abscess	1 (1.0%)
Transient ischaemic attack	1 (1.0%)
Tri-iodothyronine increased	1 (1.0%)
Tumour fistulisation	1 (1.0%)
Tumour inflammation	1 (1.0%)
Type 1 diabetes mellitus	1 (1.0%)
Urethritis	1 (1.0%)
Urge incontinence	1 (1.0%)
Urinary incontinence	1 (1.0%)
Urogenital infection fungal	1 (1.0%)
Urticaria	1 (1.0%)
Vaginal discharge	1 (1.0%)
Vascular access site inflammation	1 (1.0%)
Vascular access site pain	1 (1.0%)
Vascular device occlusion	1 (1.0%)
Ventricular extrasystoles	1 (1.0%)
Visual impairment	1 (1.0%)
Vitreous detachment	1 (1.0%)
Vulvovaginal discomfort	1 (1.0%)
Vulvovaginal pruritus	1 (1.0%)
Wheezing	1 (1.0%)
White blood cell count increased	1 (1.0%)
Wound	1 (1.0%)
Wound infection	1 (1.0%)
Wound secretion	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_C_SE.out
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Adverse Events Leading to Dose Interruption of Atezolizumab by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Aspartate aminotransferase increased	7 (6.9%)
Neutropenia	7 (6.9%)
Pyrexia	6 (5.9%)
Rash	6 (5.9%)
Alanine aminotransferase increased	5 (4.9%)
Diarrhoea	5 (4.9%)
COVID-19	4 (3.9%)
Pneumonitis	4 (3.9%)
Upper respiratory tract infection	4 (3.9%)
Fatigue	3 (2.9%)
Hyperglycaemia	3 (2.9%)
Nausea	3 (2.9%)
Acute kidney injury	2 (2.0%)
Blood alkaline phosphatase increased	2 (2.0%)
Dehydration	2 (2.0%)
Febrile neutropenia	2 (2.0%)
Influenza	2 (2.0%)
Pruritus	2 (2.0%)
Respiratory disorder	2 (2.0%)
Tumour necrosis	2 (2.0%)
Urinary tract infection	2 (2.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSIATZ_C_SE.out
08MAY2023 6:10

Adverse Events Leading to Dose Interruption of Atezolizumab by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Amylase increased	1 (1.0%)
Back pain	1 (1.0%)
Blood bilirubin increased	1 (1.0%)
Blood lactate dehydrogenase increased	1 (1.0%)
Bronchitis	1 (1.0%)
Cerebrovascular insufficiency	1 (1.0%)
Cholecystitis	1 (1.0%)
Diabetic ketoacidosis	1 (1.0%)
Dyspnoea	1 (1.0%)
Gastroenteritis	1 (1.0%)
General physical health deterioration	1 (1.0%)
Herpes zoster	1 (1.0%)
Hypertransaminasaemia	1 (1.0%)
Hypothyroidism	1 (1.0%)
Immune-mediated lung disease	1 (1.0%)
Influenza like illness	1 (1.0%)
Infusion related reaction	1 (1.0%)
Lipase increased	1 (1.0%)
Lung infiltration	1 (1.0%)
Myocarditis	1 (1.0%)
Myositis	1 (1.0%)
Neutrophil count decreased	1 (1.0%)
Onycholysis	1 (1.0%)
Procedural pain	1 (1.0%)
Pulmonary embolism	1 (1.0%)
Rash erythematous	1 (1.0%)
Rash maculo-papular	1 (1.0%)
Rash papular	1 (1.0%)
Rash pruritic	1 (1.0%)
Respiratory tract infection viral	1 (1.0%)
Rhinitis	1 (1.0%)
Vascular access site inflammation	1 (1.0%)
Weight decreased	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSIATZ_C_SE.out
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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Diarrhoea	0	14 (8.4%)
Neutropenia	4 (4.6%)	10 (6.0%)
Hyperglycaemia	2 (2.3%)	8 (4.8%)
Neutrophil count decreased	4 (4.6%)	5 (3.0%)
COVID-19	0	6 (3.6%)
Nausea	1 (1.1%)	4 (2.4%)
Rash	1 (1.1%)	4 (2.4%)
Anaemia	1 (1.1%)	3 (1.8%)
Pneumonia	2 (2.3%)	2 (1.2%)
Vomiting	1 (1.1%)	3 (1.8%)
Asthenia	1 (1.1%)	2 (1.2%)
Herpes zoster	1 (1.1%)	2 (1.2%)
Pleural effusion	2 (2.3%)	1 (0.6%)
Pyrexia	1 (1.1%)	2 (1.2%)
Upper respiratory tract infection	0	3 (1.8%)
Alanine aminotransferase increased	1 (1.1%)	1 (0.6%)
Headache	0	2 (1.2%)
Hypertriglyceridaemia	0	2 (1.2%)
Mucosal inflammation	0	2 (1.2%)
Neuropathy peripheral	1 (1.1%)	1 (0.6%)
Pruritus	0	2 (1.2%)
Spinal fracture	1 (1.1%)	1 (0.6%)
Abdominal discomfort	0	1 (0.6%)
Abdominal pain	0	1 (0.6%)
Abscess jaw	0	1 (0.6%)
Accidental overdose	0	1 (0.6%)
Anuria	0	1 (0.6%)
Anxiety	0	1 (0.6%)
Arthralgia	1 (1.1%)	0
Aspartate aminotransferase increased	1 (1.1%)	0
Ataxia	0	1 (0.6%)
Atrial fibrillation	0	1 (0.6%)
Breast pain	1 (1.1%)	0

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSIIPAT_A_SE.out
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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Bronchiolitis	0	1 (0.6%)
Bronchitis	0	1 (0.6%)
COVID-19 pneumonia	0	1 (0.6%)
Cellulitis	1 (1.1%)	0
Cholecystitis acute	0	1 (0.6%)
Colitis	1 (1.1%)	0
Conjunctivitis	0	1 (0.6%)
Cough	0	1 (0.6%)
Cystoid macular oedema	1 (1.1%)	0
Decreased appetite	0	1 (0.6%)
Dermatitis allergic	0	1 (0.6%)
Dizziness	1 (1.1%)	0
Dyspepsia	0	1 (0.6%)
Dyspnoea	0	1 (0.6%)
Dysuria	0	1 (0.6%)
Electrolyte imbalance	0	1 (0.6%)
Enteritis	0	1 (0.6%)
Erysipelas	1 (1.1%)	0
Face oedema	0	1 (0.6%)
Fatigue	0	1 (0.6%)
Glaucoma	0	1 (0.6%)
Haemoptysis	1 (1.1%)	0
Hyperamylasaemia	1 (1.1%)	0
Hyperlipasaemia	1 (1.1%)	0
Hypersensitivity	0	1 (0.6%)
Hypokalaemia	0	1 (0.6%)
Infected neoplasm	1 (1.1%)	0
Influenza A virus test positive	0	1 (0.6%)
Influenza like illness	0	1 (0.6%)
Intervertebral disc compression	1 (1.1%)	0
Leukopenia	0	1 (0.6%)
Localised oedema	0	1 (0.6%)
Lymphangiosis carcinomatosa	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Lymphoedema	0	1 (0.6%)
Malaise	0	1 (0.6%)
Oropharyngeal pain	0	1 (0.6%)
Pancreatitis	0	1 (0.6%)
Peripheral sensory neuropathy	0	1 (0.6%)
Pneumonitis	0	1 (0.6%)
Proteinuria	0	1 (0.6%)
Rash maculo-papular	0	1 (0.6%)
Renal failure	0	1 (0.6%)
Respiratory tract infection viral	0	1 (0.6%)
Schwannoma	0	1 (0.6%)
Skin infection	0	1 (0.6%)
Skin laceration	1 (1.1%)	0
Swelling face	0	1 (0.6%)
Tachycardia	1 (1.1%)	0
Tooth abscess	1 (1.1%)	0
Tooth infection	0	1 (0.6%)
Tumour haemorrhage	0	1 (0.6%)
Tumour necrosis	0	1 (0.6%)
Upper gastrointestinal haemorrhage	1 (1.1%)	0
Urinary tract infection	0	1 (0.6%)
Viral infection	1 (1.1%)	0
White blood cell count decreased	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
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Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Neutrophil count decreased	6 (8.0%)	11 (7.6%)
Diarrhoea	0	14 (9.7%)
Neutropenia	6 (8.0%)	7 (4.8%)
Vomiting	0	7 (4.8%)
Alanine aminotransferase increased	2 (2.7%)	4 (2.8%)
Hyperglycaemia	1 (1.3%)	4 (2.8%)
Upper respiratory tract infection	2 (2.7%)	3 (2.1%)
Herpes zoster	1 (1.3%)	3 (2.1%)
Abdominal pain	1 (1.3%)	2 (1.4%)
Abdominal pain upper	1 (1.3%)	2 (1.4%)
Aspartate aminotransferase increased	1 (1.3%)	2 (1.4%)
Asthenia	1 (1.3%)	2 (1.4%)
Drug eruption	0	3 (2.1%)
Fatigue	2 (2.7%)	1 (0.7%)
Nausea	0	3 (2.1%)
Rash	0	3 (2.1%)
Amylase increased	0	2 (1.4%)
Cellulitis	0	2 (1.4%)
Cholecystitis acute	1 (1.3%)	1 (0.7%)
Decreased appetite	1 (1.3%)	1 (0.7%)
Dizziness	2 (2.7%)	0
Enterocolitis	0	2 (1.4%)
Influenza	0	2 (1.4%)
Malaise	1 (1.3%)	1 (0.7%)
Myalgia	0	2 (1.4%)
Neuropathy peripheral	1 (1.3%)	1 (0.7%)
Paraesthesia	0	2 (1.4%)
Pruritus	0	2 (1.4%)
Pyrexia	1 (1.3%)	1 (0.7%)
Rash maculo-papular	1 (1.3%)	1 (0.7%)
Stomatitis	1 (1.3%)	1 (0.7%)
Abdominal abscess	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSIIPAT_B_SE.out
08MAY2023 6:07

Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Abdominal hernia	0	1 (0.7%)
Alopecia	0	1 (0.7%)
Anaemia	0	1 (0.7%)
Anxiety	0	1 (0.7%)
Appendicitis	0	1 (0.7%)
Arthritis	0	1 (0.7%)
Blood creatinine increased	0	1 (0.7%)
Bronchitis	0	1 (0.7%)
C-reactive protein increased	0	1 (0.7%)
COVID-19	1 (1.3%)	0
Cough	0	1 (0.7%)
Dehydration	0	1 (0.7%)
Dermatitis bullous	0	1 (0.7%)
Diarrhoea infectious	0	1 (0.7%)
Erythema	1 (1.3%)	0
Femoral neck fracture	0	1 (0.7%)
Femur fracture	1 (1.3%)	0
Glycosylated haemoglobin increased	0	1 (0.7%)
Hyperbilirubinaemia	0	1 (0.7%)
Hypersensitivity	0	1 (0.7%)
Hypertransaminasaemia	0	1 (0.7%)
Hypertriglyceridaemia	1 (1.3%)	0
Hypoglycaemia	0	1 (0.7%)
Imperception	0	1 (0.7%)
Infection	0	1 (0.7%)
Intestinal obstruction	0	1 (0.7%)
Leukopenia	1 (1.3%)	0
Lipase increased	0	1 (0.7%)
Lower respiratory tract infection	0	1 (0.7%)
Mucosal inflammation	0	1 (0.7%)
Nasopharyngitis	0	1 (0.7%)
Odynophagia	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSIIPAT_B_SE.out
08MAY2023 6:07

Adverse Events Leading to Dose Interruption of Ipatasertib/Placebo by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Oedema	0	1 (0.7%)
Oedema peripheral	1 (1.3%)	0
Oropharyngeal pain	0	1 (0.7%)
Paraesthesia oral	0	1 (0.7%)
Pathological fracture	0	1 (0.7%)
Peripheral sensory neuropathy	1 (1.3%)	0
Peripheral swelling	1 (1.3%)	0
Pharyngitis	0	1 (0.7%)
Pneumonia	1 (1.3%)	0
Pneumonitis	0	1 (0.7%)
Pulmonary embolism	1 (1.3%)	0
Respiratory tract infection viral	1 (1.3%)	0
Sinus tachycardia	0	1 (0.7%)
Supraventricular tachycardia	0	1 (0.7%)
Thrombosis	1 (1.3%)	0
Tumour necrosis	1 (1.3%)	0
Venous thrombosis limb	0	1 (0.7%)
Vertigo	0	1 (0.7%)
Vitreous floaters	1 (1.3%)	0
White blood cell count decreased	1 (1.3%)	0
Wound infection	1 (1.3%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSIIPAT_B_SE.out
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Adverse Events Leading to Dose Interruption of Ipatasertib by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diarrhoea	15 (14.7%)
Neutropenia	10 (9.8%)
Alanine aminotransferase increased	6 (5.9%)
Aspartate aminotransferase increased	6 (5.9%)
Pyrexia	6 (5.9%)
Rash	6 (5.9%)
Hyperglycaemia	5 (4.9%)
Nausea	5 (4.9%)
Neutrophil count decreased	4 (3.9%)
COVID-19	3 (2.9%)
Upper respiratory tract infection	3 (2.9%)
Acute kidney injury	2 (2.0%)
Dehydration	2 (2.0%)
Influenza	2 (2.0%)
Pneumonitis	2 (2.0%)
Pruritus	2 (2.0%)
Rash maculo-papular	2 (2.0%)
Tumour necrosis	2 (2.0%)
Urinary tract infection	2 (2.0%)
Vomiting	2 (2.0%)
Accidental overdose	1 (1.0%)
Amylase increased	1 (1.0%)
Asthenia	1 (1.0%)
Autoimmune hepatitis	1 (1.0%)
Blood alkaline phosphatase increased	1 (1.0%)
Blood bilirubin increased	1 (1.0%)
Blood glucose increased	1 (1.0%)
Blood lactate dehydrogenase increased	1 (1.0%)
Bronchitis	1 (1.0%)
Cholecystitis	1 (1.0%)
Dyspnoea	1 (1.0%)
Dystonia	1 (1.0%)
Fatigue	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
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08MAY2023 6:07

Adverse Events Leading to Dose Interruption of Ipatasertib by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Febrile neutropenia	1 (1.0%)
Gastroenteritis norovirus	1 (1.0%)
Gastrooesophageal reflux disease	1 (1.0%)
General physical health deterioration	1 (1.0%)
Herpes zoster	1 (1.0%)
Hyperbilirubinaemia	1 (1.0%)
Hypertransaminasaemia	1 (1.0%)
Hypothyroidism	1 (1.0%)
Immune-mediated lung disease	1 (1.0%)
Infected neoplasm	1 (1.0%)
Influenza like illness	1 (1.0%)
Lipase increased	1 (1.0%)
Lung infiltration	1 (1.0%)
Myocarditis	1 (1.0%)
Myositis	1 (1.0%)
Onycholysis	1 (1.0%)
Pain	1 (1.0%)
Pneumonia	1 (1.0%)
Procedural pain	1 (1.0%)
Rash erythematous	1 (1.0%)
Rash pruritic	1 (1.0%)
Respiratory disorder	1 (1.0%)
Rhinitis	1 (1.0%)
Toothache	1 (1.0%)
Weight decreased	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
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Adverse Events Leading to Dose Interruption of Paclitaxel by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Neutropenia	13 (14.9%)	20 (12.0%)
Neutrophil count decreased	8 (9.2%)	15 (9.0%)
Anaemia	1 (1.1%)	7 (4.2%)
Nausea	0	8 (4.8%)
Diarrhoea	0	7 (4.2%)
Asthenia	2 (2.3%)	4 (2.4%)
COVID-19	0	6 (3.6%)
Upper respiratory tract infection	1 (1.1%)	5 (3.0%)
Pneumonia	3 (3.4%)	2 (1.2%)
Pyrexia	2 (2.3%)	3 (1.8%)
Alanine aminotransferase increased	2 (2.3%)	2 (1.2%)
Hyperglycaemia	2 (2.3%)	2 (1.2%)
Rash	0	4 (2.4%)
Aspartate aminotransferase increased	2 (2.3%)	1 (0.6%)
Dyspnoea	1 (1.1%)	2 (1.2%)
Fatigue	0	3 (1.8%)
Leukopenia	1 (1.1%)	2 (1.2%)
Neuropathy peripheral	1 (1.1%)	2 (1.2%)
Pleural effusion	2 (2.3%)	1 (0.6%)
Vomiting	0	3 (1.8%)
White blood cell count decreased	2 (2.3%)	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSIPAC_A_SE.out
08MAY2023 6:08

Adverse Events Leading to Dose Interruption of Paclitaxel by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Bone pain	0	2 (1.2%)
Bronchitis	0	2 (1.2%)
Decreased appetite	0	2 (1.2%)
Dermatitis allergic	0	2 (1.2%)
Flushing	1 (1.1%)	1 (0.6%)
Herpes zoster	0	2 (1.2%)
Hyperbilirubinaemia	2 (2.3%)	0
Hypersensitivity	0	2 (1.2%)
Influenza like illness	0	2 (1.2%)
Peripheral sensory neuropathy	1 (1.1%)	1 (0.6%)
Respiratory tract infection viral	0	2 (1.2%)
Spinal fracture	1 (1.1%)	1 (0.6%)
Wound	0	2 (1.2%)
Abdominal pain	0	1 (0.6%)
Abscess jaw	0	1 (0.6%)
Altered state of consciousness	0	1 (0.6%)
Anxiety	0	1 (0.6%)
Arthralgia	1 (1.1%)	0
Ataxia	0	1 (0.6%)
Atrial fibrillation	0	1 (0.6%)
Back pain	0	1 (0.6%)
Breast pain	1 (1.1%)	0
Bronchiolitis	0	1 (0.6%)
COVID-19 pneumonia	0	1 (0.6%)
Cellulitis	1 (1.1%)	0
Chest pain	1 (1.1%)	0
Cholecystitis acute	0	1 (0.6%)
Colitis	1 (1.1%)	0
Cough	0	1 (0.6%)
Cystitis	1 (1.1%)	0
Cystoid macular oedema	1 (1.1%)	0
Device related infection	0	1 (0.6%)
Dizziness	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
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Adverse Events Leading to Dose Interruption of Paclitaxel by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Dysgeusia	0	1 (0.6%)
Dysuria	0	1 (0.6%)
Eastern Cooperative Oncology Group performance status worsened	0	1 (0.6%)
Electrolyte imbalance	0	1 (0.6%)
Embolism	0	1 (0.6%)
Enteritis	0	1 (0.6%)
Erysipelas	1 (1.1%)	0
Erythema	0	1 (0.6%)
Face oedema	0	1 (0.6%)
Fall	0	1 (0.6%)
Febrile neutropenia	0	1 (0.6%)
Fracture	0	1 (0.6%)
Furuncle	0	1 (0.6%)
Haemoptysis	1 (1.1%)	0
Headache	0	1 (0.6%)
Hyperamylasaemia	1 (1.1%)	0
Hyperhidrosis	1 (1.1%)	0
Hyperlipasaemia	1 (1.1%)	0
Hypertension	0	1 (0.6%)
Hypertensive crisis	0	1 (0.6%)
Hypertriglyceridaemia	0	1 (0.6%)
Hypokalaemia	0	1 (0.6%)
Hypotension	1 (1.1%)	0
Hypoxia	1 (1.1%)	0
INFLUENSA VIROSA*	0	1 (0.6%)
Infected neoplasm	1 (1.1%)	0
Influenza	1 (1.1%)	0
Infusion related reaction	0	1 (0.6%)
Intervertebral disc compression	1 (1.1%)	0
Laryngitis	0	1 (0.6%)
Localised oedema	0	1 (0.6%)
Lymphangiosis carcinomatosa	1 (1.1%)	0
Lymphopenia	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
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Adverse Events Leading to Dose Interruption of Paclitaxel by Preferred Term, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Mucosal inflammation	0	1 (0.6%)
Nail infection	0	1 (0.6%)
Nasopharyngitis	1 (1.1%)	0
Non-cardiac chest pain	1 (1.1%)	0
Onycholysis	1 (1.1%)	0
Oropharyngeal pain	0	1 (0.6%)
Pancreatitis	0	1 (0.6%)
Paraesthesia	0	1 (0.6%)
Pathological fracture	0	1 (0.6%)
Periodontitis	0	1 (0.6%)
Proteinuria	0	1 (0.6%)
Pruritus	0	1 (0.6%)
Rash maculo-papular	0	1 (0.6%)
Renal failure	0	1 (0.6%)
Respiratory disorder	1 (1.1%)	0
Schwannoma	0	1 (0.6%)
Seizure	0	1 (0.6%)
Skin infection	0	1 (0.6%)
Stomatitis	0	1 (0.6%)
Tachypnoea	0	1 (0.6%)
Thrombocytopenia	1 (1.1%)	0
Tooth abscess	1 (1.1%)	0
Tooth infection	0	1 (0.6%)
Tumour haemorrhage	0	1 (0.6%)
Tumour necrosis	0	1 (0.6%)
Upper gastrointestinal haemorrhage	1 (1.1%)	0
Urinary tract infection	0	1 (0.6%)
Vertigo	0	1 (0.6%)
Viral infection	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
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Adverse Events Leading to Dose Interruption of Paclitaxel by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Neutrophil count decreased	13 (17.3%)	17 (11.7%)
Neutropenia	10 (13.3%)	19 (13.1%)
Diarrhoea	0	10 (6.9%)
Alanine aminotransferase increased	2 (2.7%)	5 (3.4%)
Asthenia	1 (1.3%)	4 (2.8%)
Herpes zoster	1 (1.3%)	4 (2.8%)
Neuropathy peripheral	1 (1.3%)	4 (2.8%)
Pyrexia	2 (2.7%)	3 (2.1%)
Rash	0	5 (3.4%)
Abdominal pain	1 (1.3%)	3 (2.1%)
Aspartate aminotransferase increased	1 (1.3%)	3 (2.1%)
Fatigue	3 (4.0%)	1 (0.7%)
Hyperbilirubinaemia	1 (1.3%)	3 (2.1%)
Leukopenia	3 (4.0%)	1 (0.7%)
Paraesthesia	2 (2.7%)	2 (1.4%)
Upper respiratory tract infection	2 (2.7%)	2 (1.4%)
Vomiting	0	4 (2.8%)
Myalgia	0	3 (2.1%)
Nasopharyngitis	1 (1.3%)	2 (1.4%)
Pneumonia	3 (4.0%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
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08MAY2023 6:09

Adverse Events Leading to Dose Interruption of Paclitaxel by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Arthritis	0	2 (1.4%)
Bronchitis	0	2 (1.4%)
Cholecystitis acute	1 (1.3%)	1 (0.7%)
Cystitis	1 (1.3%)	1 (0.7%)
Decreased appetite	1 (1.3%)	1 (0.7%)
Dyspnoea	1 (1.3%)	1 (0.7%)
Enterocolitis	0	2 (1.4%)
Erythema	2 (2.7%)	0
Influenza	0	2 (1.4%)
Malaise	1 (1.3%)	1 (0.7%)
Nausea	0	2 (1.4%)
Oedema peripheral	1 (1.3%)	1 (0.7%)
Pruritus	0	2 (1.4%)
Pulmonary embolism	2 (2.7%)	0
Respiratory tract infection viral	2 (2.7%)	0
Thrombocytopenia	0	2 (1.4%)
Urinary tract infection	0	2 (1.4%)
White blood cell count decreased	1 (1.3%)	1 (0.7%)
Wound infection	1 (1.3%)	1 (0.7%)
Abdominal abscess	0	1 (0.7%)
Abdominal hernia	0	1 (0.7%)
Abdominal pain upper	0	1 (0.7%)
Amylase increased	0	1 (0.7%)
Anaemia	0	1 (0.7%)
Anxiety	1 (1.3%)	0
Aphthous ulcer	0	1 (0.7%)
Appendicitis	0	1 (0.7%)
Ascites	0	1 (0.7%)
Blood alkaline phosphatase increased	1 (1.3%)	0
Blood creatine phosphokinase increased	0	1 (0.7%)
Blood creatinine increased	0	1 (0.7%)
COVID-19	1 (1.3%)	0
Catheter site erythema	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
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Adverse Events Leading to Dose Interruption of Paclitaxel by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Cellulitis	0	1 (0.7%)
Chest discomfort	0	1 (0.7%)
Chest pain	1 (1.3%)	0
Cough	0	1 (0.7%)
Dehydration	0	1 (0.7%)
Dermatitis allergic	1 (1.3%)	0
Dizziness	1 (1.3%)	0
Drug eruption	0	1 (0.7%)
Drug hypersensitivity	0	1 (0.7%)
Dyspepsia	0	1 (0.7%)
Erysipelas	0	1 (0.7%)
Femoral neck fracture	0	1 (0.7%)
Flank pain	1 (1.3%)	0
Flushing	1 (1.3%)	0
Glycosylated haemoglobin increased	0	1 (0.7%)
Haemorrhage	0	1 (0.7%)
Headache	1 (1.3%)	0
Hyperglycaemia	0	1 (0.7%)
Hypersensitivity	0	1 (0.7%)
Hypertension	0	1 (0.7%)
Hyperthermia	1 (1.3%)	0
Hypertransaminasaemia	0	1 (0.7%)
Hypertriglyceridaemia	1 (1.3%)	0
Hypoaesthesia oral	0	1 (0.7%)
Imperception	0	1 (0.7%)
Infection	0	1 (0.7%)
Influenza like illness	0	1 (0.7%)
Infusion site extravasation	0	1 (0.7%)
Intestinal obstruction	0	1 (0.7%)
Laryngitis	0	1 (0.7%)
Lipase increased	0	1 (0.7%)
Lower respiratory tract infection	0	1 (0.7%)
Muscle tone disorder	1 (1.3%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
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Adverse Events Leading to Dose Interruption of Paclitaxel by Preferred Term, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Nail discolouration	0	1 (0.7%)
Nail disorder	0	1 (0.7%)
Nail ridging	0	1 (0.7%)
Odynophagia	0	1 (0.7%)
Oedema	0	1 (0.7%)
Oropharyngeal pain	0	1 (0.7%)
Paraesthesia oral	0	1 (0.7%)
Pathological fracture	0	1 (0.7%)
Peripheral sensory neuropathy	0	1 (0.7%)
Peripheral swelling	1 (1.3%)	0
Pneumonitis	0	1 (0.7%)
Poisoning	1 (1.3%)	0
Radiculopathy	1 (1.3%)	0
Rash maculo-papular	0	1 (0.7%)
Respiratory disorder	1 (1.3%)	0
SARS-CoV-2 test positive	0	1 (0.7%)
Skin infection	1 (1.3%)	0
Spinal pain	1 (1.3%)	0
Stomatitis	1 (1.3%)	0
Supraventricular tachycardia	0	1 (0.7%)
Thrombosis	1 (1.3%)	0
Tonsillitis	1 (1.3%)	0
Tracheobronchitis	1 (1.3%)	0
Tumour necrosis	1 (1.3%)	0
Vascular access site infection	0	1 (0.7%)
Venous thrombosis limb	0	1 (0.7%)
Ventricular arrhythmia	1 (1.3%)	0
Viral infection	0	1 (0.7%)
Visual impairment	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Adverse Events Leading to Dose Interruption of Paclitaxel by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Neutropenia	16 (15.7%)
Diarrhoea	9 (8.8%)
Alanine aminotransferase increased	8 (7.8%)
Aspartate aminotransferase increased	7 (6.9%)
Pyrexia	7 (6.9%)
Neutrophil count decreased	6 (5.9%)
COVID-19	4 (3.9%)
Fatigue	4 (3.9%)
Nausea	4 (3.9%)
Rash	4 (3.9%)
Upper respiratory tract infection	4 (3.9%)
Dyspnoea	3 (2.9%)
Pneumonia	3 (2.9%)
Urinary tract infection	3 (2.9%)
Anaemia	2 (2.0%)
Asthenia	2 (2.0%)
Autoimmune hepatitis	2 (2.0%)
Back pain	2 (2.0%)
Dehydration	2 (2.0%)
Flushing	2 (2.0%)
Herpes zoster	2 (2.0%)
Hyperglycaemia	2 (2.0%)
Influenza	2 (2.0%)
Infusion related reaction	2 (2.0%)
Leukopenia	2 (2.0%)
Pruritus	2 (2.0%)
Tumour necrosis	2 (2.0%)
Abdominal pain	1 (1.0%)
Abdominal pain upper	1 (1.0%)
Acute kidney injury	1 (1.0%)
Amylase increased	1 (1.0%)
Blood alkaline phosphatase increased	1 (1.0%)
Bronchitis	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSIPAC_C_SE.out
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Adverse Events Leading to Dose Interruption of Paclitaxel by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cholecystitis	1 (1.0%)
Cognitive disorder	1 (1.0%)
Diabetic ketoacidosis	1 (1.0%)
Dizziness	1 (1.0%)
Dystonia	1 (1.0%)
Erythema	1 (1.0%)
Febrile neutropenia	1 (1.0%)
Gastroenteritis	1 (1.0%)
Gastrooesophageal reflux disease	1 (1.0%)
General physical health deterioration	1 (1.0%)
Hyperbilirubinaemia	1 (1.0%)
Hyperhidrosis	1 (1.0%)
Hypertransaminasaemia	1 (1.0%)
Hypoaesthesia	1 (1.0%)
Hypothyroidism	1 (1.0%)
Immune-mediated lung disease	1 (1.0%)
Infected neoplasm	1 (1.0%)
Influenza like illness	1 (1.0%)
Lipase increased	1 (1.0%)
Lung infiltration	1 (1.0%)
Myocarditis	1 (1.0%)
Myositis	1 (1.0%)
Nasopharyngitis	1 (1.0%)
Neuropathy peripheral	1 (1.0%)
Non-cardiac chest pain	1 (1.0%)
Onycholysis	1 (1.0%)
Oral candidiasis	1 (1.0%)
Pain	1 (1.0%)
Paraesthesia oral	1 (1.0%)
Phlebitis	1 (1.0%)
Pneumonitis	1 (1.0%)
Procedural pain	1 (1.0%)
Rash erythematous	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSIPAC_C_SE.out
08MAY2023 6:09

Adverse Events Leading to Dose Interruption of Paclitaxel by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Rash pruritic	1 (1.0%)
Respiratory disorder	1 (1.0%)
Rhinitis	1 (1.0%)
Scar pain	1 (1.0%)
Sensation of foreign body	1 (1.0%)
Skin infection	1 (1.0%)
Stomatitis	1 (1.0%)
Thrombocytopenia	1 (1.0%)
Tremor	1 (1.0%)
Vascular access site inflammation	1 (1.0%)
Vomiting	1 (1.0%)
Weight decreased	1 (1.0%)
White blood cell count decreased	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_DSIPAC_C_SE.out
08MAY2023 6:09 Page 3 of 3

Adverse Events Related to Atezolizumab Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diarrhoea	34 (33.3%)
Rash	20 (19.6%)
Alanine aminotransferase increased	15 (14.7%)
Nausea	15 (14.7%)
Aspartate aminotransferase increased	13 (12.7%)
Asthenia	11 (10.8%)
Vomiting	10 (9.8%)
Fatigue	9 (8.8%)
Hyperglycaemia	8 (7.8%)
Neuropathy peripheral	8 (7.8%)
Neutropenia	8 (7.8%)
Anaemia	7 (6.9%)
Pneumonitis	7 (6.9%)
Pruritus	7 (6.9%)
Mucosal inflammation	6 (5.9%)
Arthralgia	5 (4.9%)
Blood alkaline phosphatase increased	5 (4.9%)
Hyperbilirubinaemia	5 (4.9%)
Hypothyroidism	4 (3.9%)
Lipase increased	4 (3.9%)
Abdominal pain	3 (2.9%)
Abdominal pain upper	3 (2.9%)
Alopecia	3 (2.9%)
Autoimmune hepatitis	3 (2.9%)
Blood lactate dehydrogenase increased	3 (2.9%)
Gastrooesophageal reflux disease	3 (2.9%)
Headache	3 (2.9%)
Leukopenia	3 (2.9%)
Pyrexia	3 (2.9%)
Urinary tract infection	3 (2.9%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_RELATZ_C_SE.out
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Adverse Events Related to Atezolizumab Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Abdominal discomfort	2 (2.0%)
Blood bilirubin increased	2 (2.0%)
Blood thyroid stimulating hormone increased	2 (2.0%)
Blood triglycerides increased	2 (2.0%)
Constipation	2 (2.0%)
Decreased appetite	2 (2.0%)
Dehydration	2 (2.0%)
Epistaxis	2 (2.0%)
Erythema	2 (2.0%)
Flatulence	2 (2.0%)
Hand dermatitis	2 (2.0%)
Hypercreatininaemia	2 (2.0%)
Hypersensitivity	2 (2.0%)
Hypokalaemia	2 (2.0%)
Insomnia	2 (2.0%)
Muscle spasms	2 (2.0%)
Myalgia	2 (2.0%)
Oedema peripheral	2 (2.0%)
Polyneuropathy	2 (2.0%)
Rash maculo-papular	2 (2.0%)
Stomatitis	2 (2.0%)
Tumour necrosis	2 (2.0%)
Acute kidney injury	1 (1.0%)
Alkalosis	1 (1.0%)
Amylase increased	1 (1.0%)
Autoimmune hypothyroidism	1 (1.0%)
Balance disorder	1 (1.0%)
Blood chloride decreased	1 (1.0%)
Cognitive disorder	1 (1.0%)
Cough	1 (1.0%)
Dental discomfort	1 (1.0%)
Dermatitis allergic	1 (1.0%)
Diabetic ketoacidosis	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_RELATZ_C_SE.out
08MAY2023 6:42

Adverse Events Related to Atezolizumab Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Dizziness	1 (1.0%)
Dry eye	1 (1.0%)
Dry mouth	1 (1.0%)
Dysgeusia	1 (1.0%)
Dyslipidaemia	1 (1.0%)
Dyspepsia	1 (1.0%)
Dystonia	1 (1.0%)
Eczema	1 (1.0%)
Eosinophilia	1 (1.0%)
Eyelid function disorder	1 (1.0%)
Flushing	1 (1.0%)
Furuncle	1 (1.0%)
Generalised oedema	1 (1.0%)
Gingival pain	1 (1.0%)
High density lipoprotein increased	1 (1.0%)
Hypercalcaemia	1 (1.0%)
Hyperkalaemia	1 (1.0%)
Hypersomnia	1 (1.0%)
Hypertension	1 (1.0%)
Hyperthyroidism	1 (1.0%)
Hypertransaminasaemia	1 (1.0%)
Hypertriglyceridaemia	1 (1.0%)
Hypoacusis	1 (1.0%)
Hypoaesthesia	1 (1.0%)
Hypoalbuminaemia	1 (1.0%)
Hypomagnesaemia	1 (1.0%)
Hyponatraemia	1 (1.0%)
Hypophosphataemia	1 (1.0%)
Immune-mediated lung disease	1 (1.0%)
Large intestine perforation	1 (1.0%)
Lethargy	1 (1.0%)
Lung infiltration	1 (1.0%)
Lymphadenopathy	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_RELATZ_C_SE.out
08MAY2023 6:42

Adverse Events Related to Atezolizumab Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Lymphopenia	1 (1.0%)
Mixed connective tissue disease	1 (1.0%)
Mouth ulceration	1 (1.0%)
Musculoskeletal stiffness	1 (1.0%)
Myocarditis	1 (1.0%)
Myositis	1 (1.0%)
Nail bed tenderness	1 (1.0%)
Nail disorder	1 (1.0%)
Neutrophil count decreased	1 (1.0%)
Oedema	1 (1.0%)
Oesophagitis	1 (1.0%)
Oral discomfort	1 (1.0%)
Pain	1 (1.0%)
Pain in extremity	1 (1.0%)
Paraesthesia	1 (1.0%)
Peripheral sensory neuropathy	1 (1.0%)
Pneumonia	1 (1.0%)
Pneumonia viral	1 (1.0%)
Posterior reversible encephalopathy syndrome	1 (1.0%)
Productive cough	1 (1.0%)
Pulmonary embolism	1 (1.0%)
Rash erythematous	1 (1.0%)
Rash papular	1 (1.0%)
Rash pruritic	1 (1.0%)
Seborrhoeic dermatitis	1 (1.0%)
Skin lesion	1 (1.0%)
Thirst	1 (1.0%)
Thrombocytosis	1 (1.0%)
Tinnitus	1 (1.0%)
Tumour inflammation	1 (1.0%)
Type 1 diabetes mellitus	1 (1.0%)
Vertigo	1 (1.0%)
Vision blurred	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_RELATZ_C_SE.out
08MAY2023 6:42

Adverse Events Related to Atezolizumab Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Weight decreased	1 (1.0%)
White blood cell count decreased	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_RELATZ_C_SE.out
08MAY2023 6:42

Adverse Events Related to Ipatasertib Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diarrhoea	85 (83.3%)
Nausea	31 (30.4%)
Rash	23 (22.5%)
Fatigue	18 (17.6%)
Hyperglycaemia	18 (17.6%)
Vomiting	18 (17.6%)
Alanine aminotransferase increased	16 (15.7%)
Asthenia	14 (13.7%)
Aspartate aminotransferase increased	13 (12.7%)
Neutropenia	12 (11.8%)
Anaemia	9 (8.8%)
Pruritus	9 (8.8%)
Neuropathy peripheral	8 (7.8%)
Abdominal pain	7 (6.9%)
Leukopenia	7 (6.9%)
Decreased appetite	6 (5.9%)
Hyperbilirubinaemia	6 (5.9%)
Alopecia	5 (4.9%)
Blood alkaline phosphatase increased	5 (4.9%)
Mucosal inflammation	5 (4.9%)
Accidental overdose	4 (3.9%)
Blood cholesterol increased	4 (3.9%)
Headache	4 (3.9%)
Neutrophil count decreased	4 (3.9%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_RELIPAT_C_SE.out
08MAY2023 6:41

Adverse Events Related to Ipatasertib Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Arthralgia	3 (2.9%)
Blood lactate dehydrogenase increased	3 (2.9%)
Constipation	3 (2.9%)
Dizziness	3 (2.9%)
Dyspepsia	3 (2.9%)
Epistaxis	3 (2.9%)
Hyperkalaemia	3 (2.9%)
Hypertriglyceridaemia	3 (2.9%)
Hypokalaemia	3 (2.9%)
Lipase increased	3 (2.9%)
Low density lipoprotein increased	3 (2.9%)
Lymphopenia	3 (2.9%)
Myalgia	3 (2.9%)
Pneumonitis	3 (2.9%)
Rash maculo-papular	3 (2.9%)
White blood cell count decreased	3 (2.9%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_RELIPAT_C_SE.out
08MAY2023 6:41

Adverse Events Related to Ipatasertib Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Abdominal discomfort	2 (2.0%)
Abdominal pain upper	2 (2.0%)
Blood bilirubin increased	2 (2.0%)
Blood triglycerides increased	2 (2.0%)
Dehydration	2 (2.0%)
Dysgeusia	2 (2.0%)
Flatulence	2 (2.0%)
Gastrooesophageal reflux disease	2 (2.0%)
Hypercholesterolaemia	2 (2.0%)
Hypercreatininaemia	2 (2.0%)
Hypoalbuminaemia	2 (2.0%)
Hyponatraemia	2 (2.0%)
Muscle spasms	2 (2.0%)
Oedema peripheral	2 (2.0%)
Paraesthesia	2 (2.0%)
Pyrexia	2 (2.0%)
Stomatitis	2 (2.0%)
Tumour necrosis	2 (2.0%)
Vision blurred	2 (2.0%)
Acne	1 (1.0%)
Alkalosis	1 (1.0%)
Amylase increased	1 (1.0%)
Back pain	1 (1.0%)
Balance disorder	1 (1.0%)
Basophil percentage increased	1 (1.0%)
Blood chloride decreased	1 (1.0%)
Blood glucose increased	1 (1.0%)
Cognitive disorder	1 (1.0%)
Dental discomfort	1 (1.0%)
Dermatitis allergic	1 (1.0%)
Diabetic ketoacidosis	1 (1.0%)
Dry eye	1 (1.0%)
Dry mouth	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_RELIPAT_C_SE.out
08MAY2023 6:41

Adverse Events Related to Ipatasertib Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Dyslipidaemia	1 (1.0%)
Dyspnoea	1 (1.0%)
Eczema	1 (1.0%)
Eosinophil percentage increased	1 (1.0%)
Eosinophilia	1 (1.0%)
Erythema	1 (1.0%)
Eyelid function disorder	1 (1.0%)
Faecal volume increased	1 (1.0%)
Febrile neutropenia	1 (1.0%)
Flushing	1 (1.0%)
Gamma-glutamyltransferase increased	1 (1.0%)
Gastroenteritis	1 (1.0%)
Gastrooesophageal sphincter insufficiency	1 (1.0%)
Generalised oedema	1 (1.0%)
Gingivitis	1 (1.0%)
Haematocrit decreased	1 (1.0%)
Hand dermatitis	1 (1.0%)
Hypercalcaemia	1 (1.0%)
Hypersensitivity	1 (1.0%)
Hypersomnia	1 (1.0%)
Hypertension	1 (1.0%)
Hypoacusis	1 (1.0%)
Hypoaesthesia	1 (1.0%)
Hypomagnesaemia	1 (1.0%)
Hypophosphataemia	1 (1.0%)
Hypothyroidism	1 (1.0%)
Immature granulocyte count increased	1 (1.0%)
Insomnia	1 (1.0%)
Intentional overdose	1 (1.0%)
Intestinal mucosal atrophy	1 (1.0%)
Large intestine perforation	1 (1.0%)
Lethargy	1 (1.0%)
Lung infiltration	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_RELIPAT_C_SE.out
08MAY2023 6:41

Adverse Events Related to Ipatasertib Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Lymphadenopathy	1 (1.0%)
Lymphocyte count decreased	1 (1.0%)
Monocyte percentage decreased	1 (1.0%)
Mouth ulceration	1 (1.0%)
Nail bed tenderness	1 (1.0%)
Nail disorder	1 (1.0%)
Oedema	1 (1.0%)
Oesophagitis	1 (1.0%)
Oral discomfort	1 (1.0%)
Oral herpes	1 (1.0%)
Pain in extremity	1 (1.0%)
Paronychia	1 (1.0%)
Periorbital oedema	1 (1.0%)
Peripheral sensory neuropathy	1 (1.0%)
Platelet count decreased	1 (1.0%)
Pneumonia	1 (1.0%)
Pneumonia viral	1 (1.0%)
Posterior reversible encephalopathy syndrome	1 (1.0%)
Productive cough	1 (1.0%)
Rash erythematous	1 (1.0%)
Rash papular	1 (1.0%)
Rash pruritic	1 (1.0%)
Red blood cell count decreased	1 (1.0%)
Seborrhoeic dermatitis	1 (1.0%)
Thirst	1 (1.0%)
Thrombocytosis	1 (1.0%)
Tinnitus	1 (1.0%)
Tumour inflammation	1 (1.0%)
Type 1 diabetes mellitus	1 (1.0%)
Urinary tract infection	1 (1.0%)
Vertigo	1 (1.0%)
Visual impairment	1 (1.0%)
Weight decreased	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_RELIPAT_C_SE.out
08MAY2023 6:41

Adverse Events Related to Ipatasertib Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Weight increased	1 (1.0%)
White blood cell count increased	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_RELIPAT_C_SE.out
08MAY2023 6:41 Page 6 of 6

Adverse Events Related to Paclitaxel Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diarrhoea	46 (45.1%)
Alopecia	41 (40.2%)
Nausea	32 (31.4%)
Anaemia	31 (30.4%)
Neuropathy peripheral	28 (27.5%)
Neutropenia	25 (24.5%)
Fatigue	20 (19.6%)
Vomiting	19 (18.6%)
Alanine aminotransferase increased	18 (17.6%)
Asthenia	18 (17.6%)
Aspartate aminotransferase increased	13 (12.7%)
Leukopenia	11 (10.8%)
Mucosal inflammation	10 (9.8%)
Rash	10 (9.8%)
Blood alkaline phosphatase increased	9 (8.8%)
Myalgia	8 (7.8%)
Neutrophil count decreased	8 (7.8%)
Polyneuropathy	8 (7.8%)
Pruritus	8 (7.8%)
Decreased appetite	7 (6.9%)
Epistaxis	7 (6.9%)
Dysgeusia	6 (5.9%)
Flushing	6 (5.9%)
Peripheral sensory neuropathy	6 (5.9%)
Stomatitis	6 (5.9%)
Abdominal pain	5 (4.9%)
Arthralgia	5 (4.9%)
Dyspnoea	5 (4.9%)
Hyperbilirubinaemia	5 (4.9%)
White blood cell count decreased	5 (4.9%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_RELPAC_C_SE.out
08MAY2023 6:42

Adverse Events Related to Paclitaxel Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Dyspepsia	4 (3.9%)
Gastrooesophageal reflux disease	4 (3.9%)
Hyperglycaemia	4 (3.9%)
Hypoaesthesia	4 (3.9%)
Paraesthesia	4 (3.9%)
Abdominal pain upper	3 (2.9%)
Back pain	3 (2.9%)
Blood bilirubin increased	3 (2.9%)
Blood lactate dehydrogenase increased	3 (2.9%)
Constipation	3 (2.9%)
Dehydration	3 (2.9%)
Headache	3 (2.9%)
Lipase increased	3 (2.9%)
Muscle spasms	3 (2.9%)
Oedema	3 (2.9%)
Oedema peripheral	3 (2.9%)
Pyrexia	3 (2.9%)
Weight decreased	3 (2.9%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae_pt.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_pt_RELPAC_C_SE.out
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Adverse Events Related to Paclitaxel Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Abdominal discomfort	2 (2.0%)
Chills	2 (2.0%)
Cognitive disorder	2 (2.0%)
Cough	2 (2.0%)
Dizziness	2 (2.0%)
Dry eye	2 (2.0%)
Dry mouth	2 (2.0%)
Febrile neutropenia	2 (2.0%)
Flatulence	2 (2.0%)
Hand dermatitis	2 (2.0%)
Hot flush	2 (2.0%)
Hyperkalaemia	2 (2.0%)
Infusion related reaction	2 (2.0%)
Lethargy	2 (2.0%)
Lymphopenia	2 (2.0%)
Mouth ulceration	2 (2.0%)
Nail disorder	2 (2.0%)
Nail dystrophy	2 (2.0%)
Oral candidiasis	2 (2.0%)
Pain	2 (2.0%)
Platelet count decreased	2 (2.0%)
Rhinorrhoea	2 (2.0%)
Thirst	2 (2.0%)
Tumour necrosis	2 (2.0%)
Urinary tract infection	2 (2.0%)
Vertigo	2 (2.0%)
Vision blurred	2 (2.0%)
Vulvovaginal dryness	2 (2.0%)
Abnormal sensation in eye	1 (1.0%)
Alkalosis	1 (1.0%)
Amenorrhoea	1 (1.0%)
Amylase increased	1 (1.0%)
Artificial menopause	1 (1.0%)

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Adverse Events Related to Paclitaxel Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Balance disorder	1 (1.0%)
Basophil percentage increased	1 (1.0%)
Bronchitis	1 (1.0%)
Bronchospasm	1 (1.0%)
Burning sensation mucosal	1 (1.0%)
Cerebrovascular insufficiency	1 (1.0%)
Chest discomfort	1 (1.0%)
Conjunctivitis	1 (1.0%)
Dermatitis acneiform	1 (1.0%)
Dermatitis allergic	1 (1.0%)
Dyslipidaemia	1 (1.0%)
Eczema	1 (1.0%)
Encephalopathy	1 (1.0%)
Eosinophil percentage increased	1 (1.0%)
Eosinophilia	1 (1.0%)
Erythema	1 (1.0%)
Eye disorder	1 (1.0%)
Eye irritation	1 (1.0%)
Eyelid function disorder	1 (1.0%)
Fluid retention	1 (1.0%)
Foreign body sensation in eyes	1 (1.0%)
Generalised oedema	1 (1.0%)
Gingival pain	1 (1.0%)
Gingivitis	1 (1.0%)
Haematocrit decreased	1 (1.0%)
High density lipoprotein increased	1 (1.0%)
Hypercalcaemia	1 (1.0%)
Hypercreatininaemia	1 (1.0%)
Hyperhidrosis	1 (1.0%)
Hypersensitivity	1 (1.0%)
Hypersomnia	1 (1.0%)
Hypertension	1 (1.0%)
Hypoacusis	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
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Adverse Events Related to Paclitaxel Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hypoalbuminaemia	1 (1.0%)
Immature granulocyte count increased	1 (1.0%)
Influenza like illness	1 (1.0%)
Insomnia	1 (1.0%)
Irritability	1 (1.0%)
Jugular vein thrombosis	1 (1.0%)
Lacrimation increased	1 (1.0%)
Lymphadenopathy	1 (1.0%)
Lymphocyte count decreased	1 (1.0%)
Lymphoedema	1 (1.0%)
Madarosis	1 (1.0%)
Memory impairment	1 (1.0%)
Monocyte percentage decreased	1 (1.0%)
Musculoskeletal stiffness	1 (1.0%)
Nail bed tenderness	1 (1.0%)
Nail discolouration	1 (1.0%)
Nail infection	1 (1.0%)
Nail ridging	1 (1.0%)
Nasal crusting	1 (1.0%)
Neurotoxicity	1 (1.0%)
Non-cardiac chest pain	1 (1.0%)
Oesophagitis	1 (1.0%)
Onychalgia	1 (1.0%)
Onychoclasis	1 (1.0%)
Onycholysis	1 (1.0%)
Onychomadesis	1 (1.0%)
Oral discomfort	1 (1.0%)
Oral herpes	1 (1.0%)
Oxygen saturation decreased	1 (1.0%)
Pain in extremity	1 (1.0%)
Paraesthesia oral	1 (1.0%)
Paronychia	1 (1.0%)
Peripheral motor neuropathy	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
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Adverse Events Related to Paclitaxel Treatment by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Peripheral swelling	1 (1.0%)
Pneumonia viral	1 (1.0%)
Pneumonitis	1 (1.0%)
Productive cough	1 (1.0%)
Rash maculo-papular	1 (1.0%)
Red blood cell count decreased	1 (1.0%)
Sensation of foreign body	1 (1.0%)
Skin exfoliation	1 (1.0%)
Skin hyperpigmentation	1 (1.0%)
Skin infection	1 (1.0%)
Taste disorder	1 (1.0%)
Thrombocytopenia	1 (1.0%)
Thrombocytosis	1 (1.0%)
Tinnitus	1 (1.0%)
Tremor	1 (1.0%)
Tumour inflammation	1 (1.0%)
Upper respiratory tract infection	1 (1.0%)
Urticaria	1 (1.0%)
White blood cell count increased	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
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Serious Adverse Events by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diarrhoea	4 (3.9%)
Pyrexia	4 (3.9%)
Pneumonia	3 (2.9%)
Urinary tract infection	3 (2.9%)
Cholecystitis	2 (2.0%)
Dehydration	2 (2.0%)
Fatigue	2 (2.0%)
Febrile neutropenia	2 (2.0%)
Pneumonitis	2 (2.0%)
Rash	2 (2.0%)
Tumour necrosis	2 (2.0%)
Vomiting	2 (2.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Serious Adverse Events by Preferred Term, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Acute kidney injury	1 (1.0%)
Alanine aminotransferase increased	1 (1.0%)
Aspartate aminotransferase increased	1 (1.0%)
Autoimmune hepatitis	1 (1.0%)
COVID-19	1 (1.0%)
Cardiac arrest	1 (1.0%)
Diabetic ketoacidosis	1 (1.0%)
Dystonia	1 (1.0%)
Emphysematous cystitis	1 (1.0%)
Gastroenteritis	1 (1.0%)
Gastroenteritis norovirus	1 (1.0%)
General physical health deterioration	1 (1.0%)
Hypersensitivity	1 (1.0%)
Hypertransaminasaemia	1 (1.0%)
Immune-mediated lung disease	1 (1.0%)
Influenza	1 (1.0%)
Large intestine perforation	1 (1.0%)
Lymphoedema	1 (1.0%)
Musculoskeletal chest pain	1 (1.0%)
Myocarditis	1 (1.0%)
Myositis	1 (1.0%)
Nausea	1 (1.0%)
Pleural effusion	1 (1.0%)
Posterior reversible encephalopathy syndrome	1 (1.0%)
Pulmonary embolism	1 (1.0%)
Skin infection	1 (1.0%)
Suspected COVID-19	1 (1.0%)
Tumour fistulisation	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Serious Adverse Events, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one such adverse event	20 (23.0%)	34 (20.5%)
Overall total number of events	27	48
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	10 (6.0%)
Total number of events	2	14
Diarrhoea	0	6 (3.6%)
Nausea	0	2 (1.2%)
Vomiting	0	2 (1.2%)
Abdominal pain	0	1 (0.6%)
Colitis	1 (1.1%)	0
Large intestine perforation	0	1 (0.6%)
Upper gastrointestinal haemorrhage	1 (1.1%)	0
Infections and infestations		
Total number of patients with at least one such adverse event	6 (6.9%)	6 (3.6%)
Total number of events	7	7
Pneumonia	4 (4.6%)	2 (1.2%)
Abscess jaw	0	1 (0.6%)
COVID-19	0	1 (0.6%)
COVID-19 pneumonia	0	1 (0.6%)
Cellulitis	1 (1.1%)	0
Peritonitis	0	1 (0.6%)
Urinary tract infection	0	1 (0.6%)
Viral infection	1 (1.1%)	0
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	5 (5.7%)	5 (3.0%)
Total number of events	5	5
Pleural effusion	2 (2.3%)	1 (0.6%)
Pulmonary embolism	0	3 (1.8%)
Dyspnoea	1 (1.1%)	1 (0.6%)
Haemoptysis	1 (1.1%)	0
Pneumothorax	1 (1.1%)	0
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	2 (2.3%)	4 (2.4%)
Total number of events	3	5
Febrile neutropenia	0	3 (1.8%)
Anaemia	1 (1.1%)	1 (0.6%)
Neutropenia	1 (1.1%)	1 (0.6%)
Thrombocytopenia	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Total number of patients with at least one such adverse event	3 (3.4%)	3 (1.8%)
Total number of events	4	4
Gastric cancer	1 (1.1%)	0
Infected neoplasm	1 (1.1%)	0
Lymphangiosis carcinomatosa	1 (1.1%)	0
Schwannoma	0	1 (0.6%)
Tumour haemorrhage	0	1 (0.6%)
Tumour necrosis	0	1 (0.6%)
Injury, poisoning and procedural complications		
Total number of patients with at least one such adverse event	3 (3.4%)	2 (1.2%)
Total number of events	3	2
Spinal fracture	1 (1.1%)	1 (0.6%)
Fracture	0	1 (0.6%)
Procedural pain	1 (1.1%)	0
Skin laceration	1 (1.1%)	0
Cardiac disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	2 (1.2%)
Total number of events	1	2
Atrial fibrillation	0	1 (0.6%)
Cardiopulmonary failure	0	1 (0.6%)
Sinus tachycardia	1 (1.1%)	0
Eye disorders		
Total number of patients with at least one such adverse event	0	2 (1.2%)
Total number of events	0	3
Epiretinal membrane	0	1 (0.6%)
Glaucoma	0	1 (0.6%)
Macular oedema	0	1 (0.6%)
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	0	2 (1.2%)
Total number of events	0	2
Fatigue	0	1 (0.6%)
Hyperthermia	0	1 (0.6%)
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	1 (0.6%)
Total number of events	1	1
Hyperglycaemia	0	1 (0.6%)
Tumour lysis syndrome	1 (1.1%)	0
Immune system disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Hypersensitivity	0	1 (0.6%)

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Serious Adverse Events, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Investigations		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Lymphocyte count decreased	0	1 (0.6%)
Musculoskeletal and connective tissue disorders		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Intervertebral disc compression	1 (1.1%)	0
Skin and subcutaneous tissue disorders		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Erythema multiforme	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Serious Adverse Events, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one such adverse event	11 (14.7%)	30 (20.7%)
Overall total number of events	14	45
Infections and infestations		
Total number of patients with at least one such adverse event	5 (6.7%)	5 (3.4%)
Total number of events	5	7
Pneumonia	1 (1.3%)	2 (1.4%)
Abdominal abscess	0	1 (0.7%)
COVID-19	0	1 (0.7%)
Cellulitis	0	1 (0.7%)
Erysipelas	0	1 (0.7%)
Lower respiratory tract infection	0	1 (0.7%)
Sepsis	1 (1.3%)	0
Upper respiratory tract infection	1 (1.3%)	0
Urinary tract infection	1 (1.3%)	0
Wound infection	1 (1.3%)	0
Gastrointestinal disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	7 (4.8%)
Total number of events	1	10
Diarrhoea	1 (1.3%)	4 (2.8%)
Abdominal hernia	0	1 (0.7%)
Abdominal pain	0	1 (0.7%)
Chronic gastritis	0	1 (0.7%)
Enterocolitis	0	1 (0.7%)
Intestinal obstruction	0	1 (0.7%)
Respiratory, thoracic and mediastinal disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	5 (3.4%)
Total number of events	1	5
Pneumonitis	0	2 (1.4%)
Dyspnoea	0	1 (0.7%)
Pleural effusion	0	1 (0.7%)
Pulmonary embolism	1 (1.3%)	0
Respiratory distress	0	1 (0.7%)
Blood and lymphatic system disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	3 (2.1%)
Total number of events	1	4
Febrile neutropenia	0	2 (1.4%)
Neutropenia	0	2 (1.4%)
Leukopenia	1 (1.3%)	0

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
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MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
General disorders and administration site conditions		
Total number of patients with at least one such adverse event	1 (1.3%)	3 (2.1%)
Total number of events	1	3
Death	0	1 (0.7%)
Extravasation	0	1 (0.7%)
Fatigue	1 (1.3%)	0
General physical health deterioration	0	1 (0.7%)
Renal and urinary disorders		
Total number of patients with at least one such adverse event	2 (2.7%)	1 (0.7%)
Total number of events	2	1
Acute kidney injury	1 (1.3%)	0
Hydronephrosis	1 (1.3%)	0
Renal impairment	0	1 (0.7%)
Hepatobiliary disorders		
Total number of patients with at least one such adverse event	1 (1.3%)	1 (0.7%)
Total number of events	1	1
Cholecystitis acute	1 (1.3%)	1 (0.7%)
Injury, poisoning and procedural complications		
Total number of patients with at least one such adverse event	1 (1.3%)	1 (0.7%)
Total number of events	1	1
Femur fracture	1 (1.3%)	0
Road traffic accident	0	1 (0.7%)
Metabolism and nutrition disorders		
Total number of patients with at least one such adverse event	0	2 (1.4%)
Total number of events	0	5
Decreased appetite	0	1 (0.7%)
Dehydration	0	1 (0.7%)
Hyperglycaemia	0	1 (0.7%)
Hypoglycaemia	0	1 (0.7%)
Eye disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Eyelid oedema	0	1 (0.7%)
Immune system disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Hypersensitivity	0	1 (0.7%)
Investigations		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Blood creatine phosphokinase increased	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Musculoskeletal and connective tissue disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Pathological fracture	0	1 (0.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Total number of patients with at least one such adverse event	1 (1.3%)	0
Total number of events	1	0
Tumour necrosis	1 (1.3%)	0
Nervous system disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Cerebrovascular accident	0	1 (0.7%)
Psychiatric disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Anxiety	0	1 (0.7%)
Skin and subcutaneous tissue disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Erythema multiforme	0	1 (0.7%)
Vascular disorders		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Deep vein thrombosis	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
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Serious Adverse Events, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	29 (28.4%)
Overall total number of events	58
Infections and infestations	
Total number of patients with at least one such adverse event	12 (11.8%)
Total number of events	13
Pneumonia	3 (2.9%)
Urinary tract infection	3 (2.9%)
COVID-19	1 (1.0%)
Emphysematous cystitis	1 (1.0%)
Gastroenteritis	1 (1.0%)
Gastroenteritis norovirus	1 (1.0%)
Influenza	1 (1.0%)
Skin infection	1 (1.0%)
Suspected COVID-19	1 (1.0%)
Gastrointestinal disorders	
Total number of patients with at least one such adverse event	6 (5.9%)
Total number of events	8
Diarrhoea	4 (3.9%)
Vomiting	2 (2.0%)
Large intestine perforation	1 (1.0%)
Nausea	1 (1.0%)
General disorders and administration site conditions	
Total number of patients with at least one such adverse event	6 (5.9%)
Total number of events	7
Pyrexia	4 (3.9%)
Fatigue	2 (2.0%)
General physical health deterioration	1 (1.0%)
Respiratory, thoracic and mediastinal disorders	
Total number of patients with at least one such adverse event	5 (4.9%)
Total number of events	5
Pneumonitis	2 (2.0%)
Immune-mediated lung disease	1 (1.0%)
Pleural effusion	1 (1.0%)
Pulmonary embolism	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1. Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of such AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of such AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ae.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ae_SER_C_SE.out
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MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hepatobiliary disorders	
Total number of patients with at least one such adverse event	4 (3.9%)
Total number of events	4
Cholecystitis	2 (2.0%)
Autoimmune hepatitis	1 (1.0%)
Hypertransaminasaemia	1 (1.0%)
Metabolism and nutrition disorders	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Dehydration	2 (2.0%)
Diabetic ketoacidosis	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Tumour necrosis	2 (2.0%)
Tumour fistulisation	1 (1.0%)
Blood and lymphatic system disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Febrile neutropenia	2 (2.0%)
Cardiac disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Cardiac arrest	1 (1.0%)
Myocarditis	1 (1.0%)
Musculoskeletal and connective tissue disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Musculoskeletal chest pain	1 (1.0%)
Myositis	1 (1.0%)
Nervous system disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Dystonia	1 (1.0%)
Posterior reversible encephalopathy syndrome	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Skin and subcutaneous tissue disorders	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Rash	2 (2.0%)
Immune system disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Hypersensitivity	1 (1.0%)
Investigations	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	2
Alanine aminotransferase increased	1 (1.0%)
Aspartate aminotransferase increased	1 (1.0%)
Renal and urinary disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Acute kidney injury	1 (1.0%)
Vascular disorders	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Lymphoedema	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Selected Adverse Events, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one such adverse event	79 (90.8%)	157 (94.6%)
Overall total number of events	404	1435
Diarrhea		
Total number of patients with at least one such adverse event	28 (32.2%)	141 (84.9%)
Total number of events	56	485
Diarrhoea	28 (32.2%)	141 (84.9%)
Peripheral neuropathy		
Total number of patients with at least one such adverse event	49 (56.3%)	86 (51.8%)
Total number of events	58	112
Neuropathy peripheral	20 (23.0%)	39 (23.5%)
Peripheral sensory neuropathy	19 (21.8%)	32 (19.3%)
Polyneuropathy	7 (8.0%)	5 (3.0%)
Paraesthesia	2 (2.3%)	8 (4.8%)
Muscular weakness	3 (3.4%)	1 (0.6%)
Neurotoxicity	1 (1.1%)	2 (1.2%)
Dysaesthesia	1 (1.1%)	1 (0.6%)
Peripheral motor neuropathy	0	2 (1.2%)
Neuralgia	0	1 (0.6%)
Toxic neuropathy	0	1 (0.6%)
Asthenia		
Total number of patients with at least one such adverse event	25 (28.7%)	63 (38.0%)
Total number of events	28	74
Fatigue	15 (17.2%)	31 (18.7%)
Asthenia	10 (11.5%)	35 (21.1%)
Nausea		
Total number of patients with at least one such adverse event	22 (25.3%)	66 (39.8%)
Total number of events	29	108
Nausea	22 (25.3%)	66 (39.8%)
Neutropenia		
Total number of patients with at least one such adverse event	31 (35.6%)	51 (30.7%)
Total number of events	63	146
Neutropenia	21 (24.1%)	28 (16.9%)
Neutrophil count decreased	10 (11.5%)	22 (13.3%)
Febrile neutropenia	0	4 (2.4%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_A_SE.out
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Grouped Term MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Immune-Mediated Rash		
Total number of patients with at least one such adverse event	19 (21.8%)	50 (30.1%)
Total number of events	24	70
Rash	11 (12.6%)	26 (15.7%)
Dermatitis acneiform	1 (1.1%)	7 (4.2%)
Erythema	5 (5.7%)	3 (1.8%)
Dermatitis allergic	0	6 (3.6%)
Rash maculo-papular	0	5 (3.0%)
Dermatitis	2 (2.3%)	2 (1.2%)
Rash pustular	0	3 (1.8%)
Hand dermatitis	1 (1.1%)	1 (0.6%)
Drug eruption	0	1 (0.6%)
Folliculitis	0	1 (0.6%)
Rash papular	1 (1.1%)	0
Rash		
Total number of patients with at least one such adverse event	19 (21.8%)	50 (30.1%)
Total number of events	24	70
Rash	11 (12.6%)	26 (15.7%)
Dermatitis acneiform	1 (1.1%)	7 (4.2%)
Erythema	5 (5.7%)	3 (1.8%)
Dermatitis allergic	0	6 (3.6%)
Rash maculo-papular	0	5 (3.0%)
Dermatitis	2 (2.3%)	2 (1.2%)
Rash pustular	0	3 (1.8%)
Hand dermatitis	1 (1.1%)	1 (0.6%)
Drug eruption	0	1 (0.6%)
Folliculitis	0	1 (0.6%)
Rash papular	1 (1.1%)	0
Erythropenia		
Total number of patients with at least one such adverse event	23 (26.4%)	45 (27.1%)
Total number of events	36	62
Anaemia	23 (26.4%)	44 (26.5%)
Haemoglobin decreased	0	2 (1.2%)
Anaemia macrocytic	0	1 (0.6%)
Haematocrit decreased	1 (1.1%)	0
Anaemia		
Total number of patients with at least one such adverse event	23 (26.4%)	44 (26.5%)
Total number of events	35	59
Anaemia	23 (26.4%)	44 (26.5%)
Vomiting		
Total number of patients with at least one such adverse event	8 (9.2%)	54 (32.5%)
Total number of events	10	114
Vomiting	8 (9.2%)	54 (32.5%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hepatotoxicity		
Total number of patients with at least one such adverse event	12 (13.8%)	29 (17.5%)
Total number of events	37	70
Alanine aminotransferase increased	7 (8.0%)	23 (13.9%)
Aspartate aminotransferase increased	6 (6.9%)	18 (10.8%)
Gamma-glutamyltransferase increased	1 (1.1%)	4 (2.4%)
Blood alkaline phosphatase increased	1 (1.1%)	9 (5.4%)
Hyperbilirubinaemia	3 (3.4%)	0
Blood bilirubin increased	0	1 (0.6%)
Hyperglycemia		
Total number of patients with at least one such adverse event	10 (11.5%)	31 (18.7%)
Total number of events	17	62
Hyperglycaemia	9 (10.3%)	31 (18.7%)
Diabetes mellitus	0	1 (0.6%)
Glucose tolerance impaired	0	2 (1.2%)
Blood glucose increased	1 (1.1%)	0
Glycosylated haemoglobin abnormal	0	1 (0.6%)
Decreased appetite		
Total number of patients with at least one such adverse event	10 (11.5%)	29 (17.5%)
Total number of events	10	35
Decreased appetite	10 (11.5%)	29 (17.5%)
Oral mucositis		
Total number of patients with at least one such adverse event	8 (9.2%)	30 (18.1%)
Total number of events	16	45
Stomatitis	6 (6.9%)	18 (10.8%)
Mucosal inflammation	2 (2.3%)	11 (6.6%)
Mouth ulceration	0	1 (0.6%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)		
Total number of patients with at least one such adverse event	12 (13.8%)	24 (14.5%)
Total number of events	36	58
Alanine aminotransferase increased	7 (8.0%)	23 (13.9%)
Aspartate aminotransferase increased	6 (6.9%)	18 (10.8%)
Gamma-glutamyltransferase increased	1 (1.1%)	4 (2.4%)
Hyperbilirubinaemia	3 (3.4%)	0
Blood bilirubin increased	0	1 (0.6%)
Immune-Mediated Hepatitis (Lab Abnormalities)		
Total number of patients with at least one such adverse event	12 (13.8%)	24 (14.5%)
Total number of events	36	58
Alanine aminotransferase increased	7 (8.0%)	23 (13.9%)
Aspartate aminotransferase increased	6 (6.9%)	18 (10.8%)
Gamma-glutamyltransferase increased	1 (1.1%)	4 (2.4%)
Hyperbilirubinaemia	3 (3.4%)	0
Blood bilirubin increased	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Elevated transaminase		
Total number of patients with at least one such adverse event	8 (9.2%)	24 (14.5%)
Total number of events	23	52
Alanine aminotransferase increased	7 (8.0%)	23 (13.9%)
Aspartate aminotransferase increased	6 (6.9%)	18 (10.8%)
Hyperlipidemia		
Total number of patients with at least one such adverse event	5 (5.7%)	13 (7.8%)
Total number of events	5	22
Hypertriglyceridaemia	2 (2.3%)	9 (5.4%)
Blood cholesterol increased	2 (2.3%)	6 (3.6%)
Hypercholesterolaemia	1 (1.1%)	2 (1.2%)
Blood triglycerides increased	0	1 (0.6%)
Hyperlipidaemia	0	1 (0.6%)
Weight decreased		
Total number of patients with at least one such adverse event	3 (3.4%)	12 (7.2%)
Total number of events	3	13
Weight decreased	3 (3.4%)	12 (7.2%)
Pneumonia		
Total number of patients with at least one such adverse event	5 (5.7%)	8 (4.8%)
Total number of events	5	8
Pneumonia	5 (5.7%)	6 (3.6%)
COVID-19 pneumonia	0	1 (0.6%)
Pneumonia klebsiella	0	1 (0.6%)
Thrombocytopenia		
Total number of patients with at least one such adverse event	4 (4.6%)	2 (1.2%)
Total number of events	5	2
Thrombocytopenia	4 (4.6%)	1 (0.6%)
Platelet count decreased	0	1 (0.6%)
Immune-Mediated Pneumonitis		
Total number of patients with at least one such adverse event	1 (1.1%)	3 (1.8%)
Total number of events	1	3
Bronchiolitis	0	1 (0.6%)
Lung infiltration	0	1 (0.6%)
Pneumonitis	0	1 (0.6%)
Radiation pneumonitis	1 (1.1%)	0
Pneumonitis		
Total number of patients with at least one such adverse event	1 (1.1%)	3 (1.8%)
Total number of events	1	3
Bronchiolitis	0	1 (0.6%)
Lung infiltration	0	1 (0.6%)
Pneumonitis	0	1 (0.6%)
Radiation pneumonitis	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_A_SE.out

Selected Adverse Events, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Colitis		
Total number of patients with at least one such adverse event	1 (1.1%)	1 (0.6%)
Total number of events	1	1
Colitis	1 (1.1%)	1 (0.6%)
Immune-Mediated Colitis		
Total number of patients with at least one such adverse event	1 (1.1%)	1 (0.6%)
Total number of events	1	1
Colitis	1 (1.1%)	1 (0.6%)
Confirmed covid-19		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
COVID-19 pneumonia	0	1 (0.6%)
Covid-19 (smq)		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
COVID-19 pneumonia	0	1 (0.6%)
Dehydration		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	2
Dehydration	0	1 (0.6%)
Erythema multiforme		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Erythema multiforme	0	1 (0.6%)
Immune-Mediated Diabetes Mellitus		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Diabetes mellitus	0	1 (0.6%)
Immune-Mediated Severe Cutaneous Reactions		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Erythema multiforme	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_A_SE.out
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Selected Adverse Events, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one such adverse event	73 (97.3%)	141 (97.2%)
Overall total number of events	584	1419
Diarrhea		
Total number of patients with at least one such adverse event	30 (40.0%)	126 (86.9%)
Total number of events	65	466
Diarrhoea	30 (40.0%)	126 (86.9%)
Peripheral neuropathy		
Total number of patients with at least one such adverse event	49 (65.3%)	94 (64.8%)
Total number of events	64	133
Neuropathy peripheral	12 (16.0%)	46 (31.7%)
Peripheral sensory neuropathy	23 (30.7%)	23 (15.9%)
Paraesthesia	6 (8.0%)	13 (9.0%)
Polyneuropathy	6 (8.0%)	12 (8.3%)
Muscular weakness	3 (4.0%)	2 (1.4%)
Neurotoxicity	2 (2.7%)	3 (2.1%)
Hypoaesthesia	2 (2.7%)	2 (1.4%)
Peripheral motor neuropathy	0	4 (2.8%)
Dysaesthesia	1 (1.3%)	0
Gait disturbance	1 (1.3%)	0
Hypotonia	1 (1.3%)	0
Neuritis	0	1 (0.7%)
Neutropenia		
Total number of patients with at least one such adverse event	33 (44.0%)	59 (40.7%)
Total number of events	123	194
Neutropenia	18 (24.0%)	38 (26.2%)
Neutrophil count decreased	18 (24.0%)	23 (15.9%)
Febrile neutropenia	0	3 (2.1%)
Asthenia		
Total number of patients with at least one such adverse event	31 (41.3%)	55 (37.9%)
Total number of events	48	72
Fatigue	19 (25.3%)	29 (20.0%)
Asthenia	13 (17.3%)	27 (18.6%)
Nausea		
Total number of patients with at least one such adverse event	17 (22.7%)	60 (41.4%)
Total number of events	28	94
Nausea	17 (22.7%)	60 (41.4%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Grouped Term MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Immune-Mediated Rash		
Total number of patients with at least one such adverse event	18 (24.0%)	47 (32.4%)
Total number of events	30	87
Rash	9 (12.0%)	31 (21.4%)
Rash maculo-papular	4 (5.3%)	7 (4.8%)
Erythema	3 (4.0%)	5 (3.4%)
Dermatitis acneiform	2 (2.7%)	3 (2.1%)
Folliculitis	1 (1.3%)	4 (2.8%)
Dermatitis	1 (1.3%)	3 (2.1%)
Dermatitis allergic	2 (2.7%)	1 (0.7%)
Drug eruption	0	3 (2.1%)
Rash erythematous	0	1 (0.7%)
Rash papular	0	1 (0.7%)
Rash pruritic	0	1 (0.7%)
Rash		
Total number of patients with at least one such adverse event	18 (24.0%)	47 (32.4%)
Total number of events	31	89
Rash	9 (12.0%)	31 (21.4%)
Rash maculo-papular	4 (5.3%)	7 (4.8%)
Erythema	3 (4.0%)	5 (3.4%)
Dermatitis acneiform	2 (2.7%)	3 (2.1%)
Folliculitis	1 (1.3%)	4 (2.8%)
Dermatitis	1 (1.3%)	3 (2.1%)
Dermatitis allergic	2 (2.7%)	1 (0.7%)
Dermatitis bullous	1 (1.3%)	2 (1.4%)
Drug eruption	0	3 (2.1%)
Rash erythematous	0	1 (0.7%)
Rash papular	0	1 (0.7%)
Rash pruritic	0	1 (0.7%)
Erythropenia		
Total number of patients with at least one such adverse event	16 (21.3%)	47 (32.4%)
Total number of events	31	62
Anaemia	15 (20.0%)	45 (31.0%)
Haemoglobin decreased	1 (1.3%)	2 (1.4%)
Haematocrit decreased	0	1 (0.7%)
Anaemia		
Total number of patients with at least one such adverse event	15 (20.0%)	45 (31.0%)
Total number of events	28	57
Anaemia	15 (20.0%)	45 (31.0%)
Vomiting		
Total number of patients with at least one such adverse event	6 (8.0%)	45 (31.0%)
Total number of events	10	67
Vomiting	6 (8.0%)	45 (31.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hepatotoxicity		
Total number of patients with at least one such adverse event	21 (28.0%)	25 (17.2%)
Total number of events	97	70
Alanine aminotransferase increased	15 (20.0%)	19 (13.1%)
Aspartate aminotransferase increased	10 (13.3%)	13 (9.0%)
Hyperbilirubinaemia	4 (5.3%)	6 (4.1%)
Gamma-glutamyltransferase increased	2 (2.7%)	3 (2.1%)
Blood alkaline phosphatase increased	7 (9.3%)	3 (2.1%)
Blood bilirubin increased	0	2 (1.4%)
Hepatic function abnormal	1 (1.3%)	0
Cholestasis	1 (1.3%)	0
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)		
Total number of patients with at least one such adverse event	19 (25.3%)	24 (16.6%)
Total number of events	87	66
Alanine aminotransferase increased	15 (20.0%)	19 (13.1%)
Aspartate aminotransferase increased	10 (13.3%)	13 (9.0%)
Hyperbilirubinaemia	4 (5.3%)	6 (4.1%)
Gamma-glutamyltransferase increased	2 (2.7%)	3 (2.1%)
Blood bilirubin increased	0	2 (1.4%)
Hepatic function abnormal	1 (1.3%)	0
Immune-Mediated Hepatitis (Lab Abnormalities)		
Total number of patients with at least one such adverse event	19 (25.3%)	24 (16.6%)
Total number of events	87	66
Alanine aminotransferase increased	15 (20.0%)	19 (13.1%)
Aspartate aminotransferase increased	10 (13.3%)	13 (9.0%)
Hyperbilirubinaemia	4 (5.3%)	6 (4.1%)
Gamma-glutamyltransferase increased	2 (2.7%)	3 (2.1%)
Blood bilirubin increased	0	2 (1.4%)
Hepatic function abnormal	1 (1.3%)	0
Oral mucositis		
Total number of patients with at least one such adverse event	9 (12.0%)	27 (18.6%)
Total number of events	13	44
Stomatitis	6 (8.0%)	16 (11.0%)
Mucosal inflammation	3 (4.0%)	8 (5.5%)
Mouth ulceration	1 (1.3%)	5 (3.4%)
Elevated transaminase		
Total number of patients with at least one such adverse event	16 (21.3%)	19 (13.1%)
Total number of events	46	45
Alanine aminotransferase increased	15 (20.0%)	19 (13.1%)
Aspartate aminotransferase increased	10 (13.3%)	13 (9.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hyperglycemia		
Total number of patients with at least one such adverse event	10 (13.3%)	23 (15.9%)
Total number of events	39	34
Hyperglycaemia	10 (13.3%)	19 (13.1%)
Blood glucose increased	0	2 (1.4%)
Diabetes mellitus	0	1 (0.7%)
Glycosylated haemoglobin increased	0	1 (0.7%)
Type 2 diabetes mellitus	0	1 (0.7%)
Decreased appetite		
Total number of patients with at least one such adverse event	7 (9.3%)	22 (15.2%)
Total number of events	15	31
Decreased appetite	7 (9.3%)	22 (15.2%)
Hyperlipidemia		
Total number of patients with at least one such adverse event	8 (10.7%)	17 (11.7%)
Total number of events	13	31
Hypertriglyceridaemia	5 (6.7%)	7 (4.8%)
Blood cholesterol increased	3 (4.0%)	6 (4.1%)
Hypercholesterolaemia	2 (2.7%)	4 (2.8%)
Blood triglycerides increased	0	4 (2.8%)
Hyperlipidaemia	0	1 (0.7%)
Pneumonia		
Total number of patients with at least one such adverse event	4 (5.3%)	6 (4.1%)
Total number of events	4	6
Pneumonia	4 (5.3%)	6 (4.1%)
Weight decreased		
Total number of patients with at least one such adverse event	2 (2.7%)	7 (4.8%)
Total number of events	2	8
Weight decreased	2 (2.7%)	7 (4.8%)
Immune-Mediated Pneumonitis		
Total number of patients with at least one such adverse event	0	6 (4.1%)
Total number of events	0	6
Pneumonitis	0	6 (4.1%)
Pneumonitis		
Total number of patients with at least one such adverse event	0	6 (4.1%)
Total number of events	0	6
Pneumonitis	0	6 (4.1%)
Dehydration		
Total number of patients with at least one such adverse event	0	4 (2.8%)
Total number of events	0	5
Dehydration	0	4 (2.8%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_B_SE.out
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Selected Adverse Events, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Immune-Mediated Severe Cutaneous Reactions		
Total number of patients with at least one such adverse event	1 (1.3%)	3 (2.1%)
Total number of events	1	3
Dermatitis bullous	1 (1.3%)	2 (1.4%)
Erythema multiforme	0	1 (0.7%)
Thrombocytopenia		
Total number of patients with at least one such adverse event	1 (1.3%)	3 (2.1%)
Total number of events	1	4
Thrombocytopenia	0	3 (2.1%)
Platelet count decreased	1 (1.3%)	0
Colitis		
Total number of patients with at least one such adverse event	0	2 (1.4%)
Total number of events	0	2
Enterocolitis	0	2 (1.4%)
Erythema multiforme		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Erythema multiforme	0	1 (0.7%)
Immune-Mediated Diabetes Mellitus		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Diabetes mellitus	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_B_SE.out
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Selected Adverse Events, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	101 (99.0%)
Overall total number of events	1115
Diarrhea	
Total number of patients with at least one such adverse event	86 (84.3%)
Total number of events	328
Diarrhoea	86 (84.3%)
Peripheral neuropathy	
Total number of patients with at least one such adverse event	53 (52.0%)
Total number of events	72
Neuropathy peripheral	30 (29.4%)
Peripheral sensory neuropathy	8 (7.8%)
Polyneuropathy	8 (7.8%)
Hypoaesthesia	5 (4.9%)
Paraesthesia	5 (4.9%)
Peripheral motor neuropathy	2 (2.0%)
Neurotoxicity	1 (1.0%)
Immune-Mediated Rash	
Total number of patients with at least one such adverse event	46 (45.1%)
Total number of events	66
Rash	31 (30.4%)
Rash maculo-papular	5 (4.9%)
Dermatitis acneiform	3 (2.9%)
Erythema	3 (2.9%)
Hand dermatitis	3 (2.9%)
Dermatitis allergic	2 (2.0%)
Rash erythematous	2 (2.0%)
Rash papular	2 (2.0%)
Rash pruritic	1 (1.0%)
Rash pustular	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi.sas
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Grouped Term MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Rash	
Total number of patients with at least one such adverse event	46 (45.1%)
Total number of events	66
Rash	31 (30.4%)
Rash maculo-papular	5 (4.9%)
Dermatitis acneiform	3 (2.9%)
Erythema	3 (2.9%)
Hand dermatitis	3 (2.9%)
Dermatitis allergic	2 (2.0%)
Rash erythematous	2 (2.0%)
Rash papular	2 (2.0%)
Rash pruritic	1 (1.0%)
Rash pustular	1 (1.0%)
Nausea	
Total number of patients with at least one such adverse event	42 (41.2%)
Total number of events	66
Nausea	42 (41.2%)
Asthenia	
Total number of patients with at least one such adverse event	40 (39.2%)
Total number of events	59
Fatigue	23 (22.5%)
Asthenia	19 (18.6%)
Hepatotoxicity	
Total number of patients with at least one such adverse event	35 (34.3%)
Total number of events	142
Alanine aminotransferase increased	26 (25.5%)
Aspartate aminotransferase increased	22 (21.6%)
Hyperbilirubinaemia	6 (5.9%)
Blood alkaline phosphatase increased	12 (11.8%)
Blood bilirubin increased	4 (3.9%)
Gamma-glutamyltransferase increased	1 (1.0%)
Cholestasis	1 (1.0%)
Prothrombin time prolonged	1 (1.0%)
Anaemia	
Total number of patients with at least one such adverse event	34 (33.3%)
Total number of events	50
Anaemia	34 (33.3%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Erythropenia	
Total number of patients with at least one such adverse event	34 (33.3%)
Total number of events	53
Anaemia	34 (33.3%)
Haematocrit decreased	1 (1.0%)
Red blood cell count decreased	1 (1.0%)
Neutropenia	
Total number of patients with at least one such adverse event	34 (33.3%)
Total number of events	149
Neutropenia	25 (24.5%)
Neutrophil count decreased	8 (7.8%)
Febrile neutropenia	2 (2.0%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)	
Total number of patients with at least one such adverse event	32 (31.4%)
Total number of events	120
Alanine aminotransferase increased	26 (25.5%)
Aspartate aminotransferase increased	22 (21.6%)
Hyperbilirubinaemia	6 (5.9%)
Blood bilirubin increased	4 (3.9%)
Gamma-glutamyltransferase increased	1 (1.0%)
Immune-Mediated Hepatitis (Lab Abnormalities)	
Total number of patients with at least one such adverse event	32 (31.4%)
Total number of events	120
Alanine aminotransferase increased	26 (25.5%)
Aspartate aminotransferase increased	22 (21.6%)
Hyperbilirubinaemia	6 (5.9%)
Blood bilirubin increased	4 (3.9%)
Gamma-glutamyltransferase increased	1 (1.0%)
Vomiting	
Total number of patients with at least one such adverse event	29 (28.4%)
Total number of events	46
Vomiting	29 (28.4%)
Retching	1 (1.0%)
Elevated transaminase	
Total number of patients with at least one such adverse event	28 (27.5%)
Total number of events	100
Alanine aminotransferase increased	26 (25.5%)
Aspartate aminotransferase increased	22 (21.6%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hyperglycemia	
Total number of patients with at least one such adverse event	24 (23.5%)
Total number of events	48
Hyperglycaemia	22 (21.6%)
Blood glucose increased	2 (2.0%)
Diabetes mellitus	1 (1.0%)
Diabetic ketoacidosis	1 (1.0%)
Type 1 diabetes mellitus	1 (1.0%)
Glycosylated haemoglobin increased	1 (1.0%)
Oral mucositis	
Total number of patients with at least one such adverse event	21 (20.6%)
Total number of events	23
Mucosal inflammation	12 (11.8%)
Stomatitis	7 (6.9%)
Mouth ulceration	2 (2.0%)
Decreased appetite	
Total number of patients with at least one such adverse event	14 (13.7%)
Total number of events	15
Decreased appetite	14 (13.7%)
Hyperlipidemia	
Total number of patients with at least one such adverse event	14 (13.7%)
Total number of events	18
Blood cholesterol increased	5 (4.9%)
Blood triglycerides increased	4 (3.9%)
Hypercholesterolaemia	4 (3.9%)
Hypertriglyceridaemia	4 (3.9%)
Immune-Mediated Pneumonitis	
Total number of patients with at least one such adverse event	9 (8.8%)
Total number of events	9
Pneumonitis	7 (6.9%)
Immune-mediated lung disease	1 (1.0%)
Lung infiltration	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Pneumonitis	
Total number of patients with at least one such adverse event	9 (8.8%)
Total number of events	9
Pneumonitis	7 (6.9%)
Immune-mediated lung disease	1 (1.0%)
Lung infiltration	1 (1.0%)
Pneumonia	
Total number of patients with at least one such adverse event	7 (6.9%)
Total number of events	7
Pneumonia	6 (5.9%)
Pneumonia viral	1 (1.0%)
Weight decreased	
Total number of patients with at least one such adverse event	7 (6.9%)
Total number of events	7
Weight decreased	7 (6.9%)
Dehydration	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	4
Dehydration	3 (2.9%)
Thrombocytopenia	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Platelet count decreased	2 (2.0%)
Thrombocytopenia	1 (1.0%)
Immune-Mediated Diabetes Mellitus	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	3
Diabetes mellitus	1 (1.0%)
Diabetic ketoacidosis	1 (1.0%)
Type 1 diabetes mellitus	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	79 (90.8%)	157 (94.6%)
	Grade 1-2	50 (57.5%)	86 (51.8%)
	1	21 (24.1%)	23 (13.9%)
	2	29 (33.3%)	63 (38.0%)
	Grade 3-4	29 (33.3%)	71 (42.8%)
	3	27 (31.0%)	63 (38.0%)
	4	2 (2.3%)	8 (4.8%)
Diarrhea			
- Overall -	- Any Grade -	28 (32.2%)	141 (84.9%)
	Grade 1-2	26 (29.9%)	126 (75.9%)
	1	18 (20.7%)	67 (40.4%)
	2	8 (9.2%)	59 (35.5%)
	Grade 3-4	2 (2.3%)	15 (9.0%)
	3	2 (2.3%)	15 (9.0%)
Diarrhoea	- Any Grade -	28 (32.2%)	141 (84.9%)
	Grade 1-2	26 (29.9%)	126 (75.9%)
	1	18 (20.7%)	67 (40.4%)
	2	8 (9.2%)	59 (35.5%)
	Grade 3-4	2 (2.3%)	15 (9.0%)
	3	2 (2.3%)	15 (9.0%)
Peripheral neuropathy			
- Overall -	- Any Grade -	49 (56.3%)	86 (51.8%)
	Grade 1-2	44 (50.6%)	70 (42.2%)
	1	33 (37.9%)	44 (26.5%)
	2	11 (12.6%)	26 (15.7%)
	Grade 3-4	5 (5.7%)	16 (9.6%)
	3	5 (5.7%)	16 (9.6%)
Neuropathy peripheral	- Any Grade -	20 (23.0%)	39 (23.5%)
	Grade 1-2	17 (19.5%)	31 (18.7%)
	1	13 (14.9%)	19 (11.4%)
	2	4 (4.6%)	12 (7.2%)
	Grade 3-4	3 (3.4%)	8 (4.8%)
	3	3 (3.4%)	8 (4.8%)
Peripheral sensory neuropathy	- Any Grade -	19 (21.8%)	32 (19.3%)
	Grade 1-2	17 (19.5%)	27 (16.3%)
	1	13 (14.9%)	18 (10.8%)
	2	4 (4.6%)	9 (5.4%)
	Grade 3-4	2 (2.3%)	5 (3.0%)
	3	2 (2.3%)	5 (3.0%)
Polyneuropathy	- Any Grade -	7 (8.0%)	5 (3.0%)
	Grade 1-2	7 (8.0%)	4 (2.4%)
	1	4 (4.6%)	4 (2.4%)
	2	3 (3.4%)	0
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_ctc_A_SE.out
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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Paraesthesia	- Any Grade -	2 (2.3%)	8 (4.8%)
	Grade 1-2	2 (2.3%)	7 (4.2%)
	1	2 (2.3%)	3 (1.8%)
	2	0	4 (2.4%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Muscular weakness	- Any Grade -	3 (3.4%)	1 (0.6%)
	Grade 1-2	3 (3.4%)	1 (0.6%)
	1	3 (3.4%)	0
	2	0	1 (0.6%)
Neurotoxicity	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	1	1 (1.1%)	1 (0.6%)
	2	0	1 (0.6%)
Dysaesthesia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Peripheral motor neuropathy	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Neuralgia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Toxic neuropathy	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Asthenia			
- Overall -	- Any Grade -	25 (28.7%)	63 (38.0%)
	Grade 1-2	22 (25.3%)	51 (30.7%)
	1	16 (18.4%)	36 (21.7%)
	2	6 (6.9%)	15 (9.0%)
	Grade 3-4	3 (3.4%)	12 (7.2%)
	3	3 (3.4%)	12 (7.2%)
Fatigue	- Any Grade -	15 (17.2%)	31 (18.7%)
	Grade 1-2	13 (14.9%)	25 (15.1%)
	1	11 (12.6%)	20 (12.0%)
	2	2 (2.3%)	5 (3.0%)
	Grade 3-4	2 (2.3%)	6 (3.6%)
	3	2 (2.3%)	6 (3.6%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Asthenia	- Any Grade -	10 (11.5%)	35 (21.1%)
	Grade 1-2	9 (10.3%)	29 (17.5%)
	1	5 (5.7%)	17 (10.2%)
	2	4 (4.6%)	12 (7.2%)
	Grade 3-4	1 (1.1%)	6 (3.6%)
	3	1 (1.1%)	6 (3.6%)
Nausea			
- Overall -	- Any Grade -	22 (25.3%)	66 (39.8%)
	Grade 1-2	22 (25.3%)	61 (36.7%)
	1	17 (19.5%)	46 (27.7%)
	2	5 (5.7%)	15 (9.0%)
	Grade 3-4	0	5 (3.0%)
	3	0	5 (3.0%)
Nausea	- Any Grade -	22 (25.3%)	66 (39.8%)
	Grade 1-2	22 (25.3%)	61 (36.7%)
	1	17 (19.5%)	46 (27.7%)
	2	5 (5.7%)	15 (9.0%)
	Grade 3-4	0	5 (3.0%)
	3	0	5 (3.0%)
Neutropenia			
- Overall -	- Any Grade -	31 (35.6%)	51 (30.7%)
	Grade 1-2	22 (25.3%)	28 (16.9%)
	1	5 (5.7%)	5 (3.0%)
	2	17 (19.5%)	23 (13.9%)
	Grade 3-4	9 (10.3%)	23 (13.9%)
	3	8 (9.2%)	18 (10.8%)
	4	1 (1.1%)	5 (3.0%)
Neutropenia	- Any Grade -	21 (24.1%)	28 (16.9%)
	Grade 1-2	17 (19.5%)	16 (9.6%)
	1	4 (4.6%)	3 (1.8%)
	2	13 (14.9%)	13 (7.8%)
	Grade 3-4	4 (4.6%)	12 (7.2%)
	3	3 (3.4%)	10 (6.0%)
	4	1 (1.1%)	2 (1.2%)
Neutrophil count decreased	- Any Grade -	10 (11.5%)	22 (13.3%)
	Grade 1-2	5 (5.7%)	14 (8.4%)
	1	1 (1.1%)	2 (1.2%)
	2	4 (4.6%)	12 (7.2%)
	Grade 3-4	5 (5.7%)	8 (4.8%)
	3	5 (5.7%)	6 (3.6%)
	4	0	2 (1.2%)
Febrile neutropenia	- Any Grade -	0	4 (2.4%)
	Grade 3-4	0	4 (2.4%)
	3	0	3 (1.8%)
	4	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Immune-Mediated Rash			
- Overall -	- Any Grade -	19 (21.8%)	50 (30.1%)
	Grade 1-2	18 (20.7%)	48 (28.9%)
	1	16 (18.4%)	39 (23.5%)
	2	2 (2.3%)	9 (5.4%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	1 (1.1%)	2 (1.2%)
Rash	- Any Grade -	11 (12.6%)	26 (15.7%)
	Grade 1-2	11 (12.6%)	24 (14.5%)
	1	9 (10.3%)	20 (12.0%)
	2	2 (2.3%)	4 (2.4%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Dermatitis acneiform	- Any Grade -	1 (1.1%)	7 (4.2%)
	Grade 1-2	1 (1.1%)	7 (4.2%)
	1	1 (1.1%)	7 (4.2%)
Erythema	- Any Grade -	5 (5.7%)	3 (1.8%)
	Grade 1-2	4 (4.6%)	3 (1.8%)
	1	4 (4.6%)	2 (1.2%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Dermatitis allergic	- Any Grade -	0	6 (3.6%)
	Grade 1-2	0	6 (3.6%)
	1	0	4 (2.4%)
	2	0	2 (1.2%)
Rash maculo-papular	- Any Grade -	0	5 (3.0%)
	Grade 1-2	0	5 (3.0%)
	1	0	4 (2.4%)
	2	0	1 (0.6%)
Dermatitis	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	2 (2.3%)	1 (0.6%)
	2	0	1 (0.6%)
Rash pustular	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)
Hand dermatitis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Drug eruption	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Folliculitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Rash papular	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Rash			
- Overall -	- Any Grade -	19 (21.8%)	50 (30.1%)
	Grade 1-2	18 (20.7%)	48 (28.9%)
	1	16 (18.4%)	39 (23.5%)
	2	2 (2.3%)	9 (5.4%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	1 (1.1%)	2 (1.2%)
Rash	- Any Grade -	11 (12.6%)	26 (15.7%)
	Grade 1-2	11 (12.6%)	24 (14.5%)
	1	9 (10.3%)	20 (12.0%)
	2	2 (2.3%)	4 (2.4%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Dermatitis acneiform	- Any Grade -	1 (1.1%)	7 (4.2%)
	Grade 1-2	1 (1.1%)	7 (4.2%)
	1	1 (1.1%)	7 (4.2%)
Erythema	- Any Grade -	5 (5.7%)	3 (1.8%)
	Grade 1-2	4 (4.6%)	3 (1.8%)
	1	4 (4.6%)	2 (1.2%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Dermatitis allergic	- Any Grade -	0	6 (3.6%)
	Grade 1-2	0	6 (3.6%)
	1	0	4 (2.4%)
	2	0	2 (1.2%)
Rash maculo-papular	- Any Grade -	0	5 (3.0%)
	Grade 1-2	0	5 (3.0%)
	1	0	4 (2.4%)
	2	0	1 (0.6%)
Dermatitis	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	1	2 (2.3%)	1 (0.6%)
	2	0	1 (0.6%)
Rash pustular	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	3 (1.8%)
	1	0	2 (1.2%)
	2	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hand dermatitis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	1 (0.6%)
Drug eruption	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Folliculitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Rash papular	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Erythropenia			
- Overall -	- Any Grade -	23 (26.4%)	45 (27.1%)
	Grade 1-2	20 (23.0%)	41 (24.7%)
	1	9 (10.3%)	20 (12.0%)
	2	11 (12.6%)	21 (12.7%)
	Grade 3-4	3 (3.4%)	4 (2.4%)
	3	2 (2.3%)	4 (2.4%)
	4	1 (1.1%)	0
Anaemia	- Any Grade -	23 (26.4%)	44 (26.5%)
	Grade 1-2	20 (23.0%)	40 (24.1%)
	1	9 (10.3%)	21 (12.7%)
	2	11 (12.6%)	19 (11.4%)
	Grade 3-4	3 (3.4%)	4 (2.4%)
	3	2 (2.3%)	4 (2.4%)
	4	1 (1.1%)	0
Haemoglobin decreased	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Anaemia macrocytic	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Haematocrit decreased	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Anaemia			
- Overall -	- Any Grade -	23 (26.4%)	44 (26.5%)
	Grade 1-2	20 (23.0%)	40 (24.1%)
	1	9 (10.3%)	21 (12.7%)
	2	11 (12.6%)	19 (11.4%)
	Grade 3-4	3 (3.4%)	4 (2.4%)
	3	2 (2.3%)	4 (2.4%)
	4	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Anaemia	- Any Grade -	23 (26.4%)	44 (26.5%)
	Grade 1-2	20 (23.0%)	40 (24.1%)
	1	9 (10.3%)	21 (12.7%)
	2	11 (12.6%)	19 (11.4%)
	Grade 3-4	3 (3.4%)	4 (2.4%)
	3	2 (2.3%)	4 (2.4%)
	4	1 (1.1%)	0
Vomiting			
- Overall -	- Any Grade -	8 (9.2%)	54 (32.5%)
	Grade 1-2	7 (8.0%)	50 (30.1%)
	1	6 (6.9%)	41 (24.7%)
	2	1 (1.1%)	9 (5.4%)
	Grade 3-4	1 (1.1%)	4 (2.4%)
	3	1 (1.1%)	3 (1.8%)
	4	0	1 (0.6%)
Vomiting	- Any Grade -	8 (9.2%)	54 (32.5%)
	Grade 1-2	7 (8.0%)	50 (30.1%)
	1	6 (6.9%)	41 (24.7%)
	2	1 (1.1%)	9 (5.4%)
	Grade 3-4	1 (1.1%)	4 (2.4%)
	3	1 (1.1%)	3 (1.8%)
	4	0	1 (0.6%)
Hepatotoxicity			
- Overall -	- Any Grade -	12 (13.8%)	29 (17.5%)
	Grade 1-2	9 (10.3%)	20 (12.0%)
	1	5 (5.7%)	11 (6.6%)
	2	4 (4.6%)	9 (5.4%)
	Grade 3-4	3 (3.4%)	9 (5.4%)
	3	3 (3.4%)	8 (4.8%)
	4	0	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	7 (8.0%)	23 (13.9%)
	Grade 1-2	4 (4.6%)	15 (9.0%)
	1	4 (4.6%)	8 (4.8%)
	2	0	7 (4.2%)
	Grade 3-4	3 (3.4%)	8 (4.8%)
	3	3 (3.4%)	8 (4.8%)
Aspartate aminotransferase increased	- Any Grade -	6 (6.9%)	18 (10.8%)
	Grade 1-2	3 (3.4%)	13 (7.8%)
	1	2 (2.3%)	7 (4.2%)
	2	1 (1.1%)	6 (3.6%)
	Grade 3-4	3 (3.4%)	5 (3.0%)
	3	3 (3.4%)	5 (3.0%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Blood alkaline phosphatase increased	- Any Grade -	1 (1.1%)	9 (5.4%)
	Grade 1-2	1 (1.1%)	9 (5.4%)
	1	1 (1.1%)	8 (4.8%)
	2	0	1 (0.6%)
Gamma-glutamyltransferase increased	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
Hyperbilirubinaemia	- Any Grade -	3 (3.4%)	0
	Grade 1-2	3 (3.4%)	0
	1	1 (1.1%)	0
	2	2 (2.3%)	0
Blood bilirubin increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Hyperglycemia			
- Overall -	- Any Grade -	10 (11.5%)	31 (18.7%)
	Grade 1-2	10 (11.5%)	28 (16.9%)
	1	6 (6.9%)	17 (10.2%)
	2	4 (4.6%)	11 (6.6%)
	Grade 3-4	0	3 (1.8%)
	3	0	2 (1.2%)
	4	0	1 (0.6%)
Hyperglycaemia	- Any Grade -	9 (10.3%)	31 (18.7%)
	Grade 1-2	9 (10.3%)	28 (16.9%)
	1	5 (5.7%)	17 (10.2%)
	2	4 (4.6%)	11 (6.6%)
	Grade 3-4	0	3 (1.8%)
	3	0	2 (1.2%)
	4	0	1 (0.6%)
Glucose tolerance impaired	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Blood glucose increased	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Diabetes mellitus	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Glycosylated haemoglobin abnormal	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Decreased appetite			
- Overall -	- Any Grade -	10 (11.5%)	29 (17.5%)
	Grade 1-2	10 (11.5%)	28 (16.9%)
	1	7 (8.0%)	18 (10.8%)
	2	3 (3.4%)	10 (6.0%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Decreased appetite	- Any Grade -	10 (11.5%)	29 (17.5%)
	Grade 1-2	10 (11.5%)	28 (16.9%)
	1	7 (8.0%)	18 (10.8%)
	2	3 (3.4%)	10 (6.0%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Oral mucositis			
- Overall -	- Any Grade -	8 (9.2%)	30 (18.1%)
	Grade 1-2	8 (9.2%)	29 (17.5%)
	1	7 (8.0%)	18 (10.8%)
	2	1 (1.1%)	11 (6.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Stomatitis	- Any Grade -	6 (6.9%)	18 (10.8%)
	Grade 1-2	6 (6.9%)	18 (10.8%)
	1	5 (5.7%)	10 (6.0%)
	2	1 (1.1%)	8 (4.8%)
Mucosal inflammation	- Any Grade -	2 (2.3%)	11 (6.6%)
	Grade 1-2	2 (2.3%)	10 (6.0%)
	1	2 (2.3%)	7 (4.2%)
	2	0	3 (1.8%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Mouth ulceration	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)			
- Overall -	- Any Grade -	12 (13.8%)	24 (14.5%)
	Grade 1-2	9 (10.3%)	15 (9.0%)
	1	5 (5.7%)	6 (3.6%)
	2	4 (4.6%)	9 (5.4%)
	Grade 3-4	3 (3.4%)	9 (5.4%)
	3	3 (3.4%)	8 (4.8%)
	4	0	1 (0.6%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Alanine aminotransferase increased	- Any Grade -	7 (8.0%)	23 (13.9%)
	Grade 1-2	4 (4.6%)	15 (9.0%)
	1	4 (4.6%)	8 (4.8%)
	2	0	7 (4.2%)
	Grade 3-4	3 (3.4%)	8 (4.8%)
	3	3 (3.4%)	8 (4.8%)
Aspartate aminotransferase increased	- Any Grade -	6 (6.9%)	18 (10.8%)
	Grade 1-2	3 (3.4%)	13 (7.8%)
	1	2 (2.3%)	7 (4.2%)
	2	1 (1.1%)	6 (3.6%)
	Grade 3-4	3 (3.4%)	5 (3.0%)
	3	3 (3.4%)	5 (3.0%)
Gamma-glutamyltransferase increased	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
Hyperbilirubinaemia	- Any Grade -	3 (3.4%)	0
	Grade 1-2	3 (3.4%)	0
	1	1 (1.1%)	0
	2	2 (2.3%)	0
Blood bilirubin increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Immune-Mediated Hepatitis (Lab Abnormalities)			
- Overall -	- Any Grade -	12 (13.8%)	24 (14.5%)
	Grade 1-2	9 (10.3%)	15 (9.0%)
	1	5 (5.7%)	6 (3.6%)
	2	4 (4.6%)	9 (5.4%)
	Grade 3-4	3 (3.4%)	9 (5.4%)
	3	3 (3.4%)	8 (4.8%)
	4	0	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	7 (8.0%)	23 (13.9%)
	Grade 1-2	4 (4.6%)	15 (9.0%)
	1	4 (4.6%)	8 (4.8%)
	2	0	7 (4.2%)
	Grade 3-4	3 (3.4%)	8 (4.8%)
	3	3 (3.4%)	8 (4.8%)
Aspartate aminotransferase increased	- Any Grade -	6 (6.9%)	18 (10.8%)
	Grade 1-2	3 (3.4%)	13 (7.8%)
	1	2 (2.3%)	7 (4.2%)
	2	1 (1.1%)	6 (3.6%)
	Grade 3-4	3 (3.4%)	5 (3.0%)
	3	3 (3.4%)	5 (3.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Gamma-glutamyltransferase increased	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
Hyperbilirubinaemia	- Any Grade -	3 (3.4%)	0
	Grade 1-2	3 (3.4%)	0
	1	1 (1.1%)	0
	2	2 (2.3%)	0
Blood bilirubin increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Elevated transaminase			
- Overall -	- Any Grade -	8 (9.2%)	24 (14.5%)
	Grade 1-2	5 (5.7%)	15 (9.0%)
	1	4 (4.6%)	7 (4.2%)
	2	1 (1.1%)	8 (4.8%)
	Grade 3-4	3 (3.4%)	9 (5.4%)
	3	3 (3.4%)	9 (5.4%)
Alanine aminotransferase increased	- Any Grade -	7 (8.0%)	23 (13.9%)
	Grade 1-2	4 (4.6%)	15 (9.0%)
	1	4 (4.6%)	8 (4.8%)
	2	0	7 (4.2%)
	Grade 3-4	3 (3.4%)	8 (4.8%)
	3	3 (3.4%)	8 (4.8%)
Aspartate aminotransferase increased	- Any Grade -	6 (6.9%)	18 (10.8%)
	Grade 1-2	3 (3.4%)	13 (7.8%)
	1	2 (2.3%)	7 (4.2%)
	2	1 (1.1%)	6 (3.6%)
	Grade 3-4	3 (3.4%)	5 (3.0%)
	3	3 (3.4%)	5 (3.0%)
Hyperlipidemia			
- Overall -	- Any Grade -	5 (5.7%)	13 (7.8%)
	Grade 1-2	5 (5.7%)	9 (5.4%)
	1	5 (5.7%)	2 (1.2%)
	2	0	7 (4.2%)
	Grade 3-4	0	4 (2.4%)
	3	0	4 (2.4%)
Hypertriglyceridaemia	- Any Grade -	2 (2.3%)	9 (5.4%)
	Grade 1-2	2 (2.3%)	6 (3.6%)
	1	2 (2.3%)	0
	2	0	6 (3.6%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Blood cholesterol increased	- Any Grade -	2 (2.3%)	6 (3.6%)
	Grade 1-2	2 (2.3%)	6 (3.6%)
	1	2 (2.3%)	5 (3.0%)
	2	0	1 (0.6%)
Hypercholesterolaemia	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	1	1 (1.1%)	0
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Blood triglycerides increased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Hyperlipidaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Weight decreased			
- Overall -	- Any Grade -	3 (3.4%)	12 (7.2%)
	Grade 1-2	3 (3.4%)	12 (7.2%)
	1	2 (2.3%)	8 (4.8%)
	2	1 (1.1%)	4 (2.4%)
Weight decreased	- Any Grade -	3 (3.4%)	12 (7.2%)
	Grade 1-2	3 (3.4%)	12 (7.2%)
	1	2 (2.3%)	8 (4.8%)
	2	1 (1.1%)	4 (2.4%)
Pneumonia			
- Overall -	- Any Grade -	5 (5.7%)	8 (4.8%)
	Grade 1-2	1 (1.1%)	5 (3.0%)
	1	0	1 (0.6%)
	2	1 (1.1%)	4 (2.4%)
	Grade 3-4	4 (4.6%)	3 (1.8%)
	3	3 (3.4%)	3 (1.8%)
	4	1 (1.1%)	0
Pneumonia	- Any Grade -	5 (5.7%)	6 (3.6%)
	Grade 1-2	1 (1.1%)	4 (2.4%)
	1	0	1 (0.6%)
	2	1 (1.1%)	3 (1.8%)
	Grade 3-4	4 (4.6%)	2 (1.2%)
	3	3 (3.4%)	2 (1.2%)
	4	1 (1.1%)	0
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Pneumonia klebsiella	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Thrombocytopenia			
- Overall -	- Any Grade -	4 (4.6%)	2 (1.2%)
	Grade 1-2	3 (3.4%)	2 (1.2%)
	1	1 (1.1%)	0
	2	2 (2.3%)	2 (1.2%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Thrombocytopenia	- Any Grade -	4 (4.6%)	1 (0.6%)
	Grade 1-2	3 (3.4%)	1 (0.6%)
	1	1 (1.1%)	0
	2	2 (2.3%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Platelet count decreased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Immune-Mediated Pneumonitis			
- Overall -	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	1 (1.1%)	3 (1.8%)
Bronchiolitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Lung infiltration	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Pneumonitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Radiation pneumonitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Pneumonitis			
- Overall -	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	1	1 (1.1%)	3 (1.8%)
Bronchiolitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Lung infiltration	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Pneumonitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Radiation pneumonitis	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	1	1 (1.1%)	0
Colitis			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Colitis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Immune-Mediated Colitis			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Colitis	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Confirmed covid-19			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Covid-19 (smq)			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Dehydration			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Dehydration	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Erythema multiforme			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Erythema multiforme	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Immune-Mediated Diabetes Mellitus			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Diabetes mellitus	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Immune-Mediated Severe Cutaneous Reactions			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Erythema multiforme	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	73 (97.3%)	141 (97.2%)
	Grade 1-2	49 (65.3%)	75 (51.7%)
	1	13 (17.3%)	11 (7.6%)
	2	36 (48.0%)	64 (44.1%)
	Grade 3-4	24 (32.0%)	64 (44.1%)
	3	22 (29.3%)	59 (40.7%)
	4	2 (2.7%)	5 (3.4%)
	Grade 5	0	2 (1.4%)
Diarrhea			
- Overall -	- Any Grade -	30 (40.0%)	126 (86.9%)
	Grade 1-2	29 (38.7%)	109 (75.2%)
	1	22 (29.3%)	47 (32.4%)
	2	7 (9.3%)	62 (42.8%)
	Grade 3-4	1 (1.3%)	17 (11.7%)
	3	1 (1.3%)	17 (11.7%)
Diarrhoea	- Any Grade -	30 (40.0%)	126 (86.9%)
	Grade 1-2	29 (38.7%)	109 (75.2%)
	1	22 (29.3%)	47 (32.4%)
	2	7 (9.3%)	62 (42.8%)
	Grade 3-4	1 (1.3%)	17 (11.7%)
	3	1 (1.3%)	17 (11.7%)
Peripheral neuropathy			
- Overall -	- Any Grade -	49 (65.3%)	94 (64.8%)
	Grade 1-2	42 (56.0%)	79 (54.5%)
	1	22 (29.3%)	42 (29.0%)
	2	20 (26.7%)	37 (25.5%)
	Grade 3-4	7 (9.3%)	15 (10.3%)
	3	7 (9.3%)	15 (10.3%)
Neuropathy peripheral	- Any Grade -	12 (16.0%)	46 (31.7%)
	Grade 1-2	9 (12.0%)	36 (24.8%)
	1	2 (2.7%)	19 (13.1%)
	2	7 (9.3%)	17 (11.7%)
	Grade 3-4	3 (4.0%)	10 (6.9%)
	3	3 (4.0%)	10 (6.9%)
Peripheral sensory neuropathy	- Any Grade -	23 (30.7%)	23 (15.9%)
	Grade 1-2	19 (25.3%)	19 (13.1%)
	1	10 (13.3%)	8 (5.5%)
	2	9 (12.0%)	11 (7.6%)
	Grade 3-4	4 (5.3%)	4 (2.8%)
	3	4 (5.3%)	4 (2.8%)
Paraesthesia	- Any Grade -	6 (8.0%)	13 (9.0%)
	Grade 1-2	6 (8.0%)	13 (9.0%)
	1	5 (6.7%)	10 (6.9%)
	2	1 (1.3%)	3 (2.1%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Polyneuropathy	- Any Grade -	6 (8.0%)	12 (8.3%)
	Grade 1-2	6 (8.0%)	11 (7.6%)
	1	5 (6.7%)	8 (5.5%)
	2	1 (1.3%)	3 (2.1%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Muscular weakness	- Any Grade -	3 (4.0%)	2 (1.4%)
	Grade 1-2	3 (4.0%)	2 (1.4%)
	1	3 (4.0%)	2 (1.4%)
Neurotoxicity	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	1 (1.3%)	0
	2	1 (1.3%)	3 (2.1%)
Hypoaesthesia	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	0
Peripheral motor neuropathy	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	2 (1.4%)
	2	0	2 (1.4%)
Dysaesthesia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Gait disturbance	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Hypotonia	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Neuritis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Neutropenia			
- Overall -	- Any Grade -	33 (44.0%)	59 (40.7%)
	Grade 1-2	21 (28.0%)	33 (22.8%)
	1	2 (2.7%)	8 (5.5%)
	2	19 (25.3%)	25 (17.2%)
	Grade 3-4	12 (16.0%)	25 (17.2%)
	3	10 (13.3%)	21 (14.5%)
	4	2 (2.7%)	4 (2.8%)
	Grade 5	0	1 (0.7%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Neutropenia	- Any Grade -	18 (24.0%)	38 (26.2%)
	Grade 1-2	11 (14.7%)	26 (17.9%)
	1	1 (1.3%)	7 (4.8%)
	2	10 (13.3%)	19 (13.1%)
	Grade 3-4	7 (9.3%)	12 (8.3%)
	3	7 (9.3%)	10 (6.9%)
	4	0	2 (1.4%)
Neutrophil count decreased	- Any Grade -	18 (24.0%)	23 (15.9%)
	Grade 1-2	12 (16.0%)	10 (6.9%)
	1	2 (2.7%)	1 (0.7%)
	2	10 (13.3%)	9 (6.2%)
	Grade 3-4	6 (8.0%)	13 (9.0%)
	3	4 (5.3%)	10 (6.9%)
	4	2 (2.7%)	3 (2.1%)
Febrile neutropenia	- Any Grade -	0	3 (2.1%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
	Grade 5	0	1 (0.7%)
Asthenia			
- Overall -	- Any Grade -	31 (41.3%)	55 (37.9%)
	Grade 1-2	27 (36.0%)	53 (36.6%)
	1	16 (21.3%)	31 (21.4%)
	2	11 (14.7%)	22 (15.2%)
	Grade 3-4	4 (5.3%)	2 (1.4%)
	3	4 (5.3%)	2 (1.4%)
Fatigue	- Any Grade -	19 (25.3%)	29 (20.0%)
	Grade 1-2	16 (21.3%)	29 (20.0%)
	1	10 (13.3%)	18 (12.4%)
	2	6 (8.0%)	11 (7.6%)
	Grade 3-4	3 (4.0%)	0
	3	3 (4.0%)	0
Asthenia	- Any Grade -	13 (17.3%)	27 (18.6%)
	Grade 1-2	11 (14.7%)	25 (17.2%)
	1	6 (8.0%)	13 (9.0%)
	2	5 (6.7%)	12 (8.3%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	2 (2.7%)	2 (1.4%)
Nausea			
- Overall -	- Any Grade -	17 (22.7%)	60 (41.4%)
	Grade 1-2	17 (22.7%)	58 (40.0%)
	1	14 (18.7%)	41 (28.3%)
	2	3 (4.0%)	17 (11.7%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Nausea	- Any Grade -	17 (22.7%)	60 (41.4%)
	Grade 1-2	17 (22.7%)	58 (40.0%)
	1	14 (18.7%)	41 (28.3%)
	2	3 (4.0%)	17 (11.7%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Immune-Mediated Rash			
- Overall -	- Any Grade -	18 (24.0%)	47 (32.4%)
	Grade 1-2	18 (24.0%)	41 (28.3%)
	1	14 (18.7%)	27 (18.6%)
	2	4 (5.3%)	14 (9.7%)
	Grade 3-4	0	6 (4.1%)
	3	0	6 (4.1%)
Rash	- Any Grade -	9 (12.0%)	31 (21.4%)
	Grade 1-2	9 (12.0%)	29 (20.0%)
	1	9 (12.0%)	21 (14.5%)
	2	0	8 (5.5%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Rash maculo-papular	- Any Grade -	4 (5.3%)	7 (4.8%)
	Grade 1-2	4 (5.3%)	5 (3.4%)
	1	3 (4.0%)	3 (2.1%)
	2	1 (1.3%)	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Erythema	- Any Grade -	3 (4.0%)	5 (3.4%)
	Grade 1-2	3 (4.0%)	5 (3.4%)
	1	2 (2.7%)	3 (2.1%)
	2	1 (1.3%)	2 (1.4%)
Dermatitis acneiform	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	2 (2.7%)	3 (2.1%)
Folliculitis	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	0	3 (2.1%)
	2	1 (1.3%)	1 (0.7%)
Dermatitis	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	1 (1.3%)	3 (2.1%)
Dermatitis allergic	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	2	2 (2.7%)	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Drug eruption	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash erythematous	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash papular	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Rash pruritic	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Rash			
- Overall -	- Any Grade -	18 (24.0%)	47 (32.4%)
	Grade 1-2	18 (24.0%)	41 (28.3%)
	1	14 (18.7%)	26 (17.9%)
	2	4 (5.3%)	15 (10.3%)
	Grade 3-4	0	6 (4.1%)
	3	0	6 (4.1%)
Rash	- Any Grade -	9 (12.0%)	31 (21.4%)
	Grade 1-2	9 (12.0%)	29 (20.0%)
	1	9 (12.0%)	21 (14.5%)
	2	0	8 (5.5%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Rash maculo-papular	- Any Grade -	4 (5.3%)	7 (4.8%)
	Grade 1-2	4 (5.3%)	5 (3.4%)
	1	3 (4.0%)	3 (2.1%)
	2	1 (1.3%)	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Erythema	- Any Grade -	3 (4.0%)	5 (3.4%)
	Grade 1-2	3 (4.0%)	5 (3.4%)
	1	2 (2.7%)	3 (2.1%)
	2	1 (1.3%)	2 (1.4%)
Dermatitis acneiform	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	1	2 (2.7%)	3 (2.1%)
Folliculitis	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	0	3 (2.1%)
	2	1 (1.3%)	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Dermatitis	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	1 (1.3%)	3 (2.1%)
Dermatitis allergic	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	2 (2.7%)	1 (0.7%)
	2	2 (2.7%)	1 (0.7%)
Dermatitis bullous	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Drug eruption	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash erythematous	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash papular	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Rash pruritic	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Erythropenia			
- Overall -	- Any Grade -	16 (21.3%)	47 (32.4%)
	Grade 1-2	16 (21.3%)	45 (31.0%)
	1	9 (12.0%)	19 (13.1%)
	2	7 (9.3%)	26 (17.9%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Anaemia	- Any Grade -	15 (20.0%)	45 (31.0%)
	Grade 1-2	15 (20.0%)	43 (29.7%)
	1	8 (10.7%)	18 (12.4%)
	2	7 (9.3%)	25 (17.2%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Haemoglobin decreased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Haematocrit decreased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Anaemia			
- Overall -	- Any Grade -	15 (20.0%)	45 (31.0%)
	Grade 1-2	15 (20.0%)	43 (29.7%)
	1	8 (10.7%)	18 (12.4%)
	2	7 (9.3%)	25 (17.2%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Anaemia	- Any Grade -	15 (20.0%)	45 (31.0%)
	Grade 1-2	15 (20.0%)	43 (29.7%)
	1	8 (10.7%)	18 (12.4%)
	2	7 (9.3%)	25 (17.2%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Vomiting			
- Overall -	- Any Grade -	6 (8.0%)	45 (31.0%)
	Grade 1-2	6 (8.0%)	42 (29.0%)
	1	6 (8.0%)	30 (20.7%)
	2	0	12 (8.3%)
	Grade 3-4	0	3 (2.1%)
	3	0	2 (1.4%)
	4	0	1 (0.7%)
Vomiting	- Any Grade -	6 (8.0%)	45 (31.0%)
	Grade 1-2	6 (8.0%)	42 (29.0%)
	1	6 (8.0%)	30 (20.7%)
	2	0	12 (8.3%)
	Grade 3-4	0	3 (2.1%)
	3	0	2 (1.4%)
	4	0	1 (0.7%)
Hepatotoxicity			
- Overall -	- Any Grade -	21 (28.0%)	25 (17.2%)
	Grade 1-2	18 (24.0%)	17 (11.7%)
	1	11 (14.7%)	11 (7.6%)
	2	7 (9.3%)	6 (4.1%)
	Grade 3-4	3 (4.0%)	8 (5.5%)
	3	3 (4.0%)	8 (5.5%)
Alanine aminotransferase increased	- Any Grade -	15 (20.0%)	19 (13.1%)
	Grade 1-2	12 (16.0%)	12 (8.3%)
	1	8 (10.7%)	9 (6.2%)
	2	4 (5.3%)	3 (2.1%)
	Grade 3-4	3 (4.0%)	7 (4.8%)
	3	3 (4.0%)	7 (4.8%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Aspartate aminotransferase increased	- Any Grade -	10 (13.3%)	13 (9.0%)
	Grade 1-2	9 (12.0%)	11 (7.6%)
	1	8 (10.7%)	8 (5.5%)
	2	1 (1.3%)	3 (2.1%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
Blood alkaline phosphatase increased	- Any Grade -	7 (9.3%)	3 (2.1%)
	Grade 1-2	7 (9.3%)	3 (2.1%)
	1	2 (2.7%)	3 (2.1%)
	2	5 (6.7%)	0
Hyperbilirubinaemia	- Any Grade -	4 (5.3%)	6 (4.1%)
	Grade 1-2	4 (5.3%)	6 (4.1%)
	1	3 (4.0%)	4 (2.8%)
	2	1 (1.3%)	2 (1.4%)
Gamma-glutamyltransferase increased	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	2 (2.7%)	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Blood bilirubin increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Cholestasis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Hepatic function abnormal	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)			
- Overall -	- Any Grade -	19 (25.3%)	24 (16.6%)
	Grade 1-2	16 (21.3%)	16 (11.0%)
	1	11 (14.7%)	10 (6.9%)
	2	5 (6.7%)	6 (4.1%)
	Grade 3-4	3 (4.0%)	8 (5.5%)
	3	3 (4.0%)	8 (5.5%)
Alanine aminotransferase increased	- Any Grade -	15 (20.0%)	19 (13.1%)
	Grade 1-2	12 (16.0%)	12 (8.3%)
	1	8 (10.7%)	9 (6.2%)
	2	4 (5.3%)	3 (2.1%)
	Grade 3-4	3 (4.0%)	7 (4.8%)
	3	3 (4.0%)	7 (4.8%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Aspartate aminotransferase increased	- Any Grade -	10 (13.3%)	13 (9.0%)
	Grade 1-2	9 (12.0%)	11 (7.6%)
	1	8 (10.7%)	8 (5.5%)
	2	1 (1.3%)	3 (2.1%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
Hyperbilirubinaemia	- Any Grade -	4 (5.3%)	6 (4.1%)
	Grade 1-2	4 (5.3%)	6 (4.1%)
	1	3 (4.0%)	4 (2.8%)
	2	1 (1.3%)	2 (1.4%)
Gamma-glutamyltransferase increased	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	2 (2.7%)	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Blood bilirubin increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Hepatic function abnormal	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Immune-Mediated Hepatitis (Lab Abnormalities)			
- Overall -	- Any Grade -	19 (25.3%)	24 (16.6%)
	Grade 1-2	16 (21.3%)	16 (11.0%)
	1	11 (14.7%)	10 (6.9%)
	2	5 (6.7%)	6 (4.1%)
	Grade 3-4	3 (4.0%)	8 (5.5%)
	3	3 (4.0%)	8 (5.5%)
Alanine aminotransferase increased	- Any Grade -	15 (20.0%)	19 (13.1%)
	Grade 1-2	12 (16.0%)	12 (8.3%)
	1	8 (10.7%)	9 (6.2%)
	2	4 (5.3%)	3 (2.1%)
	Grade 3-4	3 (4.0%)	7 (4.8%)
	3	3 (4.0%)	7 (4.8%)
Aspartate aminotransferase increased	- Any Grade -	10 (13.3%)	13 (9.0%)
	Grade 1-2	9 (12.0%)	11 (7.6%)
	1	8 (10.7%)	8 (5.5%)
	2	1 (1.3%)	3 (2.1%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
Hyperbilirubinaemia	- Any Grade -	4 (5.3%)	6 (4.1%)
	Grade 1-2	4 (5.3%)	6 (4.1%)
	1	3 (4.0%)	4 (2.8%)
	2	1 (1.3%)	2 (1.4%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Gamma-glutamyltransferase increased	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	2 (2.7%)	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Blood bilirubin increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Hepatic function abnormal	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Oral mucositis			
- Overall -	- Any Grade -	9 (12.0%)	27 (18.6%)
	Grade 1-2	9 (12.0%)	27 (18.6%)
	1	7 (9.3%)	21 (14.5%)
	2	2 (2.7%)	6 (4.1%)
Stomatitis	- Any Grade -	6 (8.0%)	16 (11.0%)
	Grade 1-2	6 (8.0%)	16 (11.0%)
	1	5 (6.7%)	13 (9.0%)
	2	1 (1.3%)	3 (2.1%)
Mucosal inflammation	- Any Grade -	3 (4.0%)	8 (5.5%)
	Grade 1-2	3 (4.0%)	8 (5.5%)
	1	2 (2.7%)	6 (4.1%)
	2	1 (1.3%)	2 (1.4%)
Mouth ulceration	- Any Grade -	1 (1.3%)	5 (3.4%)
	Grade 1-2	1 (1.3%)	5 (3.4%)
	1	1 (1.3%)	4 (2.8%)
	2	0	1 (0.7%)
Elevated transaminase			
- Overall -	- Any Grade -	16 (21.3%)	19 (13.1%)
	Grade 1-2	13 (17.3%)	12 (8.3%)
	1	9 (12.0%)	9 (6.2%)
	2	4 (5.3%)	3 (2.1%)
	Grade 3-4	3 (4.0%)	7 (4.8%)
	3	3 (4.0%)	7 (4.8%)
Alanine aminotransferase increased	- Any Grade -	15 (20.0%)	19 (13.1%)
	Grade 1-2	12 (16.0%)	12 (8.3%)
	1	8 (10.7%)	9 (6.2%)
	2	4 (5.3%)	3 (2.1%)
	Grade 3-4	3 (4.0%)	7 (4.8%)
	3	3 (4.0%)	7 (4.8%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Aspartate aminotransferase increased	- Any Grade -	10 (13.3%)	13 (9.0%)
	Grade 1-2	9 (12.0%)	11 (7.6%)
	1	8 (10.7%)	8 (5.5%)
	2	1 (1.3%)	3 (2.1%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
Hyperglycemia			
- Overall -	- Any Grade -	10 (13.3%)	23 (15.9%)
	Grade 1-2	10 (13.3%)	20 (13.8%)
	1	8 (10.7%)	10 (6.9%)
	2	2 (2.7%)	10 (6.9%)
	Grade 3-4	0	3 (2.1%)
	3	0	3 (2.1%)
Hyperglycaemia	- Any Grade -	10 (13.3%)	19 (13.1%)
	Grade 1-2	10 (13.3%)	16 (11.0%)
	1	8 (10.7%)	6 (4.1%)
	2	2 (2.7%)	10 (6.9%)
	Grade 3-4	0	3 (2.1%)
	3	0	3 (2.1%)
Blood glucose increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Diabetes mellitus	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Glycosylated haemoglobin increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Type 2 diabetes mellitus	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Decreased appetite			
- Overall -	- Any Grade -	7 (9.3%)	22 (15.2%)
	Grade 1-2	7 (9.3%)	20 (13.8%)
	1	4 (5.3%)	16 (11.0%)
	2	3 (4.0%)	4 (2.8%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Decreased appetite	- Any Grade -	7 (9.3%)	22 (15.2%)
	Grade 1-2	7 (9.3%)	20 (13.8%)
	1	4 (5.3%)	16 (11.0%)
	2	3 (4.0%)	4 (2.8%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hyperlipidemia			
- Overall -	- Any Grade -	8 (10.7%)	17 (11.7%)
	Grade 1-2	7 (9.3%)	16 (11.0%)
	1	3 (4.0%)	8 (5.5%)
	2	4 (5.3%)	8 (5.5%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	0	1 (0.7%)
	4	1 (1.3%)	0
Hypertriglyceridaemia	- Any Grade -	5 (6.7%)	7 (4.8%)
	Grade 1-2	4 (5.3%)	6 (4.1%)
	1	3 (4.0%)	2 (1.4%)
	2	1 (1.3%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	0	1 (0.7%)
	4	1 (1.3%)	0
Blood cholesterol increased	- Any Grade -	3 (4.0%)	6 (4.1%)
	Grade 1-2	3 (4.0%)	6 (4.1%)
	1	2 (2.7%)	5 (3.4%)
	2	1 (1.3%)	1 (0.7%)
Hypercholesterolaemia	- Any Grade -	2 (2.7%)	4 (2.8%)
	Grade 1-2	2 (2.7%)	4 (2.8%)
	1	0	4 (2.8%)
	2	2 (2.7%)	0
Blood triglycerides increased	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	1 (0.7%)
	2	0	3 (2.1%)
Hyperlipidaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pneumonia			
- Overall -	- Any Grade -	4 (5.3%)	6 (4.1%)
	Grade 1-2	3 (4.0%)	5 (3.4%)
	1	0	1 (0.7%)
	2	3 (4.0%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
	Grade 5	0	1 (0.7%)
Pneumonia	- Any Grade -	4 (5.3%)	6 (4.1%)
	Grade 1-2	3 (4.0%)	5 (3.4%)
	1	0	1 (0.7%)
	2	3 (4.0%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
	Grade 5	0	1 (0.7%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Weight decreased			
- Overall -	- Any Grade -	2 (2.7%)	7 (4.8%)
	Grade 1-2	2 (2.7%)	7 (4.8%)
	1	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	5 (3.4%)
Weight decreased	- Any Grade -	2 (2.7%)	7 (4.8%)
	Grade 1-2	2 (2.7%)	7 (4.8%)
	1	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	5 (3.4%)
Immune-Mediated Pneumonitis			
- Overall -	- Any Grade -	0	6 (4.1%)
	Grade 1-2	0	5 (3.4%)
	1	0	4 (2.8%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	6 (4.1%)
	Grade 1-2	0	5 (3.4%)
	1	0	4 (2.8%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Pneumonitis			
- Overall -	- Any Grade -	0	6 (4.1%)
	Grade 1-2	0	5 (3.4%)
	1	0	4 (2.8%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	6 (4.1%)
	Grade 1-2	0	5 (3.4%)
	1	0	4 (2.8%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dehydration			
- Overall -	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	3 (2.1%)
	1	0	1 (0.7%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Dehydration	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	3 (2.1%)
	1	0	1 (0.7%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Immune-Mediated Severe Cutaneous Reactions			
- Overall -	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dermatitis bullous	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	0	1 (0.7%)
Erythema multiforme	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Thrombocytopenia			
- Overall -	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	1 (1.3%)	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Thrombocytopenia	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Platelet count decreased	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	1	1 (1.3%)	0
Colitis			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Enterocolitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erythema multiforme			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erythema multiforme	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Immune-Mediated Diabetes Mellitus			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Diabetes mellitus	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	101 (99.0%)
	Grade 1-2	49 (48.0%)
	1	5 (4.9%)
	2	44 (43.1%)
	Grade 3-4	51 (50.0%)
	3	46 (45.1%)
	4	5 (4.9%)
	Grade 5	1 (1.0%)
Diarrhea		
- Overall -	- Any Grade -	86 (84.3%)
	Grade 1-2	69 (67.6%)
	1	28 (27.5%)
	2	41 (40.2%)
	Grade 3-4	17 (16.7%)
	3	17 (16.7%)
Diarrhoea	- Any Grade -	86 (84.3%)
	Grade 1-2	69 (67.6%)
	1	28 (27.5%)
	2	41 (40.2%)
	Grade 3-4	17 (16.7%)
	3	17 (16.7%)
Peripheral neuropathy		
- Overall -	- Any Grade -	53 (52.0%)
	Grade 1-2	44 (43.1%)
	1	30 (29.4%)
	2	14 (13.7%)
	Grade 3-4	9 (8.8%)
	3	9 (8.8%)
Neuropathy peripheral	- Any Grade -	30 (29.4%)
	Grade 1-2	23 (22.5%)
	1	14 (13.7%)
	2	9 (8.8%)
	Grade 3-4	7 (6.9%)
	3	7 (6.9%)
Peripheral sensory neuropathy	- Any Grade -	8 (7.8%)
	Grade 1-2	7 (6.9%)
	1	6 (5.9%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Polyneuropathy	- Any Grade -	8 (7.8%)
	Grade 1-2	8 (7.8%)
	1	4 (3.9%)
	2	4 (3.9%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hypoaesthesia	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	4 (3.9%)
	2	1 (1.0%)
Paraesthesia	- Any Grade -	5 (4.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
Peripheral motor neuropathy	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neurotoxicity	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Immune-Mediated Rash		
- Overall -	- Any Grade -	46 (45.1%)
	Grade 1-2	41 (40.2%)
	1	26 (25.5%)
	2	15 (14.7%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Rash	- Any Grade -	31 (30.4%)
	Grade 1-2	29 (28.4%)
	1	20 (19.6%)
	2	9 (8.8%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Rash maculo-papular	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dermatitis acneiform	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Erythema	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
Hand dermatitis	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Dermatitis allergic	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Rash erythematous	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Rash papular	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash pruritic	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash pustular	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash		
- Overall -	- Any Grade -	46 (45.1%)
	Grade 1-2	41 (40.2%)
	1	26 (25.5%)
	2	15 (14.7%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Rash	- Any Grade -	31 (30.4%)
	Grade 1-2	29 (28.4%)
	1	20 (19.6%)
	2	9 (8.8%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Rash maculo-papular	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dermatitis acneiform	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
Erythema	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hand dermatitis	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
Dermatitis allergic	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Rash erythematous	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Rash papular	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash pruritic	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash pustular	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Nausea		
- Overall -	- Any Grade -	42 (41.2%)
	Grade 1-2	40 (39.2%)
	1	29 (28.4%)
	2	11 (10.8%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Nausea	- Any Grade -	42 (41.2%)
	Grade 1-2	40 (39.2%)
	1	29 (28.4%)
	2	11 (10.8%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Asthenia		
- Overall -	- Any Grade -	40 (39.2%)
	Grade 1-2	36 (35.3%)
	1	21 (20.6%)
	2	15 (14.7%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Fatigue	- Any Grade -	23 (22.5%)
	Grade 1-2	20 (19.6%)
	1	11 (10.8%)
	2	9 (8.8%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Asthenia	- Any Grade -	19 (18.6%)
	Grade 1-2	18 (17.6%)
	1	12 (11.8%)
	2	6 (5.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hepatotoxicity		
- Overall -	- Any Grade -	35 (34.3%)
	Grade 1-2	21 (20.6%)
	1	16 (15.7%)
	2	5 (4.9%)
	Grade 3-4	14 (13.7%)
	3	14 (13.7%)
Alanine aminotransferase increased	- Any Grade -	26 (25.5%)
	Grade 1-2	18 (17.6%)
	1	14 (13.7%)
	2	4 (3.9%)
	Grade 3-4	8 (7.8%)
	3	8 (7.8%)
Aspartate aminotransferase increased	- Any Grade -	22 (21.6%)
	Grade 1-2	14 (13.7%)
	1	8 (7.8%)
	2	6 (5.9%)
	Grade 3-4	8 (7.8%)
	3	8 (7.8%)
Blood alkaline phosphatase increased	- Any Grade -	12 (11.8%)
	Grade 1-2	9 (8.8%)
	1	8 (7.8%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Hyperbilirubinaemia	- Any Grade -	6 (5.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Blood bilirubin increased	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cholestasis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Gamma-glutamyltransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Prothrombin time prolonged	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Anaemia		
- Overall -	- Any Grade -	34 (33.3%)
	Grade 1-2	32 (31.4%)
	1	15 (14.7%)
	2	17 (16.7%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Anaemia	- Any Grade -	34 (33.3%)
	Grade 1-2	32 (31.4%)
	1	15 (14.7%)
	2	17 (16.7%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Erythropenia		
- Overall -	- Any Grade -	34 (33.3%)
	Grade 1-2	32 (31.4%)
	1	15 (14.7%)
	2	17 (16.7%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Anaemia	- Any Grade -	34 (33.3%)
	Grade 1-2	32 (31.4%)
	1	15 (14.7%)
	2	17 (16.7%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Haematocrit decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Red blood cell count decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_ctc_C_SE.out
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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Neutropenia		
- Overall -	- Any Grade -	34 (33.3%)
	Grade 1-2	23 (22.5%)
	1	4 (3.9%)
	2	19 (18.6%)
	Grade 3-4	11 (10.8%)
	3	8 (7.8%)
	4	3 (2.9%)
Neutropenia	- Any Grade -	25 (24.5%)
	Grade 1-2	19 (18.6%)
	1	4 (3.9%)
	2	15 (14.7%)
	Grade 3-4	6 (5.9%)
	3	5 (4.9%)
	4	1 (1.0%)
Neutrophil count decreased	- Any Grade -	8 (7.8%)
	Grade 1-2	4 (3.9%)
	2	4 (3.9%)
	Grade 3-4	4 (3.9%)
	3	3 (2.9%)
	4	1 (1.0%)
Febrile neutropenia	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)		
- Overall -	- Any Grade -	32 (31.4%)
	Grade 1-2	20 (19.6%)
	1	13 (12.7%)
	2	7 (6.9%)
	Grade 3-4	12 (11.8%)
	3	12 (11.8%)
Alanine aminotransferase increased	- Any Grade -	26 (25.5%)
	Grade 1-2	18 (17.6%)
	1	14 (13.7%)
	2	4 (3.9%)
	Grade 3-4	8 (7.8%)
	3	8 (7.8%)
Aspartate aminotransferase increased	- Any Grade -	22 (21.6%)
	Grade 1-2	14 (13.7%)
	1	8 (7.8%)
	2	6 (5.9%)
	Grade 3-4	8 (7.8%)
	3	8 (7.8%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hyperbilirubinaemia	- Any Grade -	6 (5.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Blood bilirubin increased	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
Gamma-glutamyltransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-Mediated Hepatitis (Lab Abnormalities)		
- Overall -	- Any Grade -	32 (31.4%)
	Grade 1-2	20 (19.6%)
	1	13 (12.7%)
	2	7 (6.9%)
	Grade 3-4	12 (11.8%)
	3	12 (11.8%)
Alanine aminotransferase increased	- Any Grade -	26 (25.5%)
	Grade 1-2	18 (17.6%)
	1	14 (13.7%)
	2	4 (3.9%)
	Grade 3-4	8 (7.8%)
	3	8 (7.8%)
Aspartate aminotransferase increased	- Any Grade -	22 (21.6%)
	Grade 1-2	14 (13.7%)
	1	8 (7.8%)
	2	6 (5.9%)
	Grade 3-4	8 (7.8%)
	3	8 (7.8%)
Hyperbilirubinaemia	- Any Grade -	6 (5.9%)
	Grade 1-2	5 (4.9%)
	1	5 (4.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Blood bilirubin increased	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
Gamma-glutamyltransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Vomiting		
- Overall -	- Any Grade -	29 (28.4%)
	Grade 1-2	27 (26.5%)
	1	22 (21.6%)
	2	5 (4.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Vomiting	- Any Grade -	29 (28.4%)
	Grade 1-2	27 (26.5%)
	1	22 (21.6%)
	2	5 (4.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Retching	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Elevated transaminase		
- Overall -	- Any Grade -	28 (27.5%)
	Grade 1-2	17 (16.7%)
	1	10 (9.8%)
	2	7 (6.9%)
	Grade 3-4	11 (10.8%)
	3	11 (10.8%)
Alanine aminotransferase increased	- Any Grade -	26 (25.5%)
	Grade 1-2	18 (17.6%)
	1	14 (13.7%)
	2	4 (3.9%)
	Grade 3-4	8 (7.8%)
	3	8 (7.8%)
Aspartate aminotransferase increased	- Any Grade -	22 (21.6%)
	Grade 1-2	14 (13.7%)
	1	8 (7.8%)
	2	6 (5.9%)
	Grade 3-4	8 (7.8%)
	3	8 (7.8%)
Hyperglycemia		
- Overall -	- Any Grade -	24 (23.5%)
	Grade 1-2	19 (18.6%)
	1	10 (9.8%)
	2	9 (8.8%)
	Grade 3-4	5 (4.9%)
	3	4 (3.9%)
	4	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hyperglycaemia	- Any Grade -	22 (21.6%)
	Grade 1-2	18 (17.6%)
	1	9 (8.8%)
	2	9 (8.8%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Blood glucose increased	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Diabetes mellitus	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Glycosylated haemoglobin increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Type 1 diabetes mellitus	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Oral mucositis		
- Overall -	- Any Grade -	21 (20.6%)
	Grade 1-2	21 (20.6%)
	1	18 (17.6%)
	2	3 (2.9%)
Mucosal inflammation	- Any Grade -	12 (11.8%)
	Grade 1-2	12 (11.8%)
	1	10 (9.8%)
	2	2 (2.0%)
Stomatitis	- Any Grade -	7 (6.9%)
	Grade 1-2	7 (6.9%)
	1	6 (5.9%)
	2	1 (1.0%)
Mouth ulceration	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Decreased appetite		
- Overall -	- Any Grade -	14 (13.7%)
	Grade 1-2	13 (12.7%)
	1	11 (10.8%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Decreased appetite	- Any Grade -	14 (13.7%)
	Grade 1-2	13 (12.7%)
	1	11 (10.8%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hyperlipidemia		
- Overall -	- Any Grade -	14 (13.7%)
	Grade 1-2	13 (12.7%)
	1	11 (10.8%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Blood cholesterol increased	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Blood triglycerides increased	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	3 (2.9%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Hypercholesterolaemia	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	4 (3.9%)
Hypertriglyceridaemia	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
Immune-Mediated Pneumonitis		
- Overall -	- Any Grade -	9 (8.8%)
	Grade 1-2	8 (7.8%)
	1	5 (4.9%)
	2	3 (2.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_ctc_C_SE.out
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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Pneumonitis	- Any Grade -	7 (6.9%)
	Grade 1-2	6 (5.9%)
	1	4 (3.9%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Lung infiltration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pneumonitis		
- Overall -	- Any Grade -	9 (8.8%)
	Grade 1-2	8 (7.8%)
	1	5 (4.9%)
	2	3 (2.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonitis	- Any Grade -	7 (6.9%)
	Grade 1-2	6 (5.9%)
	1	4 (3.9%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Lung infiltration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pneumonia		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	5 (4.9%)
	1	2 (2.0%)
	2	3 (2.9%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
	Grade 5	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Pneumonia	- Any Grade -	6 (5.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
	Grade 5	1 (1.0%)
Pneumonia viral	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Weight decreased		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	7 (6.9%)
	1	5 (4.9%)
	2	2 (2.0%)
Weight decreased	- Any Grade -	7 (6.9%)
	Grade 1-2	7 (6.9%)
	1	5 (4.9%)
	2	2 (2.0%)
Dehydration		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Dehydration	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Thrombocytopenia		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Platelet count decreased	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Thrombocytopenia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_ctc_C_SE.out
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Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Immune-Mediated Diabetes Mellitus		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Diabetes mellitus	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Type 1 diabetes mellitus	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_ctc_C_SE.out
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Selected Adverse Events Leading to Atezolizumab Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	6 (5.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Elevated transaminase		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Alanine aminotransferase increased	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Aspartate aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Hepatotoxicity		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Alanine aminotransferase increased	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Aspartate aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Blood alkaline phosphatase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Alanine aminotransferase increased	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Aspartate aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_ctc_DSCATZ_C_SE.out
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Selected Adverse Events Leading to Atezolizumab Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Immune-Mediated Hepatitis (Lab Abnormalities)		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Alanine aminotransferase increased	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Aspartate aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Diarrhea		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Diarrhoea	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Immune-Mediated Pneumonitis		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonia		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Pneumonia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Pneumonitis		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_ctc_DSCATZ_C_SE.out
08MAY2023 7:11

Selected Adverse Events Leading to Ipatasertib/Placebo Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	3 (3.4%)	13 (7.8%)
	Grade 1-2	0	5 (3.0%)
	2	0	5 (3.0%)
	Grade 3-4	3 (3.4%)	8 (4.8%)
	3	3 (3.4%)	7 (4.2%)
	4	0	1 (0.6%)
Diarrhea			
- Overall -	- Any Grade -	0	6 (3.6%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Diarrhoea	- Any Grade -	0	6 (3.6%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Hyperglycemia			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Hyperglycaemia	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Immune-Mediated Rash			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Erythema	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Rash	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Peripheral neuropathy			
- Overall -	- Any Grade -	2 (2.3%)	0
	Grade 3-4	2 (2.3%)	0
	3	2 (2.3%)	0
Neuropathy peripheral	- Any Grade -	2 (2.3%)	0
	Grade 3-4	2 (2.3%)	0
	3	2 (2.3%)	0

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events Leading to Ipatasertib/Placebo Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Rash			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Erythema	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Rash	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Asthenia			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Fatigue	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Elevated transaminase			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Aspartate aminotransferase increased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Erythema multiforme			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Erythema multiforme	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hepatotoxicity			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Aspartate aminotransferase increased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Aspartate aminotransferase increased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Immune-Mediated Hepatitis (Lab Abnormalities)			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Aspartate aminotransferase increased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Immune-Mediated Severe Cutaneous Reactions			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Erythema multiforme	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Neutropenia			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Neutrophil count decreased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Pneumonia			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	3 (4.0%)	12 (8.3%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	2	1 (1.3%)	4 (2.8%)
	Grade 3-4	2 (2.7%)	6 (4.1%)
	3	2 (2.7%)	6 (4.1%)
	Grade 5	0	2 (1.4%)
Diarrhea			
- Overall -	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	0	3 (2.1%)
	2	0	3 (2.1%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Diarrhoea	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	0	3 (2.1%)
	2	0	3 (2.1%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Neutropenia			
- Overall -	- Any Grade -	0	3 (2.1%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
	Grade 5	0	1 (0.7%)
Febrile neutropenia	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Neutropenia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperglycemia			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperglycaemia	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Asthenia			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Fatigue	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Elevated transaminase			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Alanine aminotransferase increased	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hepatotoxicity			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Alanine aminotransferase increased	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Alanine aminotransferase increased	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Immune-Mediated Hepatitis (Lab Abnormalities)			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Alanine aminotransferase increased	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Immune-Mediated Pneumonitis			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Oral mucositis			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Stomatitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Peripheral neuropathy			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Peripheral sensory neuropathy	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Pneumonia			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Pneumonia	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Pneumonitis			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Vomiting			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vomiting	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1.
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08MAY2023 7:00 Page 3 of 3

Selected Adverse Events Leading to Ipatasertib Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	5 (4.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	4 (3.9%)
	3	3 (2.9%)
	4	1 (1.0%)
Elevated transaminase		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Aspartate aminotransferase increased	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Alanine aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Hepatotoxicity		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Aspartate aminotransferase increased	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Alanine aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Blood alkaline phosphatase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events Leading to Ipatasertib Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Aspartate aminotransferase increased	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Alanine aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Immune-Mediated Hepatitis (Lab Abnormalities)		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Aspartate aminotransferase increased	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Alanine aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Hyperglycemia		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Hyperglycaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-Mediated Diabetes Mellitus		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)

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08MAY2023 7:01

Selected Adverse Events Leading to Ipatasertib Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Immune-Mediated Pneumonitis		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonitis		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_ctc_DSCIPAT_C_SE.out
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Selected Adverse Events Leading to Paclitaxel Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	11 (12.6%)	20 (12.0%)
	Grade 1-2	6 (6.9%)	4 (2.4%)
	1	1 (1.1%)	0
	2	5 (5.7%)	4 (2.4%)
	Grade 3-4	5 (5.7%)	16 (9.6%)
	3	5 (5.7%)	14 (8.4%)
	4	0	2 (1.2%)
Peripheral neuropathy			
- Overall -	- Any Grade -	9 (10.3%)	13 (7.8%)
	Grade 1-2	5 (5.7%)	3 (1.8%)
	1	1 (1.1%)	0
	2	4 (4.6%)	3 (1.8%)
	Grade 3-4	4 (4.6%)	10 (6.0%)
	3	4 (4.6%)	10 (6.0%)
Neuropathy peripheral	- Any Grade -	4 (4.6%)	8 (4.8%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	2	1 (1.1%)	3 (1.8%)
	Grade 3-4	3 (3.4%)	5 (3.0%)
	3	3 (3.4%)	5 (3.0%)
Peripheral sensory neuropathy	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	3 (1.8%)
	3	1 (1.1%)	3 (1.8%)
Polyneuropathy	- Any Grade -	3 (3.4%)	1 (0.6%)
	Grade 1-2	3 (3.4%)	0
	1	1 (1.1%)	0
	2	2 (2.3%)	0
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Peripheral motor neuropathy	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Toxic neuropathy	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Diarrhea			
- Overall -	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events Leading to Paclitaxel Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Diarrhoea	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Immune-Mediated Rash			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Erythema	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Rash	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Neutropenia			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	4	0	2 (1.2%)
Neutropenia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Neutrophil count decreased	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Rash			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Erythema	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Rash	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Asthenia			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
Fatigue	- Any Grade -	1 (1.1%)	0
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0

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Selected Adverse Events Leading to Paclitaxel Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Pneumonia			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events Leading to Paclitaxel Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	10 (13.3%)	35 (24.1%)
	Grade 1-2	4 (5.3%)	15 (10.3%)
	1	1 (1.3%)	1 (0.7%)
	2	3 (4.0%)	14 (9.7%)
	Grade 3-4	6 (8.0%)	18 (12.4%)
	3	5 (6.7%)	18 (12.4%)
	4	1 (1.3%)	0
	Grade 5	0	2 (1.4%)
Peripheral neuropathy			
- Overall -	- Any Grade -	7 (9.3%)	22 (15.2%)
	Grade 1-2	3 (4.0%)	12 (8.3%)
	1	1 (1.3%)	0
	2	2 (2.7%)	12 (8.3%)
	Grade 3-4	4 (5.3%)	10 (6.9%)
	3	4 (5.3%)	10 (6.9%)
Peripheral sensory neuropathy	- Any Grade -	5 (6.7%)	7 (4.8%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	2	1 (1.3%)	4 (2.8%)
	Grade 3-4	4 (5.3%)	3 (2.1%)
	3	4 (5.3%)	3 (2.1%)
Neuropathy peripheral	- Any Grade -	1 (1.3%)	10 (6.9%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	2	1 (1.3%)	4 (2.8%)
	Grade 3-4	0	6 (4.1%)
	3	0	6 (4.1%)
Neurotoxicity	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
Paraesthesia	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
Polyneuropathy	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Selected Adverse Events Leading to Paclitaxel Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Neutropenia			
- Overall -	- Any Grade -	2 (2.7%)	8 (5.5%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	2 (2.7%)	5 (3.4%)
	3	1 (1.3%)	5 (3.4%)
	4	1 (1.3%)	0
	Grade 5	0	1 (0.7%)
Neutrophil count decreased	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
	4	1 (1.3%)	0
Febrile neutropenia	- Any Grade -	0	3 (2.1%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
	Grade 5	0	1 (0.7%)
Neutropenia	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Asthenia			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Fatigue	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Asthenia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Anaemia			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Anaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Diarrhea			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Selected Adverse Events Leading to Paclitaxel Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Diarrhoea	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Erythropenia			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Anaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hyperglycemia			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperglycaemia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Immune-Mediated Pneumonitis			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Immune-Mediated Rash			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Nausea			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nausea	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Pneumonia			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)

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Selected Adverse Events Leading to Paclitaxel Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Pneumonia	- Any Grade -	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Pneumonitis			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events Leading to Paclitaxel Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	15 (14.7%)
	Grade 1-2	9 (8.8%)
	1	2 (2.0%)
	2	7 (6.9%)
	Grade 3-4	6 (5.9%)
	3	6 (5.9%)
Peripheral neuropathy		
- Overall -	- Any Grade -	11 (10.8%)
	Grade 1-2	7 (6.9%)
	1	2 (2.0%)
	2	5 (4.9%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Neuropathy peripheral	- Any Grade -	7 (6.9%)
	Grade 1-2	4 (3.9%)
	2	4 (3.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Polyneuropathy	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Peripheral motor neuropathy	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Peripheral sensory neuropathy	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Asthenia		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Fatigue	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Elevated transaminase		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

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Selected Adverse Events Leading to Paclitaxel Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hepatotoxicity		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Immune-Mediated Hepatitis (Lab Abnormalities)		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Immune-Mediated Pneumonitis		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neutropenia		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neutrophil count decreased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonia		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

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Selected Adverse Events Leading to Paclitaxel Treatment Discontinuation by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Pneumonia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Pneumonitis		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonitis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_ctc_DSCPAC_C_SE.out
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Selected Adverse Events Leading to Atezolizumab Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	38 (37.3%)
	Grade 1-2	18 (17.6%)
	1	4 (3.9%)
	2	14 (13.7%)
	Grade 3-4	20 (19.6%)
	3	17 (16.7%)
	4	3 (2.9%)
Immune-Mediated Rash		
- Overall -	- Any Grade -	10 (9.8%)
	Grade 1-2	5 (4.9%)
	1	2 (2.0%)
	2	3 (2.9%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Rash	- Any Grade -	6 (5.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Rash erythematous	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash maculo-papular	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash papular	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash pruritic	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neutropenia		
- Overall -	- Any Grade -	10 (9.8%)
	Grade 1-2	5 (4.9%)
	2	5 (4.9%)
	Grade 3-4	5 (4.9%)
	3	3 (2.9%)
	4	2 (2.0%)
Neutropenia	- Any Grade -	7 (6.9%)
	Grade 1-2	5 (4.9%)
	2	5 (4.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_ctc_DSIATZ_C_SE.out
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Selected Adverse Events Leading to Atezolizumab Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Febrile neutropenia	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Neutrophil count decreased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Rash		
- Overall -	- Any Grade -	10 (9.8%)
	Grade 1-2	5 (4.9%)
	1	2 (2.0%)
	2	3 (2.9%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Rash	- Any Grade -	6 (5.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Rash erythematous	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash maculo-papular	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash papular	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash pruritic	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hepatotoxicity		
- Overall -	- Any Grade -	8 (7.8%)
	Grade 1-2	3 (2.9%)
	2	3 (2.9%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Aspartate aminotransferase increased	- Any Grade -	7 (6.9%)
	Grade 1-2	5 (4.9%)
	1	3 (2.9%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)

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Selected Adverse Events Leading to Atezolizumab Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Alanine aminotransferase increased	- Any Grade -	5 (4.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Blood alkaline phosphatase increased	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Blood bilirubin increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Elevated transaminase		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	3 (2.9%)
	2	3 (2.9%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Aspartate aminotransferase increased	- Any Grade -	7 (6.9%)
	Grade 1-2	5 (4.9%)
	1	3 (2.9%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Alanine aminotransferase increased	- Any Grade -	5 (4.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	3 (2.9%)
	2	3 (2.9%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Aspartate aminotransferase increased	- Any Grade -	7 (6.9%)
	Grade 1-2	5 (4.9%)
	1	3 (2.9%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)

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Selected Adverse Events Leading to Atezolizumab Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Alanine aminotransferase increased	- Any Grade -	5 (4.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Blood bilirubin increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Immune-Mediated Hepatitis (Lab Abnormalities)		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	3 (2.9%)
	2	3 (2.9%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Aspartate aminotransferase increased	- Any Grade -	7 (6.9%)
	Grade 1-2	5 (4.9%)
	1	3 (2.9%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Alanine aminotransferase increased	- Any Grade -	5 (4.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Blood bilirubin increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Immune-Mediated Pneumonitis		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	3 (2.9%)
	2	3 (2.9%)
Pneumonitis	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

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Selected Adverse Events Leading to Atezolizumab Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Lung infiltration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pneumonitis		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	6 (5.9%)
	1	3 (2.9%)
	2	3 (2.9%)
Pneumonitis	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Lung infiltration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Diarrhea		
- Overall -	- Any Grade -	5 (4.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Diarrhoea	- Any Grade -	5 (4.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Asthenia		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Fatigue	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events Leading to Atezolizumab Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hyperglycemia		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	2 (2.0%)
	4	1 (1.0%)
Hyperglycaemia	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Nausea		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nausea	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dehydration		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dehydration	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-Mediated Diabetes Mellitus		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events Leading to Atezolizumab Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Weight decreased		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Weight decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	15 (17.2%)	51 (30.7%)
	Grade 1-2	4 (4.6%)	25 (15.1%)
	1	0	4 (2.4%)
	2	4 (4.6%)	21 (12.7%)
	Grade 3-4	11 (12.6%)	26 (15.7%)
	3	10 (11.5%)	24 (14.5%)
	4	1 (1.1%)	2 (1.2%)
Neutropenia			
- Overall -	- Any Grade -	8 (9.2%)	15 (9.0%)
	Grade 1-2	2 (2.3%)	4 (2.4%)
	2	2 (2.3%)	4 (2.4%)
	Grade 3-4	6 (6.9%)	11 (6.6%)
	3	5 (5.7%)	11 (6.6%)
	4	1 (1.1%)	0
Neutropenia	- Any Grade -	4 (4.6%)	10 (6.0%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	2	1 (1.1%)	3 (1.8%)
	Grade 3-4	3 (3.4%)	7 (4.2%)
	3	2 (2.3%)	7 (4.2%)
	4	1 (1.1%)	0
Neutrophil count decreased	- Any Grade -	4 (4.6%)	5 (3.0%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	3 (3.4%)	4 (2.4%)
	3	3 (3.4%)	4 (2.4%)
Diarrhea			
- Overall -	- Any Grade -	0	14 (8.4%)
	Grade 1-2	0	8 (4.8%)
	1	0	1 (0.6%)
	2	0	7 (4.2%)
	Grade 3-4	0	6 (3.6%)
	3	0	6 (3.6%)
Diarrhoea	- Any Grade -	0	14 (8.4%)
	Grade 1-2	0	8 (4.8%)
	1	0	1 (0.6%)
	2	0	7 (4.2%)
	Grade 3-4	0	6 (3.6%)
	3	0	6 (3.6%)
Hyperglycemia			
- Overall -	- Any Grade -	2 (2.3%)	8 (4.8%)
	Grade 1-2	2 (2.3%)	7 (4.2%)
	2	2 (2.3%)	7 (4.2%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hyperglycaemia	- Any Grade -	2 (2.3%)	8 (4.8%)
	Grade 1-2	2 (2.3%)	7 (4.2%)
	2	2 (2.3%)	7 (4.2%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Immune-Mediated Rash			
- Overall -	- Any Grade -	1 (1.1%)	6 (3.6%)
	Grade 1-2	1 (1.1%)	6 (3.6%)
	1	0	2 (1.2%)
	2	1 (1.1%)	4 (2.4%)
Rash	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	4 (2.4%)
	1	0	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
Dermatitis allergic	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Rash maculo-papular	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Rash			
- Overall -	- Any Grade -	1 (1.1%)	6 (3.6%)
	Grade 1-2	1 (1.1%)	6 (3.6%)
	1	0	2 (1.2%)
	2	1 (1.1%)	4 (2.4%)
Rash	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	4 (2.4%)
	1	0	2 (1.2%)
	2	1 (1.1%)	2 (1.2%)
Dermatitis allergic	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Rash maculo-papular	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Nausea			
- Overall -	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	2	1 (1.1%)	3 (1.8%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Nausea	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	3 (1.8%)
	2	1 (1.1%)	3 (1.8%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Pneumonia			
- Overall -	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	2 (1.2%)
Pneumonia	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Anaemia			
- Overall -	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	0	2 (1.2%)
	4	1 (1.1%)	0
Anaemia	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	0	2 (1.2%)
	4	1 (1.1%)	0
Asthenia			
- Overall -	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Asthenia	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Fatigue	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Erythropenia			
- Overall -	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	0	2 (1.2%)
	4	1 (1.1%)	0
Anaemia	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	0	2 (1.2%)
	4	1 (1.1%)	0
Vomiting			
- Overall -	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	1 (1.1%)	1 (0.6%)
	4	0	1 (0.6%)
Vomiting	- Any Grade -	1 (1.1%)	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	1 (1.1%)	1 (0.6%)
	4	0	1 (0.6%)
Peripheral neuropathy			
- Overall -	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Neuropathy peripheral	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Peripheral sensory neuropathy	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Elevated transaminase			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Hepatotoxicity			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Hyperlipidemia			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hypertriglyceridaemia	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Immune-Mediated Hepatitis (Lab Abnormalities)			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Alanine aminotransferase increased	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Immune-Mediated Pneumonitis			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Bronchiolitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Pneumonitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Oral mucositis			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Mucosal inflammation	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Pneumonitis			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
Bronchiolitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Pneumonitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Colitis			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Colitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Confirmed covid-19			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Covid-19 (smq)			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Decreased appetite			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Decreased appetite	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Immune-Mediated Colitis			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Colitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	19 (25.3%)	52 (35.9%)
	Grade 1-2	5 (6.7%)	26 (17.9%)
	1	0	5 (3.4%)
	2	5 (6.7%)	21 (14.5%)
	Grade 3-4	14 (18.7%)	26 (17.9%)
	3	13 (17.3%)	23 (15.9%)
	4	1 (1.3%)	3 (2.1%)
Neutropenia			
- Overall -	- Any Grade -	11 (14.7%)	18 (12.4%)
	Grade 1-2	3 (4.0%)	5 (3.4%)
	2	3 (4.0%)	5 (3.4%)
	Grade 3-4	8 (10.7%)	13 (9.0%)
	3	8 (10.7%)	11 (7.6%)
	4	0	2 (1.4%)
Neutrophil count decreased	- Any Grade -	6 (8.0%)	11 (7.6%)
	Grade 1-2	2 (2.7%)	3 (2.1%)
	2	2 (2.7%)	3 (2.1%)
	Grade 3-4	4 (5.3%)	8 (5.5%)
	3	4 (5.3%)	8 (5.5%)
Neutropenia	- Any Grade -	6 (8.0%)	7 (4.8%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
	Grade 3-4	5 (6.7%)	5 (3.4%)
	3	5 (6.7%)	3 (2.1%)
	4	0	2 (1.4%)
Diarrhea			
- Overall -	- Any Grade -	0	14 (9.7%)
	Grade 1-2	0	7 (4.8%)
	1	0	1 (0.7%)
	2	0	6 (4.1%)
	Grade 3-4	0	7 (4.8%)
	3	0	7 (4.8%)
Diarrhoea	- Any Grade -	0	14 (9.7%)
	Grade 1-2	0	7 (4.8%)
	1	0	1 (0.7%)
	2	0	6 (4.1%)
	Grade 3-4	0	7 (4.8%)
	3	0	7 (4.8%)
Rash			
- Overall -	- Any Grade -	2 (2.7%)	8 (5.5%)
	Grade 1-2	2 (2.7%)	6 (4.1%)
	2	2 (2.7%)	6 (4.1%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Drug eruption	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash maculo-papular	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Dermatitis bullous	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Erythema	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Immune-Mediated Rash			
- Overall -	- Any Grade -	2 (2.7%)	7 (4.8%)
	Grade 1-2	2 (2.7%)	5 (3.4%)
	2	2 (2.7%)	5 (3.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Drug eruption	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash maculo-papular	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Erythema	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hepatotoxicity			
- Overall -	- Any Grade -	2 (2.7%)	5 (3.4%)
	Grade 1-2	0	3 (2.1%)
	1	0	1 (0.7%)
	2	0	2 (1.4%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	2 (2.7%)	2 (1.4%)
Alanine aminotransferase increased	- Any Grade -	2 (2.7%)	4 (2.8%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	2 (2.7%)	2 (1.4%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Hyperbilirubinaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)			
- Overall -	- Any Grade -	2 (2.7%)	5 (3.4%)
	Grade 1-2	0	3 (2.1%)
	1	0	1 (0.7%)
	2	0	2 (1.4%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	2 (2.7%)	2 (1.4%)
Alanine aminotransferase increased	- Any Grade -	2 (2.7%)	4 (2.8%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	2 (2.7%)	2 (1.4%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Hyperbilirubinaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Immune-Mediated Hepatitis (Lab Abnormalities)			
- Overall -	- Any Grade -	2 (2.7%)	5 (3.4%)
	Grade 1-2	0	3 (2.1%)
	1	0	1 (0.7%)
	2	0	2 (1.4%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	2 (2.7%)	2 (1.4%)
Alanine aminotransferase increased	- Any Grade -	2 (2.7%)	4 (2.8%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	2 (2.7%)	2 (1.4%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Hyperbilirubinaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vomiting			
- Overall -	- Any Grade -	0	7 (4.8%)
	Grade 1-2	0	5 (3.4%)
	1	0	1 (0.7%)
	2	0	4 (2.8%)
	Grade 3-4	0	2 (1.4%)
	3	0	1 (0.7%)
	4	0	1 (0.7%)
Vomiting	- Any Grade -	0	7 (4.8%)
	Grade 1-2	0	5 (3.4%)
	1	0	1 (0.7%)
	2	0	4 (2.8%)
	Grade 3-4	0	2 (1.4%)
	3	0	1 (0.7%)
	4	0	1 (0.7%)
Asthenia			
- Overall -	- Any Grade -	3 (4.0%)	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	3 (4.0%)	1 (0.7%)
	3	3 (4.0%)	1 (0.7%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Asthenia	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Fatigue	- Any Grade -	2 (2.7%)	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	2 (2.7%)	0
	3	2 (2.7%)	0
Elevated transaminase			
- Overall -	- Any Grade -	2 (2.7%)	4 (2.8%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	2 (2.7%)	2 (1.4%)
Alanine aminotransferase increased	- Any Grade -	2 (2.7%)	4 (2.8%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	2 (2.7%)	2 (1.4%)
	3	2 (2.7%)	2 (1.4%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Hyperglycemia			
- Overall -	- Any Grade -	1 (1.3%)	5 (3.4%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	2	1 (1.3%)	4 (2.8%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperglycaemia	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	2	1 (1.3%)	3 (2.1%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Glycosylated haemoglobin increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Peripheral neuropathy			
- Overall -	- Any Grade -	2 (2.7%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	0	1 (0.7%)
	2	1 (1.3%)	2 (1.4%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Neuropathy peripheral	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Paraesthesia	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
Peripheral sensory neuropathy	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Nausea			
- Overall -	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Nausea	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Oral mucositis			
- Overall -	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	1	0	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Stomatitis	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Mucosal inflammation	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Colitis			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Enterocolitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Decreased appetite			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Decreased appetite	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Anaemia			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Anaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Dehydration			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dehydration	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erythropenia			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Anaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Interruption by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hyperlipidemia			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	4	1 (1.3%)	0
Hypertriglyceridaemia	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	4	1 (1.3%)	0
Immune-Mediated Pneumonitis			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Immune-Mediated Severe Cutaneous Reactions			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Dermatitis bullous	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Pneumonia			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Pneumonia	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Pneumonitis			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events Leading to Ipatasertib Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	48 (47.1%)
	Grade 1-2	24 (23.5%)
	1	5 (4.9%)
	2	19 (18.6%)
	Grade 3-4	24 (23.5%)
	3	22 (21.6%)
	4	2 (2.0%)
Diarrhea		
- Overall -	- Any Grade -	15 (14.7%)
	Grade 1-2	9 (8.8%)
	2	9 (8.8%)
	Grade 3-4	6 (5.9%)
	3	6 (5.9%)
Diarrhoea	- Any Grade -	15 (14.7%)
	Grade 1-2	9 (8.8%)
	2	9 (8.8%)
	Grade 3-4	6 (5.9%)
	3	6 (5.9%)
Neutropenia		
- Overall -	- Any Grade -	14 (13.7%)
	Grade 1-2	7 (6.9%)
	2	7 (6.9%)
	Grade 3-4	7 (6.9%)
	3	5 (4.9%)
	4	2 (2.0%)
Neutropenia	- Any Grade -	10 (9.8%)
	Grade 1-2	7 (6.9%)
	2	7 (6.9%)
	Grade 3-4	3 (2.9%)
	3	2 (2.0%)
	4	1 (1.0%)
Neutrophil count decreased	- Any Grade -	4 (3.9%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Febrile neutropenia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Immune-Mediated Rash		
- Overall -	- Any Grade -	10 (9.8%)
	Grade 1-2	6 (5.9%)
	1	2 (2.0%)
	2	4 (3.9%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)

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Selected Adverse Events Leading to Ipatasertib Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Rash	- Any Grade -	6 (5.9%)
	Grade 1-2	4 (3.9%)
	1	1 (1.0%)
	2	3 (2.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Rash maculo-papular	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash erythematous	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash pruritic	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash		
- Overall -	- Any Grade -	10 (9.8%)
	Grade 1-2	6 (5.9%)
	1	2 (2.0%)
	2	4 (3.9%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Rash	- Any Grade -	6 (5.9%)
	Grade 1-2	4 (3.9%)
	1	1 (1.0%)
	2	3 (2.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Rash maculo-papular	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash erythematous	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash pruritic	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Selected Adverse Events Leading to Ipatasertib Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Elevated transaminase		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Alanine aminotransferase increased	- Any Grade -	6 (5.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Aspartate aminotransferase increased	- Any Grade -	6 (5.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Hepatotoxicity		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Alanine aminotransferase increased	- Any Grade -	6 (5.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Aspartate aminotransferase increased	- Any Grade -	6 (5.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Blood alkaline phosphatase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Blood bilirubin increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hyperbilirubinaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Selected Adverse Events Leading to Ipatasertib Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Alanine aminotransferase increased	- Any Grade -	6 (5.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Aspartate aminotransferase increased	- Any Grade -	6 (5.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Blood bilirubin increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hyperbilirubinaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Immune-Mediated Hepatitis (Lab Abnormalities)		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Alanine aminotransferase increased	- Any Grade -	6 (5.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Aspartate aminotransferase increased	- Any Grade -	6 (5.9%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)

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Selected Adverse Events Leading to Ipatasertib Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Blood bilirubin increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Hyperbilirubinaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hyperglycemia		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Hyperglycaemia	- Any Grade -	5 (4.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Blood glucose increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nausea		
- Overall -	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nausea	- Any Grade -	5 (4.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-Mediated Pneumonitis		
- Overall -	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	1 (1.0%)
	2	3 (2.9%)
Pneumonitis	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)

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Selected Adverse Events Leading to Ipatasertib Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Lung infiltration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pneumonitis		
- Overall -	- Any Grade -	4 (3.9%)
	Grade 1-2	4 (3.9%)
	1	1 (1.0%)
	2	3 (2.9%)
Pneumonitis	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Lung infiltration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Asthenia		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Asthenia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Fatigue	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Dehydration		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dehydration	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Selected Adverse Events Leading to Ipatasertib Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Vomiting		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Vomiting	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Pneumonia		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Weight decreased		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Weight decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	27 (31.0%)	62 (37.3%)
	Grade 1-2	14 (16.1%)	30 (18.1%)
	1	1 (1.1%)	4 (2.4%)
	2	13 (14.9%)	26 (15.7%)
	Grade 3-4	13 (14.9%)	32 (19.3%)
	3	12 (13.8%)	30 (18.1%)
	4	1 (1.1%)	2 (1.2%)
Neutropenia			
- Overall -	- Any Grade -	21 (24.1%)	34 (20.5%)
	Grade 1-2	14 (16.1%)	17 (10.2%)
	1	1 (1.1%)	0
	2	13 (14.9%)	17 (10.2%)
	Grade 3-4	7 (8.0%)	17 (10.2%)
	3	6 (6.9%)	16 (9.6%)
	4	1 (1.1%)	1 (0.6%)
Neutropenia	- Any Grade -	13 (14.9%)	20 (12.0%)
	Grade 1-2	10 (11.5%)	8 (4.8%)
	1	1 (1.1%)	0
	2	9 (10.3%)	8 (4.8%)
	Grade 3-4	3 (3.4%)	12 (7.2%)
	3	2 (2.3%)	11 (6.6%)
	4	1 (1.1%)	1 (0.6%)
Neutrophil count decreased	- Any Grade -	8 (9.2%)	15 (9.0%)
	Grade 1-2	4 (4.6%)	11 (6.6%)
	2	4 (4.6%)	11 (6.6%)
	Grade 3-4	4 (4.6%)	4 (2.4%)
	3	4 (4.6%)	4 (2.4%)
Febrile neutropenia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Anaemia			
- Overall -	- Any Grade -	1 (1.1%)	7 (4.2%)
	Grade 1-2	0	5 (3.0%)
	1	0	1 (0.6%)
	2	0	4 (2.4%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	0	2 (1.2%)
	4	1 (1.1%)	0
Anaemia	- Any Grade -	1 (1.1%)	7 (4.2%)
	Grade 1-2	0	5 (3.0%)
	1	0	1 (0.6%)
	2	0	4 (2.4%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	0	2 (1.2%)
	4	1 (1.1%)	0

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Asthenia			
- Overall -	- Any Grade -	2 (2.3%)	6 (3.6%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	2	2 (2.3%)	2 (1.2%)
	Grade 3-4	0	4 (2.4%)
	3	0	4 (2.4%)
Asthenia	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	2 (2.3%)	2 (1.2%)
	2	2 (2.3%)	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Fatigue	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Erythropenia			
- Overall -	- Any Grade -	1 (1.1%)	7 (4.2%)
	Grade 1-2	0	5 (3.0%)
	1	0	1 (0.6%)
	2	0	4 (2.4%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	0	2 (1.2%)
	4	1 (1.1%)	0
Anaemia	- Any Grade -	1 (1.1%)	7 (4.2%)
	Grade 1-2	0	5 (3.0%)
	1	0	1 (0.6%)
	2	0	4 (2.4%)
	Grade 3-4	1 (1.1%)	2 (1.2%)
	3	0	2 (1.2%)
	4	1 (1.1%)	0
Nausea			
- Overall -	- Any Grade -	0	8 (4.8%)
	Grade 1-2	0	4 (2.4%)
	1	0	1 (0.6%)
	2	0	3 (1.8%)
	Grade 3-4	0	4 (2.4%)
	3	0	4 (2.4%)
Nausea	- Any Grade -	0	8 (4.8%)
	Grade 1-2	0	4 (2.4%)
	1	0	1 (0.6%)
	2	0	3 (1.8%)
	Grade 3-4	0	4 (2.4%)
	3	0	4 (2.4%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Diarrhea			
- Overall -	- Any Grade -	0	7 (4.2%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	0	4 (2.4%)
	3	0	4 (2.4%)
Diarrhoea	- Any Grade -	0	7 (4.2%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	0	4 (2.4%)
	3	0	4 (2.4%)
Immune-Mediated Rash			
- Overall -	- Any Grade -	0	7 (4.2%)
	Grade 1-2	0	6 (3.6%)
	1	0	2 (1.2%)
	2	0	4 (2.4%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Rash	- Any Grade -	0	4 (2.4%)
	Grade 1-2	0	3 (1.8%)
	1	0	1 (0.6%)
	2	0	2 (1.2%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Dermatitis allergic	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Erythema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Rash maculo-papular	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Rash			
- Overall -	- Any Grade -	0	7 (4.2%)
	Grade 1-2	0	6 (3.6%)
	1	0	2 (1.2%)
	2	0	4 (2.4%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Rash	- Any Grade -	0	4 (2.4%)
	Grade 1-2	0	3 (1.8%)
	1	0	1 (0.6%)
	2	0	2 (1.2%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Dermatitis allergic	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Erythema	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Rash maculo-papular	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hepatotoxicity			
- Overall -	- Any Grade -	4 (4.6%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	0
	2	2 (2.3%)	0
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	2 (1.2%)
Alanine aminotransferase increased	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	2 (1.2%)
Aspartate aminotransferase increased	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
Hyperbilirubinaemia	- Any Grade -	2 (2.3%)	0
	Grade 1-2	2 (2.3%)	0
	2	2 (2.3%)	0
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)			
- Overall -	- Any Grade -	4 (4.6%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	0
	2	2 (2.3%)	0
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	2 (1.2%)
Alanine aminotransferase increased	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	2 (1.2%)
Aspartate aminotransferase increased	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hyperbilirubinaemia	- Any Grade -	2 (2.3%)	0
	Grade 1-2	2 (2.3%)	0
	2	2 (2.3%)	0
Immune-Mediated Hepatitis (Lab Abnormalities)			
- Overall -	- Any Grade -	4 (4.6%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	0
	2	2 (2.3%)	0
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	2 (1.2%)
Alanine aminotransferase increased	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	2 (1.2%)
Aspartate aminotransferase increased	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
Hyperbilirubinaemia	- Any Grade -	2 (2.3%)	0
	Grade 1-2	2 (2.3%)	0
	2	2 (2.3%)	0
Peripheral neuropathy			
- Overall -	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	3 (1.8%)
	3	1 (1.1%)	3 (1.8%)
Neuropathy peripheral	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	0
	2	1 (1.1%)	0
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Peripheral sensory neuropathy	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Paraesthesia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Pneumonia			
- Overall -	- Any Grade -	3 (3.4%)	3 (1.8%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	2 (1.2%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Pneumonia	- Any Grade -	3 (3.4%)	2 (1.2%)
	Grade 1-2	1 (1.1%)	1 (0.6%)
	2	1 (1.1%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Elevated transaminase			
- Overall -	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	2 (1.2%)
Alanine aminotransferase increased	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	2 (1.2%)
Aspartate aminotransferase increased	- Any Grade -	2 (2.3%)	1 (0.6%)
	Grade 3-4	2 (2.3%)	1 (0.6%)
	3	2 (2.3%)	1 (0.6%)
Hyperglycemia			
- Overall -	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	0
	2	2 (2.3%)	0
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
Hyperglycaemia	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 1-2	2 (2.3%)	0
	2	2 (2.3%)	0
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
Vomiting			
- Overall -	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Vomiting	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	2 (1.2%)
	1	0	2 (1.2%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Decreased appetite			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Decreased appetite	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Oral mucositis			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	1	0	1 (0.6%)
	2	0	1 (0.6%)
Mucosal inflammation	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Stomatitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Colitis			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Colitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Confirmed covid-19			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Covid-19 (smq)			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Hyperlipidemia			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hypertriglyceridaemia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Immune-Mediated Colitis			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Colitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Immune-Mediated Pneumonitis			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Bronchiolitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Pneumonitis			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Bronchiolitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Thrombocytopenia			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Thrombocytopenia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	30 (40.0%)	61 (42.1%)
	Grade 1-2	13 (17.3%)	29 (20.0%)
	1	1 (1.3%)	3 (2.1%)
	2	12 (16.0%)	26 (17.9%)
	Grade 3-4	17 (22.7%)	32 (22.1%)
	3	16 (21.3%)	31 (21.4%)
	4	1 (1.3%)	1 (0.7%)
Neutropenia			
- Overall -	- Any Grade -	22 (29.3%)	35 (24.1%)
	Grade 1-2	11 (14.7%)	17 (11.7%)
	2	11 (14.7%)	17 (11.7%)
	Grade 3-4	11 (14.7%)	18 (12.4%)
	3	11 (14.7%)	17 (11.7%)
	4	0	1 (0.7%)
Neutrophil count decreased	- Any Grade -	13 (17.3%)	17 (11.7%)
	Grade 1-2	7 (9.3%)	8 (5.5%)
	2	7 (9.3%)	8 (5.5%)
	Grade 3-4	6 (8.0%)	9 (6.2%)
	3	6 (8.0%)	9 (6.2%)
Neutropenia	- Any Grade -	10 (13.3%)	19 (13.1%)
	Grade 1-2	4 (5.3%)	10 (6.9%)
	2	4 (5.3%)	10 (6.9%)
	Grade 3-4	6 (8.0%)	9 (6.2%)
	3	6 (8.0%)	8 (5.5%)
	4	0	1 (0.7%)
Hepatotoxicity			
- Overall -	- Any Grade -	4 (5.3%)	8 (5.5%)
	Grade 1-2	2 (2.7%)	4 (2.8%)
	1	0	1 (0.7%)
	2	2 (2.7%)	3 (2.1%)
	Grade 3-4	2 (2.7%)	4 (2.8%)
	3	2 (2.7%)	4 (2.8%)
Alanine aminotransferase increased	- Any Grade -	2 (2.7%)	5 (3.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	2 (2.7%)	4 (2.8%)
	3	2 (2.7%)	4 (2.8%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Hyperbilirubinaemia	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	0	1 (0.7%)
	2	1 (1.3%)	2 (1.4%)
Blood alkaline phosphatase increased	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)			
- Overall -	- Any Grade -	3 (4.0%)	8 (5.5%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	0	1 (0.7%)
	2	1 (1.3%)	3 (2.1%)
	Grade 3-4	2 (2.7%)	4 (2.8%)
	3	2 (2.7%)	4 (2.8%)
Alanine aminotransferase increased	- Any Grade -	2 (2.7%)	5 (3.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	2 (2.7%)	4 (2.8%)
	3	2 (2.7%)	4 (2.8%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
Hyperbilirubinaemia	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	0	1 (0.7%)
	2	1 (1.3%)	2 (1.4%)
Immune-Mediated Hepatitis (Lab Abnormalities)			
- Overall -	- Any Grade -	3 (4.0%)	8 (5.5%)
	Grade 1-2	1 (1.3%)	4 (2.8%)
	1	0	1 (0.7%)
	2	1 (1.3%)	3 (2.1%)
	Grade 3-4	2 (2.7%)	4 (2.8%)
	3	2 (2.7%)	4 (2.8%)
Alanine aminotransferase increased	- Any Grade -	2 (2.7%)	5 (3.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	2 (2.7%)	4 (2.8%)
	3	2 (2.7%)	4 (2.8%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Aspartate aminotransferase increased	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
Hyperbilirubinaemia	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	0	1 (0.7%)
	2	1 (1.3%)	2 (1.4%)
Diarrhea			
- Overall -	- Any Grade -	0	10 (6.9%)
	Grade 1-2	0	6 (4.1%)
	2	0	6 (4.1%)
	Grade 3-4	0	4 (2.8%)
	3	0	4 (2.8%)
Diarrhoea	- Any Grade -	0	10 (6.9%)
	Grade 1-2	0	6 (4.1%)
	2	0	6 (4.1%)
	Grade 3-4	0	4 (2.8%)
	3	0	4 (2.8%)
Immune-Mediated Rash			
- Overall -	- Any Grade -	3 (4.0%)	7 (4.8%)
	Grade 1-2	3 (4.0%)	5 (3.4%)
	1	1 (1.3%)	0
	2	2 (2.7%)	5 (3.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Rash	- Any Grade -	0	5 (3.4%)
	Grade 1-2	0	4 (2.8%)
	2	0	4 (2.8%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erythema	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	1	1 (1.3%)	0
	2	1 (1.3%)	0
Dermatitis allergic	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Drug eruption	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Rash maculo-papular	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Peripheral neuropathy			
- Overall -	- Any Grade -	3 (4.0%)	7 (4.8%)
	Grade 1-2	3 (4.0%)	4 (2.8%)
	1	1 (1.3%)	1 (0.7%)
	2	2 (2.7%)	3 (2.1%)
	Grade 3-4	0	3 (2.1%)
	3	0	3 (2.1%)
Neuropathy peripheral	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	1 (1.3%)	2 (1.4%)
	2	1 (1.3%)	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Paraesthesia	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	1	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Peripheral sensory neuropathy	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash			
- Overall -	- Any Grade -	3 (4.0%)	7 (4.8%)
	Grade 1-2	3 (4.0%)	5 (3.4%)
	1	1 (1.3%)	0
	2	2 (2.7%)	5 (3.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Rash	- Any Grade -	0	5 (3.4%)
	Grade 1-2	0	4 (2.8%)
	2	0	4 (2.8%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erythema	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	1	1 (1.3%)	0
	2	1 (1.3%)	0
Dermatitis allergic	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Drug eruption	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Rash maculo-papular	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Asthenia			
- Overall -	- Any Grade -	4 (5.3%)	5 (3.4%)
	Grade 1-2	0	3 (2.1%)
	2	0	3 (2.1%)
	Grade 3-4	4 (5.3%)	2 (1.4%)
	3	4 (5.3%)	2 (1.4%)
Asthenia	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
Fatigue	- Any Grade -	3 (4.0%)	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	3 (4.0%)	0
	3	3 (4.0%)	0
Elevated transaminase			
- Overall -	- Any Grade -	2 (2.7%)	5 (3.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	2 (2.7%)	4 (2.8%)
	3	2 (2.7%)	4 (2.8%)
Alanine aminotransferase increased	- Any Grade -	2 (2.7%)	5 (3.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	2 (2.7%)	4 (2.8%)
	3	2 (2.7%)	4 (2.8%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	2 (1.4%)
	3	1 (1.3%)	2 (1.4%)
Vomiting			
- Overall -	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	1 (0.7%)
	2	0	3 (2.1%)
Vomiting	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	4 (2.8%)
	1	0	1 (0.7%)
	2	0	3 (2.1%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Pneumonia			
- Overall -	- Any Grade -	3 (4.0%)	0
	Grade 1-2	2 (2.7%)	0
	2	2 (2.7%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Pneumonia	- Any Grade -	3 (4.0%)	0
	Grade 1-2	2 (2.7%)	0
	2	2 (2.7%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Colitis			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Enterocolitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Decreased appetite			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Decreased appetite	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperglycemia			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
Glycosylated haemoglobin increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hyperglycaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Nausea			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Nausea	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Thrombocytopenia			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Thrombocytopenia	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	1	0	2 (1.4%)
Anaemia			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Anaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Dehydration			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dehydration	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erythropenia			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Anaemia	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Hyperlipidemia			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	4	1 (1.3%)	0
Hypertriglyceridaemia	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	4	1 (1.3%)	0

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_ctc_DSIPAC_B_SE.out
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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Immune-Mediated Pneumonitis			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Oral mucositis			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Stomatitis	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Pneumonitis			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	51 (50.0%)
	Grade 1-2	23 (22.5%)
	1	6 (5.9%)
	2	17 (16.7%)
	Grade 3-4	28 (27.5%)
	3	25 (24.5%)
	4	3 (2.9%)
Neutropenia		
- Overall -	- Any Grade -	22 (21.6%)
	Grade 1-2	13 (12.7%)
	2	13 (12.7%)
	Grade 3-4	9 (8.8%)
	3	7 (6.9%)
	4	2 (2.0%)
Neutropenia	- Any Grade -	16 (15.7%)
	Grade 1-2	12 (11.8%)
	2	12 (11.8%)
	Grade 3-4	4 (3.9%)
	3	3 (2.9%)
	4	1 (1.0%)
Neutrophil count decreased	- Any Grade -	6 (5.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	4 (3.9%)
	3	4 (3.9%)
Febrile neutropenia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Diarrhea		
- Overall -	- Any Grade -	9 (8.8%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	6 (5.9%)
	3	6 (5.9%)
Diarrhoea	- Any Grade -	9 (8.8%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	6 (5.9%)
	3	6 (5.9%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Elevated transaminase		
- Overall -	- Any Grade -	8 (7.8%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Alanine aminotransferase increased	- Any Grade -	8 (7.8%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Aspartate aminotransferase increased	- Any Grade -	7 (6.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Hepatotoxicity		
- Overall -	- Any Grade -	8 (7.8%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Alanine aminotransferase increased	- Any Grade -	8 (7.8%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Aspartate aminotransferase increased	- Any Grade -	7 (6.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Blood alkaline phosphatase increased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Hyperbilirubinaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)		
- Overall -	- Any Grade -	8 (7.8%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Alanine aminotransferase increased	- Any Grade -	8 (7.8%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Aspartate aminotransferase increased	- Any Grade -	7 (6.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Hyperbilirubinaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-Mediated Hepatitis (Lab Abnormalities)		
- Overall -	- Any Grade -	8 (7.8%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Alanine aminotransferase increased	- Any Grade -	8 (7.8%)
	Grade 1-2	3 (2.9%)
	1	2 (2.0%)
	2	1 (1.0%)
	Grade 3-4	5 (4.9%)
	3	5 (4.9%)
Aspartate aminotransferase increased	- Any Grade -	7 (6.9%)
	Grade 1-2	4 (3.9%)
	1	3 (2.9%)
	2	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Hyperbilirubinaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Immune-Mediated Rash		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Rash	- Any Grade -	4 (3.9%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Erythema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash erythematous	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash pruritic	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash		
- Overall -	- Any Grade -	7 (6.9%)
	Grade 1-2	4 (3.9%)
	1	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Rash	- Any Grade -	4 (3.9%)
	Grade 1-2	2 (2.0%)
	1	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Erythema	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash erythematous	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Rash pruritic	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Asthenia		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	4 (3.9%)
	1	1 (1.0%)
	2	3 (2.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Fatigue	- Any Grade -	4 (3.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Asthenia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
Nausea		
- Overall -	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nausea	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-Mediated Pneumonitis		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Lung infiltration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pneumonitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Pneumonia		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonia	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	1	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonitis		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Lung infiltration	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Pneumonitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Anaemia		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Anaemia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Dehydration		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Dehydration	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Erythropenia		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Anaemia	- Any Grade -	2 (2.0%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
Hyperglycemia		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Hyperglycaemia	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Peripheral neuropathy		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hypoaesthesia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Neuropathy peripheral	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-Mediated Diabetes Mellitus		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events Leading to Paclitaxel Dose Interruption by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Oral mucositis		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Stomatitis	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Thrombocytopenia		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Thrombocytopenia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Vomiting		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Vomiting	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Weight decreased		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
Weight decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Reduction by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	7 (8.0%)	44 (26.5%)
	Grade 1-2	3 (3.4%)	21 (12.7%)
	2	3 (3.4%)	21 (12.7%)
	Grade 3-4	4 (4.6%)	23 (13.9%)
	3	4 (4.6%)	19 (11.4%)
	4	0	4 (2.4%)
Diarrhea			
- Overall -	- Any Grade -	2 (2.3%)	23 (13.9%)
	Grade 1-2	1 (1.1%)	16 (9.6%)
	2	1 (1.1%)	16 (9.6%)
	Grade 3-4	1 (1.1%)	7 (4.2%)
	3	1 (1.1%)	7 (4.2%)
Diarrhoea	- Any Grade -	2 (2.3%)	23 (13.9%)
	Grade 1-2	1 (1.1%)	16 (9.6%)
	2	1 (1.1%)	16 (9.6%)
	Grade 3-4	1 (1.1%)	7 (4.2%)
	3	1 (1.1%)	7 (4.2%)
Neutropenia			
- Overall -	- Any Grade -	2 (2.3%)	9 (5.4%)
	Grade 3-4	2 (2.3%)	9 (5.4%)
	3	2 (2.3%)	5 (3.0%)
	4	0	4 (2.4%)
Neutropenia	- Any Grade -	0	4 (2.4%)
	Grade 3-4	0	4 (2.4%)
	3	0	2 (1.2%)
	4	0	2 (1.2%)
Neutrophil count decreased	- Any Grade -	2 (2.3%)	2 (1.2%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	1 (0.6%)
	4	0	1 (0.6%)
Febrile neutropenia	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	2 (1.2%)
	4	0	1 (0.6%)
Elevated transaminase			
- Overall -	- Any Grade -	1 (1.1%)	5 (3.0%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	4 (2.4%)
	3	1 (1.1%)	4 (2.4%)
Alanine aminotransferase increased	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 3-4	1 (1.1%)	4 (2.4%)
	3	1 (1.1%)	4 (2.4%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Reduction by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Aspartate aminotransferase increased	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	3 (1.8%)
	3	1 (1.1%)	3 (1.8%)
Hepatotoxicity			
- Overall -	- Any Grade -	1 (1.1%)	5 (3.0%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	4 (2.4%)
	3	1 (1.1%)	4 (2.4%)
Alanine aminotransferase increased	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 3-4	1 (1.1%)	4 (2.4%)
	3	1 (1.1%)	4 (2.4%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	3 (1.8%)
	3	1 (1.1%)	3 (1.8%)
Hyperglycemia			
- Overall -	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	2	2 (2.3%)	3 (1.8%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hyperglycaemia	- Any Grade -	2 (2.3%)	4 (2.4%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	2	2 (2.3%)	3 (1.8%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)			
- Overall -	- Any Grade -	1 (1.1%)	5 (3.0%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	4 (2.4%)
	3	1 (1.1%)	4 (2.4%)
Alanine aminotransferase increased	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 3-4	1 (1.1%)	4 (2.4%)
	3	1 (1.1%)	4 (2.4%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Reduction by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Aspartate aminotransferase increased	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	3 (1.8%)
	3	1 (1.1%)	3 (1.8%)
Immune-Mediated Hepatitis (Lab Abnormalities)			
- Overall -	- Any Grade -	1 (1.1%)	5 (3.0%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	4 (2.4%)
	3	1 (1.1%)	4 (2.4%)
Alanine aminotransferase increased	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 3-4	1 (1.1%)	4 (2.4%)
	3	1 (1.1%)	4 (2.4%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	3 (1.8%)
	3	1 (1.1%)	3 (1.8%)
Nausea			
- Overall -	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Nausea	- Any Grade -	0	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Decreased appetite			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Decreased appetite	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	2 (1.2%)
	2	0	2 (1.2%)
Immune-Mediated Rash			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Reduction by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Rash	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Rash			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Rash	- Any Grade -	0	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Asthenia			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Fatigue	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Colitis			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Colitis	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Immune-Mediated Colitis			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Colitis	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Oral mucositis			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Reduction by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Stomatitis	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Peripheral neuropathy			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Neuropathy peripheral	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Weight decreased			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Weight decreased	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Reduction by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	6 (8.0%)	47 (32.4%)
	Grade 1-2	1 (1.3%)	22 (15.2%)
	2	1 (1.3%)	22 (15.2%)
	Grade 3-4	5 (6.7%)	25 (17.2%)
	3	3 (4.0%)	22 (15.2%)
	4	2 (2.7%)	3 (2.1%)
Diarrhea			
- Overall -	- Any Grade -	0	33 (22.8%)
	Grade 1-2	0	23 (15.9%)
	2	0	23 (15.9%)
	Grade 3-4	0	10 (6.9%)
	3	0	10 (6.9%)
Diarrhoea	- Any Grade -	0	33 (22.8%)
	Grade 1-2	0	23 (15.9%)
	2	0	23 (15.9%)
	Grade 3-4	0	10 (6.9%)
	3	0	10 (6.9%)
Neutropenia			
- Overall -	- Any Grade -	4 (5.3%)	9 (6.2%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	4 (5.3%)	8 (5.5%)
	3	2 (2.7%)	5 (3.4%)
	4	2 (2.7%)	3 (2.1%)
Neutrophil count decreased	- Any Grade -	3 (4.0%)	6 (4.1%)
	Grade 3-4	3 (4.0%)	6 (4.1%)
	3	1 (1.3%)	3 (2.1%)
	4	2 (2.7%)	3 (2.1%)
Neutropenia	- Any Grade -	2 (2.7%)	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	2 (2.7%)	1 (0.7%)
	3	2 (2.7%)	1 (0.7%)
Febrile neutropenia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Immune-Mediated Rash			
- Overall -	- Any Grade -	0	5 (3.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	3 (2.1%)
	3	0	3 (2.1%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Reduction by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Rash	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
Rash maculo-papular	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Rash erythematous	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Rash			
- Overall -	- Any Grade -	0	5 (3.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	3 (2.1%)
	3	0	3 (2.1%)
Rash	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
Rash maculo-papular	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Rash erythematous	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperglycemia			
- Overall -	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperglycaemia	- Any Grade -	0	3 (2.1%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Nausea			
- Overall -	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	0	1 (0.7%)
	2	1 (1.3%)	0
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Reduction by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Nausea	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	0	1 (0.7%)
	2	1 (1.3%)	0
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Decreased appetite			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Decreased appetite	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
Elevated transaminase			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Alanine aminotransferase increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Aspartate aminotransferase increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Hepatotoxicity			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Alanine aminotransferase increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Aspartate aminotransferase increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Gamma-glutamyltransferase increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Reduction by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Alanine aminotransferase increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Aspartate aminotransferase increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Gamma-glutamyltransferase increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Immune-Mediated Hepatitis (Lab Abnormalities)			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Alanine aminotransferase increased	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Aspartate aminotransferase increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Gamma-glutamyltransferase increased	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Asthenia			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Asthenia	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_ctc_DSRIPAT_B_SE.out
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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Reduction by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Fatigue	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Erythema multiforme			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erythema multiforme	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Immune-Mediated Pneumonitis			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Immune-Mediated Severe Cutaneous Reactions			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erythema multiforme	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Peripheral neuropathy			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Peripheral sensory neuropathy	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Pneumonitis			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Selected Adverse Events Leading to Ipatasertib/Placebo Dose Reduction by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Vomiting			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)
Vomiting	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	1	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events Leading to Ipatasertib Dose Reduction by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	36 (35.3%)
	Grade 1-2	15 (14.7%)
	1	3 (2.9%)
	2	12 (11.8%)
	Grade 3-4	21 (20.6%)
	3	19 (18.6%)
	4	2 (2.0%)
Diarrhea		
- Overall -	- Any Grade -	21 (20.6%)
	Grade 1-2	13 (12.7%)
	1	3 (2.9%)
	2	10 (9.8%)
	Grade 3-4	8 (7.8%)
	3	8 (7.8%)
Diarrhoea	- Any Grade -	21 (20.6%)
	Grade 1-2	13 (12.7%)
	1	3 (2.9%)
	2	10 (9.8%)
	Grade 3-4	8 (7.8%)
	3	8 (7.8%)
Neutropenia		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	5 (4.9%)
	3	4 (3.9%)
	4	1 (1.0%)
Neutrophil count decreased	- Any Grade -	3 (2.9%)
	Grade 3-4	3 (2.9%)
	3	2 (2.0%)
	4	1 (1.0%)
Neutropenia	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Febrile neutropenia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Selected Adverse Events Leading to Ipatasertib Dose Reduction by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hyperglycemia		
- Overall -	- Any Grade -	5 (4.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Hyperglycaemia	- Any Grade -	5 (4.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Nausea		
- Overall -	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nausea	- Any Grade -	4 (3.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Elevated transaminase		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hepatotoxicity		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Selected Adverse Events Leading to Ipatasertib Dose Reduction by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hyperbilirubinaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hyperlipidemia		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Blood triglycerides increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hyperbilirubinaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-Mediated Hepatitis (Lab Abnormalities)		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hyperbilirubinaemia	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-Mediated Rash		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Selected Adverse Events Leading to Ipatasertib Dose Reduction by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Rash	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Vomiting		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Vomiting	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Selected Adverse Events Leading to Paclitaxel Dose Reduction by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	6 (6.9%)	32 (19.3%)
	Grade 1-2	3 (3.4%)	18 (10.8%)
	1	0	4 (2.4%)
	2	3 (3.4%)	14 (8.4%)
	Grade 3-4	3 (3.4%)	14 (8.4%)
	3	3 (3.4%)	12 (7.2%)
	4	0	2 (1.2%)
Peripheral neuropathy			
- Overall -	- Any Grade -	3 (3.4%)	13 (7.8%)
	Grade 1-2	3 (3.4%)	11 (6.6%)
	1	0	4 (2.4%)
	2	3 (3.4%)	7 (4.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Peripheral sensory neuropathy	- Any Grade -	2 (2.3%)	5 (3.0%)
	Grade 1-2	2 (2.3%)	3 (1.8%)
	1	0	1 (0.6%)
	2	2 (2.3%)	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Neuropathy peripheral	- Any Grade -	1 (1.1%)	5 (3.0%)
	Grade 1-2	1 (1.1%)	5 (3.0%)
	1	0	2 (1.2%)
	2	1 (1.1%)	3 (1.8%)
Neurotoxicity	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Paraesthesia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	1	0	1 (0.6%)
Peripheral motor neuropathy	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Neutropenia			
- Overall -	- Any Grade -	2 (2.3%)	10 (6.0%)
	Grade 1-2	0	4 (2.4%)
	2	0	4 (2.4%)
	Grade 3-4	2 (2.3%)	6 (3.6%)
	3	2 (2.3%)	4 (2.4%)
	4	0	2 (1.2%)
Neutropenia	- Any Grade -	0	5 (3.0%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)

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Selected Adverse Events Leading to Paclitaxel Dose Reduction by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Neutrophil count decreased	- Any Grade -	2 (2.3%)	3 (1.8%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	2 (2.3%)	2 (1.2%)
	3	2 (2.3%)	1 (0.6%)
	4	0	1 (0.6%)
Febrile neutropenia	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
Asthenia			
- Overall -	- Any Grade -	1 (1.1%)	2 (1.2%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Fatigue	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	1 (1.1%)	1 (0.6%)
Asthenia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Elevated transaminase			
- Overall -	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Alanine aminotransferase increased	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Aspartate aminotransferase increased	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Hepatotoxicity			
- Overall -	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Alanine aminotransferase increased	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Aspartate aminotransferase increased	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)

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Selected Adverse Events Leading to Paclitaxel Dose Reduction by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)			
- Overall -	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Alanine aminotransferase increased	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Aspartate aminotransferase increased	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Immune-Mediated Hepatitis (Lab Abnormalities)			
- Overall -	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Alanine aminotransferase increased	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Aspartate aminotransferase increased	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Diarrhea			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Diarrhoea	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Anaemia			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Anaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Decreased appetite			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Decreased appetite	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Selected Adverse Events Leading to Paclitaxel Dose Reduction by Highest NCI CTCAE Grade,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Erythropenia			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Anaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hyperglycemia			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)
Hyperglycaemia	- Any Grade -	0	1 (0.6%)
	Grade 1-2	0	1 (0.6%)
	2	0	1 (0.6%)

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Selected Adverse Events Leading to Paclitaxel Dose Reduction by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	16 (21.3%)	38 (26.2%)
	Grade 1-2	10 (13.3%)	22 (15.2%)
	1	1 (1.3%)	1 (0.7%)
	2	9 (12.0%)	21 (14.5%)
	Grade 3-4	6 (8.0%)	16 (11.0%)
	3	5 (6.7%)	12 (8.3%)
	4	1 (1.3%)	4 (2.8%)
Peripheral neuropathy			
- Overall -	- Any Grade -	7 (9.3%)	19 (13.1%)
	Grade 1-2	6 (8.0%)	18 (12.4%)
	1	0	1 (0.7%)
	2	6 (8.0%)	17 (11.7%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Neuropathy peripheral	- Any Grade -	2 (2.7%)	9 (6.2%)
	Grade 1-2	1 (1.3%)	8 (5.5%)
	2	1 (1.3%)	8 (5.5%)
	Grade 3-4	1 (1.3%)	1 (0.7%)
	3	1 (1.3%)	1 (0.7%)
Peripheral sensory neuropathy	- Any Grade -	2 (2.7%)	5 (3.4%)
	Grade 1-2	2 (2.7%)	5 (3.4%)
	2	2 (2.7%)	5 (3.4%)
Polyneuropathy	- Any Grade -	1 (1.3%)	3 (2.1%)
	Grade 1-2	1 (1.3%)	3 (2.1%)
	1	0	1 (0.7%)
	2	1 (1.3%)	2 (1.4%)
Neurotoxicity	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
Gait disturbance	- Any Grade -	1 (1.3%)	0
	Grade 1-2	1 (1.3%)	0
	2	1 (1.3%)	0
Peripheral motor neuropathy	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Neutropenia			
- Overall -	- Any Grade -	6 (8.0%)	13 (9.0%)
	Grade 1-2	2 (2.7%)	2 (1.4%)
	2	2 (2.7%)	2 (1.4%)
	Grade 3-4	4 (5.3%)	11 (7.6%)
	3	3 (4.0%)	7 (4.8%)
	4	1 (1.3%)	4 (2.8%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events Leading to Paclitaxel Dose Reduction by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Neutrophil count decreased	- Any Grade -	3 (4.0%)	8 (5.5%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
	Grade 3-4	2 (2.7%)	7 (4.8%)
	3	1 (1.3%)	4 (2.8%)
	4	1 (1.3%)	3 (2.1%)
Neutropenia	- Any Grade -	3 (4.0%)	5 (3.4%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	2	1 (1.3%)	1 (0.7%)
	Grade 3-4	2 (2.7%)	4 (2.8%)
	3	2 (2.7%)	3 (2.1%)
	4	0	1 (0.7%)
Diarrhea			
- Overall -	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	3 (2.1%)
	3	0	3 (2.1%)
Diarrhoea	- Any Grade -	0	4 (2.8%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	3 (2.1%)
	3	0	3 (2.1%)
Anaemia			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
Anaemia	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
Asthenia			
- Overall -	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	1	1 (1.3%)	0
	2	1 (1.3%)	0
Asthenia	- Any Grade -	2 (2.7%)	0
	Grade 1-2	2 (2.7%)	0
	1	1 (1.3%)	0
	2	1 (1.3%)	0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Selected Adverse Events Leading to Paclitaxel Dose Reduction by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Erythropenia			
- Overall -	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
Anaemia	- Any Grade -	1 (1.3%)	1 (0.7%)
	Grade 1-2	1 (1.3%)	1 (0.7%)
	1	1 (1.3%)	0
	2	0	1 (0.7%)
Decreased appetite			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Decreased appetite	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Elevated transaminase			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Alanine aminotransferase increased	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Hepatotoxicity			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Alanine aminotransferase increased	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Alanine aminotransferase increased	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Immune-Mediated Hepatitis (Lab Abnormalities)			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0

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Selected Adverse Events Leading to Paclitaxel Dose Reduction by Highest NCI CTCAE Grade,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Alanine aminotransferase increased	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Immune-Mediated Pneumonitis			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Nausea			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Nausea	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Pneumonitis			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	1 (0.7%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)

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Selected Adverse Events Leading to Paclitaxel Dose Reduction by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	23 (22.5%)
	Grade 1-2	15 (14.7%)
	1	4 (3.9%)
	2	11 (10.8%)
	Grade 3-4	8 (7.8%)
	3	7 (6.9%)
	4	1 (1.0%)
Peripheral neuropathy		
- Overall -	- Any Grade -	11 (10.8%)
	Grade 1-2	9 (8.8%)
	1	3 (2.9%)
	2	6 (5.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Neuropathy peripheral	- Any Grade -	8 (7.8%)
	Grade 1-2	6 (5.9%)
	1	2 (2.0%)
	2	4 (3.9%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Polyneuropathy	- Any Grade -	3 (2.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
Neutropenia		
- Overall -	- Any Grade -	6 (5.9%)
	Grade 1-2	3 (2.9%)
	1	1 (1.0%)
	2	2 (2.0%)
	Grade 3-4	3 (2.9%)
	3	2 (2.0%)
	4	1 (1.0%)
Neutropenia	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neutrophil count decreased	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events Leading to Paclitaxel Dose Reduction by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Diarrhea		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Diarrhoea	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	2 (2.0%)
Elevated transaminase		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hepatotoxicity		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
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Selected Adverse Events Leading to Paclitaxel Dose Reduction by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Alanine aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-Mediated Hepatitis (Lab Abnormalities)		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Anaemia		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Anaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Erythropenia		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Anaemia	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Weight decreased		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Selected Adverse Events Leading to Paclitaxel Dose Reduction by Highest NCI CTCAE Grade,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Weight decreased	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
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Serious Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
- Any adverse events -	- Any Grade -	7 (8.0%)	17 (10.2%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	7 (8.0%)	14 (8.4%)
	3	5 (5.7%)	10 (6.0%)
	4	2 (2.3%)	4 (2.4%)
Pneumonia			
- Overall -	- Any Grade -	4 (4.6%)	3 (1.8%)
	Grade 3-4	4 (4.6%)	3 (1.8%)
	3	3 (3.4%)	3 (1.8%)
	4	1 (1.1%)	0
Pneumonia	- Any Grade -	4 (4.6%)	2 (1.2%)
	Grade 3-4	4 (4.6%)	2 (1.2%)
	3	3 (3.4%)	2 (1.2%)
	4	1 (1.1%)	0
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Diarrhea			
- Overall -	- Any Grade -	0	6 (3.6%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Diarrhoea	- Any Grade -	0	6 (3.6%)
	Grade 1-2	0	3 (1.8%)
	2	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	3 (1.8%)
Neutropenia			
- Overall -	- Any Grade -	1 (1.1%)	4 (2.4%)
	Grade 3-4	1 (1.1%)	4 (2.4%)
	3	0	2 (1.2%)
	4	1 (1.1%)	2 (1.2%)
Febrile neutropenia	- Any Grade -	0	3 (1.8%)
	Grade 3-4	0	3 (1.8%)
	3	0	2 (1.2%)
	4	0	1 (0.6%)
Neutropenia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	4	1 (1.1%)	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Serious Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Anaemia			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	0	1 (0.6%)
	4	1 (1.1%)	0
Anaemia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	0	1 (0.6%)
	4	1 (1.1%)	0
Erythropenia			
- Overall -	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	0	1 (0.6%)
	4	1 (1.1%)	0
Anaemia	- Any Grade -	1 (1.1%)	1 (0.6%)
	Grade 3-4	1 (1.1%)	1 (0.6%)
	3	0	1 (0.6%)
	4	1 (1.1%)	0
Nausea			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Nausea	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	2 (1.2%)
Vomiting			
- Overall -	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
Vomiting	- Any Grade -	0	2 (1.2%)
	Grade 3-4	0	2 (1.2%)
	3	0	1 (0.6%)
	4	0	1 (0.6%)
Asthenia			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Fatigue	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi_ctc.sas
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Serious Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Colitis			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Colitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Confirmed covid-19			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Covid-19 (smq)			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
COVID-19 pneumonia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Erythema multiforme			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Erythema multiforme	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Hyperglycemia			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Hyperglycaemia	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	4	0	1 (0.6%)
Immune-Mediated Colitis			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Colitis	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0

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Serious Selected Adverse Events by Highest NCI CTCAE Grade, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Immune-Mediated Severe Cutaneous Reactions			
- Overall -	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Erythema multiforme	- Any Grade -	0	1 (0.6%)
	Grade 3-4	0	1 (0.6%)
	3	0	1 (0.6%)
Thrombocytopenia			
- Overall -	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0
Thrombocytopenia	- Any Grade -	1 (1.1%)	0
	Grade 3-4	1 (1.1%)	0
	3	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi_ctc.sas
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Serious Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
- Any adverse events -	- Any Grade -	3 (4.0%)	12 (8.3%)
	Grade 1-2	0	2 (1.4%)
	2	0	2 (1.4%)
	Grade 3-4	3 (4.0%)	8 (5.5%)
	3	3 (4.0%)	8 (5.5%)
	Grade 5	0	2 (1.4%)
Diarrhea			
- Overall -	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	4 (2.8%)
	3	1 (1.3%)	4 (2.8%)
Diarrhoea	- Any Grade -	1 (1.3%)	4 (2.8%)
	Grade 3-4	1 (1.3%)	4 (2.8%)
	3	1 (1.3%)	4 (2.8%)
Neutropenia			
- Overall -	- Any Grade -	0	3 (2.1%)
	Grade 3-4	0	2 (1.4%)
	3	0	2 (1.4%)
	Grade 5	0	1 (0.7%)
Febrile neutropenia	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
	Grade 5	0	1 (0.7%)
Neutropenia	- Any Grade -	0	2 (1.4%)
	Grade 3-4	0	2 (1.4%)
	3	0	1 (0.7%)
	4	0	1 (0.7%)
Pneumonia			
- Overall -	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
	Grade 5	0	1 (0.7%)
Pneumonia	- Any Grade -	1 (1.3%)	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
	Grade 5	0	1 (0.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Serious Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Immune-Mediated Pneumonitis			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Pneumonitis			
- Overall -	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Pneumonitis	- Any Grade -	0	2 (1.4%)
	Grade 1-2	0	1 (0.7%)
	2	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Asthenia			
- Overall -	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Fatigue	- Any Grade -	1 (1.3%)	0
	Grade 3-4	1 (1.3%)	0
	3	1 (1.3%)	0
Colitis			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Enterocolitis	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Decreased appetite			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Decreased appetite	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Serious Selected Adverse Events by Highest NCI CTCAE Grade, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Dehydration			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Dehydration	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erythema multiforme			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erythema multiforme	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperglycemia			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Hyperglycaemia	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Immune-Mediated Severe Cutaneous Reactions			
- Overall -	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)
Erythema multiforme	- Any Grade -	0	1 (0.7%)
	Grade 3-4	0	1 (0.7%)
	3	0	1 (0.7%)

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Serious Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
- Any adverse events -	- Any Grade -	13 (12.7%)
	Grade 1-2	3 (2.9%)
	2	3 (2.9%)
	Grade 3-4	9 (8.8%)
	3	7 (6.9%)
	4	2 (2.0%)
	Grade 5	1 (1.0%)
Diarrhea		
- Overall -	- Any Grade -	4 (3.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Diarrhoea	- Any Grade -	4 (3.9%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	3 (2.9%)
	3	3 (2.9%)
Immune-Mediated Pneumonitis		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonitis	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Pneumonia		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
	Grade 5	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Serious Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Pneumonia	- Any Grade -	3 (2.9%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
	Grade 5	1 (1.0%)
Pneumonitis		
- Overall -	- Any Grade -	3 (2.9%)
	Grade 1-2	2 (2.0%)
	2	2 (2.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Pneumonitis	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-mediated lung disease	- Any Grade -	1 (1.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
Asthenia		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Fatigue	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dehydration		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Dehydration	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Serious Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Immune-Mediated Rash		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Neutropenia		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Febrile neutropenia	- Any Grade -	2 (2.0%)
	Grade 3-4	2 (2.0%)
	3	1 (1.0%)
	4	1 (1.0%)
Rash		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Rash	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	2	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Vomiting		
- Overall -	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Vomiting	- Any Grade -	2 (2.0%)
	Grade 1-2	1 (1.0%)
	1	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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Serious Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Elevated transaminase		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hepatotoxicity		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Hyperglycemia		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Immune-Mediated Diabetes Mellitus		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Diabetic ketoacidosis	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	4	1 (1.0%)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
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Serious Selected Adverse Events by Highest NCI CTCAE Grade, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Immune-Mediated Hepatitis (Lab Abnormalities)		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Alanine aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Aspartate aminotransferase increased	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nausea		
- Overall -	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)
Nausea	- Any Grade -	1 (1.0%)
	Grade 3-4	1 (1.0%)
	3	1 (1.0%)

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All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this preferred term. To the Medical Concept Category Overall row counts, a patient contributes only with the AE occurring with the greatest intensity within the Medical Concept category. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi_ctc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_ctc_SER_C_SE.out
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Serious Selected Adverse Events, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Total number of patients with at least one such adverse event	7 (8.0%)	17 (10.2%)
Overall total number of events	8	23
Pneumonia		
Total number of patients with at least one such adverse event	4 (4.6%)	3 (1.8%)
Total number of events	4	3
Pneumonia	4 (4.6%)	2 (1.2%)
COVID-19 pneumonia	0	1 (0.6%)
Diarrhea		
Total number of patients with at least one such adverse event	0	6 (3.6%)
Total number of events	0	8
Diarrhoea	0	6 (3.6%)
Neutropenia		
Total number of patients with at least one such adverse event	1 (1.1%)	4 (2.4%)
Total number of events	1	4
Febrile neutropenia	0	3 (1.8%)
Neutropenia	1 (1.1%)	1 (0.6%)
Anaemia		
Total number of patients with at least one such adverse event	1 (1.1%)	1 (0.6%)
Total number of events	1	1
Anaemia	1 (1.1%)	1 (0.6%)
Erythropenia		
Total number of patients with at least one such adverse event	1 (1.1%)	1 (0.6%)
Total number of events	1	1
Anaemia	1 (1.1%)	1 (0.6%)
Nausea		
Total number of patients with at least one such adverse event	0	2 (1.2%)
Total number of events	0	2
Nausea	0	2 (1.2%)
Vomiting		
Total number of patients with at least one such adverse event	0	2 (1.2%)
Total number of events	0	2
Vomiting	0	2 (1.2%)
Asthenia		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Fatigue	0	1 (0.6%)

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_SER_A_SE.out
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Serious Selected Adverse Events, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Colitis		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Colitis	1 (1.1%)	0
Confirmed covid-19		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
COVID-19 pneumonia	0	1 (0.6%)
Covid-19 (smq)		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
COVID-19 pneumonia	0	1 (0.6%)
Erythema multiforme		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Erythema multiforme	0	1 (0.6%)
Hyperglycemia		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Hyperglycaemia	0	1 (0.6%)
Immune-Mediated Colitis		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Colitis	1 (1.1%)	0
Immune-Mediated Severe Cutaneous Reactions		
Total number of patients with at least one such adverse event	0	1 (0.6%)
Total number of events	0	1
Erythema multiforme	0	1 (0.6%)
Thrombocytopenia		
Total number of patients with at least one such adverse event	1 (1.1%)	0
Total number of events	1	0
Thrombocytopenia	1 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_SER_A_SE.out
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Serious Selected Adverse Events, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Total number of patients with at least one such adverse event	3 (4.0%)	12 (8.3%)
Overall total number of events	3	19
Diarrhea		
Total number of patients with at least one such adverse event	1 (1.3%)	4 (2.8%)
Total number of events	1	5
Diarrhoea	1 (1.3%)	4 (2.8%)
Neutropenia		
Total number of patients with at least one such adverse event	0	3 (2.1%)
Total number of events	0	4
Febrile neutropenia	0	2 (1.4%)
Neutropenia	0	2 (1.4%)
Pneumonia		
Total number of patients with at least one such adverse event	1 (1.3%)	2 (1.4%)
Total number of events	1	2
Pneumonia	1 (1.3%)	2 (1.4%)
Immune-Mediated Pneumonitis		
Total number of patients with at least one such adverse event	0	2 (1.4%)
Total number of events	0	2
Pneumonitis	0	2 (1.4%)
Pneumonitis		
Total number of patients with at least one such adverse event	0	2 (1.4%)
Total number of events	0	2
Pneumonitis	0	2 (1.4%)
Asthenia		
Total number of patients with at least one such adverse event	1 (1.3%)	0
Total number of events	1	0
Fatigue	1 (1.3%)	0
Colitis		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Enterocolitis	0	1 (0.7%)
Decreased appetite		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	2
Decreased appetite	0	1 (0.7%)
Dehydration		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Dehydration	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_SER_B_SE.out
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Serious Selected Adverse Events, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Erythema multiforme		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Erythema multiforme	0	1 (0.7%)
Hyperglycemia		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Hyperglycaemia	0	1 (0.7%)
Immune-Mediated Severe Cutaneous Reactions		
Total number of patients with at least one such adverse event	0	1 (0.7%)
Total number of events	0	1
Erythema multiforme	0	1 (0.7%)

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_SER_B_SE.out
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Serious Selected Adverse Events, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Grouped Term MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one such adverse event	13 (12.7%)
Overall total number of events	24
Diarrhea	
Total number of patients with at least one such adverse event	4 (3.9%)
Total number of events	4
Diarrhoea	4 (3.9%)
Immune-Mediated Pneumonitis	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Pneumonitis	2 (2.0%)
Immune-mediated lung disease	1 (1.0%)
Pneumonia	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Pneumonia	3 (2.9%)
Pneumonitis	
Total number of patients with at least one such adverse event	3 (2.9%)
Total number of events	3
Pneumonitis	2 (2.0%)
Immune-mediated lung disease	1 (1.0%)
Asthenia	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Fatigue	2 (2.0%)
Dehydration	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Dehydration	2 (2.0%)
Immune-Mediated Rash	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Rash	2 (2.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_SER_C_SE.out
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Grouped Term MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Neutropenia	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Febrile neutropenia	2 (2.0%)
Rash	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Rash	2 (2.0%)
Vomiting	
Total number of patients with at least one such adverse event	2 (2.0%)
Total number of events	2
Vomiting	2 (2.0%)
Elevated transaminase	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	2
Alanine aminotransferase increased	1 (1.0%)
Aspartate aminotransferase increased	1 (1.0%)
Hepatotoxicity	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	2
Alanine aminotransferase increased	1 (1.0%)
Aspartate aminotransferase increased	1 (1.0%)
Hyperglycemia	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Diabetic ketoacidosis	1 (1.0%)
Immune-Mediated Diabetes Mellitus	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Diabetic ketoacidosis	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Immune-Mediated Hepatitis (Diagnosis and Lab Abnormalities)	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	2
Alanine aminotransferase increased	1 (1.0%)
Aspartate aminotransferase increased	1 (1.0%)
Immune-Mediated Hepatitis (Lab Abnormalities)	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	2
Alanine aminotransferase increased	1 (1.0%)
Aspartate aminotransferase increased	1 (1.0%)
Nausea	
Total number of patients with at least one such adverse event	1 (1.0%)
Total number of events	1
Nausea	1 (1.0%)

Investigator text for AEs encoded using MedDRA version 25.1.
Percentages are based on N in the column headings. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_aesi.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_aesi_SER_C_SE.out
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Grouped Term Outcome Categories	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Anaemia		
Total Number of AE	35	59
NOT RECOVERED/NOT RESOLVED	10 (28.6%)	18 (30.5%)
RECOVERED/RESOLVED	23 (65.7%)	35 (59.3%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	2 (5.7%)	6 (10.2%)
FATAL	0	0
UNKNOWN	0	0
Asthenia		
Total Number of AE	28	74
NOT RECOVERED/NOT RESOLVED	11 (39.3%)	30 (40.5%)
RECOVERED/RESOLVED	14 (50.0%)	39 (52.7%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	3 (10.7%)	5 (6.8%)
FATAL	0	0
UNKNOWN	0	0
Colitis		
Total Number of AE	1	1
NOT RECOVERED/NOT RESOLVED	0	0
RECOVERED/RESOLVED	1 (100%)	1 (100%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Decreased Appetite		
Total Number of AE	10	35
NOT RECOVERED/NOT RESOLVED	8 (80.0%)	5 (14.3%)
RECOVERED/RESOLVED	2 (20.0%)	30 (85.7%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Dehydration		
Total Number of AE	0	2
NOT RECOVERED/NOT RESOLVED	0	0
RECOVERED/RESOLVED	0	2 (100%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Diarrhea		
Total Number of AE	56	485
NOT RECOVERED/NOT RESOLVED	2 (3.6%)	10 (2.1%)
RECOVERED/RESOLVED	54 (96.4%)	472 (97.3%)
RECOVERED/RESOLVED WITH SEQUELAE	0	2 (0.4%)
RECOVERING/RESOLVING	0	1 (0.2%)
FATAL	0	0
UNKNOWN	0	0
Elevated Transaminase		
Total Number of AE	23	52
NOT RECOVERED/NOT RESOLVED	2 (8.7%)	13 (25.0%)
RECOVERED/RESOLVED	21 (91.3%)	39 (75.0%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Erythema Multiforme		
Total Number of AE	0	1
NOT RECOVERED/NOT RESOLVED	0	0
RECOVERED/RESOLVED	0	1 (100%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0

Multiple occurrences of the same AE in an individual are counted separately. Percentages are calculated based on 'Total Number of AE' for each grouped term. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term Outcome Categories	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Erythropenia		
Total Number of AE	36	62
NOT RECOVERED/NOT RESOLVED	10 (27.8%)	19 (30.6%)
RECOVERED/RESOLVED	24 (66.7%)	37 (59.7%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	2 (5.6%)	6 (9.7%)
FATAL	0	0
UNKNOWN	0	0
Hepatotoxicity		
Total Number of AE	37	70
NOT RECOVERED/NOT RESOLVED	3 (8.1%)	17 (24.3%)
RECOVERED/RESOLVED	34 (91.9%)	52 (74.3%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	1 (1.4%)
FATAL	0	0
UNKNOWN	0	0
Hyperglycemia		
Total Number of AE	17	62
NOT RECOVERED/NOT RESOLVED	4 (23.5%)	7 (11.3%)
RECOVERED/RESOLVED	12 (70.6%)	54 (87.1%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	1 (5.9%)	1 (1.6%)
FATAL	0	0
UNKNOWN	0	0
Hyperlipidemia		
Total Number of AE	5	22
NOT RECOVERED/NOT RESOLVED	1 (20.0%)	13 (59.1%)
RECOVERED/RESOLVED	2 (40.0%)	8 (36.4%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	2 (40.0%)	1 (4.5%)
FATAL	0	0
UNKNOWN	0	0
Immune-Mediated Colitis		
Total Number of AE	1	1
NOT RECOVERED/NOT RESOLVED	0	0
RECOVERED/RESOLVED	1 (100%)	1 (100%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Immune-Mediated Diabetes Mellitus		
Total Number of AE	0	1
NOT RECOVERED/NOT RESOLVED	0	0
RECOVERED/RESOLVED	0	0
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	1 (100%)
FATAL	0	0
UNKNOWN	0	0
Immune-Mediated Hepatitis (Diagnosis And Lab Abnormalities)		
Total Number of AE	36	58
NOT RECOVERED/NOT RESOLVED	3 (8.3%)	16 (27.6%)
RECOVERED/RESOLVED	33 (91.7%)	41 (70.7%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	1 (1.7%)
FATAL	0	0
UNKNOWN	0	0

Multiple occurrences of the same AE in an individual are counted separately. Percentages are calculated based on 'Total Number of AE' for each grouped term. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term Outcome Categories	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Immune-Mediated Hepatitis (Lab Abnormalities)		
Total Number of AE	36	58
NOT RECOVERED/NOT RESOLVED	3 (8.3%)	16 (27.6%)
RECOVERED/RESOLVED	33 (91.7%)	41 (70.7%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	1 (1.7%)
FATAL	0	0
UNKNOWN	0	0
Immune-Mediated Pneumonitis		
Total Number of AE	1	3
NOT RECOVERED/NOT RESOLVED	0	1 (33.3%)
RECOVERED/RESOLVED	1 (100%)	2 (66.7%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Immune-Mediated Rash		
Total Number of AE	24	70
NOT RECOVERED/NOT RESOLVED	2 (8.3%)	8 (11.4%)
RECOVERED/RESOLVED	21 (87.5%)	62 (88.6%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	1 (4.2%)	0
FATAL	0	0
UNKNOWN	0	0
Immune-Mediated Severe Cutaneous Reactions		
Total Number of AE	0	1
NOT RECOVERED/NOT RESOLVED	0	0
RECOVERED/RESOLVED	0	1 (100%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Nausea		
Total Number of AE	29	108
NOT RECOVERED/NOT RESOLVED	2 (6.9%)	9 (8.3%)
RECOVERED/RESOLVED	27 (93.1%)	97 (89.8%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	2 (1.9%)
FATAL	0	0
UNKNOWN	0	0
Neutropenia		
Total Number of AE	63	146
NOT RECOVERED/NOT RESOLVED	0	5 (3.4%)
RECOVERED/RESOLVED	62 (98.4%)	140 (95.9%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	1 (1.6%)	1 (0.7%)
FATAL	0	0
UNKNOWN	0	0
Oral Mucositis		
Total Number of AE	16	45
NOT RECOVERED/NOT RESOLVED	0	3 (6.7%)
RECOVERED/RESOLVED	15 (93.8%)	42 (93.3%)
RECOVERED/RESOLVED WITH SEQUELAE	1 (6.3%)	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Peripheral Neuropathy		
Total Number of AE	58	112
NOT RECOVERED/NOT RESOLVED	32 (55.2%)	64 (57.1%)
RECOVERED/RESOLVED	17 (29.3%)	41 (36.6%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	9 (15.5%)	7 (6.3%)
FATAL	0	0
UNKNOWN	0	0

Multiple occurrences of the same AE in an individual are counted separately. Percentages are calculated based on 'Total Number of AE' for each grouped term. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term Outcome Categories	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Pneumonia		
Total Number of AE	5	8
NOT RECOVERED/NOT RESOLVED	0	1 (12.5%)
RECOVERED/RESOLVED	5 (100%)	7 (87.5%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Pneumonitis		
Total Number of AE	1	3
NOT RECOVERED/NOT RESOLVED	0	1 (33.3%)
RECOVERED/RESOLVED	1 (100%)	2 (66.7%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Rash		
Total Number of AE	24	70
NOT RECOVERED/NOT RESOLVED	2 (8.3%)	8 (11.4%)
RECOVERED/RESOLVED	21 (87.5%)	62 (88.6%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	1 (4.2%)	0
FATAL	0	0
UNKNOWN	0	0
Thrombocytopenia		
Total Number of AE	5	2
NOT RECOVERED/NOT RESOLVED	3 (60.0%)	0
RECOVERED/RESOLVED	1 (20.0%)	2 (100%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	1 (20.0%)	0
FATAL	0	0
UNKNOWN	0	0
Vomiting		
Total Number of AE	10	114
NOT RECOVERED/NOT RESOLVED	0	1 (0.9%)
RECOVERED/RESOLVED	10 (100%)	112 (98.2%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	1 (0.9%)
FATAL	0	0
UNKNOWN	0	0
Weight Decreased		
Total Number of AE	3	13
NOT RECOVERED/NOT RESOLVED	3 (100%)	5 (38.5%)
RECOVERED/RESOLVED	0	5 (38.5%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	2 (15.4%)
FATAL	0	0
UNKNOWN	0	1 (7.7%)

Multiple occurrences of the same AE in an individual are counted separately. Percentages are calculated based on 'Total Number of AE' for each grouped term. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term Outcome Categories	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Anaemia		
Total Number of AE	28	57
NOT RECOVERED/NOT RESOLVED	5 (17.9%)	10 (17.5%)
RECOVERED/RESOLVED	23 (82.1%)	45 (78.9%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	2 (3.5%)
FATAL	0	0
UNKNOWN	0	0
Asthenia		
Total Number of AE	48	72
NOT RECOVERED/NOT RESOLVED	15 (31.3%)	23 (31.9%)
RECOVERED/RESOLVED	31 (64.6%)	46 (63.9%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	2 (4.2%)	3 (4.2%)
FATAL	0	0
UNKNOWN	0	0
Colitis		
Total Number of AE	0	2
NOT RECOVERED/NOT RESOLVED	0	0
RECOVERED/RESOLVED	0	2 (100%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Decreased Appetite		
Total Number of AE	15	31
NOT RECOVERED/NOT RESOLVED	2 (13.3%)	6 (19.4%)
RECOVERED/RESOLVED	13 (86.7%)	25 (80.6%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Dehydration		
Total Number of AE	0	5
NOT RECOVERED/NOT RESOLVED	0	1 (20.0%)
RECOVERED/RESOLVED	0	4 (80.0%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Diarrhea		
Total Number of AE	65	466
NOT RECOVERED/NOT RESOLVED	1 (1.5%)	10 (2.1%)
RECOVERED/RESOLVED	64 (98.5%)	455 (97.6%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	1 (0.2%)
FATAL	0	0
UNKNOWN	0	0
Elevated Transaminase		
Total Number of AE	46	45
NOT RECOVERED/NOT RESOLVED	4 (8.7%)	8 (17.8%)
RECOVERED/RESOLVED	41 (89.1%)	37 (82.2%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	1 (2.2%)	0
FATAL	0	0
UNKNOWN	0	0
Erythema Multiforme		
Total Number of AE	0	1
NOT RECOVERED/NOT RESOLVED	0	0
RECOVERED/RESOLVED	0	1 (100%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0

Multiple occurrences of the same AE in an individual are counted separately. Percentages are calculated based on 'Total Number of AE' for each grouped term. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term Outcome Categories	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Erythropenia		
Total Number of AE	31	62
NOT RECOVERED/NOT RESOLVED	5 (16.1%)	12 (19.4%)
RECOVERED/RESOLVED	26 (83.9%)	48 (77.4%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	2 (3.2%)
FATAL	0	0
UNKNOWN	0	0
Hepatotoxicity		
Total Number of AE	97	70
NOT RECOVERED/NOT RESOLVED	9 (9.3%)	12 (17.1%)
RECOVERED/RESOLVED	86 (88.7%)	58 (82.9%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	2 (2.1%)	0
FATAL	0	0
UNKNOWN	0	0
Hyperglycemia		
Total Number of AE	39	34
NOT RECOVERED/NOT RESOLVED	1 (2.6%)	5 (14.7%)
RECOVERED/RESOLVED	38 (97.4%)	29 (85.3%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Hyperlipidemia		
Total Number of AE	13	31
NOT RECOVERED/NOT RESOLVED	3 (23.1%)	11 (35.5%)
RECOVERED/RESOLVED	10 (76.9%)	20 (64.5%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Immune-Mediated Diabetes Mellitus		
Total Number of AE	0	1
NOT RECOVERED/NOT RESOLVED	0	1 (100%)
RECOVERED/RESOLVED	0	0
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Immune-Mediated Hepatitis (Diagnosis And Lab Abnormalities)		
Total Number of AE	87	66
NOT RECOVERED/NOT RESOLVED	6 (6.9%)	12 (18.2%)
RECOVERED/RESOLVED	80 (92.0%)	54 (81.8%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	1 (1.1%)	0
FATAL	0	0
UNKNOWN	0	0
Immune-Mediated Hepatitis (Lab Abnormalities)		
Total Number of AE	87	66
NOT RECOVERED/NOT RESOLVED	6 (6.9%)	12 (18.2%)
RECOVERED/RESOLVED	80 (92.0%)	54 (81.8%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	1 (1.1%)	0
FATAL	0	0
UNKNOWN	0	0

Multiple occurrences of the same AE in an individual are counted separately. Percentages are calculated based on 'Total Number of AE' for each grouped term. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term Outcome Categories	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Immune-Mediated Pneumonitis		
Total Number of AE	0	6
NOT RECOVERED/NOT RESOLVED	0	2 (33.3%)
RECOVERED/RESOLVED	0	4 (66.7%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Immune-Mediated Rash		
Total Number of AE	30	87
NOT RECOVERED/NOT RESOLVED	3 (10.0%)	6 (6.9%)
RECOVERED/RESOLVED	27 (90.0%)	79 (90.8%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	2 (2.3%)
FATAL	0	0
UNKNOWN	0	0
Immune-Mediated Severe Cutaneous Reactions		
Total Number of AE	1	3
NOT RECOVERED/NOT RESOLVED	0	0
RECOVERED/RESOLVED	1 (100%)	3 (100%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Nausea		
Total Number of AE	28	94
NOT RECOVERED/NOT RESOLVED	4 (14.3%)	9 (9.6%)
RECOVERED/RESOLVED	24 (85.7%)	84 (89.4%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	1 (1.1%)
FATAL	0	0
UNKNOWN	0	0
Neutropenia		
Total Number of AE	123	194
NOT RECOVERED/NOT RESOLVED	4 (3.3%)	2 (1.0%)
RECOVERED/RESOLVED	119 (96.7%)	191 (98.5%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	1 (0.5%)
UNKNOWN	0	0
Oral Mucositis		
Total Number of AE	13	44
NOT RECOVERED/NOT RESOLVED	0	3 (6.8%)
RECOVERED/RESOLVED	12 (92.3%)	41 (93.2%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	1 (7.7%)	0
FATAL	0	0
UNKNOWN	0	0
Peripheral Neuropathy		
Total Number of AE	64	133
NOT RECOVERED/NOT RESOLVED	45 (70.3%)	87 (65.4%)
RECOVERED/RESOLVED	17 (26.6%)	42 (31.6%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	2 (3.1%)	4 (3.0%)
FATAL	0	0
UNKNOWN	0	0
Pneumonia		
Total Number of AE	4	6
NOT RECOVERED/NOT RESOLVED	0	0
RECOVERED/RESOLVED	4 (100%)	5 (83.3%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	1 (16.7%)
UNKNOWN	0	0

Multiple occurrences of the same AE in an individual are counted separately. Percentages are calculated based on 'Total Number of AE' for each grouped term. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term Outcome Categories	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Pneumonitis		
Total Number of AE	0	6
NOT RECOVERED/NOT RESOLVED	0	2 (33.3%)
RECOVERED/RESOLVED	0	4 (66.7%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Rash		
Total Number of AE	31	89
NOT RECOVERED/NOT RESOLVED	3 (9.7%)	6 (6.7%)
RECOVERED/RESOLVED	28 (90.3%)	81 (91.0%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	2 (2.2%)
FATAL	0	0
UNKNOWN	0	0
Thrombocytopenia		
Total Number of AE	1	4
NOT RECOVERED/NOT RESOLVED	0	1 (25.0%)
RECOVERED/RESOLVED	1 (100%)	3 (75.0%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	0
FATAL	0	0
UNKNOWN	0	0
Vomiting		
Total Number of AE	10	67
NOT RECOVERED/NOT RESOLVED	0	0
RECOVERED/RESOLVED	10 (100%)	65 (97.0%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	2 (3.0%)
FATAL	0	0
UNKNOWN	0	0
Weight Decreased		
Total Number of AE	2	8
NOT RECOVERED/NOT RESOLVED	1 (50.0%)	4 (50.0%)
RECOVERED/RESOLVED	1 (50.0%)	3 (37.5%)
RECOVERED/RESOLVED WITH SEQUELAE	0	0
RECOVERING/RESOLVING	0	1 (12.5%)
FATAL	0	0
UNKNOWN	0	0

Multiple occurrences of the same AE in an individual are counted separately. Percentages are calculated based on 'Total Number of AE' for each grouped term. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term Outcome Categories	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Anaemia	
Total Number of AE	50
NOT RECOVERED/NOT RESOLVED	13 (26.0%)
RECOVERED/RESOLVED	33 (66.0%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	4 (8.0%)
FATAL	0
UNKNOWN	0
Asthenia	
Total Number of AE	59
NOT RECOVERED/NOT RESOLVED	19 (32.2%)
RECOVERED/RESOLVED	34 (57.6%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	6 (10.2%)
FATAL	0
UNKNOWN	0
Decreased Appetite	
Total Number of AE	15
NOT RECOVERED/NOT RESOLVED	5 (33.3%)
RECOVERED/RESOLVED	8 (53.3%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	2 (13.3%)
FATAL	0
UNKNOWN	0
Dehydration	
Total Number of AE	4
NOT RECOVERED/NOT RESOLVED	1 (25.0%)
RECOVERED/RESOLVED	3 (75.0%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	0
FATAL	0
UNKNOWN	0
Diarrhea	
Total Number of AE	328
NOT RECOVERED/NOT RESOLVED	8 (2.4%)
RECOVERED/RESOLVED	317 (96.6%)
RECOVERED/RESOLVED WITH SEQUELAE	2 (0.6%)
RECOVERING/RESOLVING	1 (0.3%)
FATAL	0
UNKNOWN	0
Elevated Transaminase	
Total Number of AE	100
NOT RECOVERED/NOT RESOLVED	4 (4.0%)
RECOVERED/RESOLVED	90 (90.0%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	6 (6.0%)
FATAL	0
UNKNOWN	0
Erythropenia	
Total Number of AE	53
NOT RECOVERED/NOT RESOLVED	13 (24.5%)
RECOVERED/RESOLVED	36 (67.9%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	4 (7.5%)
FATAL	0
UNKNOWN	0
Hepatotoxicity	
Total Number of AE	142
NOT RECOVERED/NOT RESOLVED	10 (7.0%)
RECOVERED/RESOLVED	121 (85.2%)
RECOVERED/RESOLVED WITH SEQUELAE	1 (0.7%)
RECOVERING/RESOLVING	10 (7.0%)
FATAL	0
UNKNOWN	0

Multiple occurrences of the same AE in an individual are counted separately. Percentages are calculated based on 'Total Number of AE' for each grouped term. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term Outcome Categories	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Hyperglycemia	
Total Number of AE	48
NOT RECOVERED/NOT RESOLVED	4 (8.3%)
RECOVERED/RESOLVED	40 (83.3%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	4 (8.3%)
FATAL	0
UNKNOWN	0
Hyperlipidemia	
Total Number of AE	18
NOT RECOVERED/NOT RESOLVED	8 (44.4%)
RECOVERED/RESOLVED	9 (50.0%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	1 (5.6%)
FATAL	0
UNKNOWN	0
Immune-Mediated Diabetes Mellitus	
Total Number of AE	3
NOT RECOVERED/NOT RESOLVED	1 (33.3%)
RECOVERED/RESOLVED	1 (33.3%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	1 (33.3%)
FATAL	0
UNKNOWN	0
Immune-Mediated Hepatitis (Diagnosis And Lab Abnormalities)	
Total Number of AE	120
NOT RECOVERED/NOT RESOLVED	6 (5.0%)
RECOVERED/RESOLVED	107 (89.2%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	7 (5.8%)
FATAL	0
UNKNOWN	0
Immune-Mediated Hepatitis (Lab Abnormalities)	
Total Number of AE	120
NOT RECOVERED/NOT RESOLVED	6 (5.0%)
RECOVERED/RESOLVED	107 (89.2%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	7 (5.8%)
FATAL	0
UNKNOWN	0
Immune-Mediated Pneumonitis	
Total Number of AE	9
NOT RECOVERED/NOT RESOLVED	2 (22.2%)
RECOVERED/RESOLVED	6 (66.7%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	1 (11.1%)
FATAL	0
UNKNOWN	0
Immune-Mediated Rash	
Total Number of AE	66
NOT RECOVERED/NOT RESOLVED	4 (6.1%)
RECOVERED/RESOLVED	58 (87.9%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	3 (4.5%)
FATAL	0
UNKNOWN	1 (1.5%)

Multiple occurrences of the same AE in an individual are counted separately. Percentages are calculated based on 'Total Number of AE' for each grouped term. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term Outcome Categories	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Nausea	
Total Number of AE	66
NOT RECOVERED/NOT RESOLVED	7 (10.6%)
RECOVERED/RESOLVED	53 (80.3%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	6 (9.1%)
FATAL	0
UNKNOWN	0
Neutropenia	
Total Number of AE	149
NOT RECOVERED/NOT RESOLVED	1 (0.7%)
RECOVERED/RESOLVED	147 (98.7%)
RECOVERED/RESOLVED WITH SEQUELAE	1 (0.7%)
RECOVERING/RESOLVING	0
FATAL	0
UNKNOWN	0
Oral Mucositis	
Total Number of AE	23
NOT RECOVERED/NOT RESOLVED	1 (4.3%)
RECOVERED/RESOLVED	20 (87.0%)
RECOVERED/RESOLVED WITH SEQUELAE	1 (4.3%)
RECOVERING/RESOLVING	1 (4.3%)
FATAL	0
UNKNOWN	0
Peripheral Neuropathy	
Total Number of AE	72
NOT RECOVERED/NOT RESOLVED	36 (50.0%)
RECOVERED/RESOLVED	20 (27.8%)
RECOVERED/RESOLVED WITH SEQUELAE	1 (1.4%)
RECOVERING/RESOLVING	15 (20.8%)
FATAL	0
UNKNOWN	0
Pneumonia	
Total Number of AE	7
NOT RECOVERED/NOT RESOLVED	0
RECOVERED/RESOLVED	6 (85.7%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	0
FATAL	1 (14.3%)
UNKNOWN	0
Pneumonitis	
Total Number of AE	9
NOT RECOVERED/NOT RESOLVED	2 (22.2%)
RECOVERED/RESOLVED	6 (66.7%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	1 (11.1%)
FATAL	0
UNKNOWN	0
Rash	
Total Number of AE	66
NOT RECOVERED/NOT RESOLVED	4 (6.1%)
RECOVERED/RESOLVED	58 (87.9%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	3 (4.5%)
FATAL	0
UNKNOWN	1 (1.5%)
Thrombocytopenia	
Total Number of AE	3
NOT RECOVERED/NOT RESOLVED	0
RECOVERED/RESOLVED	3 (100%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	0
FATAL	0
UNKNOWN	0

Multiple occurrences of the same AE in an individual are counted separately. Percentages are calculated based on 'Total Number of AE' for each grouped term. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Grouped Term Outcome Categories	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Vomiting	
Total Number of AE	46
NOT RECOVERED/NOT RESOLVED	0
RECOVERED/RESOLVED	46 (100%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	0
FATAL	0
UNKNOWN	0
Weight Decreased	
Total Number of AE	7
NOT RECOVERED/NOT RESOLVED	4 (57.1%)
RECOVERED/RESOLVED	2 (28.6%)
RECOVERED/RESOLVED WITH SEQUELAE	0
RECOVERING/RESOLVING	1 (14.3%)
FATAL	0
UNKNOWN	0

Multiple occurrences of the same AE in an individual are counted separately. Percentages are calculated based on 'Total Number of AE' for each grouped term. Only treatment emergent adverse events are included.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
Total number of patients with at least one treatment	87 (100%)	166 (98.8%)	253 (99.2%)
Total number of treatments	1066	2356	3422
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM			
Total number of patients with at least one treatment	16 (18.4%)	45 (26.8%)	61 (23.9%)
Total number of treatments	20	62	82
LOSARTAN	5 (5.7%)	10 (6.0%)	15 (5.9%)
LOSARTAN POTASSIUM	1 (1.1%)	5 (3.0%)	6 (2.4%)
CAPTOPRIL	2 (2.3%)	3 (1.8%)	5 (2.0%)
IRBESARTAN	1 (1.1%)	3 (1.8%)	4 (1.6%)
LISINOPRIL	0	3 (1.8%)	3 (1.2%)
OLMESARTAN MEDOXOMIL	1 (1.1%)	2 (1.2%)	3 (1.2%)
PERINDOPRIL	1 (1.1%)	2 (1.2%)	3 (1.2%)
TELMISARTAN	0	3 (1.8%)	3 (1.2%)
BISOPROLOL FUMARATE;PERINDOPRIL ARGININE	1 (1.1%)	1 (0.6%)	2 (0.8%)
ENALAPRIL	1 (1.1%)	1 (0.6%)	2 (0.8%)
HYDROCHLOROTHIAZIDE;LOSARTAN POTASSIUM	0	2 (1.2%)	2 (0.8%)
PERINDOPRIL ERBUMINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
RAMIPRIL	0	2 (1.2%)	2 (0.8%)
VALSARTAN	1 (1.1%)	1 (0.6%)	2 (0.8%)
AMLODIPINE BESILATE;INDAPAMIDE;PERINDOPRIL ARGININE	0	1 (0.6%)	1 (0.4%)
AMLODIPINE BESILATE;RAMIPRIL	1 (1.1%)	0	1 (0.4%)
AMLODIPINE BESILATE;TELMISARTAN	0	1 (0.6%)	1 (0.4%)
AMLODIPINE;VALSARTAN	0	1 (0.6%)	1 (0.4%)
AZILSARTAN	0	1 (0.6%)	1 (0.4%)
CANDESARTAN	0	1 (0.6%)	1 (0.4%)
ENALAPRIL MALEATE;HYDROCHLOROTHIAZIDE	0	1 (0.6%)	1 (0.4%)
ENALAPRIL;HYDROCHLOROTHIAZIDE	0	1 (0.6%)	1 (0.4%)
ENALAPRILAT	0	1 (0.6%)	1 (0.4%)
HYDROCHLOROTHIAZIDE;LISINOPRIL	1 (1.1%)	0	1 (0.4%)
INDAPAMIDE;PERINDOPRIL ARGININE	0	1 (0.6%)	1 (0.4%)
INDAPAMIDE;PERINDOPRIL ERBUMINE	0	1 (0.6%)	1 (0.4%)
LISINOPRIL DIHYDRATE	0	1 (0.6%)	1 (0.4%)
OLMESARTAN	0	1 (0.6%)	1 (0.4%)
PERINDOPRIL ARGININE	0	1 (0.6%)	1 (0.4%)

Treatments are coded using the WHODRUG GLOBAL B3 SEPTEMBER 1, 2022. dictionary. Treatments can appear under multiple classes. The table includes medications that have temporal overlap with study drug administration. Multiple uses of a specific medication for a patient were counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a patient were counted once in the frequency for the medication class. Use of the anti-diarrheal medication Loperamide is primarily summarized in separate outputs.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_A_IT.out
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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
ALL OTHER NON-THERAPEUTIC PRODUCTS			
Total number of patients with at least one treatment	12 (13.8%)	16 (9.5%)	28 (11.0%)
Total number of treatments	66	49	115
SODIUM CHLORIDE	7 (8.0%)	10 (6.0%)	17 (6.7%)
ASCORBIC ACID	3 (3.4%)	1 (0.6%)	4 (1.6%)
SODIUM HYPOCHLORITE	1 (1.1%)	3 (1.8%)	4 (1.6%)
HYPROMELLOSE	0	2 (1.2%)	2 (0.8%)
PENICILLIN NOS	1 (1.1%)	1 (0.6%)	2 (0.8%)
HYALURONIC ACID	1 (1.1%)	0	1 (0.4%)
WATER PURIFIED	0	1 (0.6%)	1 (0.4%)
XANTHAN GUM	0	1 (0.6%)	1 (0.4%)
ALL OTHER THERAPEUTIC PRODUCTS			
Total number of patients with at least one treatment	11 (12.6%)	23 (13.7%)	34 (13.3%)
Total number of treatments	15	38	53
ACETYLCYSTEINE	4 (4.6%)	10 (6.0%)	14 (5.5%)
CALCIUM CARBONATE	1 (1.1%)	4 (2.4%)	5 (2.0%)
ASCORBIC ACID	3 (3.4%)	1 (0.6%)	4 (1.6%)
ALL OTHER THERAPEUTIC PRODUCTS	0	3 (1.8%)	3 (1.2%)
HYDROXOCOBALAMIN	1 (1.1%)	2 (1.2%)	3 (1.2%)
ALUMINIUM HYDROXIDE	0	1 (0.6%)	1 (0.4%)
ATROPINE	0	1 (0.6%)	1 (0.4%)
CALCIUM;VITAMIN D NOS	0	1 (0.6%)	1 (0.4%)
CHONDROITIN SULFATE SODIUM	1 (1.1%)	0	1 (0.4%)
INOSINE	1 (1.1%)	0	1 (0.4%)
IRON	1 (1.1%)	0	1 (0.4%)
METHYLPARABEN	0	1 (0.6%)	1 (0.4%)
NALOXONE	0	1 (0.6%)	1 (0.4%)
NUCLEOSIDES	0	1 (0.6%)	1 (0.4%)
POTASSIUM IODIDE	0	1 (0.6%)	1 (0.4%)
SODIUM PHOSPHATE	1 (1.1%)	0	1 (0.4%)
TAURINE	1 (1.1%)	0	1 (0.4%)
ANALGESICS			
Total number of patients with at least one treatment	55 (63.2%)	116 (69.0%)	171 (67.1%)
Total number of treatments	289	804	1093
PARACETAMOL	31 (35.6%)	61 (36.3%)	92 (36.1%)
TRAMADOL	7 (8.0%)	20 (11.9%)	27 (10.6%)
GABAPENTIN	11 (12.6%)	13 (7.7%)	24 (9.4%)
METAMIZOLE SODIUM	4 (4.6%)	14 (8.3%)	18 (7.1%)
PREGABALIN	6 (6.9%)	11 (6.5%)	17 (6.7%)
TRAMADOL HYDROCHLORIDE	4 (4.6%)	11 (6.5%)	15 (5.9%)
MORPHINE	7 (8.0%)	4 (2.4%)	11 (4.3%)

Treatments are coded using the WHODRUG GLOBAL B3 SEPTEMBER 1, 2022. dictionary. Treatments can appear under multiple classes. The table includes medications that have temporal overlap with study drug administration. Multiple uses of a specific medication for a patient were counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a patient were counted once in the frequency for the medication class. Use of the anti-diarrheal medication Loperamide is primarily summarized in separate outputs.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_A_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
PARACETAMOL;TRAMADOL HYDROCHLORIDE	2 (2.3%)	9 (5.4%)	11 (4.3%)
ACETYLSALICYLIC ACID	4 (4.6%)	6 (3.6%)	10 (3.9%)
CODEINE PHOSPHATE;PARACETAMOL	2 (2.3%)	7 (4.2%)	9 (3.5%)
CODEINE PHOSPHATE;IBUPROFEN;PARACETAMOL	4 (4.6%)	4 (2.4%)	8 (3.1%)
FENTANYL	1 (1.1%)	5 (3.0%)	6 (2.4%)
METAMIZOLE	1 (1.1%)	5 (3.0%)	6 (2.4%)
OXYCODONE HYDROCHLORIDE	1 (1.1%)	5 (3.0%)	6 (2.4%)
CODEINE	3 (3.4%)	2 (1.2%)	5 (2.0%)
CODEINE PHOSPHATE	3 (3.4%)	2 (1.2%)	5 (2.0%)
MORPHINE SULFATE	1 (1.1%)	4 (2.4%)	5 (2.0%)
NALOXONE HYDROCHLORIDE;OXYCODONE HYDROCHLORIDE	0	5 (3.0%)	5 (2.0%)
DULOXETINE	0	4 (2.4%)	4 (1.6%)
METOPROLOL	1 (1.1%)	3 (1.8%)	4 (1.6%)
AMITRIPTYLINE	0	3 (1.8%)	3 (1.2%)
BUPRENORPHINE	1 (1.1%)	2 (1.2%)	3 (1.2%)
CANNABIDIOL	2 (2.3%)	1 (0.6%)	3 (1.2%)
CODEINE;PARACETAMOL	0	3 (1.8%)	3 (1.2%)
FENTANYL CITRATE	1 (1.1%)	2 (1.2%)	3 (1.2%)
METOPROLOL TARTRATE	2 (2.3%)	1 (0.6%)	3 (1.2%)
MORPHINE HYDROCHLORIDE	0	3 (1.8%)	3 (1.2%)
TAPENTADOL	0	3 (1.8%)	3 (1.2%)
VENLAFAXINE	3 (3.4%)	0	3 (1.2%)
ACETYLSALICYLIC ACID;MAGNESIUM HYDROXIDE	0	2 (1.2%)	2 (0.8%)
ARTEMISIA ARGYI	0	2 (1.2%)	2 (0.8%)
CAFFEINE;CODEINE PHOSPHATE;PARACETAMOL	2 (2.3%)	0	2 (0.8%)
CAFFEINE;CODEINE;PARACETAMOL	1 (1.1%)	1 (0.6%)	2 (0.8%)
CAFFEINE;PARACETAMOL;PROMETHAZINE METHYLENE DISALICYLATE;SALICYLAMIDE	2 (2.3%)	0	2 (0.8%)
CARBAMAZEPINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
DULOXETINE HYDROCHLORIDE	0	2 (1.2%)	2 (0.8%)
METHADONE	1 (1.1%)	1 (0.6%)	2 (0.8%)
METOPROLOL SUCCINATE	0	2 (1.2%)	2 (0.8%)
PROPRANOLOL	0	2 (1.2%)	2 (0.8%)
ACETYLSALICYLATE LYSINE	1 (1.1%)	0	1 (0.4%)
ACETYLSALICYLIC ACID;CAFFEINE	0	1 (0.6%)	1 (0.4%)
AMITRIPTYLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
ASCORBIC ACID;NOSCAPINE;PARACETAMOL; PSEUDOEPHEDRINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
CAFFEINE;CHLORPHENAMINE MALEATE;PARACETAMOL; PHENYLEPHRINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
CAFFEINE;DIHYDROERGOTAMINE MESILATE;METAMIZOLE SODIUM	0	1 (0.6%)	1 (0.4%)
CAFFEINE;DIHYDROERGOTAMINE MESILATE; METOCLOPRAMIDE HYDROCHLORIDE;PARACETAMOL	0	1 (0.6%)	1 (0.4%)
CAFFEINE;PAPAVER SOMNIFERUM LATEX;PARACETAMOL	0	1 (0.6%)	1 (0.4%)
CLONIDINE	0	1 (0.6%)	1 (0.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_A_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
CODEINE PHOSPHATE HEMIHYDRATE	0	1 (0.6%)	1 (0.4%)
DIHYDROCODEINE BITARTRATE	1 (1.1%)	0	1 (0.4%)
FENPIVERINIUM BROMIDE;METAMIZOLE SODIUM; PITOFENONE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
FLUNARIZINE DIHYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
GABAPENTIN;NORTRIPTYLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
HYDROMORPHONE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
IBUPROFEN;PARACETAMOL	0	1 (0.6%)	1 (0.4%)
METAMIZOLE MAGNESIUM	0	1 (0.6%)	1 (0.4%)
MORPHINE HYDROCHLORIDE TRIHYDRATE	0	1 (0.6%)	1 (0.4%)
NALOXONE;OXYCODONE	1 (1.1%)	0	1 (0.4%)
NAPROXEN;PARACETAMOL	1 (1.1%)	0	1 (0.4%)
OXYCODONE	0	1 (0.6%)	1 (0.4%)
OXYCODONE HYDROCHLORIDE TRIHYDRATE	0	1 (0.6%)	1 (0.4%)
OXYCODONE HYDROCHLORIDE;PARACETAMOL	0	1 (0.6%)	1 (0.4%)
PARACETAMOL;TRAMADOL	0	1 (0.6%)	1 (0.4%)
PENTAZOCINE	0	1 (0.6%)	1 (0.4%)
PETHIDINE	0	1 (0.6%)	1 (0.4%)
PETHIDINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
PRONILIDE	1 (1.1%)	0	1 (0.4%)
PROPRANOLOL HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
TAPENTADOL HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
TIMOLOL MALEATE	0	1 (0.6%)	1 (0.4%)
VERAPAMIL	0	1 (0.6%)	1 (0.4%)
ANESTHETICS			
Total number of patients with at least one treatment	7 (8.0%)	15 (8.9%)	22 (8.6%)
Total number of treatments	12	37	49
FENTANYL	1 (1.1%)	5 (3.0%)	6 (2.4%)
LIDOCAINE	1 (1.1%)	5 (3.0%)	6 (2.4%)
LIDOCAINE HYDROCHLORIDE	2 (2.3%)	2 (1.2%)	4 (1.6%)
FENTANYL CITRATE	1 (1.1%)	2 (1.2%)	3 (1.2%)
PROCAINE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
BENZOCAINE	0	1 (0.6%)	1 (0.4%)
EPINEPHRINE BITARTRATE;LIDOCAINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
EPINEPHRINE;LIDOCAINE	1 (1.1%)	0	1 (0.4%)
LIDOCAINE;PRILOCAINE	1 (1.1%)	0	1 (0.4%)
PRILOCAINE	0	1 (0.6%)	1 (0.4%)
THIOPENTAL SODIUM	1 (1.1%)	0	1 (0.4%)
ANTHELMINTICS			
Total number of patients with at least one treatment	1 (1.1%)	0	1 (0.4%)
Total number of treatments	1	0	1
IVERMECTIN	1 (1.1%)	0	1 (0.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_A_IT.out

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
ANTI-ACNE PREPARATIONS			
Total number of patients with at least one treatment	77 (88.5%)	144 (85.7%)	221 (86.7%)
Total number of treatments	581	1119	1700
DEXAMETHASONE	55 (63.2%)	114 (67.9%)	169 (66.3%)
DEXAMETHASONE SODIUM PHOSPHATE	12 (13.8%)	15 (8.9%)	27 (10.6%)
IBUPROFEN	6 (6.9%)	16 (9.5%)	22 (8.6%)
METHYLPREDNISOLONE	7 (8.0%)	12 (7.1%)	19 (7.5%)
METHYLPREDNISOLONE SODIUM SUCCINATE	4 (4.6%)	8 (4.8%)	12 (4.7%)
AZITHROMYCIN	1 (1.1%)	6 (3.6%)	7 (2.7%)
CHLORHEXIDINE GLUCONATE	1 (1.1%)	5 (3.0%)	6 (2.4%)
CLINDAMYCIN	2 (2.3%)	2 (1.2%)	4 (1.6%)
DIMETICONE	0	3 (1.8%)	3 (1.2%)
FLUOROMETHOLONE	0	3 (1.8%)	3 (1.2%)
ERYTHROMYCIN	1 (1.1%)	1 (0.6%)	2 (0.8%)
MINOCYCLINE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
CHLORAMPHENICOL	0	1 (0.6%)	1 (0.4%)
DOXYCYCLINE	0	1 (0.6%)	1 (0.4%)
MINOCYCLINE	0	1 (0.6%)	1 (0.4%)
ZINC	0	1 (0.6%)	1 (0.4%)
ANTI-PARKINSON DRUGS			
Total number of patients with at least one treatment	22 (25.3%)	66 (39.3%)	88 (34.5%)
Total number of treatments	95	297	392
DIPHENHYDRAMINE	12 (13.8%)	40 (23.8%)	52 (20.4%)
DIPHENHYDRAMINE HYDROCHLORIDE	10 (11.5%)	27 (16.1%)	37 (14.5%)
ORPHENADRINE	0	1 (0.6%)	1 (0.4%)
ANTIANEMIC PREPARATIONS			
Total number of patients with at least one treatment	7 (8.0%)	22 (13.1%)	29 (11.4%)
Total number of treatments	12	50	62
FERROUS SULFATE	3 (3.4%)	6 (3.6%)	9 (3.5%)
FOLIC ACID	2 (2.3%)	7 (4.2%)	9 (3.5%)
FERRIC HYDROXIDE POLYMALTOSE COMPLEX	0	6 (3.6%)	6 (2.4%)
EPOETIN ALFA	1 (1.1%)	2 (1.2%)	3 (1.2%)
HYDROXOCOBALAMIN	1 (1.1%)	2 (1.2%)	3 (1.2%)
MECOBALAMIN	0	3 (1.8%)	3 (1.2%)
SACCHARATED IRON OXIDE	1 (1.1%)	2 (1.2%)	3 (1.2%)
CYANOCOBALAMIN	1 (1.1%)	1 (0.6%)	2 (0.8%)
VITAMIN B NOS	1 (1.1%)	1 (0.6%)	2 (0.8%)
ASCORBIC ACID;FERROUS SULFATE	0	1 (0.6%)	1 (0.4%)
DARBEPOETIN ALFA	0	1 (0.6%)	1 (0.4%)
IRON	1 (1.1%)	0	1 (0.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
ANTIBACTERIALS FOR SYSTEMIC USE			
Total number of patients with at least one treatment	34 (39.1%)	68 (40.5%)	102 (40.0%)
Total number of treatments	91	182	273
AMOXICILLIN;CLAVULANATE POTASSIUM	6 (6.9%)	10 (6.0%)	16 (6.3%)
LEVOFLOXACIN	6 (6.9%)	9 (5.4%)	15 (5.9%)
CIPROFLOXACIN	3 (3.4%)	11 (6.5%)	14 (5.5%)
AMOXICILLIN	4 (4.6%)	7 (4.2%)	11 (4.3%)
METRONIDAZOLE	5 (5.7%)	5 (3.0%)	10 (3.9%)
CEFALEXIN	3 (3.4%)	5 (3.0%)	8 (3.1%)
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 (1.1%)	7 (4.2%)	8 (3.1%)
AZITHROMYCIN	1 (1.1%)	6 (3.6%)	7 (2.7%)
FUSIDIC ACID	2 (2.3%)	4 (2.4%)	6 (2.4%)
AMOXICILLIN TRIHYDRATE;CLAVULANATE POTASSIUM	2 (2.3%)	3 (1.8%)	5 (2.0%)
NITROFURANTOIN	1 (1.1%)	4 (2.4%)	5 (2.0%)
AMOXICILLIN;CLAVULANIC ACID	0	4 (2.4%)	4 (1.6%)
CEFTRIAXONE	1 (1.1%)	3 (1.8%)	4 (1.6%)
CEFUROXIME	1 (1.1%)	3 (1.8%)	4 (1.6%)
CLINDAMYCIN	2 (2.3%)	2 (1.2%)	4 (1.6%)
FOSFOMYCIN TROMETAMOL	2 (2.3%)	2 (1.2%)	4 (1.6%)
OFLOXACIN	1 (1.1%)	3 (1.8%)	4 (1.6%)
GENTAMICIN	1 (1.1%)	2 (1.2%)	3 (1.2%)
PIPERACILLIN SODIUM;TAZOBACTAM SODIUM	1 (1.1%)	2 (1.2%)	3 (1.2%)
AMIKACIN	0	2 (1.2%)	2 (0.8%)
AMOXICILLIN TRIHYDRATE	0	2 (1.2%)	2 (0.8%)
AMPICILLIN SODIUM;SULBACTAM SODIUM	1 (1.1%)	1 (0.6%)	2 (0.8%)
ARTEMISIA ARGYI	0	2 (1.2%)	2 (0.8%)
CEFADROXIL	0	2 (1.2%)	2 (0.8%)
CEFAZOLIN SODIUM	1 (1.1%)	1 (0.6%)	2 (0.8%)
CEFCAPENE PIVOXIL HYDROCHLORIDE HYDRATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
CEFDINIR	1 (1.1%)	1 (0.6%)	2 (0.8%)
CEFEPIME HYDROCHLORIDE	0	2 (1.2%)	2 (0.8%)
CEFIXIME	1 (1.1%)	1 (0.6%)	2 (0.8%)
CEFOPERAZONE SODIUM;SULBACTAM SODIUM	0	2 (1.2%)	2 (0.8%)
CEFOPERAZONE;SULBACTAM	1 (1.1%)	1 (0.6%)	2 (0.8%)
CLARITHROMYCIN	1 (1.1%)	1 (0.6%)	2 (0.8%)
CLAVULANIC ACID	1 (1.1%)	1 (0.6%)	2 (0.8%)
ERYTHROMYCIN	1 (1.1%)	1 (0.6%)	2 (0.8%)
FOSFOMYCIN	0	2 (1.2%)	2 (0.8%)
MEROPENEM	2 (2.3%)	0	2 (0.8%)
MINOCYCLINE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
MOXIFLOXACIN HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
PENICILLIN NOS	1 (1.1%)	1 (0.6%)	2 (0.8%)
PIPERACILLIN;TAZOBACTAM	1 (1.1%)	1 (0.6%)	2 (0.8%)
SULFAMETHOXAZOLE	0	2 (1.2%)	2 (0.8%)

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_A_IT.out

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
TETRACYCLINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
TRIMETHOPRIM	0	2 (1.2%)	2 (0.8%)
ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER; GELATIN;POLYPORUS UMBELLATUS SCLEROTIUM;PORIA COCOS SCLEROTIUM;TALC	0	1 (0.6%)	1 (0.4%)
AMIKACIN SULFATE	0	1 (0.6%)	1 (0.4%)
AMPHOTERICIN B;TETRACYCLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
AMPICILLIN;SULBACTAM SODIUM	1 (1.1%)	0	1 (0.4%)
AZITHROMYCIN DIHYDRATE	0	1 (0.6%)	1 (0.4%)
CEFACLOR MONOHYDRATE	0	1 (0.6%)	1 (0.4%)
CEFALOTIN	0	1 (0.6%)	1 (0.4%)
CEFEPIME	1 (1.1%)	0	1 (0.4%)
CEFIXIME;ORNIDAZOLE	0	1 (0.6%)	1 (0.4%)
CEFOPERAZONE SODIUM	1 (1.1%)	0	1 (0.4%)
CEFOTAXIME SODIUM	0	1 (0.6%)	1 (0.4%)
CEFPODOXIME	0	1 (0.6%)	1 (0.4%)
CEFTAZIDIME	0	1 (0.6%)	1 (0.4%)
CEFTRIAXONE SODIUM	1 (1.1%)	0	1 (0.4%)
CHLORAMPHENICOL	0	1 (0.6%)	1 (0.4%)
CIPROFLOXACIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
COLISTIMETHATE SODIUM	0	1 (0.6%)	1 (0.4%)
COLISTIN	1 (1.1%)	0	1 (0.4%)
DOXYCYCLINE	0	1 (0.6%)	1 (0.4%)
DOXYCYCLINE HYCLATE	1 (1.1%)	0	1 (0.4%)
ERTAPENEM	1 (1.1%)	0	1 (0.4%)
FLUCLOXACILLIN	1 (1.1%)	0	1 (0.4%)
FUSIDATE SODIUM	1 (1.1%)	0	1 (0.4%)
GEMIFLOXACIN MESILATE	0	1 (0.6%)	1 (0.4%)
GENTAMICIN SULFATE	0	1 (0.6%)	1 (0.4%)
IMIPENEM	0	1 (0.6%)	1 (0.4%)
LEVOFLOXACIN HEMIHYDRATE	0	1 (0.6%)	1 (0.4%)
LOMEFLOXACIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
MEROPENEM TRIHYDRATE	0	1 (0.6%)	1 (0.4%)
MINOCYCLINE	0	1 (0.6%)	1 (0.4%)
MOXIFLOXACIN	1 (1.1%)	0	1 (0.4%)
NITROXOLINE	1 (1.1%)	0	1 (0.4%)
NORFLOXACIN	0	1 (0.6%)	1 (0.4%)
OFLOXACIN;ORNIDAZOLE	0	1 (0.6%)	1 (0.4%)
ORNIDAZOLE	1 (1.1%)	0	1 (0.4%)
PIPERACILLIN	0	1 (0.6%)	1 (0.4%)
PIPERACILLIN SODIUM;TAZOBACTAM	0	1 (0.6%)	1 (0.4%)
SECNIDAZOLE	0	1 (0.6%)	1 (0.4%)
SULTAMICILLIN	0	1 (0.6%)	1 (0.4%)
TEDIZOLID	1 (1.1%)	0	1 (0.4%)
VACCINIUM MACROCARPON	1 (1.1%)	0	1 (0.4%)
XIBORNOL	0	1 (0.6%)	1 (0.4%)

Treatments are coded using the WHODRUG GLOBAL B3 SEPTEMBER 1, 2022. dictionary. Treatments can appear under multiple classes. The table includes medications that have temporal overlap with study drug administration. Multiple uses of a specific medication for a patient were counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a patient were counted once in the frequency for the medication class. Use of the anti-diarrheal medication Loperamide is primarily summarized in separate outputs.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE			
Total number of patients with at least one treatment	20 (23.0%)	40 (23.8%)	60 (23.5%)
Total number of treatments	39	65	104
LEVOFLOXACIN	6 (6.9%)	9 (5.4%)	15 (5.9%)
CIPROFLOXACIN	3 (3.4%)	11 (6.5%)	14 (5.5%)
METRONIDAZOLE	5 (5.7%)	5 (3.0%)	10 (3.9%)
FUSIDIC ACID	2 (2.3%)	4 (2.4%)	6 (2.4%)
OFLOXACIN	1 (1.1%)	3 (1.8%)	4 (1.6%)
GENTAMICIN	1 (1.1%)	2 (1.2%)	3 (1.2%)
MUPIROCIN	1 (1.1%)	2 (1.2%)	3 (1.2%)
ACICLOVIR	1 (1.1%)	1 (0.6%)	2 (0.8%)
AMIKACIN	0	2 (1.2%)	2 (0.8%)
CLARITHROMYCIN	1 (1.1%)	1 (0.6%)	2 (0.8%)
ERYTHROMYCIN	1 (1.1%)	1 (0.6%)	2 (0.8%)
MINOCYCLINE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
TETRACYCLINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
AMIKACIN SULFATE	0	1 (0.6%)	1 (0.4%)
BACITRACIN ZINC;NEOMYCIN SULFATE;POLYMYXIN B SULFATE	0	1 (0.6%)	1 (0.4%)
BACITRACIN;NEOMYCIN SULFATE	0	1 (0.6%)	1 (0.4%)
CHLORAMPHENICOL	0	1 (0.6%)	1 (0.4%)
CIPROFLOXACIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
DOXYCYCLINE	0	1 (0.6%)	1 (0.4%)
FUSIDATE SODIUM	1 (1.1%)	0	1 (0.4%)
GENTAMICIN SULFATE	0	1 (0.6%)	1 (0.4%)
INOSINE	1 (1.1%)	0	1 (0.4%)
LOMEFLOXACIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
MINOCYCLINE	0	1 (0.6%)	1 (0.4%)
MOXIFLOXACIN	1 (1.1%)	0	1 (0.4%)
NORFLOXACIN	0	1 (0.6%)	1 (0.4%)
RIFAXIMIN	1 (1.1%)	0	1 (0.4%)
ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ ANTIINFECTIVE AGENTS			
Total number of patients with at least one treatment	25 (28.7%)	64 (38.1%)	89 (34.9%)
Total number of treatments	53	211	264
HYDROCORTISONE	4 (4.6%)	11 (6.5%)	15 (5.9%)
BETAMETHASONE VALERATE	4 (4.6%)	7 (4.2%)	11 (4.3%)
NYSTATIN	5 (5.7%)	6 (3.6%)	11 (4.3%)
DIOSMECTITE	0	10 (6.0%)	10 (3.9%)
HYDROCORTISONE SODIUM SUCCINATE	1 (1.1%)	8 (4.8%)	9 (3.5%)
PREDNISONE	3 (3.4%)	6 (3.6%)	9 (3.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
RACECADOTRIL	0	7 (4.2%)	7 (2.7%)
CODEINE	3 (3.4%)	2 (1.2%)	5 (2.0%)
PREDNISOLONE	2 (2.3%)	3 (1.8%)	5 (2.0%)
BETAMETHASONE BUTYRATE PROPIONATE	3 (3.4%)	1 (0.6%)	4 (1.6%)
BETAMETHASONE DIPROPIONATE	2 (2.3%)	2 (1.2%)	4 (1.6%)
PROBIOTICS NOS	1 (1.1%)	3 (1.8%)	4 (1.6%)
MICONAZOLE	3 (3.4%)	0	3 (1.2%)
BACILLUS CLAUSII	1 (1.1%)	1 (0.6%)	2 (0.8%)
BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM; ENTEROCOCCUS FAECALIS	2 (2.3%)	0	2 (0.8%)
BECLOMETASONE DIPROPIONATE	0	2 (1.2%)	2 (0.8%)
BISMUTH SUBSALICYLATE	0	2 (1.2%)	2 (0.8%)
BUDESONIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
CHARCOAL, ACTIVATED	0	2 (1.2%)	2 (0.8%)
CROMOGLICATE SODIUM	0	2 (1.2%)	2 (0.8%)
HYDROCORTISONE BUTYRATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
SACCHAROMYCES BOULARDII	0	2 (1.2%)	2 (0.8%)
ALBUMIN TANNATE;BISMUTH SUBGALLATE;KAOLIN	0	1 (0.6%)	1 (0.4%)
ANTIBIOTICS-RESISTANT LACTIC ACID BACTERIAE	0	1 (0.6%)	1 (0.4%)
ATROPINE SULFATE;DIPHENOXYLATE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
BACITRACIN;NEOMYCIN SULFATE	0	1 (0.6%)	1 (0.4%)
BECLOMETASONE	1 (1.1%)	0	1 (0.4%)
BETAMETHASONE	0	1 (0.6%)	1 (0.4%)
BIFIDOBACTERIUM BIFIDUM;BIFIDOBACTERIUM INFANTIS	0	1 (0.6%)	1 (0.4%)
BIFIDOBACTERIUM LONGUM;LACTOBACILLUS HELVETICUS; LACTOBACILLUS RHAMNOSUS;SACCHAROMYCES BOULARDII	0	1 (0.6%)	1 (0.4%)
BIFIDOBACTERIUM NOS	0	1 (0.6%)	1 (0.4%)
CELLULOSE MICROCRYSTALLINE;HEMICELLULOSE;LIGNIN; PECTIN	0	1 (0.6%)	1 (0.4%)
CODEINE PHOSPHATE HEMIHYDRATE	0	1 (0.6%)	1 (0.4%)
COLISTIMETHATE SODIUM	0	1 (0.6%)	1 (0.4%)
COLISTIN	1 (1.1%)	0	1 (0.4%)
ETHACRIDINE LACTATE	1 (1.1%)	0	1 (0.4%)
GLUCOSE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
HYDROCORTISONE ACETATE	1 (1.1%)	0	1 (0.4%)
HYDROCORTISONE HYDROGEN SUCCINATE	0	1 (0.6%)	1 (0.4%)
LACTOBACILLUS HELVETICUS	0	1 (0.6%)	1 (0.4%)
LACTOBACILLUS HELVETICUS;LACTOBACILLUS RHAMNOSUS	0	1 (0.6%)	1 (0.4%)
LACTOBACILLUS NOS	0	1 (0.6%)	1 (0.4%)
LACTOMIN	0	1 (0.6%)	1 (0.4%)
LOPERAMIDE	0	1 (0.6%)	1 (0.4%)
LOPERAMIDE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
METHYLURACIL	0	1 (0.6%)	1 (0.4%)
RIFAXIMIN	1 (1.1%)	0	1 (0.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
ANTIEMETICS AND ANTINAUSEANTS			
Total number of patients with at least one treatment	62 (71.3%)	138 (82.1%)	200 (78.4%)
Total number of treatments	509	1115	1624
ONDANSETRON	29 (33.3%)	70 (41.7%)	99 (38.8%)
DIPHENHYDRAMINE	12 (13.8%)	40 (23.8%)	52 (20.4%)
DIPHENHYDRAMINE HYDROCHLORIDE	10 (11.5%)	27 (16.1%)	37 (14.5%)
METOCLOPRAMIDE	10 (11.5%)	16 (9.5%)	26 (10.2%)
METOCLOPRAMIDE HYDROCHLORIDE	2 (2.3%)	18 (10.7%)	20 (7.8%)
DIMENHYDRINATE	6 (6.9%)	10 (6.0%)	16 (6.3%)
GRANISETRON	3 (3.4%)	10 (6.0%)	13 (5.1%)
ONDANSETRON HYDROCHLORIDE	5 (5.7%)	8 (4.8%)	13 (5.1%)
GRANISETRON HYDROCHLORIDE	4 (4.6%)	7 (4.2%)	11 (4.3%)
DOMPERIDONE	2 (2.3%)	6 (3.6%)	8 (3.1%)
PROCHLORPERAZINE	2 (2.3%)	5 (3.0%)	7 (2.7%)
PALONOSETRON HYDROCHLORIDE	1 (1.1%)	5 (3.0%)	6 (2.4%)
HYDROXYZINE	1 (1.1%)	4 (2.4%)	5 (2.0%)
HYOSCINE	1 (1.1%)	4 (2.4%)	5 (2.0%)
PROMETHAZINE	2 (2.3%)	3 (1.8%)	5 (2.0%)
ALIZAPRIDE HYDROCHLORIDE	1 (1.1%)	2 (1.2%)	3 (1.2%)
HYDROXYZINE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
PROCHLORPERAZINE MALEATE	0	2 (1.2%)	2 (0.8%)
ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER; ARTEMISIA CAPILLARIS FLOWER;ATRACTYLODES LANCEA RHIZOME;CINNAMOMUM CASSIA BARK;POLYPORUS UMBELLATUS SCLEROTIUM;PORIA COCOS SCLEROTIUM	0	1 (0.6%)	1 (0.4%)
APREPITANT	0	1 (0.6%)	1 (0.4%)
BUTYLSCOPOLAMINE	0	1 (0.6%)	1 (0.4%)
DIFENIDOL	0	1 (0.6%)	1 (0.4%)
DIMENHYDRINATE;PYRIDOXINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
LEVOSULPIRIDE	1 (1.1%)	0	1 (0.4%)
METOPIMAZINE	0	1 (0.6%)	1 (0.4%)
PALONOSETRON	0	1 (0.6%)	1 (0.4%)
RAMOSETRON HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
ANTIEPILEPTICS			
Total number of patients with at least one treatment	21 (24.1%)	39 (23.2%)	60 (23.5%)
Total number of treatments	32	78	110
GABAPENTIN	11 (12.6%)	13 (7.7%)	24 (9.4%)
PREGABALIN	6 (6.9%)	11 (6.5%)	17 (6.7%)
LORAZEPAM	4 (4.6%)	8 (4.8%)	12 (4.7%)
DIAZEPAM	0	6 (3.6%)	6 (2.4%)
CLONAZEPAM	1 (1.1%)	4 (2.4%)	5 (2.0%)
MAGNESIUM SULFATE	0	5 (3.0%)	5 (2.0%)
CANNABIDIOL	2 (2.3%)	1 (0.6%)	3 (1.2%)
ACETAZOLAMIDE	0	2 (1.2%)	2 (0.8%)
CARBAMAZEPINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
GABAPENTIN;NORTRIPTYLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
LAMOTRIGINE	0	1 (0.6%)	1 (0.4%)
ANTIFUNGALS FOR DERMATOLOGICAL USE			
Total number of patients with at least one treatment	13 (14.9%)	15 (8.9%)	28 (11.0%)
Total number of treatments	29	19	48
NYSTATIN	5 (5.7%)	6 (3.6%)	11 (4.3%)
FLUCONAZOLE	6 (6.9%)	4 (2.4%)	10 (3.9%)
CLOTRIMAZOLE	3 (3.4%)	5 (3.0%)	8 (3.1%)
MICONAZOLE	3 (3.4%)	0	3 (1.2%)
CICLOPIROX	0	1 (0.6%)	1 (0.4%)
LANOCONAZOLE	0	1 (0.6%)	1 (0.4%)
NAFTIFINE HYDROCHLORIDE	1 (1.1%)	0	1 (0.4%)
SERTACONAZOLE NITRATE	1 (1.1%)	0	1 (0.4%)
SULCONAZOLE NITRATE	1 (1.1%)	0	1 (0.4%)
UREA	1 (1.1%)	0	1 (0.4%)
ANTIGOUT PREPARATIONS			
Total number of patients with at least one treatment	2 (2.3%)	3 (1.8%)	5 (2.0%)
Total number of treatments	2	3	5
DOCOSAHEXAENOIC ACID;EICOSAPENTAENOIC ACID	1 (1.1%)	2 (1.2%)	3 (1.2%)
ALLOPURINOL	1 (1.1%)	0	1 (0.4%)
COLCHICINE	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
ANTIHEMORRHAGICS			
Total number of patients with at least one treatment	4 (4.6%)	5 (3.0%)	9 (3.5%)
Total number of treatments	5	5	10
TRANEXAMIC ACID	2 (2.3%)	4 (2.4%)	6 (2.4%)
ETAMSILATE	1 (1.1%)	0	1 (0.4%)
MENADIONE	0	1 (0.6%)	1 (0.4%)
VITAMIN K NOS	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
ANTIHISTAMINES FOR SYSTEMIC USE			
Total number of patients with at least one treatment	80 (92.0%)	153 (91.1%)	233 (91.4%)
Total number of treatments	642	1164	1806
CHLORPHENAMINE	20 (23.0%)	38 (22.6%)	58 (22.7%)
DIPHENHYDRAMINE	12 (13.8%)	40 (23.8%)	52 (20.4%)
DIPHENHYDRAMINE HYDROCHLORIDE	10 (11.5%)	27 (16.1%)	37 (14.5%)
DEXCHLORPHENIRAMINE MALEATE	9 (10.3%)	21 (12.5%)	30 (11.8%)
LORATADINE	8 (9.2%)	14 (8.3%)	22 (8.6%)
CHLOROPYRAMINE HYDROCHLORIDE	6 (6.9%)	13 (7.7%)	19 (7.5%)
DIMENHYDRINATE	6 (6.9%)	10 (6.0%)	16 (6.3%)
CHLORPHENAMINE MALEATE	9 (10.3%)	6 (3.6%)	15 (5.9%)
DEXCHLORPHENIRAMINE	2 (2.3%)	8 (4.8%)	10 (3.9%)
LEVOCETIRIZINE DIHYDROCHLORIDE	1 (1.1%)	8 (4.8%)	9 (3.5%)
CLEMASTINE FUMARATE	5 (5.7%)	3 (1.8%)	8 (3.1%)
PHENIRAMINE	4 (4.6%)	4 (2.4%)	8 (3.1%)
CETIRIZINE	1 (1.1%)	6 (3.6%)	7 (2.7%)
CETIRIZINE HYDROCHLORIDE	3 (3.4%)	4 (2.4%)	7 (2.7%)
CLEMASTINE	1 (1.1%)	6 (3.6%)	7 (2.7%)
FEXOFENADINE HYDROCHLORIDE	0	5 (3.0%)	5 (2.0%)
HYDROXYZINE	1 (1.1%)	4 (2.4%)	5 (2.0%)
PROMETHAZINE	2 (2.3%)	3 (1.8%)	5 (2.0%)
BILASTINE	1 (1.1%)	3 (1.8%)	4 (1.6%)
QUERCETIN	1 (1.1%)	3 (1.8%)	4 (1.6%)
DIMETINDENE MALEATE	1 (1.1%)	2 (1.2%)	3 (1.2%)
PHENIRAMINE MALEATE	2 (2.3%)	1 (0.6%)	3 (1.2%)
BUCLIZINE HYDROCHLORIDE	0	2 (1.2%)	2 (0.8%)
CHLOROPYRAMINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
DESLORATADINE	0	2 (1.2%)	2 (0.8%)
EBASTINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
FEXOFENADINE	0	2 (1.2%)	2 (0.8%)
HYDROXYZINE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
LEVOCETIRIZINE	0	2 (1.2%)	2 (0.8%)
BEPOTASTINE BESILATE	0	1 (0.6%)	1 (0.4%)
BISULEPIN	0	1 (0.6%)	1 (0.4%)
BUCLIZINE	0	1 (0.6%)	1 (0.4%)
DIMENHYDRINATE;PYRIDOXINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
EPINASTINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
FEXOFENADINE HYDROCHLORIDE;PSEUDOEPHEDRINE HYDROCHLORIDE	1 (1.1%)	0	1 (0.4%)
KETOTIFEN	0	1 (0.6%)	1 (0.4%)
KETOTIFEN FUMARATE	0	1 (0.6%)	1 (0.4%)
PHENIRAMINE AMINOSALICYLATE	1 (1.1%)	0	1 (0.4%)
RUPATADINE FUMARATE	0	1 (0.6%)	1 (0.4%)
THIETHYLPERAZINE	1 (1.1%)	0	1 (0.4%)
THIETHYLPERAZINE MALEATE	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
ANTIHYPERTENSIVES			
Total number of patients with at least one treatment	1 (1.1%)	7 (4.2%)	8 (3.1%)
Total number of treatments	1	9	10
MAGNESIUM SULFATE	0	5 (3.0%)	5 (2.0%)
CLONIDINE	0	1 (0.6%)	1 (0.4%)
DOXAZOSIN	0	1 (0.6%)	1 (0.4%)
MOXONIDINE	0	1 (0.6%)	1 (0.4%)
RILMENIDINE PHOSPHATE	1 (1.1%)	0	1 (0.4%)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS			
Total number of patients with at least one treatment	35 (40.2%)	79 (47.0%)	114 (44.7%)
Total number of treatments	125	330	455
IBUPROFEN	6 (6.9%)	16 (9.5%)	22 (8.6%)
ADEMETIONINE	5 (5.7%)	10 (6.0%)	15 (5.9%)
DICLOFENAC	4 (4.6%)	10 (6.0%)	14 (5.5%)
KETOPROFEN	3 (3.4%)	8 (4.8%)	11 (4.3%)
NAPROXEN	1 (1.1%)	9 (5.4%)	10 (3.9%)
DICLOFENAC SODIUM	2 (2.3%)	6 (3.6%)	8 (3.1%)
LOXOPROFEN	1 (1.1%)	5 (3.0%)	6 (2.4%)
LOXOPROFEN SODIUM DIHYDRATE	2 (2.3%)	4 (2.4%)	6 (2.4%)
BENZYDAMINE HYDROCHLORIDE	1 (1.1%)	4 (2.4%)	5 (2.0%)
ETORICOXIB	2 (2.3%)	3 (1.8%)	5 (2.0%)
CELECOXIB	2 (2.3%)	2 (1.2%)	4 (1.6%)
KETOROLAC	1 (1.1%)	3 (1.8%)	4 (1.6%)
KETOROLAC TROMETHAMINE	0	4 (2.4%)	4 (1.6%)
MELOXICAM	3 (3.4%)	1 (0.6%)	4 (1.6%)
MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER	1 (1.1%)	3 (1.8%)	4 (1.6%)
NIMESULIDE	1 (1.1%)	3 (1.8%)	4 (1.6%)
HEPARINOID	0	3 (1.8%)	3 (1.2%)
NAPROXEN SODIUM	0	3 (1.8%)	3 (1.2%)
ACECLOFENAC	0	2 (1.2%)	2 (0.8%)
DEXKETOPROFEN	0	2 (1.2%)	2 (0.8%)
DEXKETOPROFEN TROMETAMOL	2 (2.3%)	0	2 (0.8%)
ESOMEPRAZOLE MAGNESIUM;NAPROXEN	0	2 (1.2%)	2 (0.8%)
LOXOPROFEN SODIUM	1 (1.1%)	1 (0.6%)	2 (0.8%)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	0	1 (0.6%)	1 (0.4%)
AZULENE SODIUM SULFONATE	0	1 (0.6%)	1 (0.4%)
CHONDROITIN SULFATE SODIUM	1 (1.1%)	0	1 (0.4%)
CURCUMA LONGA	1 (1.1%)	0	1 (0.4%)
DIACEREIN	0	1 (0.6%)	1 (0.4%)
DICLOFENAC POTASSIUM	0	1 (0.6%)	1 (0.4%)
DICLOFENAC SODIUM;LIDOCAINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
DIMETHYL SULFOXIDE	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
DIPHENHYDRAMINE;IBUPROFEN	0	1 (0.6%)	1 (0.4%)
FISH OIL	0	1 (0.6%)	1 (0.4%)
FLURBIPROFEN SODIUM	0	1 (0.6%)	1 (0.4%)
GLUCOSAMINE	1 (1.1%)	0	1 (0.4%)
GUAIAZULENE	0	1 (0.6%)	1 (0.4%)
IBUPROFEN ARGININE	0	1 (0.6%)	1 (0.4%)
INDOMETACIN	0	1 (0.6%)	1 (0.4%)
KETOPROFEN LYSINE	0	1 (0.6%)	1 (0.4%)
LORNOXICAM	0	1 (0.6%)	1 (0.4%)
NSAIDS	1 (1.1%)	0	1 (0.4%)
PELUBIPROFEN	0	1 (0.6%)	1 (0.4%)
TENOXICAM	0	1 (0.6%)	1 (0.4%)
VACCINIUM MACROCARPON	1 (1.1%)	0	1 (0.4%)
ZALTOPROFEN	0	1 (0.6%)	1 (0.4%)
ANTIMYCOTICS FOR SYSTEMIC USE			
Total number of patients with at least one treatment	10 (11.5%)	14 (8.3%)	24 (9.4%)
Total number of treatments	18	16	34
NYSTATIN	5 (5.7%)	6 (3.6%)	11 (4.3%)
FLUCONAZOLE	6 (6.9%)	4 (2.4%)	10 (3.9%)
MICONAZOLE	3 (3.4%)	0	3 (1.2%)
AMPHOTERICIN B;TETRACYCLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
ANIDULAFUNGIN	0	1 (0.6%)	1 (0.4%)
CASPOFUNGIN ACETATE	0	1 (0.6%)	1 (0.4%)
ITRACONAZOLE	0	1 (0.6%)	1 (0.4%)
ANTINEOPLASTIC AGENTS			
Total number of patients with at least one treatment	2 (2.3%)	5 (3.0%)	7 (2.7%)
Total number of treatments	3	8	11
CELECOXIB	2 (2.3%)	2 (1.2%)	4 (1.6%)
PROPRANOLOL	0	2 (1.2%)	2 (0.8%)
PROPRANOLOL HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
ANTIOBESITY PREPARATIONS, EXCL. DIET PRODUCTS			
Total number of patients with at least one treatment	0	1 (0.6%)	1 (0.4%)
Total number of treatments	0	1	1
BENZOCAINE	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
ANTIPROTOZOALS			
Total number of patients with at least one treatment	12 (13.8%)	18 (10.7%)	30 (11.8%)
Total number of treatments	19	22	41
METRONIDAZOLE	5 (5.7%)	5 (3.0%)	10 (3.9%)
CLOTRIMAZOLE	3 (3.4%)	5 (3.0%)	8 (3.1%)
OFLOXACIN	1 (1.1%)	3 (1.8%)	4 (1.6%)
MICONAZOLE	3 (3.4%)	0	3 (1.2%)
NITAZOXANIDE	1 (1.1%)	2 (1.2%)	3 (1.2%)
HYDROXYCHLOROQUINE SULFATE	0	1 (0.6%)	1 (0.4%)
MICONAZOLE NITRATE;TINIDAZOLE	0	1 (0.6%)	1 (0.4%)
NITROFURAL	0	1 (0.6%)	1 (0.4%)
ORNIDAZOLE	1 (1.1%)	0	1 (0.4%)
SECNIDAZOLE	0	1 (0.6%)	1 (0.4%)
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.			
Total number of patients with at least one treatment	80 (92.0%)	153 (91.1%)	233 (91.4%)
Total number of treatments	627	1114	1741
CHLORPHENAMINE	20 (23.0%)	38 (22.6%)	58 (22.7%)
DIPHENHYDRAMINE	12 (13.8%)	40 (23.8%)	52 (20.4%)
DIPHENHYDRAMINE HYDROCHLORIDE	10 (11.5%)	27 (16.1%)	37 (14.5%)
DEXCHLORPHENIRAMINE MALEATE	9 (10.3%)	21 (12.5%)	30 (11.8%)
LORATADINE	8 (9.2%)	14 (8.3%)	22 (8.6%)
CHLOROPYRAMINE HYDROCHLORIDE	6 (6.9%)	13 (7.7%)	19 (7.5%)
CHLORPHENAMINE MALEATE	9 (10.3%)	6 (3.6%)	15 (5.9%)
DEXCHLORPHENIRAMINE	2 (2.3%)	8 (4.8%)	10 (3.9%)
LEVOCETIRIZINE DIHYDROCHLORIDE	1 (1.1%)	8 (4.8%)	9 (3.5%)
CLEMASTINE FUMARATE	5 (5.7%)	3 (1.8%)	8 (3.1%)
PHENIRAMINE	4 (4.6%)	4 (2.4%)	8 (3.1%)
CETIRIZINE	1 (1.1%)	6 (3.6%)	7 (2.7%)
CETIRIZINE HYDROCHLORIDE	3 (3.4%)	4 (2.4%)	7 (2.7%)
CLEMASTINE	1 (1.1%)	6 (3.6%)	7 (2.7%)
LIDOCAINE	1 (1.1%)	5 (3.0%)	6 (2.4%)
FEXOFENADINE HYDROCHLORIDE	0	5 (3.0%)	5 (2.0%)
HYDROXYZINE	1 (1.1%)	4 (2.4%)	5 (2.0%)
PROMETHAZINE	2 (2.3%)	3 (1.8%)	5 (2.0%)
BILASTINE	1 (1.1%)	3 (1.8%)	4 (1.6%)
LIDOCAINE HYDROCHLORIDE	2 (2.3%)	2 (1.2%)	4 (1.6%)
DIMETINDENE MALEATE	1 (1.1%)	2 (1.2%)	3 (1.2%)
PHENIRAMINE MALEATE	2 (2.3%)	1 (0.6%)	3 (1.2%)
CAMPHOR;CHLORPHENAMINE MALEATE;HEXACHLOROPHENE; LIDOCAINE HYDROCHLORIDE;MENTHOL;METHYL SALICYLATE	0	2 (1.2%)	2 (0.8%)
CHLOROPYRAMINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
DESLORATADINE	0	2 (1.2%)	2 (0.8%)

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ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
EBASTINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
FEXOFENADINE	0	2 (1.2%)	2 (0.8%)
HYDROXYZINE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
LEVOCETIRIZINE	0	2 (1.2%)	2 (0.8%)
ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER; ARTEMISIA CAPILLARIS FLOWER;ATRACTYLODES LANCEA RHIZOME;CINNAMOMUM CASSIA BARK;POLYPORUS UMBELLATUS SCLEROTIUM;PORIA COCOS SCLEROTIUM	0	1 (0.6%)	1 (0.4%)
BENZOCAINE	0	1 (0.6%)	1 (0.4%)
CAMPHOR;MENTHOL	0	1 (0.6%)	1 (0.4%)
DOXEPIN	1 (1.1%)	0	1 (0.4%)
EPINASTINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
KETOTIFEN	0	1 (0.6%)	1 (0.4%)
KETOTIFEN FUMARATE	0	1 (0.6%)	1 (0.4%)
LIDOCAINE;PRILOCAINE	1 (1.1%)	0	1 (0.4%)
MENTHOL;METHYL SALICYLATE	1 (1.1%)	0	1 (0.4%)
PHENIRAMINE AMINOSALICYLATE	1 (1.1%)	0	1 (0.4%)
RUPATADINE FUMARATE	0	1 (0.6%)	1 (0.4%)
ANTIPSORIATICS			
Total number of patients with at least one treatment	1 (1.1%)	0	1 (0.4%)
Total number of treatments	1	0	1
MENTHOL;METHYL SALICYLATE	1 (1.1%)	0	1 (0.4%)
ANTISEPTICS AND DISINFECTANTS			
Total number of patients with at least one treatment	3 (3.4%)	16 (9.5%)	19 (7.5%)
Total number of treatments	5	28	33
CHLORHEXIDINE GLUCONATE	1 (1.1%)	5 (3.0%)	6 (2.4%)
SODIUM HYPOCHLORITE	1 (1.1%)	3 (1.8%)	4 (1.6%)
POVIDONE-IODINE	0	3 (1.8%)	3 (1.2%)
BORIC ACID;SODIUM BORATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
BENZALKONIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
BENZETHONIUM CHLORIDE	1 (1.1%)	0	1 (0.4%)
CETRIMONIUM BROMIDE;CHLORHEXIDINE GLUCONATE	0	1 (0.6%)	1 (0.4%)
CHLORHEXIDINE DIACETATE	0	1 (0.6%)	1 (0.4%)
DEQUALINIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
ETHACRIDINE LACTATE	1 (1.1%)	0	1 (0.4%)
ETHYLHEXYLGLYCERIN;GLYCEROL;OCTENIDINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
HYDROXYBENZOATES NOS	0	1 (0.6%)	1 (0.4%)
MIRAMISTIN	0	1 (0.6%)	1 (0.4%)
NITROFURAL	0	1 (0.6%)	1 (0.4%)
OCTENIDINE HYDROCHLORIDE;PHENOXYETHANOL	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
ANTITHROMBOTIC AGENTS			
Total number of patients with at least one treatment	21 (24.1%)	35 (20.8%)	56 (22.0%)
Total number of treatments	29	49	78
ACETYLSALICYLIC ACID	4 (4.6%)	6 (3.6%)	10 (3.9%)
ENOXAPARIN SODIUM	4 (4.6%)	4 (2.4%)	8 (3.1%)
RIVAROXABAN	5 (5.7%)	3 (1.8%)	8 (3.1%)
ENOXAPARIN	2 (2.3%)	2 (1.2%)	4 (1.6%)
MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER	1 (1.1%)	3 (1.8%)	4 (1.6%)
TINZAPARIN SODIUM	1 (1.1%)	3 (1.8%)	4 (1.6%)
HEPARIN SODIUM	0	3 (1.8%)	3 (1.2%)
HEPARINOID	0	3 (1.8%)	3 (1.2%)
ACETYLSALICYLIC ACID;MAGNESIUM HYDROXIDE	0	2 (1.2%)	2 (0.8%)
APIXABAN	1 (1.1%)	1 (0.6%)	2 (0.8%)
BEMIPARIN SODIUM	0	2 (1.2%)	2 (0.8%)
EDOXABAN TOSILATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
HEPARIN	1 (1.1%)	1 (0.6%)	2 (0.8%)
ACETYLSALICYLATE LYSINE	1 (1.1%)	0	1 (0.4%)
ALTEPLASE	0	1 (0.6%)	1 (0.4%)
CILOSTAZOL	0	1 (0.6%)	1 (0.4%)
CLOPIDOGREL BISULFATE	0	1 (0.6%)	1 (0.4%)
DALTEPARIN	1 (1.1%)	0	1 (0.4%)
FLUINDIONE	0	1 (0.6%)	1 (0.4%)
FONDAPARINUX SODIUM	1 (1.1%)	0	1 (0.4%)
LIMAPROST ALFADEX	0	1 (0.6%)	1 (0.4%)
NADROPARIN CALCIUM	0	1 (0.6%)	1 (0.4%)
PENTOSAN POLYSULFATE SODIUM	0	1 (0.6%)	1 (0.4%)
STREPTODORNASE;STREPTOKINASE	1 (1.1%)	0	1 (0.4%)
UROKINASE	0	1 (0.6%)	1 (0.4%)
WARFARIN	0	1 (0.6%)	1 (0.4%)
ANTIVIRALS FOR SYSTEMIC USE			
Total number of patients with at least one treatment	4 (4.6%)	7 (4.2%)	11 (4.3%)
Total number of treatments	6	8	14
VALACICLOVIR HYDROCHLORIDE	1 (1.1%)	2 (1.2%)	3 (1.2%)
ACICLOVIR	1 (1.1%)	1 (0.6%)	2 (0.8%)
OSELTAMIVIR PHOSPHATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
BALOXAVIR MARBOXIL	1 (1.1%)	0	1 (0.4%)
BRIVUDINE	1 (1.1%)	0	1 (0.4%)
FAMCICLOVIR	0	1 (0.6%)	1 (0.4%)
PERAMIVIR	0	1 (0.6%)	1 (0.4%)
TILORONE	0	1 (0.6%)	1 (0.4%)
VALACICLOVIR	0	1 (0.6%)	1 (0.4%)

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Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
APPETITE STIMULANTS			
Total number of patients with at least one treatment	1 (1.1%)	6 (3.6%)	7 (2.7%)
Total number of treatments	1	16	17
MEGESTROL ACETATE	1 (1.1%)	6 (3.6%)	7 (2.7%)
MEGESTROL	0	1 (0.6%)	1 (0.4%)
BETA BLOCKING AGENTS			
Total number of patients with at least one treatment	10 (11.5%)	28 (16.7%)	38 (14.9%)
Total number of treatments	10	34	44
BISOPROLOL	2 (2.3%)	6 (3.6%)	8 (3.1%)
BISOPROLOL FUMARATE	2 (2.3%)	4 (2.4%)	6 (2.4%)
ATENOLOL	1 (1.1%)	4 (2.4%)	5 (2.0%)
METOPROLOL	1 (1.1%)	3 (1.8%)	4 (1.6%)
METOPROLOL TARTRATE	2 (2.3%)	1 (0.6%)	3 (1.2%)
CARVEDILOL	2 (2.3%)	0	2 (0.8%)
METOPROLOL SUCCINATE	0	2 (1.2%)	2 (0.8%)
NEBIVOLOL HYDROCHLORIDE	0	2 (1.2%)	2 (0.8%)
PROPRANOLOL	0	2 (1.2%)	2 (0.8%)
ATENOLOL;CHLORTALIDONE	0	1 (0.6%)	1 (0.4%)
NEBIVOLOL	0	1 (0.6%)	1 (0.4%)
PROPRANOLOL HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
TIMOLOL MALEATE	0	1 (0.6%)	1 (0.4%)

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ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
BILE AND LIVER THERAPY			
Total number of patients with at least one treatment	15 (17.2%)	24 (14.3%)	39 (15.3%)
Total number of treatments	47	52	99
ACETYLCYSTEINE	4 (4.6%)	10 (6.0%)	14 (5.5%)
LACTULOSE	6 (6.9%)	4 (2.4%)	10 (3.9%)
ARGININE GLUTAMATE	2 (2.3%)	5 (3.0%)	7 (2.7%)
URSODEOXYCHOLIC ACID	1 (1.1%)	3 (1.8%)	4 (1.6%)
SILYBUM MARIANUM	1 (1.1%)	2 (1.2%)	3 (1.2%)
DROTAVERINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
DROTAVERINE HYDROCHLORIDE	0	2 (1.2%)	2 (0.8%)
ADENINE HYDROCHLORIDE;BIFENDATE;CARNITINE OROTATE;CYANOCOBALAMIN;LIVER;PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN	0	1 (0.6%)	1 (0.4%)
ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER; ARTEMISIA CAPILLARIS FLOWER;ATRACTYLODES LANCEA RHIZOME;CINNAMOMUM CASSIA BARK;POLYPORUS UMBELLATUS SCLEROTIUM;PORIA COCOS SCLEROTIUM	0	1 (0.6%)	1 (0.4%)
ARGININE	1 (1.1%)	0	1 (0.4%)
CURCUMA LONGA	1 (1.1%)	0	1 (0.4%)
CYNARA CARDUNCULUS EXTRACT	1 (1.1%)	0	1 (0.4%)
INOSINE	1 (1.1%)	0	1 (0.4%)
INOSINE;MEGLUMINE;METHIONINE;NICOTINAMIDE; SUCCINIC ACID	1 (1.1%)	0	1 (0.4%)
LEVOGLUTAMIDE	0	1 (0.6%)	1 (0.4%)
RIFAXIMIN	1 (1.1%)	0	1 (0.4%)
THIOTRIAZOLINE	1 (1.1%)	0	1 (0.4%)
TIMONACIC	1 (1.1%)	0	1 (0.4%)
BLOOD SUBSTITUTES AND PERFUSION SOLUTIONS			
Total number of patients with at least one treatment	23 (26.4%)	46 (27.4%)	69 (27.1%)
Total number of treatments	100	176	276
SODIUM CHLORIDE	7 (8.0%)	10 (6.0%)	17 (6.7%)
POTASSIUM CHLORIDE	3 (3.4%)	7 (4.2%)	10 (3.9%)
SODIUM BICARBONATE	2 (2.3%)	7 (4.2%)	9 (3.5%)
CALCIUM CHLORIDE DIHYDRATE;POTASSIUM CHLORIDE; SODIUM CHLORIDE;SODIUM LACTATE	0	6 (3.6%)	6 (2.4%)
CHLORHEXIDINE GLUCONATE	1 (1.1%)	5 (3.0%)	6 (2.4%)
CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE;SORBITOL	2 (2.3%)	3 (1.8%)	5 (2.0%)
MAGNESIUM SULFATE	0	5 (3.0%)	5 (2.0%)
ALBUMIN HUMAN	0	4 (2.4%)	4 (1.6%)
BLOOD, WHOLE	1 (1.1%)	3 (1.8%)	4 (1.6%)
CALCIUM GLUCONATE	1 (1.1%)	3 (1.8%)	4 (1.6%)
GLUCOSE	1 (1.1%)	3 (1.8%)	4 (1.6%)

Treatments are coded using the WHODRUG GLOBAL B3 SEPTEMBER 1, 2022. dictionary. Treatments can appear under multiple classes. The table includes medications that have temporal overlap with study drug administration. Multiple uses of a specific medication for a patient were counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a patient were counted once in the frequency for the medication class. Use of the anti-diarrheal medication Loperamide is primarily summarized in separate outputs.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
RED BLOOD CELLS	1 (1.1%)	3 (1.8%)	4 (1.6%)
ELECTROLYTES NOS	1 (1.1%)	2 (1.2%)	3 (1.2%)
GLYCEROL	2 (2.3%)	1 (0.6%)	3 (1.2%)
SELENIUM	1 (1.1%)	2 (1.2%)	3 (1.2%)
CALCIUM CHLORIDE DIHYDRATE;MAGNESIUM CHLORIDE HEXAHYDRATE;MALIC ACID;POTASSIUM CHLORIDE;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	0	2 (1.2%)	2 (0.8%)
CALCIUM CHLORIDE DIHYDRATE;MAGNESIUM CHLORIDE HEXAHYDRATE;POTASSIUM CHLORIDE;SODIUM CHLORIDE; SODIUM LACTATE	0	2 (1.2%)	2 (0.8%)
CALCIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
LYSINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
POTASSIUM	1 (1.1%)	1 (0.6%)	2 (0.8%)
RED BLOOD CELLS, CONCENTRATED	0	2 (1.2%)	2 (0.8%)
VITAMINS NOS	1 (1.1%)	1 (0.6%)	2 (0.8%)
ALANINE;ARGININE;CALCIUM CHLORIDE DIHYDRATE;FISH OIL;GLUCOSE MONOHYDRATE;GLYCINE;GLYCINE MAX OIL; HISTIDINE;ISOLEUCINE;LEUCINE;LYSINE HYDROCHLORIDE;MAGNESIUM SULFATE HEPTAHYDRATE; MEDIUM-CHAIN TRIGLYCERIDES;METHIONINE;OLEA EUROPAEA OIL;PHENYLALANINE;POTASSIUM CHLORIDE; PROLINE;SERINE;SODIUM ACETATE TRIHYDRATE;SODIUM GLYCEROPHOSPHATE;THREONINE;TRYPTOPHAN, L-; TYROSINE;VALINE;ZINC SULFATE HEPTAHYDRATE	0	1 (0.6%)	1 (0.4%)
ALANINE;ARGININE;CYSTEINE HYDROCHLORIDE;GLYCINE; HISTIDINE;ISOLEUCINE;LEUCINE;LYSINE ACETATE; METHIONINE;PHENYLALANINE;PROLINE;SERINE; THREONINE;TRYPTOPHAN, L-;VALINE	0	1 (0.6%)	1 (0.4%)
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
ARGININE	1 (1.1%)	0	1 (0.4%)
CHLORHEXIDINE DIACETATE	0	1 (0.6%)	1 (0.4%)
ETHACRIDINE LACTATE	1 (1.1%)	0	1 (0.4%)
GLUCONATE SODIUM;MAGNESIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM ACETATE;SODIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
GLUCOSE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
HETASTARCH	0	1 (0.6%)	1 (0.4%)
MAGNESIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
MAGNESIUM CITRATE	0	1 (0.6%)	1 (0.4%)
MAGNESIUM GLUCONATE;POTASSIUM GLUCONATE	1 (1.1%)	0	1 (0.4%)
MANNITOL	0	1 (0.6%)	1 (0.4%)
NITROFURAL	0	1 (0.6%)	1 (0.4%)
NUTRIENTS NOS	0	1 (0.6%)	1 (0.4%)
POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE	0	1 (0.6%)	1 (0.4%)
SODIUM PHOSPHATE	1 (1.1%)	0	1 (0.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
SOLUTIONS FOR PARENTERAL NUTRITION	1 (1.1%)	0	1 (0.4%)
UREA	1 (1.1%)	0	1 (0.4%)
ZINC	0	1 (0.6%)	1 (0.4%)
ZINC SULFATE	1 (1.1%)	0	1 (0.4%)
CALCIUM CHANNEL BLOCKERS			
Total number of patients with at least one treatment	8 (9.2%)	20 (11.9%)	28 (11.0%)
Total number of treatments	9	20	29
AMLODIPINE	5 (5.7%)	13 (7.7%)	18 (7.1%)
AMLODIPINE BESILATE	1 (1.1%)	5 (3.0%)	6 (2.4%)
LERCANIDIPINE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
NIFEDIPINE	2 (2.3%)	0	2 (0.8%)
VERAPAMIL	0	1 (0.6%)	1 (0.4%)
CARDIAC THERAPY			
Total number of patients with at least one treatment	17 (19.5%)	45 (26.8%)	62 (24.3%)
Total number of treatments	50	196	246
IBUPROFEN	6 (6.9%)	16 (9.5%)	22 (8.6%)
MELDONIUM	4 (4.6%)	6 (3.6%)	10 (3.9%)
RACECADOTRIL	0	7 (4.2%)	7 (2.7%)
LIDOCAINE	1 (1.1%)	5 (3.0%)	6 (2.4%)
LIDOCAINE HYDROCHLORIDE	2 (2.3%)	2 (1.2%)	4 (1.6%)
MAGNESIUM ASPARTATE;POTASSIUM ASPARTATE	0	4 (2.4%)	4 (1.6%)
TRIMETAZIDINE HYDROCHLORIDE	1 (1.1%)	3 (1.8%)	4 (1.6%)
IVABRADINE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
NOREPINEPHRINE BITARTRATE	0	2 (1.2%)	2 (0.8%)
ATROPINE	0	1 (0.6%)	1 (0.4%)
CAMPHOR;MENTHOL	0	1 (0.6%)	1 (0.4%)
EMPAGLIFLOZIN	0	1 (0.6%)	1 (0.4%)
GLUCOSE;INSULIN;POTASSIUM	0	1 (0.6%)	1 (0.4%)
IBUPROFEN ARGININE	0	1 (0.6%)	1 (0.4%)
INDOMETACIN	0	1 (0.6%)	1 (0.4%)
INOSINE	1 (1.1%)	0	1 (0.4%)
IPRATROPIUM BROMIDE	0	1 (0.6%)	1 (0.4%)
LEVOCARNITINE	1 (1.1%)	0	1 (0.4%)
LIMAPROST ALFADEX	0	1 (0.6%)	1 (0.4%)
MAGNESIUM GLUCONATE;POTASSIUM GLUCONATE	1 (1.1%)	0	1 (0.4%)
NOREPINEPHRINE	0	1 (0.6%)	1 (0.4%)
PILSICAINIDE HYDROCHLORIDE	1 (1.1%)	0	1 (0.4%)
PROPAFENONE HYDROCHLORIDE	1 (1.1%)	0	1 (0.4%)
TAURINE	1 (1.1%)	0	1 (0.4%)
THIOTRIAZOLINE	1 (1.1%)	0	1 (0.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
CONTRAST MEDIA			
Total number of patients with at least one treatment	1 (1.1%)	0	1 (0.4%)
Total number of treatments	5	0	5
IOHEXOL	1 (1.1%)	0	1 (0.4%)
CORTICOSTEROIDS FOR SYSTEMIC USE			
Total number of patients with at least one treatment	81 (93.1%)	147 (87.5%)	228 (89.4%)
Total number of treatments	641	1063	1704
DEXAMETHASONE	55 (63.2%)	114 (67.9%)	169 (66.3%)
DEXAMETHASONE SODIUM PHOSPHATE	12 (13.8%)	15 (8.9%)	27 (10.6%)
METHYLPREDNISOLONE	7 (8.0%)	12 (7.1%)	19 (7.5%)
HYDROCORTISONE	4 (4.6%)	11 (6.5%)	15 (5.9%)
METHYLPREDNISOLONE SODIUM SUCCINATE	4 (4.6%)	8 (4.8%)	12 (4.7%)
BETAMETHASONE VALERATE	4 (4.6%)	7 (4.2%)	11 (4.3%)
HYDROCORTISONE SODIUM SUCCINATE	1 (1.1%)	8 (4.8%)	9 (3.5%)
PREDNISONE	3 (3.4%)	6 (3.6%)	9 (3.5%)
PREDNISOLONE	2 (2.3%)	3 (1.8%)	5 (2.0%)
BETAMETHASONE BUTYRATE PROPIONATE	3 (3.4%)	1 (0.6%)	4 (1.6%)
BETAMETHASONE DIPROPIONATE	2 (2.3%)	2 (1.2%)	4 (1.6%)
TRIAMCINOLONE ACETONIDE	0	4 (2.4%)	4 (1.6%)
HYDROCORTISONE BUTYRATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
TRIAMCINOLONE	0	2 (1.2%)	2 (0.8%)
BETAMETHASONE	0	1 (0.6%)	1 (0.4%)
BETAMETHASONE;DEXCHLORPHENIRAMINE MALEATE	0	1 (0.6%)	1 (0.4%)
DEFLAZACORT	1 (1.1%)	0	1 (0.4%)
DEXAMETHASONE PHOSPHATE	1 (1.1%)	0	1 (0.4%)
HYDROCORTISONE ACETATE	1 (1.1%)	0	1 (0.4%)
HYDROCORTISONE HYDROGEN SUCCINATE	0	1 (0.6%)	1 (0.4%)
LIDOCAINE HYDROCHLORIDE;TRIAMCINOLONE ACETONIDE	1 (1.1%)	0	1 (0.4%)
PREDNISOLONE VALEROACETATE	0	1 (0.6%)	1 (0.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_A_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS			
Total number of patients with at least one treatment	81 (93.1%)	149 (88.7%)	230 (90.2%)
Total number of treatments	609	1092	1701
DEXAMETHASONE	55 (63.2%)	114 (67.9%)	169 (66.3%)
DEXAMETHASONE SODIUM PHOSPHATE	12 (13.8%)	15 (8.9%)	27 (10.6%)
METHYLPREDNISOLONE	7 (8.0%)	12 (7.1%)	19 (7.5%)
HYDROCORTISONE	4 (4.6%)	11 (6.5%)	15 (5.9%)
METHYLPREDNISOLONE SODIUM SUCCINATE	4 (4.6%)	8 (4.8%)	12 (4.7%)
BETAMETHASONE VALERATE	4 (4.6%)	7 (4.2%)	11 (4.3%)
HYDROCORTISONE SODIUM SUCCINATE	1 (1.1%)	8 (4.8%)	9 (3.5%)
PREDNISONE	3 (3.4%)	6 (3.6%)	9 (3.5%)
MOMETASONE FUROATE	2 (2.3%)	4 (2.4%)	6 (2.4%)
PREDNISOLONE	2 (2.3%)	3 (1.8%)	5 (2.0%)
BETAMETHASONE BUTYRATE PROPIONATE	3 (3.4%)	1 (0.6%)	4 (1.6%)
BETAMETHASONE DIPROPIONATE	2 (2.3%)	2 (1.2%)	4 (1.6%)
TRIAMCINOLONE ACETONIDE	0	4 (2.4%)	4 (1.6%)
BETAMETHASONE VALERATE;GENTAMICIN SULFATE	3 (3.4%)	0	3 (1.2%)
CLOBETASOL PROPIONATE	1 (1.1%)	2 (1.2%)	3 (1.2%)
DESONIDE	0	3 (1.8%)	3 (1.2%)
DIFLUPREDNATE	0	3 (1.8%)	3 (1.2%)
FLUOROMETHOLONE	0	3 (1.8%)	3 (1.2%)
FLUTICASONE PROPIONATE	1 (1.1%)	2 (1.2%)	3 (1.2%)
BECLOMETASONE DIPROPIONATE	0	2 (1.2%)	2 (0.8%)
BUDESONIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
CLOBETASOL	0	2 (1.2%)	2 (0.8%)
HYDROCORTISONE BUTYRATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
METHYLPREDNISOLONE ACEPONATE	0	2 (1.2%)	2 (0.8%)
TRIAMCINOLONE	0	2 (1.2%)	2 (0.8%)
ALCLOMETASONE DIPROPIONATE	0	1 (0.6%)	1 (0.4%)
BECLOMETASONE	1 (1.1%)	0	1 (0.4%)
BETAMETHASONE	0	1 (0.6%)	1 (0.4%)
BETAMETHASONE DIPROPIONATE;SALICYLIC ACID	0	1 (0.6%)	1 (0.4%)
DEXAMETHASONE PROPIONATE	0	1 (0.6%)	1 (0.4%)
DIFLUCORTOLONE	0	1 (0.6%)	1 (0.4%)
DIPHENHYDRAMINE HYDROCHLORIDE;HYDROCORTISONE ACETATE;NEOMYCIN SULFATE	0	1 (0.6%)	1 (0.4%)
FUSIDIC ACID;HYDROCORTISONE ACETATE	1 (1.1%)	0	1 (0.4%)
HYDROCORTISONE ACETATE	1 (1.1%)	0	1 (0.4%)
PREDNISOLONE VALEROACETATE	0	1 (0.6%)	1 (0.4%)
COUGH AND COLD PREPARATIONS			
Total number of patients with at least one treatment	29 (33.3%)	39 (23.2%)	68 (26.7%)
Total number of treatments	105	102	207
SODIUM CHLORIDE	7 (8.0%)	10 (6.0%)	17 (6.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_A_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
ACETYLCYSTEINE	4 (4.6%)	10 (6.0%)	14 (5.5%)
AMBROXOL HYDROCHLORIDE	0	5 (3.0%)	5 (2.0%)
CODEINE	3 (3.4%)	2 (1.2%)	5 (2.0%)
CODEINE PHOSPHATE	3 (3.4%)	2 (1.2%)	5 (2.0%)
LEVODROPROPIZINE	3 (3.4%)	1 (0.6%)	4 (1.6%)
AMBROXOL	0	3 (1.8%)	3 (1.2%)
AMMONIUM CHLORIDE;CHLORPHENAMINE MALEATE; DIHYDROCODEINE BITARTRATE;METHYLEPHEDRINE HYDROCHLORIDE-DL	1 (1.1%)	2 (1.2%)	3 (1.2%)
ELECTROLYTES NOS	1 (1.1%)	2 (1.2%)	3 (1.2%)
ERDOSTEINE	0	3 (1.8%)	3 (1.2%)
GLYCEROL	2 (2.3%)	1 (0.6%)	3 (1.2%)
BUTAMIRATE CITRATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
CARBOCISTEINE	2 (2.3%)	0	2 (0.8%)
DEXTROMETHORPHAN	0	2 (1.2%)	2 (0.8%)
DEXTROMETHORPHAN HYDROBROMIDE MONOHYDRATE	0	2 (1.2%)	2 (0.8%)
DROPROPIZINE	2 (2.3%)	0	2 (0.8%)
GLYCYRRHIZA GLABRA EXTRACT;PAPAVER SOMNIFERUM	0	2 (1.2%)	2 (0.8%)
OPIUM ALKALOIDS AND DERIVATIVES	1 (1.1%)	1 (0.6%)	2 (0.8%)
OTHER COUGH SUPPRESSANTS AND EXPECTORANTS	1 (1.1%)	1 (0.6%)	2 (0.8%)
BENZONATATE	0	1 (0.6%)	1 (0.4%)
CAMPHOR;MENTHOL	0	1 (0.6%)	1 (0.4%)
CHLORPHENAMINE;DEXTROMETHORPHAN;PHENYLEPHRINE	0	1 (0.6%)	1 (0.4%)
CINNAMOMUM CASSIA;EPHEDRA SPP.;GLYCYRRHIZA SPP.; PAEONIA LACTIFLORA;PUERARIA MONTANA VAR. LOBATA; ZINGIBER OFFICINALE;ZIZIPHUS JUJUBA	0	1 (0.6%)	1 (0.4%)
CODEINE PHOSPHATE HEMIHYDRATE	0	1 (0.6%)	1 (0.4%)
COUGH AND COLD PREPARATIONS	0	1 (0.6%)	1 (0.4%)
DEXTROMETHORPHAN HYDROBROMIDE	1 (1.1%)	0	1 (0.4%)
DIHYDROCODEINE BITARTRATE	1 (1.1%)	0	1 (0.4%)
DIHYDROCODEINE THIOCYANATE	0	1 (0.6%)	1 (0.4%)
DIMEMORFAN PHOSPHATE	1 (1.1%)	0	1 (0.4%)
EPRAZINONE HYDROCHLORIDE	1 (1.1%)	0	1 (0.4%)
ETHYLMORPHINE	1 (1.1%)	0	1 (0.4%)
GENTIANA LUTEA ROOT;PRIMULA SPP. FLOWER;RUMEX SPP. HERB;SAMBUCUS NIGRA FLOWER;VERBENA OFFICINALIS HERB	1 (1.1%)	0	1 (0.4%)
HELICIDINE	1 (1.1%)	0	1 (0.4%)
HERBAL COUGH AND COLD REMEDIES, OTHER	1 (1.1%)	0	1 (0.4%)
L-CARBOCISTEINE	0	1 (0.6%)	1 (0.4%)
MANNITOL	0	1 (0.6%)	1 (0.4%)
NOSCAPINE	0	1 (0.6%)	1 (0.4%)
POTASSIUM IODIDE	0	1 (0.6%)	1 (0.4%)
STREPTODORNASE;STREPTOKINASE	1 (1.1%)	0	1 (0.4%)
TERPIN HYDRATE	0	1 (0.6%)	1 (0.4%)
THYMUS VULGARIS EXTRACT	1 (1.1%)	0	1 (0.4%)

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_A_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
ZINC	0	1 (0.6%)	1 (0.4%)
DIAGNOSTIC AGENTS			
Total number of patients with at least one treatment	3 (3.4%)	14 (8.3%)	17 (6.7%)
Total number of treatments	3	19	22
FOLIC ACID	2 (2.3%)	7 (4.2%)	9 (3.5%)
MAGNESIUM SULFATE	0	5 (3.0%)	5 (2.0%)
GLUCOSE	1 (1.1%)	3 (1.8%)	4 (1.6%)
MANNITOL	0	1 (0.6%)	1 (0.4%)
DIGESTIVES, INCL. ENZYMES			
Total number of patients with at least one treatment	2 (2.3%)	3 (1.8%)	5 (2.0%)
Total number of treatments	2	5	7
SILYBUM MARIANUM	1 (1.1%)	2 (1.2%)	3 (1.2%)
ENZYME PREPARATIONS	0	1 (0.6%)	1 (0.4%)
ENZYMES NOS	1 (1.1%)	0	1 (0.4%)
DIURETICS			
Total number of patients with at least one treatment	12 (13.8%)	25 (14.9%)	37 (14.5%)
Total number of treatments	17	43	60
FUROSEMIDE	5 (5.7%)	12 (7.1%)	17 (6.7%)
HYDROCHLOROTHIAZIDE	4 (4.6%)	4 (2.4%)	8 (3.1%)
SPIRONOLACTONE	1 (1.1%)	5 (3.0%)	6 (2.4%)
INDAPAMIDE	1 (1.1%)	2 (1.2%)	3 (1.2%)
ACETAZOLAMIDE	0	2 (1.2%)	2 (0.8%)
AMILORIDE HYDROCHLORIDE;HYDROCHLOROTHIAZIDE	1 (1.1%)	0	1 (0.4%)
EPLERENONE	0	1 (0.6%)	1 (0.4%)
TOLVAPTAN	0	1 (0.6%)	1 (0.4%)
TORASEMIDE	1 (1.1%)	0	1 (0.4%)
TRICHLORMETHIAZIDE	0	1 (0.6%)	1 (0.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
DRUGS FOR ACID RELATED DISORDERS			
Total number of patients with at least one treatment	78 (89.7%)	151 (89.9%)	229 (89.8%)
Total number of treatments	635	1103	1738
RANITIDINE	34 (39.1%)	63 (37.5%)	97 (38.0%)
FAMOTIDINE	24 (27.6%)	47 (28.0%)	71 (27.8%)
RANITIDINE HYDROCHLORIDE	24 (27.6%)	33 (19.6%)	57 (22.4%)
OMEPRAZOLE	14 (16.1%)	25 (14.9%)	39 (15.3%)
MAGNESIUM OXIDE	3 (3.4%)	12 (7.1%)	15 (5.9%)
PANTOPRAZOLE SODIUM SESQUIHYDRATE	4 (4.6%)	10 (6.0%)	14 (5.5%)
ESOMEPRAZOLE	1 (1.1%)	12 (7.1%)	13 (5.1%)
PANTOPRAZOLE	6 (6.9%)	7 (4.2%)	13 (5.1%)
REBAMIPIDE	6 (6.9%)	5 (3.0%)	11 (4.3%)
SODIUM BICARBONATE	2 (2.3%)	7 (4.2%)	9 (3.5%)
LANSOPRAZOLE	3 (3.4%)	4 (2.4%)	7 (2.7%)
CIMETIDINE	3 (3.4%)	3 (1.8%)	6 (2.4%)
CALCIUM CARBONATE	1 (1.1%)	4 (2.4%)	5 (2.0%)
TEPRENONE	1 (1.1%)	4 (2.4%)	5 (2.0%)
SODIUM GUALENATE HYDRATE	1 (1.1%)	3 (1.8%)	4 (1.6%)
ANTACIDS, OTHER COMBINATIONS	0	3 (1.8%)	3 (1.2%)
ESOMEPRAZOLE MAGNESIUM	2 (2.3%)	1 (0.6%)	3 (1.2%)
ARTEMISIA ARGYI	0	2 (1.2%)	2 (0.8%)
BISMUTH SUBSALICYLATE	0	2 (1.2%)	2 (0.8%)
HYDROTALCITE	0	2 (1.2%)	2 (0.8%)
LAFUTIDINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
RABEPRAZOLE SODIUM	0	2 (1.2%)	2 (0.8%)
SODIUM GUALENATE	0	2 (1.2%)	2 (0.8%)
ALMAGATE	0	1 (0.6%)	1 (0.4%)
ALUMINIUM HYDROXIDE	0	1 (0.6%)	1 (0.4%)
ALUMINIUM HYDROXIDE;MAGNESIUM HYDROXIDE	0	1 (0.6%)	1 (0.4%)
BISMUTH SUBCITRATE POTASSIUM;METRONIDAZOLE; TETRACYCLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
ESOMEPRAZOLE SODIUM	0	1 (0.6%)	1 (0.4%)
MAGALDRATE	0	1 (0.6%)	1 (0.4%)
MAGALDRATE;SIMETICONE	0	1 (0.6%)	1 (0.4%)
NIZATIDINE	0	1 (0.6%)	1 (0.4%)
POLAPREZINC	0	1 (0.6%)	1 (0.4%)
SODIUM BICARBONATE;SODIUM GUALENATE HYDRATE	0	1 (0.6%)	1 (0.4%)
SUCRALFATE	0	1 (0.6%)	1 (0.4%)
VONOPRAZAN FUMARATE	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
DRUGS FOR CONSTIPATION			
Total number of patients with at least one treatment	25 (28.7%)	35 (20.8%)	60 (23.5%)
Total number of treatments	102	91	193
SODIUM CHLORIDE	7 (8.0%)	10 (6.0%)	17 (6.7%)
MAGNESIUM OXIDE	3 (3.4%)	12 (7.1%)	15 (5.9%)
LACTULOSE	6 (6.9%)	4 (2.4%)	10 (3.9%)
SENNOSIDE A+B	4 (4.6%)	2 (1.2%)	6 (2.4%)
BISACODYL	3 (3.4%)	2 (1.2%)	5 (2.0%)
MAGNESIUM SULFATE	0	5 (3.0%)	5 (2.0%)
PROBIOTICS NOS	1 (1.1%)	3 (1.8%)	4 (1.6%)
GLYCEROL	2 (2.3%)	1 (0.6%)	3 (1.2%)
BISACODYL;DOCUSATE SODIUM	0	2 (1.2%)	2 (0.8%)
POLYCARBOPHIL CALCIUM	0	2 (1.2%)	2 (0.8%)
SODIUM BICARBONATE;SODIUM PHOSPHATE MONOBASIC (ANHYDROUS)	2 (2.3%)	0	2 (0.8%)
BIFIDOBACTERIUM NOS	0	1 (0.6%)	1 (0.4%)
CARMELLOSE SODIUM	0	1 (0.6%)	1 (0.4%)
CELLULOSE MICROCRYSTALLINE;HEMICELLULOSE;LIGNIN; PECTIN	0	1 (0.6%)	1 (0.4%)
CONTACT LAXATIVES	1 (1.1%)	0	1 (0.4%)
DOCUSATE SODIUM	1 (1.1%)	0	1 (0.4%)
DOCUSATE SODIUM;SENNOSIDE A+B	1 (1.1%)	0	1 (0.4%)
MACROGOL 3350;POTASSIUM CHLORIDE;SODIUM BICARBONATE;SODIUM CHLORIDE	1 (1.1%)	0	1 (0.4%)
MACROGOL 4000	0	1 (0.6%)	1 (0.4%)
MAGNESIUM CITRATE	0	1 (0.6%)	1 (0.4%)
MANNITOL	0	1 (0.6%)	1 (0.4%)
NALOXONE	0	1 (0.6%)	1 (0.4%)
PARAFFIN	0	1 (0.6%)	1 (0.4%)
PRUCALOPRIDE	0	1 (0.6%)	1 (0.4%)
SENNA SPP.	1 (1.1%)	0	1 (0.4%)
SODIUM CITRATE;SODIUM LAURYL SULFOACETATE; SORBITOL	1 (1.1%)	0	1 (0.4%)
SODIUM PHOSPHATE	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS			
Total number of patients with at least one treatment	21 (24.1%)	50 (29.8%)	71 (27.8%)
Total number of treatments	34	121	155
METOCLOPRAMIDE	10 (11.5%)	16 (9.5%)	26 (10.2%)
METOCLOPRAMIDE HYDROCHLORIDE	2 (2.3%)	18 (10.7%)	20 (7.8%)
DOMPERIDONE	2 (2.3%)	6 (3.6%)	8 (3.1%)
HYOSCINE	1 (1.1%)	4 (2.4%)	5 (2.0%)
MOSAPRIDE CITRATE	3 (3.4%)	2 (1.2%)	5 (2.0%)
ALIZAPRIDE HYDROCHLORIDE	1 (1.1%)	2 (1.2%)	3 (1.2%)
DIMETICONE	0	3 (1.8%)	3 (1.2%)
SIMETICONE	1 (1.1%)	2 (1.2%)	3 (1.2%)
DROTAVERINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
DROTAVERINE HYDROCHLORIDE	0	2 (1.2%)	2 (0.8%)
ITOPRIDE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
MEBEVERINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
ALVERINE CITRATE;SIMETICONE	1 (1.1%)	0	1 (0.4%)
ATROPINE	0	1 (0.6%)	1 (0.4%)
BROMOPRIDE	0	1 (0.6%)	1 (0.4%)
BUTYLSCOPOLAMINE	0	1 (0.6%)	1 (0.4%)
CURCUMA LONGA	1 (1.1%)	0	1 (0.4%)
DEXPANTHENOL	0	1 (0.6%)	1 (0.4%)
DICYCLOVERINE	0	1 (0.6%)	1 (0.4%)
FENPIVERINIUM BROMIDE;METAMIZOLE SODIUM; PITOFENONE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
HOMATROPINE METHYLBROMIDE	0	1 (0.6%)	1 (0.4%)
HYOSCINE BUTYLBROMIDE	0	1 (0.6%)	1 (0.4%)
LEVOSULPIRIDE	1 (1.1%)	0	1 (0.4%)
METAMIZOLE SODIUM;PITOFENONE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
PARGEVERINE HYDROCHLORIDE	1 (1.1%)	0	1 (0.4%)
PINAVERIUM BROMIDE;SIMETICONE	1 (1.1%)	0	1 (0.4%)
RAMOSETRON HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
RUSCOGENIN;TRIMEBUTINE	0	1 (0.6%)	1 (0.4%)
TIROPRAMIDE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
VALERIANA OFFICINALIS	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES			
Total number of patients with at least one treatment	71 (81.6%)	136 (81.0%)	207 (81.2%)
Total number of treatments	580	1029	1609
DEXAMETHASONE	55 (63.2%)	114 (67.9%)	169 (66.3%)
DEXAMETHASONE SODIUM PHOSPHATE	12 (13.8%)	15 (8.9%)	27 (10.6%)
BETAMETHASONE VALERATE	4 (4.6%)	7 (4.2%)	11 (4.3%)
MOMETASONE FUROATE	2 (2.3%)	4 (2.4%)	6 (2.4%)
BETAMETHASONE DIPROPIONATE	2 (2.3%)	2 (1.2%)	4 (1.6%)
THEOPHYLLINE	1 (1.1%)	3 (1.8%)	4 (1.6%)
TRIAMCINOLONE ACETONIDE	0	4 (2.4%)	4 (1.6%)
BUDESONIDE;FORMOTEROL FUMARATE	1 (1.1%)	2 (1.2%)	3 (1.2%)
FLUTICASONE PROPIONATE	1 (1.1%)	2 (1.2%)	3 (1.2%)
SALBUTAMOL	1 (1.1%)	2 (1.2%)	3 (1.2%)
ARTEMISIA ARGYI	0	2 (1.2%)	2 (0.8%)
BECLOMETASONE DIPROPIONATE	0	2 (1.2%)	2 (0.8%)
BUDESONIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
CROMOGLICATE SODIUM	0	2 (1.2%)	2 (0.8%)
FENOTEROL HYDROBROMIDE;IPRATROPIUM BROMIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
IPRATROPIUM BROMIDE;SALBUTAMOL SULFATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
SALBUTAMOL SULFATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
TRIAMCINOLONE	0	2 (1.2%)	2 (0.8%)
ACLIDINIUM BROMIDE;FORMOTEROL FUMARATE	0	1 (0.6%)	1 (0.4%)
BECLOMETASONE	1 (1.1%)	0	1 (0.4%)
BECLOMETASONE DIPROPIONATE;FORMOTEROL FUMARATE	1 (1.1%)	0	1 (0.4%)
BETAMETHASONE	0	1 (0.6%)	1 (0.4%)
CICLESONIDE	0	1 (0.6%)	1 (0.4%)
DESLORATADINE;MONTELUKAST SODIUM	0	1 (0.6%)	1 (0.4%)
FENSPIRIDE HYDROCHLORIDE	1 (1.1%)	0	1 (0.4%)
FLUNISOLIDE	0	1 (0.6%)	1 (0.4%)
FLUTICASONE;SALMETEROL	0	1 (0.6%)	1 (0.4%)
FLUTICASONE;VILANTEROL	1 (1.1%)	0	1 (0.4%)
IPRATROPIUM BROMIDE	0	1 (0.6%)	1 (0.4%)
IPRATROPIUM BROMIDE;LEVOSALBUTAMOL SULFATE	0	1 (0.6%)	1 (0.4%)
LEVOCETIRIZINE DIHYDROCHLORIDE;MONTELUKAST SODIUM	0	1 (0.6%)	1 (0.4%)
MONTELUKAST	0	1 (0.6%)	1 (0.4%)
MONTELUKAST SODIUM	0	1 (0.6%)	1 (0.4%)
PRANLUKAST	0	1 (0.6%)	1 (0.4%)
TERBUTALINE	0	1 (0.6%)	1 (0.4%)

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ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
DRUGS FOR TREATMENT OF BONE DISEASES			
Total number of patients with at least one treatment	16 (18.4%)	25 (14.9%)	41 (16.1%)
Total number of treatments	28	45	73
DENOSUMAB	9 (10.3%)	16 (9.5%)	25 (9.8%)
ZOLEDRONIC ACID	3 (3.4%)	4 (2.4%)	7 (2.7%)
ZOLEDRONIC ACID MONOHYDRATE	2 (2.3%)	2 (1.2%)	4 (1.6%)
PAMIDRONATE DISODIUM	0	3 (1.8%)	3 (1.2%)
IBANDRONIC ACID	0	2 (1.2%)	2 (0.8%)
RISEDRONATE SODIUM	1 (1.1%)	1 (0.6%)	2 (0.8%)
ALENDRONIC ACID;VITAMIN D NOS	1 (1.1%)	0	1 (0.4%)
DRUGS USED IN DIABETES			
Total number of patients with at least one treatment	7 (8.0%)	23 (13.7%)	30 (11.8%)
Total number of treatments	14	55	69
METFORMIN	2 (2.3%)	14 (8.3%)	16 (6.3%)
METFORMIN HYDROCHLORIDE	2 (2.3%)	7 (4.2%)	9 (3.5%)
GLICLAZIDE	2 (2.3%)	2 (1.2%)	4 (1.6%)
DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE	1 (1.1%)	2 (1.2%)	3 (1.2%)
GLIMEPIRIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
INSULIN	0	2 (1.2%)	2 (0.8%)
INSULIN HUMAN	1 (1.1%)	1 (0.6%)	2 (0.8%)
LINAGLIPTIN	0	2 (1.2%)	2 (0.8%)
ALOGLIPTIN BENZOATE;METFORMIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
ANAGLIPTIN;METFORMIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
CANAGLIFLOZIN	1 (1.1%)	0	1 (0.4%)
EMPAGLIFLOZIN	0	1 (0.6%)	1 (0.4%)
GLIBENCLAMIDE	0	1 (0.6%)	1 (0.4%)
GLIBENCLAMIDE;METFORMIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
METFORMIN HYDROCHLORIDE;VILDAGLIPTIN	0	1 (0.6%)	1 (0.4%)
METFORMIN;SITAGLIPTIN	1 (1.1%)	0	1 (0.4%)
PIOGLITAZONE	0	1 (0.6%)	1 (0.4%)
SITAGLIPTIN PHOSPHATE	1 (1.1%)	0	1 (0.4%)
VILDAGLIPTIN	1 (1.1%)	0	1 (0.4%)
ECTOPARASITICIDES, INCL. SCABICIDES, INSECTICIDES AND REPELLENTS			
Total number of patients with at least one treatment	1 (1.1%)	3 (1.8%)	4 (1.6%)
Total number of treatments	2	3	5
DIMETICONE	0	3 (1.8%)	3 (1.2%)
BENZYL BENZOATE	1 (1.1%)	0	1 (0.4%)
IVERMECTIN	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
EMOLLIENTS AND PROTECTIVES			
Total number of patients with at least one treatment	10 (11.5%)	25 (14.9%)	35 (13.7%)
Total number of treatments	55	66	121
THIOCTIC ACID	4 (4.6%)	9 (5.4%)	13 (5.1%)
MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER	1 (1.1%)	3 (1.8%)	4 (1.6%)
DIMETICONE	0	3 (1.8%)	3 (1.2%)
GLYCEROL	2 (2.3%)	1 (0.6%)	3 (1.2%)
GLYCEROL;PARAFFIN, LIQUID;WHITE SOFT PARAFFIN	1 (1.1%)	2 (1.2%)	3 (1.2%)
HEPARINOID	0	3 (1.8%)	3 (1.2%)
OTHER EMOLLIENTS AND PROTECTIVES	0	2 (1.2%)	2 (0.8%)
AMMONIUM LACTATE	0	1 (0.6%)	1 (0.4%)
AQUAPHILUS DOLOMIAE;ELAEIS GUINEENSIS OIL; GLYCEROL;OENOTHERA BIENNIS OIL;PARAFFIN, LIQUID; TOCOPHEROL	0	1 (0.6%)	1 (0.4%)
CAMPHOR;MENTHOL	0	1 (0.6%)	1 (0.4%)
MENTHOL;METHYL SALICYLATE	1 (1.1%)	0	1 (0.4%)
OLEA EUROPAEA OIL	0	1 (0.6%)	1 (0.4%)
PARAFFIN	0	1 (0.6%)	1 (0.4%)
PARAFFIN, LIQUID;PETROLATUM;WOOL FAT	0	1 (0.6%)	1 (0.4%)
SESAMUM INDICUM SEED OIL	1 (1.1%)	0	1 (0.4%)
TOCOPHEROL	1 (1.1%)	0	1 (0.4%)
UREA	1 (1.1%)	0	1 (0.4%)
WHITE SOFT PARAFFIN	0	1 (0.6%)	1 (0.4%)
ZINC	0	1 (0.6%)	1 (0.4%)
ZINC SULFATE	1 (1.1%)	0	1 (0.4%)
ENDOCRINE THERAPY			
Total number of patients with at least one treatment	2 (2.3%)	10 (6.0%)	12 (4.7%)
Total number of treatments	2	22	24
MEGESTROL ACETATE	1 (1.1%)	6 (3.6%)	7 (2.7%)
MEDROXYPROGESTERONE ACETATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
GOSERELIN	0	1 (0.6%)	1 (0.4%)
LEUPRORELIN	0	1 (0.6%)	1 (0.4%)
LEUPRORELIN ACETATE	0	1 (0.6%)	1 (0.4%)
MEGESTROL	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
GENERAL NUTRIENTS			
Total number of patients with at least one treatment	7 (8.0%)	8 (4.8%)	15 (5.9%)
Total number of treatments	9	12	21
GLUCOSE	1 (1.1%)	3 (1.8%)	4 (1.6%)
DOCOSAHEXAENOIC ACID;EICOSAPENTAENOIC ACID	1 (1.1%)	2 (1.2%)	3 (1.2%)
LYSINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
ARGININE	1 (1.1%)	0	1 (0.4%)
ASCORBIC ACID;BETACAROTENE;BIOTIN;CALCIUM; CARBOHYDRATES NOS;CHLORIDE;CHOLINE;CHROMIUM; COLECALCIFEROL;COPPER;FATS NOS;FIBRE, DIETARY; FLUORINE;FOLIC ACID;IODINE;IRON;MAGNESIUM; MANGANESE;MOLYBDENUM;NICOTINIC ACID;PANTOTHENIC ACID;PHOSPHORUS;PHYTOMENADIONE;POTASSIUM;PROTEINS NOS;PYRIDOXINE HYDROCHLORIDE;RETINOL;RIBOFLAVIN; SELENIUM;SODIUM;VITAMIN B1 NOS;VITAMIN B12 NOS; VITAMIN E NOS;ZINC	0	1 (0.6%)	1 (0.4%)
ASCORBIC ACID;BIOTIN;CALCIUM CITRATE;CALCIUM PANTOTHENATE;CYANOCOBALAMIN;FERROUS SULFATE; FIBRE, DIETARY;FOLIC ACID;GLYCINE MAX SEED OIL; MAGNESIUM CARBONATE;MALTODEXTRIN;NICOTINAMIDE; POTASSIUM CITRATE;PROTEINS NOS;PYRIDOXINE HYDROCHLORIDE;RETINOL;RIBOFLAVIN;SODIUM CHLORIDE; SUCROSE;THIAMINE HYDROCHLORIDE;TOCOPHERYL ACETATE;WHEY PROTEIN;ZEA MAYS STARCH	0	1 (0.6%)	1 (0.4%)
CALCIUM CASEINATE	1 (1.1%)	0	1 (0.4%)
FISH OIL	0	1 (0.6%)	1 (0.4%)
NUTRIENTS NOS	0	1 (0.6%)	1 (0.4%)
POTASSIUM ASPARTATE	1 (1.1%)	0	1 (0.4%)
PROTEIN SUPPLEMENTS	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
GYNECOLOGICAL ANTIINFECTIVES AND ANTISEPTICS			
Total number of patients with at least one treatment	25 (28.7%)	41 (24.4%)	66 (25.9%)
Total number of treatments	38	70	108
CIPROFLOXACIN	3 (3.4%)	11 (6.5%)	14 (5.5%)
NYSTATIN	5 (5.7%)	6 (3.6%)	11 (4.3%)
METRONIDAZOLE	5 (5.7%)	5 (3.0%)	10 (3.9%)
CLOTRIMAZOLE	3 (3.4%)	5 (3.0%)	8 (3.1%)
CHLORHEXIDINE GLUCONATE	1 (1.1%)	5 (3.0%)	6 (2.4%)
ASCORBIC ACID	3 (3.4%)	1 (0.6%)	4 (1.6%)
CLINDAMYCIN	2 (2.3%)	2 (1.2%)	4 (1.6%)
OFLOXACIN	1 (1.1%)	3 (1.8%)	4 (1.6%)
MICONAZOLE	3 (3.4%)	0	3 (1.2%)
POVIDONE-IODINE	0	3 (1.8%)	3 (1.2%)
POTASSIUM	1 (1.1%)	1 (0.6%)	2 (0.8%)
AMPHOTERICIN B;TETRACYCLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
BENZALKONIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
CHLORAMPHENICOL	0	1 (0.6%)	1 (0.4%)
CICLOPIROX	0	1 (0.6%)	1 (0.4%)
CIPROFLOXACIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
DEQUALINIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
INOSINE	1 (1.1%)	0	1 (0.4%)
LACTOBACILLUS NOS	0	1 (0.6%)	1 (0.4%)
MICONAZOLE NITRATE;TINIDAZOLE	0	1 (0.6%)	1 (0.4%)
NITROFURAL	0	1 (0.6%)	1 (0.4%)
NORFLOXACIN	0	1 (0.6%)	1 (0.4%)
OCTENIDINE HYDROCHLORIDE;PHENOXYETHANOL	0	1 (0.6%)	1 (0.4%)
ORNIDAZOLE	1 (1.1%)	0	1 (0.4%)
SECNIDAZOLE	0	1 (0.6%)	1 (0.4%)
SERTACONAZOLE NITRATE	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
HOMEOPATHIC PREPARATION			
Total number of patients with at least one treatment	19 (21.8%)	25 (14.9%)	44 (17.3%)
Total number of treatments	79	73	152
SODIUM CHLORIDE	7 (8.0%)	10 (6.0%)	17 (6.7%)
POTASSIUM CHLORIDE	3 (3.4%)	7 (4.2%)	10 (3.9%)
CALCIUM CARBONATE	1 (1.1%)	4 (2.4%)	5 (2.0%)
ASCORBIC ACID	3 (3.4%)	1 (0.6%)	4 (1.6%)
SELENIUM	1 (1.1%)	2 (1.2%)	3 (1.2%)
SILYBUM MARIANUM	1 (1.1%)	2 (1.2%)	3 (1.2%)
CHARCOAL, ACTIVATED	0	2 (1.2%)	2 (0.8%)
CYANOCOBALAMIN	1 (1.1%)	1 (0.6%)	2 (0.8%)
POTASSIUM	1 (1.1%)	1 (0.6%)	2 (0.8%)
CALCIUM PHOSPHATE	0	1 (0.6%)	1 (0.4%)
HOMEOPATHICS NOS	0	1 (0.6%)	1 (0.4%)
IRON	1 (1.1%)	0	1 (0.4%)
PHOSPHORUS	0	1 (0.6%)	1 (0.4%)
SODIUM PHOSPHATE	1 (1.1%)	0	1 (0.4%)
THYMUS VULGARIS EXTRACT	1 (1.1%)	0	1 (0.4%)
UREA	1 (1.1%)	0	1 (0.4%)
ZINC	0	1 (0.6%)	1 (0.4%)
IMMUNOSTIMULANTS			
Total number of patients with at least one treatment	17 (19.5%)	33 (19.6%)	50 (19.6%)
Total number of treatments	34	244	278
FILGRASTIM	15 (17.2%)	27 (16.1%)	42 (16.5%)
LENOGRASTIM	1 (1.1%)	8 (4.8%)	9 (3.5%)
FILGRASTIM SNDZ	0	2 (1.2%)	2 (0.8%)
ANGELICA ACUTILOBA ROOT;ASTRAGALUS SPP. ROOT; ATRACTYLODES LANCEA RHIZOME;CINNAMOMUM CASSIA BARK;CNIDIUM OFFICINALE RHIZOME;GLYCYRRHIZA SPP. ROOT;PAEONIA LACTIFLORA ROOT;PANAX GINSENG ROOT; PORIA COCOS SCLEROTIUM;REHMANNIA GLUTINOSA ROOT	0	1 (0.6%)	1 (0.4%)
METHYLURACIL	0	1 (0.6%)	1 (0.4%)
TBO FILGRASTIM	1 (1.1%)	0	1 (0.4%)
IMMUNOSUPPRESSANTS			
Total number of patients with at least one treatment	0	2 (1.2%)	2 (0.8%)
Total number of treatments	0	2	2
COLCHICINE	0	1 (0.6%)	1 (0.4%)
HYDROXYCHLOROQUINE SULFATE	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
LIPID MODIFYING AGENTS			
Total number of patients with at least one treatment	14 (16.1%)	30 (17.9%)	44 (17.3%)
Total number of treatments	21	39	60
ATORVASTATIN	5 (5.7%)	7 (4.2%)	12 (4.7%)
SIMVASTATIN	1 (1.1%)	4 (2.4%)	5 (2.0%)
GEMFIBROZIL	0	4 (2.4%)	4 (1.6%)
ROSUVASTATIN	2 (2.3%)	2 (1.2%)	4 (1.6%)
ROSUVASTATIN CALCIUM	0	4 (2.4%)	4 (1.6%)
ATORVASTATIN CALCIUM	2 (2.3%)	1 (0.6%)	3 (1.2%)
DOCOSAHEXAENOIC ACID;EICOSAPENTAENOIC ACID	1 (1.1%)	2 (1.2%)	3 (1.2%)
PITAVASTATIN CALCIUM	0	3 (1.8%)	3 (1.2%)
ATORVASTATIN CALCIUM TRIHYDRATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
CIPROFIBRATE	0	2 (1.2%)	2 (0.8%)
EZETIMIBE	1 (1.1%)	1 (0.6%)	2 (0.8%)
FENOFIBRATE	0	2 (1.2%)	2 (0.8%)
BEZAFIBRATE	0	1 (0.6%)	1 (0.4%)
CURCUMA LONGA	1 (1.1%)	0	1 (0.4%)
DOCOSAHEXAENOIC ACID;EICOSAPENTAENOIC ACID;FISH OIL	1 (1.1%)	0	1 (0.4%)
EZETIMIBE;SIMVASTATIN	0	1 (0.6%)	1 (0.4%)
FISH OIL	0	1 (0.6%)	1 (0.4%)
FISH OIL;SALMON OIL	1 (1.1%)	0	1 (0.4%)
FLUVASTATIN SODIUM	1 (1.1%)	0	1 (0.4%)
LOVASTATIN	1 (1.1%)	0	1 (0.4%)
PITAVASTATIN	0	1 (0.6%)	1 (0.4%)
PRAVASTATIN	0	1 (0.6%)	1 (0.4%)
MEDICATED DRESSINGS			
Total number of patients with at least one treatment	11 (12.6%)	24 (14.3%)	35 (13.7%)
Total number of treatments	64	62	126
SODIUM CHLORIDE	7 (8.0%)	10 (6.0%)	17 (6.7%)
CHLORHEXIDINE GLUCONATE	1 (1.1%)	5 (3.0%)	6 (2.4%)
FUSIDIC ACID	2 (2.3%)	4 (2.4%)	6 (2.4%)
POVIDONE-IODINE	0	3 (1.8%)	3 (1.2%)
BENZALKONIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
CARMELLOSE SODIUM	0	1 (0.6%)	1 (0.4%)
CHLORHEXIDINE DIACETATE	0	1 (0.6%)	1 (0.4%)
FUSIDATE SODIUM	1 (1.1%)	0	1 (0.4%)
NITROFURAL	0	1 (0.6%)	1 (0.4%)
PARAFFIN	0	1 (0.6%)	1 (0.4%)
ZINC	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
MINERAL SUPPLEMENTS			
Total number of patients with at least one treatment	27 (31.0%)	49 (29.2%)	76 (29.8%)
Total number of treatments	99	125	224
SODIUM CHLORIDE	7 (8.0%)	10 (6.0%)	17 (6.7%)
MAGNESIUM OXIDE	3 (3.4%)	12 (7.1%)	15 (5.9%)
POTASSIUM CHLORIDE	3 (3.4%)	7 (4.2%)	10 (3.9%)
CALCIUM	4 (4.6%)	5 (3.0%)	9 (3.5%)
CALCIUM CARBONATE;COLECALCIFEROL	3 (3.4%)	5 (3.0%)	8 (3.1%)
CALCIUM CARBONATE;COLECALCIFEROL;MAGNESIUM CARBONATE	2 (2.3%)	5 (3.0%)	7 (2.7%)
CALCIUM CARBONATE	1 (1.1%)	4 (2.4%)	5 (2.0%)
MAGNESIUM SULFATE	0	5 (3.0%)	5 (2.0%)
CALCIUM GLUCONATE	1 (1.1%)	3 (1.8%)	4 (1.6%)
MAGNESIUM ASPARTATE;POTASSIUM ASPARTATE	0	4 (2.4%)	4 (1.6%)
MAGNESIUM;PYRIDOXINE HYDROCHLORIDE	2 (2.3%)	2 (1.2%)	4 (1.6%)
CALCIUM;COLECALCIFEROL	0	3 (1.8%)	3 (1.2%)
MAGNESIUM	1 (1.1%)	2 (1.2%)	3 (1.2%)
SELENIUM	1 (1.1%)	2 (1.2%)	3 (1.2%)
POTASSIUM	1 (1.1%)	1 (0.6%)	2 (0.8%)
ASPARTATE ZINC	1 (1.1%)	0	1 (0.4%)
BORON	1 (1.1%)	0	1 (0.4%)
BORON;CALCIUM;COLECALCIFEROL;COPPER;MANGANESE;ZINC	0	1 (0.6%)	1 (0.4%)
CALCIUM CARBONATE;CALCIUM LEVOMEFOLATE;COLECALCIFEROL;MECOBALAMIN;PYRIDOXAL PHOSPHATE	0	1 (0.6%)	1 (0.4%)
CALCIUM CITRATE;COLECALCIFEROL	0	1 (0.6%)	1 (0.4%)
CALCIUM PHOSPHATE	0	1 (0.6%)	1 (0.4%)
CALCIUM;VITAMIN D NOS	0	1 (0.6%)	1 (0.4%)
CITRIC ACID;POTASSIUM BICARBONATE;POTASSIUM CITRATE	1 (1.1%)	0	1 (0.4%)
LITHIUM	0	1 (0.6%)	1 (0.4%)
MAGNESIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
MAGNESIUM CITRATE	0	1 (0.6%)	1 (0.4%)
MAGNESIUM GLUCONATE;POTASSIUM GLUCONATE	1 (1.1%)	0	1 (0.4%)
MAGNESIUM LACTATE	0	1 (0.6%)	1 (0.4%)
MAGNESIUM LACTATE;PYRIDOXINE HYDROCHLORIDE	1 (1.1%)	0	1 (0.4%)
POTASSIUM ASPARTATE	1 (1.1%)	0	1 (0.4%)
POTASSIUM BICARBONATE;POTASSIUM CITRATE MONOHYDRATE	0	1 (0.6%)	1 (0.4%)
SODIUM PHOSPHATE	1 (1.1%)	0	1 (0.4%)
ZINC	0	1 (0.6%)	1 (0.4%)
ZINC SULFATE	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
MUSCLE RELAXANTS			
Total number of patients with at least one treatment	4 (4.6%)	12 (7.1%)	16 (6.3%)
Total number of treatments	4	14	18
DIAZEPAM	0	6 (3.6%)	6 (2.4%)
CAFFEINE;CARISOPRODOL;DICLOFENAC SODIUM; PARACETAMOL	1 (1.1%)	1 (0.6%)	2 (0.8%)
CAFFEINE;METAMIZOLE SODIUM;ORPHENADRINE CITRATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
CAFFEINE;CYCLOBENZAPRINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
CYCLOBENZAPRINE	0	1 (0.6%)	1 (0.4%)
LIDOCAINE HYDROCHLORIDE;TOLPERISONE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
MEPHENOXALONE	0	1 (0.6%)	1 (0.4%)
ORPHENADRINE	0	1 (0.6%)	1 (0.4%)
ORPHENADRINE CITRATE	1 (1.1%)	0	1 (0.4%)
ORPHENADRINE CITRATE;PARACETAMOL	1 (1.1%)	0	1 (0.4%)
N/A			
Total number of patients with at least one treatment	1 (1.1%)	10 (6.0%)	11 (4.3%)
Total number of treatments	1	75	76
DIOSMECTITE	0	10 (6.0%)	10 (3.9%)
ARGININE	1 (1.1%)	0	1 (0.4%)
NASAL PREPARATIONS			
Total number of patients with at least one treatment	73 (83.9%)	143 (85.1%)	216 (84.7%)
Total number of treatments	657	1099	1756
DEXAMETHASONE	55 (63.2%)	114 (67.9%)	169 (66.3%)
DEXAMETHASONE SODIUM PHOSPHATE	12 (13.8%)	15 (8.9%)	27 (10.6%)
SODIUM CHLORIDE	7 (8.0%)	10 (6.0%)	17 (6.7%)
ACETYLCYSTEINE	4 (4.6%)	10 (6.0%)	14 (5.5%)
BETAMETHASONE VALERATE	4 (4.6%)	7 (4.2%)	11 (4.3%)
SODIUM BICARBONATE	2 (2.3%)	7 (4.2%)	9 (3.5%)
MOMETASONE FUROATE	2 (2.3%)	4 (2.4%)	6 (2.4%)
PREDNISOLONE	2 (2.3%)	3 (1.8%)	5 (2.0%)
BETAMETHASONE DIPROPIONATE	2 (2.3%)	2 (1.2%)	4 (1.6%)
HYALURONATE SODIUM	1 (1.1%)	3 (1.8%)	4 (1.6%)
SODIUM HYPOCHLORITE	1 (1.1%)	3 (1.8%)	4 (1.6%)
TRIAMCINOLONE ACETONIDE	0	4 (2.4%)	4 (1.6%)
FLUTICASONE PROPIONATE	1 (1.1%)	2 (1.2%)	3 (1.2%)
MUPIROCIN	1 (1.1%)	2 (1.2%)	3 (1.2%)
POVIDONE-IODINE	0	3 (1.8%)	3 (1.2%)
BECLOMETASONE DIPROPIONATE	0	2 (1.2%)	2 (0.8%)
BUDESONIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
CALCIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)

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Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
CROMOGLICATE SODIUM	0	2 (1.2%)	2 (0.8%)
HYPROMELLOSE	0	2 (1.2%)	2 (0.8%)
TRIAMCINOLONE	0	2 (1.2%)	2 (0.8%)
BECLOMETASONE	1 (1.1%)	0	1 (0.4%)
BENZALKONIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
BETAMETHASONE	0	1 (0.6%)	1 (0.4%)
CAMPHOR;MENTHOL	0	1 (0.6%)	1 (0.4%)
CICLESONIDE	0	1 (0.6%)	1 (0.4%)
DEXPANTHENOL	0	1 (0.6%)	1 (0.4%)
DEXPANTHENOL;RETINOL	0	1 (0.6%)	1 (0.4%)
EBASTINE;PSEUDOEPHEDRINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
FEXOFENADINE HYDROCHLORIDE;PSEUDOEPHEDRINE HYDROCHLORIDE	1 (1.1%)	0	1 (0.4%)
FLUNISOLIDE	0	1 (0.6%)	1 (0.4%)
HYALURONIC ACID	1 (1.1%)	0	1 (0.4%)
IPRATROPIUM BROMIDE	0	1 (0.6%)	1 (0.4%)
KETOTIFEN	0	1 (0.6%)	1 (0.4%)
KETOTIFEN FUMARATE	0	1 (0.6%)	1 (0.4%)
MIRAMISTIN	0	1 (0.6%)	1 (0.4%)
NAPHAZOLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
OXYMETAZOLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
PSEUDOEPHEDRINE	0	1 (0.6%)	1 (0.4%)
PSEUDOEPHEDRINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
SEA WATER	1 (1.1%)	0	1 (0.4%)
SESAMUM INDICUM SEED OIL	1 (1.1%)	0	1 (0.4%)
TETRYZOLINE HYDROCHLORIDE	1 (1.1%)	0	1 (0.4%)
XYLOMETAZOLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
ZINC	0	1 (0.6%)	1 (0.4%)

Treatments are coded using the WHODRUG GLOBAL B3 SEPTEMBER 1, 2022. dictionary. Treatments can appear under multiple classes. The table includes medications that have temporal overlap with study drug administration. Multiple uses of a specific medication for a patient were counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a patient were counted once in the frequency for the medication class. Use of the anti-diarrheal medication Loperamide is primarily summarized in separate outputs.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_A_IT.out
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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
OPHTHALMOLOGICAL AND OTOLOGICAL PREPARATIONS			
Total number of patients with at least one treatment	70 (80.5%)	135 (80.4%)	205 (80.4%)
Total number of treatments	587	1024	1611
DEXAMETHASONE	55 (63.2%)	114 (67.9%)	169 (66.3%)
DEXAMETHASONE SODIUM PHOSPHATE	12 (13.8%)	15 (8.9%)	27 (10.6%)
LEVOFLOXACIN	6 (6.9%)	9 (5.4%)	15 (5.9%)
CIPROFLOXACIN	3 (3.4%)	11 (6.5%)	14 (5.5%)
CHLORHEXIDINE GLUCONATE	1 (1.1%)	5 (3.0%)	6 (2.4%)
PREDNISOLONE	2 (2.3%)	3 (1.8%)	5 (2.0%)
OFLOXACIN	1 (1.1%)	3 (1.8%)	4 (1.6%)
BETAMETHASONE VALERATE;GENTAMICIN SULFATE	3 (3.4%)	0	3 (1.2%)
GENTAMICIN	1 (1.1%)	2 (1.2%)	3 (1.2%)
TETRACYCLINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
BACITRACIN;NEOMYCIN SULFATE	0	1 (0.6%)	1 (0.4%)
BETAMETHASONE	0	1 (0.6%)	1 (0.4%)
CHLORAMPHENICOL	0	1 (0.6%)	1 (0.4%)
CHLORHEXIDINE DIACETATE	0	1 (0.6%)	1 (0.4%)
CIPROFLOXACIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
DEXAMETHASONE;NEOMYCIN SULFATE;POLYMYXIN B SULFATE	0	1 (0.6%)	1 (0.4%)
GENTAMICIN SULFATE	0	1 (0.6%)	1 (0.4%)
LEVOFLOXACIN HEMIHYDRATE	0	1 (0.6%)	1 (0.4%)
LOMEFLOXACIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
MIRAMISTIN	0	1 (0.6%)	1 (0.4%)
NORFLOXACIN	0	1 (0.6%)	1 (0.4%)
PREDNISOLONE VALEROACETATE	0	1 (0.6%)	1 (0.4%)
OPHTHALMOLOGICALS			
Total number of patients with at least one treatment	80 (92.0%)	153 (91.1%)	233 (91.4%)
Total number of treatments	791	1417	2208
DEXAMETHASONE	55 (63.2%)	114 (67.9%)	169 (66.3%)
DEXAMETHASONE SODIUM PHOSPHATE	12 (13.8%)	15 (8.9%)	27 (10.6%)
METHYLPREDNISOLONE	7 (8.0%)	12 (7.1%)	19 (7.5%)
SODIUM CHLORIDE	7 (8.0%)	10 (6.0%)	17 (6.7%)
HYDROCORTISONE	4 (4.6%)	11 (6.5%)	15 (5.9%)
LEVOFLOXACIN	6 (6.9%)	9 (5.4%)	15 (5.9%)
ACETYLCYSTEINE	4 (4.6%)	10 (6.0%)	14 (5.5%)
CIPROFLOXACIN	3 (3.4%)	11 (6.5%)	14 (5.5%)
DICLOFENAC	4 (4.6%)	10 (6.0%)	14 (5.5%)
BETAMETHASONE VALERATE	4 (4.6%)	7 (4.2%)	11 (4.3%)
REBAMIPIDE	6 (6.9%)	5 (3.0%)	11 (4.3%)
FLUCONAZOLE	6 (6.9%)	4 (2.4%)	10 (3.9%)
NAPROXEN	1 (1.1%)	9 (5.4%)	10 (3.9%)
POTASSIUM CHLORIDE	3 (3.4%)	7 (4.2%)	10 (3.9%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
HYDROCORTISONE SODIUM SUCCINATE	1 (1.1%)	8 (4.8%)	9 (3.5%)
PREDNISONE	3 (3.4%)	6 (3.6%)	9 (3.5%)
CLOTRIMAZOLE	3 (3.4%)	5 (3.0%)	8 (3.1%)
DICLOFENAC SODIUM	2 (2.3%)	6 (3.6%)	8 (3.1%)
AZITHROMYCIN	1 (1.1%)	6 (3.6%)	7 (2.7%)
CETIRIZINE	1 (1.1%)	6 (3.6%)	7 (2.7%)
CETIRIZINE HYDROCHLORIDE	3 (3.4%)	4 (2.4%)	7 (2.7%)
CHLORHEXIDINE GLUCONATE	1 (1.1%)	5 (3.0%)	6 (2.4%)
FUSIDIC ACID	2 (2.3%)	4 (2.4%)	6 (2.4%)
LIDOCAINE	1 (1.1%)	5 (3.0%)	6 (2.4%)
HYOSCINE	1 (1.1%)	4 (2.4%)	5 (2.0%)
PREDNISOLONE	2 (2.3%)	3 (1.8%)	5 (2.0%)
ALBUMIN HUMAN	0	4 (2.4%)	4 (1.6%)
ASCORBIC ACID	3 (3.4%)	1 (0.6%)	4 (1.6%)
BETAMETHASONE DIPROPIONATE	2 (2.3%)	2 (1.2%)	4 (1.6%)
BILASTINE	1 (1.1%)	3 (1.8%)	4 (1.6%)
CEFUROXIME	1 (1.1%)	3 (1.8%)	4 (1.6%)
HYALURONATE SODIUM	1 (1.1%)	3 (1.8%)	4 (1.6%)
KETOROLAC	1 (1.1%)	3 (1.8%)	4 (1.6%)
KETOROLAC TROMETHAMINE	0	4 (2.4%)	4 (1.6%)
LIDOCAINE HYDROCHLORIDE	2 (2.3%)	2 (1.2%)	4 (1.6%)
MELOXICAM	3 (3.4%)	1 (0.6%)	4 (1.6%)
MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER	1 (1.1%)	3 (1.8%)	4 (1.6%)
OFLOXACIN	1 (1.1%)	3 (1.8%)	4 (1.6%)
SODIUM GUALENATE HYDRATE	1 (1.1%)	3 (1.8%)	4 (1.6%)
TRIAMCINOLONE ACETONIDE	0	4 (2.4%)	4 (1.6%)
BETAMETHASONE VALERATE;GENTAMICIN SULFATE	3 (3.4%)	0	3 (1.2%)
DESONIDE	0	3 (1.8%)	3 (1.2%)
DIFLUPREDNATE	0	3 (1.8%)	3 (1.2%)
DIMETICONE	0	3 (1.8%)	3 (1.2%)
FLUOROMETHOLONE	0	3 (1.8%)	3 (1.2%)
GENTAMICIN	1 (1.1%)	2 (1.2%)	3 (1.2%)
GLYCEROL	2 (2.3%)	1 (0.6%)	3 (1.2%)
HEPARIN SODIUM	0	3 (1.8%)	3 (1.2%)
HEPARINOID	0	3 (1.8%)	3 (1.2%)
NAPROXEN SODIUM	0	3 (1.8%)	3 (1.2%)
POVIDONE-IODINE	0	3 (1.8%)	3 (1.2%)
ACETAZOLAMIDE	0	2 (1.2%)	2 (0.8%)
ACICLOVIR	1 (1.1%)	1 (0.6%)	2 (0.8%)
AMIKACIN	0	2 (1.2%)	2 (0.8%)
BORIC ACID;SODIUM BORATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
CROMOGLICATE SODIUM	0	2 (1.2%)	2 (0.8%)
CYANOCOBALAMIN	1 (1.1%)	1 (0.6%)	2 (0.8%)
ERYTHROMYCIN	1 (1.1%)	1 (0.6%)	2 (0.8%)
HEPARIN	1 (1.1%)	1 (0.6%)	2 (0.8%)
HYPROMELLOSE	0	2 (1.2%)	2 (0.8%)

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_A_IT.out

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
MOXIFLOXACIN HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
POTASSIUM	1 (1.1%)	1 (0.6%)	2 (0.8%)
PROCAINE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
SODIUM GUALENATE	0	2 (1.2%)	2 (0.8%)
SULFAMETHOXAZOLE	0	2 (1.2%)	2 (0.8%)
TETRACYCLINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
TRIAMCINOLONE	0	2 (1.2%)	2 (0.8%)
ACHYRANTHES BIDENTATA ROOT;ACONITUM SPP. PROCESSED ROOT;ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER;CINNAMOMUM CASSIA BARK;CORNUS OFFICINALIS FRUIT;DIOSCOREA SPP. RHIZOME;PAEONIA X SUFFRUTICOSA ROOT BARK;PLANTAGO ASIATICA SEED; PORIA COCOS SCLEROTIUM;REHMANNIA GLUTINOSA ROOT	0	1 (0.6%)	1 (0.4%)
ALCLOMETASONE DIPROPIONATE	0	1 (0.6%)	1 (0.4%)
ALTEPLASE	0	1 (0.6%)	1 (0.4%)
AMIKACIN SULFATE	0	1 (0.6%)	1 (0.4%)
ATROPINE	0	1 (0.6%)	1 (0.4%)
AZITHROMYCIN DIHYDRATE	0	1 (0.6%)	1 (0.4%)
BACITRACIN ZINC;NEOMYCIN SULFATE;POLYMYXIN B SULFATE	0	1 (0.6%)	1 (0.4%)
BACITRACIN;NEOMYCIN SULFATE	0	1 (0.6%)	1 (0.4%)
BENZALKONIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
BEPOTASTINE BESILATE	0	1 (0.6%)	1 (0.4%)
BETAMETHASONE	0	1 (0.6%)	1 (0.4%)
BIMATOPROST	0	1 (0.6%)	1 (0.4%)
BIMATOPROST;TIMOLOL	0	1 (0.6%)	1 (0.4%)
CARBOMER	0	1 (0.6%)	1 (0.4%)
CARMELLOSE SODIUM	0	1 (0.6%)	1 (0.4%)
CARMELLOSE SODIUM;GLYCEROL;RICINUS COMMUNIS OIL	0	1 (0.6%)	1 (0.4%)
CHLORAMPHENICOL	0	1 (0.6%)	1 (0.4%)
CHLORHEXIDINE DIACETATE	0	1 (0.6%)	1 (0.4%)
CHONDROITIN SULFATE SODIUM	1 (1.1%)	0	1 (0.4%)
CIPROFLOXACIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
CLONIDINE	0	1 (0.6%)	1 (0.4%)
COLISTIMETHATE SODIUM	0	1 (0.6%)	1 (0.4%)
COLISTIN	1 (1.1%)	0	1 (0.4%)
CROCIN	0	1 (0.6%)	1 (0.4%)
DEXAMETHASONE PHOSPHATE	1 (1.1%)	0	1 (0.4%)
DEXAMETHASONE;NEOMYCIN SULFATE;POLYMYXIN B SULFATE	0	1 (0.6%)	1 (0.4%)
DEXAMETHASONE;OXYTETRACYCLINE	1 (1.1%)	0	1 (0.4%)
DEXPANTHENOL	0	1 (0.6%)	1 (0.4%)
DEXPANTHENOL;RETINOL	0	1 (0.6%)	1 (0.4%)
DEXTRAN 70;HYPROMELLOSE	0	1 (0.6%)	1 (0.4%)
DIPOTASSIUM GLYCYRRHIZATE	1 (1.1%)	0	1 (0.4%)
DIQUAFOSOL TETRASODIUM	1 (1.1%)	0	1 (0.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
DORZOLAMIDE HYDROCHLORIDE;TIMOLOL MALEATE	0	1 (0.6%)	1 (0.4%)
EPINASTINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
ETHYLMORPHINE	1 (1.1%)	0	1 (0.4%)
FAMCICLOVIR	0	1 (0.6%)	1 (0.4%)
FLURBIPROFEN SODIUM	0	1 (0.6%)	1 (0.4%)
FUSIDATE SODIUM	1 (1.1%)	0	1 (0.4%)
GENTAMICIN SULFATE	0	1 (0.6%)	1 (0.4%)
GLUCOSE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
GUAIAZULENE	0	1 (0.6%)	1 (0.4%)
HAMAMELIS VIRGINIANA EXTRACT	1 (1.1%)	0	1 (0.4%)
HOMATROPINE METHYLBROMIDE	0	1 (0.6%)	1 (0.4%)
HYALURONIC ACID	1 (1.1%)	0	1 (0.4%)
HYDROCORTISONE ACETATE	1 (1.1%)	0	1 (0.4%)
INDOMETACIN	0	1 (0.6%)	1 (0.4%)
INOSINE	1 (1.1%)	0	1 (0.4%)
KETOTIFEN	0	1 (0.6%)	1 (0.4%)
KETOTIFEN FUMARATE	0	1 (0.6%)	1 (0.4%)
LATANOPROST	0	1 (0.6%)	1 (0.4%)
LEVOFLOXACIN HEMIHYDRATE	0	1 (0.6%)	1 (0.4%)
LOMEFLOXACIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
LOTEPREDNOL ETABONATE	0	1 (0.6%)	1 (0.4%)
MACROGOL 4000	0	1 (0.6%)	1 (0.4%)
MIRAMISTIN	0	1 (0.6%)	1 (0.4%)
MOXIFLOXACIN	1 (1.1%)	0	1 (0.4%)
NAPHAZOLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
NEOSTIGMINE METILSULFATE	1 (1.1%)	0	1 (0.4%)
NITROFURAL	0	1 (0.6%)	1 (0.4%)
NORFLOXACIN	0	1 (0.6%)	1 (0.4%)
OFLOXACIN;ORNIDAZOLE	0	1 (0.6%)	1 (0.4%)
OXYMETAZOLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
PARAFFIN	0	1 (0.6%)	1 (0.4%)
PARAFFIN, LIQUID;PETROLATUM;WOOL FAT	0	1 (0.6%)	1 (0.4%)
POTASSIUM IODIDE	0	1 (0.6%)	1 (0.4%)
PREDNISOLONE VALEROACETATE	0	1 (0.6%)	1 (0.4%)
PROXYMETACAINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
SEA WATER	1 (1.1%)	0	1 (0.4%)
SODIUM PHOSPHATE	1 (1.1%)	0	1 (0.4%)
TAURINE	1 (1.1%)	0	1 (0.4%)
TETRYZOLINE HYDROCHLORIDE	1 (1.1%)	0	1 (0.4%)
THIOTRIAZOLINE	1 (1.1%)	0	1 (0.4%)
TIMOLOL MALEATE	0	1 (0.6%)	1 (0.4%)
TOCOPHEROL	1 (1.1%)	0	1 (0.4%)
TROXERUTIN	0	1 (0.6%)	1 (0.4%)
WATER PURIFIED	0	1 (0.6%)	1 (0.4%)
XYLOMETAZOLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
ZINC	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
ZINC SULFATE	1 (1.1%)	0	1 (0.4%)
OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS			
Total number of patients with at least one treatment	12 (13.8%)	33 (19.6%)	45 (17.6%)
Total number of treatments	118	141	259
ADEMETIONINE	5 (5.7%)	10 (6.0%)	15 (5.9%)
ACETYLCYSTEINE	4 (4.6%)	10 (6.0%)	14 (5.5%)
THIOCTIC ACID	4 (4.6%)	9 (5.4%)	13 (5.1%)
SODIUM BICARBONATE	2 (2.3%)	7 (4.2%)	9 (3.5%)
PROBIOTICS NOS	1 (1.1%)	3 (1.8%)	4 (1.6%)
QUERCETIN	1 (1.1%)	3 (1.8%)	4 (1.6%)
LYSINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
ARGININE	1 (1.1%)	0	1 (0.4%)
CALCIUM CHLORIDE DIHYDRATE;MAGNESIUM CHLORIDE HEXAHYDRATE;POTASSIUM CHLORIDE;POTASSIUM PHOSPHATE DIBASIC;POTASSIUM PHOSPHATE MONOBASIC; SODIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
LEVOCARNITINE	1 (1.1%)	0	1 (0.4%)
LEVOGLUTAMIDE	0	1 (0.6%)	1 (0.4%)
PHOSPHORUS	0	1 (0.6%)	1 (0.4%)
POLAPREZINC	0	1 (0.6%)	1 (0.4%)
SUCRALFATE	0	1 (0.6%)	1 (0.4%)
TAURINE	1 (1.1%)	0	1 (0.4%)
ZINC	0	1 (0.6%)	1 (0.4%)

Treatments are coded using the WHODRUG GLOBAL B3 SEPTEMBER 1, 2022. dictionary. Treatments can appear under multiple classes. The table includes medications that have temporal overlap with study drug administration. Multiple uses of a specific medication for a patient were counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a patient were counted once in the frequency for the medication class. Use of the anti-diarrheal medication Loperamide is primarily summarized in separate outputs.
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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
OTHER DERMATOLOGICAL PREPARATIONS			
Total number of patients with at least one treatment	21 (24.1%)	55 (32.7%)	76 (29.8%)
Total number of treatments	41	173	214
IBUPROFEN	6 (6.9%)	16 (9.5%)	22 (8.6%)
DICLOFENAC	4 (4.6%)	10 (6.0%)	14 (5.5%)
SODIUM BICARBONATE	2 (2.3%)	7 (4.2%)	9 (3.5%)
DICLOFENAC SODIUM	2 (2.3%)	6 (3.6%)	8 (3.1%)
TRANEXAMIC ACID	2 (2.3%)	4 (2.4%)	6 (2.4%)
MAGNESIUM SULFATE	0	5 (3.0%)	5 (2.0%)
ASCORBIC ACID	3 (3.4%)	1 (0.6%)	4 (1.6%)
CALCIUM GLUCONATE	1 (1.1%)	3 (1.8%)	4 (1.6%)
HYALURONATE SODIUM	1 (1.1%)	3 (1.8%)	4 (1.6%)
PYRIDOXINE HYDROCHLORIDE	1 (1.1%)	3 (1.8%)	4 (1.6%)
POVIDONE-IODINE	0	3 (1.8%)	3 (1.2%)
SELENIUM	1 (1.1%)	2 (1.2%)	3 (1.2%)
CALCIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
CROMOGLICATE SODIUM	0	2 (1.2%)	2 (0.8%)
PYRIDOXINE	0	2 (1.2%)	2 (0.8%)
BIMATOPROST	0	1 (0.6%)	1 (0.4%)
CINNAMOMUM CASSIA;EPHEDRA SPP.;GLYCYRRHIZA SPP.; PAEONIA LACTIFLORA;PUERARIA MONTANA VAR. LOBATA; ZINGIBER OFFICINALE;ZIZIPHUS JUJUBA	0	1 (0.6%)	1 (0.4%)
DEXPANTHENOL	0	1 (0.6%)	1 (0.4%)
GUAIAZULENE	0	1 (0.6%)	1 (0.4%)
HYALURONIC ACID	1 (1.1%)	0	1 (0.4%)
IVERMECTIN	1 (1.1%)	0	1 (0.4%)
LITHIUM	0	1 (0.6%)	1 (0.4%)
MENTHOL;METHYL SALICYLATE	1 (1.1%)	0	1 (0.4%)
OTHER DERMATOLOGICALS	1 (1.1%)	0	1 (0.4%)
OXYMETAZOLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
SUCRALFATE	0	1 (0.6%)	1 (0.4%)
THIOTRIAZOLINE	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
OTHER DRUGS FOR DISORDERS OF THE MUSCULO-SKELETAL SYSTEM			
Total number of patients with at least one treatment	5 (5.7%)	8 (4.8%)	13 (5.1%)
Total number of treatments	5	11	16
HYALURONATE SODIUM	1 (1.1%)	3 (1.8%)	4 (1.6%)
CYTIDINE PHOSPHATE SODIUM;DISODIUM URIDINE MONOPHOSPHATE;URIDINE DIPHOSPHATE DISODIUM; URIDINE TRIPHOSPHATE TRISODIUM	0	3 (1.8%)	3 (1.2%)
CYTIDINE MONOPHOSPHATE DISODIUM;URIDINE TRIPHOSPHATE TRISODIUM	2 (2.3%)	0	2 (0.8%)
CHYMOTRYPSIN;TRYPSIN	0	1 (0.6%)	1 (0.4%)
ENZYMES NOS	1 (1.1%)	0	1 (0.4%)
HYALURONIC ACID	1 (1.1%)	0	1 (0.4%)
SERRAPEPTASE	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
OTHER GYNECOLOGICALS			
Total number of patients with at least one treatment	18 (20.7%)	46 (27.4%)	64 (25.1%)
Total number of treatments	27	142	169
IBUPROFEN	6 (6.9%)	16 (9.5%)	22 (8.6%)
NAPROXEN	1 (1.1%)	9 (5.4%)	10 (3.9%)
SODIUM BICARBONATE	2 (2.3%)	7 (4.2%)	9 (3.5%)
BENZYDAMINE HYDROCHLORIDE	1 (1.1%)	4 (2.4%)	5 (2.0%)
HYALURONATE SODIUM	1 (1.1%)	3 (1.8%)	4 (1.6%)
GLYCEROL	2 (2.3%)	1 (0.6%)	3 (1.2%)
NAPROXEN SODIUM	0	3 (1.8%)	3 (1.2%)
SALBUTAMOL	1 (1.1%)	2 (1.2%)	3 (1.2%)
ARTEMISIA ARGYI	0	2 (1.2%)	2 (0.8%)
NIFEDIPINE	2 (2.3%)	0	2 (0.8%)
SALBUTAMOL SULFATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
ANGELICA ACUTILOBA ROOT;ATRACTYLODES LANCEA RHIZOME;BUPLEURUM FALCATUM ROOT;GARDENIA JASMINOIDES FRUIT;GLYCYRRHIZA SPP. ROOT;MENTHA CANADENSIS HERB;PAEONIA LACTIFLORA ROOT;PAEONIA X SUFFRUTICOSA ROOT BARK;PORIA COCOS SCLEROTIUM; ZINGIBER OFFICINALE RHIZOME	0	1 (0.6%)	1 (0.4%)
BENZALKONIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
CARBOMER	0	1 (0.6%)	1 (0.4%)
CLONIDINE	0	1 (0.6%)	1 (0.4%)
ETHACRIDINE LACTATE	1 (1.1%)	0	1 (0.4%)
HYALURONATE SODIUM;MALVA SYLVESTRIS;MATRICARIA CHAMOMILLA	0	1 (0.6%)	1 (0.4%)
HYALURONIC ACID	1 (1.1%)	0	1 (0.4%)
IBUPROFEN ARGININE	0	1 (0.6%)	1 (0.4%)
LEVONORGESTREL	1 (1.1%)	0	1 (0.4%)
PAROXETINE	0	1 (0.6%)	1 (0.4%)
PHENOXYETHANOL;TRITICUM AESTIVUM	0	1 (0.6%)	1 (0.4%)
STREPTODORNASE;STREPTOKINASE	1 (1.1%)	0	1 (0.4%)
TERBUTALINE	0	1 (0.6%)	1 (0.4%)
THIOTRIAZOLINE	1 (1.1%)	0	1 (0.4%)
WATER PURIFIED	0	1 (0.6%)	1 (0.4%)
OTHER HEMATOLOGICAL AGENTS			
Total number of patients with at least one treatment	2 (2.3%)	2 (1.2%)	4 (1.6%)
Total number of treatments	4	5	9
CHYMOTRYPSIN;TRYPSIN	0	1 (0.6%)	1 (0.4%)
ENZYMES NOS	1 (1.1%)	0	1 (0.4%)
LEVOGLUTAMIDE	0	1 (0.6%)	1 (0.4%)
STREPTODORNASE;STREPTOKINASE	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
OTHER NERVOUS SYSTEM DRUGS			
Total number of patients with at least one treatment	23 (26.4%)	48 (28.6%)	71 (27.8%)
Total number of treatments	124	219	343
GABAPENTIN	11 (12.6%)	13 (7.7%)	24 (9.4%)
DIMENHYDRINATE	6 (6.9%)	10 (6.0%)	16 (6.3%)
THIOCTIC ACID	4 (4.6%)	9 (5.4%)	13 (5.1%)
MELDONIUM	4 (4.6%)	6 (3.6%)	10 (3.9%)
NALOXONE HYDROCHLORIDE;OXYCODONE HYDROCHLORIDE	0	5 (3.0%)	5 (2.0%)
TRIMETAZIDINE HYDROCHLORIDE	1 (1.1%)	3 (1.8%)	4 (1.6%)
BUPRENORPHINE	1 (1.1%)	2 (1.2%)	3 (1.2%)
GAMOLENIC ACID;NICOTINIC ACID;PANTOTHENIC ACID; PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN;SELENIUM; THIOCTIC ACID;VITAMIN B1 NOS;VITAMIN E NOS	0	3 (1.8%)	3 (1.2%)
HYDROXOCOBALAMIN	1 (1.1%)	2 (1.2%)	3 (1.2%)
MECOBALAMIN	0	3 (1.8%)	3 (1.2%)
CYANOCOBALAMIN	1 (1.1%)	1 (0.6%)	2 (0.8%)
CYTIDINE MONOPHOSPHATE DISODIUM;URIDINE TRIPHOSPHATE TRISODIUM	2 (2.3%)	0	2 (0.8%)
LYSINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
METHADONE	1 (1.1%)	1 (0.6%)	2 (0.8%)
METHYLETHYLPIRIDINOL SUCCINATE	0	2 (1.2%)	2 (0.8%)
PROPRANOLOL	0	2 (1.2%)	2 (0.8%)
BETAHISTINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
BETAHISTINE MESILATE	0	1 (0.6%)	1 (0.4%)
BETHANECHOL	0	1 (0.6%)	1 (0.4%)
BUPROPION	0	1 (0.6%)	1 (0.4%)
CLONIDINE	0	1 (0.6%)	1 (0.4%)
CURCUMIN;LECITHIN;MANGIFERA INDICA;PIPER NIGRUM; PYRIDOXINE HYDROCHLORIDE;RESVERATROL;RIBOFLAVIN	0	1 (0.6%)	1 (0.4%)
CYANOCOBALAMIN;FOLIC ACID;URIDINE PHOSPHATE	0	1 (0.6%)	1 (0.4%)
CYTIDINE MONOPHOSPHATE DISODIUM;HYDROXOCOBALAMIN ACETATE;URIDINE TRIPHOSPHATE TRISODIUM	0	1 (0.6%)	1 (0.4%)
DIMENHYDRINATE;PYRIDOXINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
FLUNARIZINE DIHYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
LIMAPROST ALFADEX	0	1 (0.6%)	1 (0.4%)
NALOXONE	0	1 (0.6%)	1 (0.4%)
NALOXONE;OXYCODONE	1 (1.1%)	0	1 (0.4%)
NEOSTIGMINE METILSULFATE	1 (1.1%)	0	1 (0.4%)
PROPRANOLOL HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
PYRIDOSTIGMINE BROMIDE	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
OTHER RESPIRATORY SYSTEM PRODUCTS			
Total number of patients with at least one treatment	0	12 (7.1%)	12 (4.7%)
Total number of treatments	0	13	13
AMBROXOL HYDROCHLORIDE	0	5 (3.0%)	5 (2.0%)
AMBROXOL	0	3 (1.8%)	3 (1.2%)
DIMETICONE	0	3 (1.8%)	3 (1.2%)
ACETAZOLAMIDE	0	2 (1.2%)	2 (0.8%)

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ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
OTOLOGICALS			
Total number of patients with at least one treatment	75 (86.2%)	144 (85.7%)	219 (85.9%)
Total number of treatments	680	1123	1803
DEXAMETHASONE	55 (63.2%)	114 (67.9%)	169 (66.3%)
DEXAMETHASONE SODIUM PHOSPHATE	12 (13.8%)	15 (8.9%)	27 (10.6%)
SODIUM CHLORIDE	7 (8.0%)	10 (6.0%)	17 (6.7%)
HYDROCORTISONE	4 (4.6%)	11 (6.5%)	15 (5.9%)
LEVOFLOXACIN	6 (6.9%)	9 (5.4%)	15 (5.9%)
CIPROFLOXACIN	3 (3.4%)	11 (6.5%)	14 (5.5%)
BETAMETHASONE VALERATE	4 (4.6%)	7 (4.2%)	11 (4.3%)
HYDROCORTISONE SODIUM SUCCINATE	1 (1.1%)	8 (4.8%)	9 (3.5%)
SODIUM BICARBONATE	2 (2.3%)	7 (4.2%)	9 (3.5%)
CLOTRIMAZOLE	3 (3.4%)	5 (3.0%)	8 (3.1%)
CHLORHEXIDINE GLUCONATE	1 (1.1%)	5 (3.0%)	6 (2.4%)
LIDOCAINE	1 (1.1%)	5 (3.0%)	6 (2.4%)
PREDNISOLONE	2 (2.3%)	3 (1.8%)	5 (2.0%)
BETAMETHASONE DIPROPIONATE	2 (2.3%)	2 (1.2%)	4 (1.6%)
LIDOCAINE HYDROCHLORIDE	2 (2.3%)	2 (1.2%)	4 (1.6%)
OFLOXACIN	1 (1.1%)	3 (1.8%)	4 (1.6%)
GENTAMICIN	1 (1.1%)	2 (1.2%)	3 (1.2%)
GLYCEROL	2 (2.3%)	1 (0.6%)	3 (1.2%)
MICONAZOLE	3 (3.4%)	0	3 (1.2%)
TETRACYCLINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
BENZOCAINE	0	1 (0.6%)	1 (0.4%)
BETAMETHASONE	0	1 (0.6%)	1 (0.4%)
CHLORAMPHENICOL	0	1 (0.6%)	1 (0.4%)
CHLORHEXIDINE DIACETATE	0	1 (0.6%)	1 (0.4%)
CIPROFLOXACIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
DEXAMETHASONE;NEOMYCIN SULFATE;POLYMYXIN B SULFATE	0	1 (0.6%)	1 (0.4%)
DOCUSATE SODIUM	1 (1.1%)	0	1 (0.4%)
GENTAMICIN SULFATE	0	1 (0.6%)	1 (0.4%)
HYDROCORTISONE ACETATE	1 (1.1%)	0	1 (0.4%)
LEVOFLOXACIN HEMIHYDRATE	0	1 (0.6%)	1 (0.4%)
LOMEFLOXACIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
MIRAMISTIN	0	1 (0.6%)	1 (0.4%)
NITROFURAL	0	1 (0.6%)	1 (0.4%)
OLEA EUROPAEA OIL	0	1 (0.6%)	1 (0.4%)
PREDNISOLONE VALEROACETATE	0	1 (0.6%)	1 (0.4%)
SEA WATER	1 (1.1%)	0	1 (0.4%)

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ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
PERIPHERAL VASODILATORS			
Total number of patients with at least one treatment	1 (1.1%)	6 (3.6%)	7 (2.7%)
Total number of treatments	1	6	7
METHYLETHYLPIRIDINOL SUCCINATE	0	2 (1.2%)	2 (0.8%)
ACHYRANTHES BIDENTATA ROOT;ACONITUM SPP. PROCESSED ROOT;ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER;CINNAMOMUM CASSIA BARK;CORNUS OFFICINALIS FRUIT;DIOSCOREA SPP. RHIZOME;PAEONIA X SUFFRUTICOSA ROOT BARK;PLANTAGO ASIATICA SEED; PORIA COCOS SCLEROTIUM;REHMANNIA GLUTINOSA ROOT	0	1 (0.6%)	1 (0.4%)
BETAHISTINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
ENZYMES NOS	1 (1.1%)	0	1 (0.4%)
FLUNARIZINE DIHYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
PENTOXIFYLLINE	0	1 (0.6%)	1 (0.4%)
PITUITARY AND HYPOTHALAMIC HORMONES AND ANALOGUES			
Total number of patients with at least one treatment	0	2 (1.2%)	2 (0.8%)
Total number of treatments	0	2	2
LEUPRORELIN	0	1 (0.6%)	1 (0.4%)
LEUPRORELIN ACETATE	0	1 (0.6%)	1 (0.4%)
PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCERS			
Total number of patients with at least one treatment	13 (14.9%)	25 (14.9%)	38 (14.9%)
Total number of treatments	71	57	128
SODIUM CHLORIDE	7 (8.0%)	10 (6.0%)	17 (6.7%)
HYALURONATE SODIUM	1 (1.1%)	3 (1.8%)	4 (1.6%)
DIMETICONE	0	3 (1.8%)	3 (1.2%)
CAMPHOR;CHLORPHENAMINE MALEATE;HEXACHLOROPHENE; LIDOCAINE HYDROCHLORIDE;MENTHOL;METHYL SALICYLATE	0	2 (1.2%)	2 (0.8%)
LYSINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
ALLANTOIN	1 (1.1%)	0	1 (0.4%)
CARMELLOSE SODIUM	0	1 (0.6%)	1 (0.4%)
CHYMOTRYPSIN;TRYPSIN	0	1 (0.6%)	1 (0.4%)
DEXPANTHENOL	0	1 (0.6%)	1 (0.4%)
FISH OIL	0	1 (0.6%)	1 (0.4%)
HAMAMELIS VIRGINIANA EXTRACT	1 (1.1%)	0	1 (0.4%)
HYALURONIC ACID	1 (1.1%)	0	1 (0.4%)
MENADIONE	0	1 (0.6%)	1 (0.4%)
METHYLURACIL	0	1 (0.6%)	1 (0.4%)
PHENOXYETHANOL;TRITICUM AESTIVUM	0	1 (0.6%)	1 (0.4%)
PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCERS	0	1 (0.6%)	1 (0.4%)
STREPTODORNASE;STREPTOKINASE	1 (1.1%)	0	1 (0.4%)
TOCOPHEROL	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
PSYCHOANALEPTICS			
Total number of patients with at least one treatment	14 (16.1%)	26 (15.5%)	40 (15.7%)
Total number of treatments	69	90	159
ADEMETIONINE	5 (5.7%)	10 (6.0%)	15 (5.9%)
DULOXETINE	0	4 (2.4%)	4 (1.6%)
IPIDACRINE	2 (2.3%)	2 (1.2%)	4 (1.6%)
AMITRIPTYLINE	0	3 (1.8%)	3 (1.2%)
VENLAFAXINE	3 (3.4%)	0	3 (1.2%)
CITALOPRAM	1 (1.1%)	1 (0.6%)	2 (0.8%)
DULOXETINE HYDROCHLORIDE	0	2 (1.2%)	2 (0.8%)
ESCITALOPRAM OXALATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
METHYLETHYLPIRIDINOL SUCCINATE	0	2 (1.2%)	2 (0.8%)
MIRTAZAPINE	2 (2.3%)	0	2 (0.8%)
SERTRALINE	0	2 (1.2%)	2 (0.8%)
AMITRIPTYLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
BUPROPION	0	1 (0.6%)	1 (0.4%)
CITICOLINE SODIUM	0	1 (0.6%)	1 (0.4%)
CLONIDINE	0	1 (0.6%)	1 (0.4%)
DOXEPIN	1 (1.1%)	0	1 (0.4%)
ENZYMES NOS	1 (1.1%)	0	1 (0.4%)
IPIDACRINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
LAMOTRIGINE	0	1 (0.6%)	1 (0.4%)
PAROXETINE	0	1 (0.6%)	1 (0.4%)
PSYCHOLEPTICS			
Total number of patients with at least one treatment	44 (50.6%)	103 (61.3%)	147 (57.6%)
Total number of treatments	140	433	573
DIPHENHYDRAMINE	12 (13.8%)	40 (23.8%)	52 (20.4%)
DIPHENHYDRAMINE HYDROCHLORIDE	10 (11.5%)	27 (16.1%)	37 (14.5%)
PREGABALIN	6 (6.9%)	11 (6.5%)	17 (6.7%)
ALPRAZOLAM	3 (3.4%)	12 (7.1%)	15 (5.9%)
LORAZEPAM	4 (4.6%)	8 (4.8%)	12 (4.7%)
ZOLPIDEM TARTRATE	4 (4.6%)	4 (2.4%)	8 (3.1%)
PROCHLORPERAZINE	2 (2.3%)	5 (3.0%)	7 (2.7%)
DIAZEPAM	0	6 (3.6%)	6 (2.4%)
ZOLPIDEM	1 (1.1%)	5 (3.0%)	6 (2.4%)
BROMAZEPAM	1 (1.1%)	4 (2.4%)	5 (2.0%)
CLONAZEPAM	1 (1.1%)	4 (2.4%)	5 (2.0%)
HYDROXYZINE	1 (1.1%)	4 (2.4%)	5 (2.0%)
HYOSCINE	1 (1.1%)	4 (2.4%)	5 (2.0%)
PROMETHAZINE	2 (2.3%)	3 (1.8%)	5 (2.0%)
DULOXETINE	0	4 (2.4%)	4 (1.6%)
ZOPICLONE	2 (2.3%)	2 (1.2%)	4 (1.6%)

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Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_A_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
AMITRIPTYLINE	0	3 (1.8%)	3 (1.2%)
CANNABIDIOL	2 (2.3%)	1 (0.6%)	3 (1.2%)
MELATONIN	1 (1.1%)	2 (1.2%)	3 (1.2%)
VENLAFAXINE	3 (3.4%)	0	3 (1.2%)
CARBAMAZEPINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
DULOXETINE HYDROCHLORIDE	0	2 (1.2%)	2 (0.8%)
ESCITALOPRAM OXALATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
HYDROXYZINE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
PROCHLORPERAZINE MALEATE	0	2 (1.2%)	2 (0.8%)
PROPRANOLOL	0	2 (1.2%)	2 (0.8%)
SERTRALINE	0	2 (1.2%)	2 (0.8%)
SUVOREXANT	1 (1.1%)	1 (0.6%)	2 (0.8%)
AMITRIPTYLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
ANGELICA ACUTILOBA ROOT;ATRACTYLODES LANCEA RHIZOME;BUPLEURUM FALCATUM ROOT;GARDENIA JASMINOIDES FRUIT;GLYCYRRHIZA SPP. ROOT;MENTHA CANADENSIS HERB;PAEONIA LACTIFLORA ROOT;PAEONIA X SUFFRUTICOSA ROOT BARK;PORIA COCOS SCLEROTIUM; ZINGIBER OFFICINALE RHIZOME	0	1 (0.6%)	1 (0.4%)
BROTIZOLAM	0	1 (0.6%)	1 (0.4%)
DEXMEDETOMIDINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
DIPHENHYDRAMINE;IBUPROFEN	0	1 (0.6%)	1 (0.4%)
DOXEPIN	1 (1.1%)	0	1 (0.4%)
ESTAZOLAM	0	1 (0.6%)	1 (0.4%)
ESZOPICLONE	0	1 (0.6%)	1 (0.4%)
ETIZOLAM	1 (1.1%)	0	1 (0.4%)
HALOPERIDOL	1 (1.1%)	0	1 (0.4%)
HUMULUS LUPULUS;MELISSA OFFICINALIS LEAF; VALERIANA OFFICINALIS EXTRACT	0	1 (0.6%)	1 (0.4%)
LEVOSULPIRIDE	1 (1.1%)	0	1 (0.4%)
LITHIUM	0	1 (0.6%)	1 (0.4%)
MEPHENOXALONE	0	1 (0.6%)	1 (0.4%)
PAROXETINE	0	1 (0.6%)	1 (0.4%)
PHENAZEPAM	0	1 (0.6%)	1 (0.4%)
PRAZEPAM	0	1 (0.6%)	1 (0.4%)
PROPRANOLOL HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
QUETIAPINE	0	1 (0.6%)	1 (0.4%)
RISPERIDONE	0	1 (0.6%)	1 (0.4%)
TEMAZEPAM	0	1 (0.6%)	1 (0.4%)
THIOPENTAL SODIUM	1 (1.1%)	0	1 (0.4%)
TRIAZOLAM	0	1 (0.6%)	1 (0.4%)
VALERIANA OFFICINALIS	1 (1.1%)	0	1 (0.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM			
Total number of patients with at least one treatment	3 (3.4%)	8 (4.8%)	11 (4.3%)
Total number of treatments	3	18	21
MEGESTROL ACETATE	1 (1.1%)	6 (3.6%)	7 (2.7%)
MEDROXYPROGESTERONE ACETATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
DESOGESTREL	0	1 (0.6%)	1 (0.4%)
LEVONORGESTREL	1 (1.1%)	0	1 (0.4%)
MEGESTROL	0	1 (0.6%)	1 (0.4%)
STOMATOLOGICAL PREPARATIONS			
Total number of patients with at least one treatment	75 (86.2%)	144 (85.7%)	219 (85.9%)
Total number of treatments	707	1213	1920
DEXAMETHASONE	55 (63.2%)	114 (67.9%)	169 (66.3%)
DEXAMETHASONE SODIUM PHOSPHATE	12 (13.8%)	15 (8.9%)	27 (10.6%)
SODIUM CHLORIDE	7 (8.0%)	10 (6.0%)	17 (6.7%)
HYDROCORTISONE	4 (4.6%)	11 (6.5%)	15 (5.9%)
DICLOFENAC	4 (4.6%)	10 (6.0%)	14 (5.5%)
KETOPROFEN	3 (3.4%)	8 (4.8%)	11 (4.3%)
NYSTATIN	5 (5.7%)	6 (3.6%)	11 (4.3%)
ACETYLSALICYLIC ACID	4 (4.6%)	6 (3.6%)	10 (3.9%)
METRONIDAZOLE	5 (5.7%)	5 (3.0%)	10 (3.9%)
NAPROXEN	1 (1.1%)	9 (5.4%)	10 (3.9%)
HYDROCORTISONE SODIUM SUCCINATE	1 (1.1%)	8 (4.8%)	9 (3.5%)
SODIUM BICARBONATE	2 (2.3%)	7 (4.2%)	9 (3.5%)
CLOTRIMAZOLE	3 (3.4%)	5 (3.0%)	8 (3.1%)
DICLOFENAC SODIUM	2 (2.3%)	6 (3.6%)	8 (3.1%)
CHLORHEXIDINE GLUCONATE	1 (1.1%)	5 (3.0%)	6 (2.4%)
LIDOCAINE	1 (1.1%)	5 (3.0%)	6 (2.4%)
TRANEXAMIC ACID	2 (2.3%)	4 (2.4%)	6 (2.4%)
BENZYDAMINE HYDROCHLORIDE	1 (1.1%)	4 (2.4%)	5 (2.0%)
PREDNISOLONE	2 (2.3%)	3 (1.8%)	5 (2.0%)
HYALURONATE SODIUM	1 (1.1%)	3 (1.8%)	4 (1.6%)
LIDOCAINE HYDROCHLORIDE	2 (2.3%)	2 (1.2%)	4 (1.6%)
NIMESULIDE	1 (1.1%)	3 (1.8%)	4 (1.6%)
SODIUM GUALENATE HYDRATE	1 (1.1%)	3 (1.8%)	4 (1.6%)
SODIUM HYPOCHLORITE	1 (1.1%)	3 (1.8%)	4 (1.6%)
TRIAMCINOLONE ACETONIDE	0	4 (2.4%)	4 (1.6%)
CLOBETASOL PROPIONATE	1 (1.1%)	2 (1.2%)	3 (1.2%)
DIMETICONE	0	3 (1.8%)	3 (1.2%)
ELECTROLYTES NOS	1 (1.1%)	2 (1.2%)	3 (1.2%)
GLYCEROL	2 (2.3%)	1 (0.6%)	3 (1.2%)
MICONAZOLE	3 (3.4%)	0	3 (1.2%)
POVIDONE-IODINE	0	3 (1.8%)	3 (1.2%)
CLOBETASOL	0	2 (1.2%)	2 (0.8%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
MINOCYCLINE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
POTASSIUM	1 (1.1%)	1 (0.6%)	2 (0.8%)
SODIUM GUALENATE	0	2 (1.2%)	2 (0.8%)
TETRACYCLINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
TRIAMCINOLONE	0	2 (1.2%)	2 (0.8%)
ACORUS CALAMUS RHIZOME;ARNICA MONTANA;MATRICARIA CHAMOMILLA;MENTHA X PIPERITA LEAF;QUERCUS SPP. BARK;SALVIA OFFICINALIS LEAF;THYMUS VULGARIS	1 (1.1%)	0	1 (0.4%)
AZULENE SODIUM SULFONATE	0	1 (0.6%)	1 (0.4%)
BENZALKONIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
BENZETHONIUM CHLORIDE	1 (1.1%)	0	1 (0.4%)
BENZOCAINE	0	1 (0.6%)	1 (0.4%)
BENZYDAMINE HYDROCHLORIDE;CHLORHEXIDINE GLUCONATE	1 (1.1%)	0	1 (0.4%)
BETAMETHASONE	0	1 (0.6%)	1 (0.4%)
CARBOMER	0	1 (0.6%)	1 (0.4%)
CETYLPYRIDINIUM CHLORIDE;CHLORHEXIDINE GLUCONATE	0	1 (0.6%)	1 (0.4%)
CHLORAMPHENICOL	0	1 (0.6%)	1 (0.4%)
CHLORHEXIDINE DIACETATE	0	1 (0.6%)	1 (0.4%)
CHLORINE DIOXIDE	1 (1.1%)	0	1 (0.4%)
CURCUMA LONGA	1 (1.1%)	0	1 (0.4%)
DOXYCYCLINE	0	1 (0.6%)	1 (0.4%)
DOXYCYCLINE HYCLATE	1 (1.1%)	0	1 (0.4%)
EPICHOLESTANOL;TETRACYCLINE HYDROCHLORIDE	1 (1.1%)	0	1 (0.4%)
FLURBIPROFEN SODIUM	0	1 (0.6%)	1 (0.4%)
HYALURONIC ACID	1 (1.1%)	0	1 (0.4%)
HYDROCORTISONE ACETATE	1 (1.1%)	0	1 (0.4%)
KETOPROFEN LYSINE	0	1 (0.6%)	1 (0.4%)
LIDOCAINE HYDROCHLORIDE;MATRICARIA CHAMOMILLA TINCTURE	0	1 (0.6%)	1 (0.4%)
LIDOCAINE HYDROCHLORIDE;TRIAMCINOLONE ACETONIDE	1 (1.1%)	0	1 (0.4%)
LIDOCAINE;PRILOCAINE	1 (1.1%)	0	1 (0.4%)
MINOCYCLINE	0	1 (0.6%)	1 (0.4%)
MIRAMISTIN	0	1 (0.6%)	1 (0.4%)
NITROFURAL	0	1 (0.6%)	1 (0.4%)
SUCRALFATE	0	1 (0.6%)	1 (0.4%)
ZINC	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
THROAT PREPARATIONS			
Total number of patients with at least one treatment	21 (24.1%)	59 (35.1%)	80 (31.4%)
Total number of treatments	36	187	223
IBUPROFEN	6 (6.9%)	16 (9.5%)	22 (8.6%)
DICLOFENAC	4 (4.6%)	10 (6.0%)	14 (5.5%)
KETOPROFEN	3 (3.4%)	8 (4.8%)	11 (4.3%)
DICLOFENAC SODIUM	2 (2.3%)	6 (3.6%)	8 (3.1%)
CHLORHEXIDINE GLUCONATE	1 (1.1%)	5 (3.0%)	6 (2.4%)
LIDOCAINE	1 (1.1%)	5 (3.0%)	6 (2.4%)
AMBROXOL HYDROCHLORIDE	0	5 (3.0%)	5 (2.0%)
BENZYDAMINE HYDROCHLORIDE	1 (1.1%)	4 (2.4%)	5 (2.0%)
LIDOCAINE HYDROCHLORIDE	2 (2.3%)	2 (1.2%)	4 (1.6%)
SODIUM GUALENATE HYDRATE	1 (1.1%)	3 (1.8%)	4 (1.6%)
AMBROXOL	0	3 (1.8%)	3 (1.2%)
POVIDONE-IODINE	0	3 (1.8%)	3 (1.2%)
TETRACYCLINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
AMYLMETACRESOL;DICHLOROBENZYL ALCOHOL;LIDOCAINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
AZULENE SODIUM SULFONATE	0	1 (0.6%)	1 (0.4%)
BACITRACIN;NEOMYCIN SULFATE	0	1 (0.6%)	1 (0.4%)
BENZALKONIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
BENZALKONIUM CHLORIDE;BENZOCAINE;TYROTHRICIN	1 (1.1%)	0	1 (0.4%)
BENZETHONIUM CHLORIDE	1 (1.1%)	0	1 (0.4%)
BENZOCAINE	0	1 (0.6%)	1 (0.4%)
BENZYDAMINE HYDROCHLORIDE;CHLORHEXIDINE GLUCONATE	1 (1.1%)	0	1 (0.4%)
CHLORHEXIDINE DIACETATE	0	1 (0.6%)	1 (0.4%)
DEQUALINIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
HEXAMIDINE ISETIONATE;LIDOCAINE HYDROCHLORIDE	1 (1.1%)	0	1 (0.4%)
HYALURONIC ACID	1 (1.1%)	0	1 (0.4%)
KETOPROFEN LYSINE	0	1 (0.6%)	1 (0.4%)
LIDOCAINE HYDROCHLORIDE;MATRICARIA CHAMOMILLA TINCTURE	0	1 (0.6%)	1 (0.4%)
MIRAMISTIN	0	1 (0.6%)	1 (0.4%)
SODIUM BICARBONATE;SODIUM GUALENATE HYDRATE	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
THYROID THERAPY			
Total number of patients with at least one treatment	6 (6.9%)	17 (10.1%)	23 (9.0%)
Total number of treatments	6	23	29
LEVOTHYROXINE SODIUM	4 (4.6%)	6 (3.6%)	10 (3.9%)
LEVOTHYROXINE	2 (2.3%)	4 (2.4%)	6 (2.4%)
THIAMAZOLE	0	3 (1.8%)	3 (1.2%)
PROPRANOLOL	0	2 (1.2%)	2 (0.8%)
CARBIMAZOLE	0	1 (0.6%)	1 (0.4%)
POTASSIUM IODIDE	0	1 (0.6%)	1 (0.4%)
PROPRANOLOL HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
TONICS			
Total number of patients with at least one treatment	4 (4.6%)	2 (1.2%)	6 (2.4%)
Total number of treatments	4	3	7
DIETARY SUPPLEMENT	1 (1.1%)	2 (1.2%)	3 (1.2%)
CURCUMA LONGA	1 (1.1%)	0	1 (0.4%)
CURCUMIN;VITAMIN D NOS	1 (1.1%)	0	1 (0.4%)
TOCOPHEROL	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN			
Total number of patients with at least one treatment	32 (36.8%)	75 (44.6%)	107 (42.0%)
Total number of treatments	70	270	340
IBUPROFEN	6 (6.9%)	16 (9.5%)	22 (8.6%)
DICLOFENAC	4 (4.6%)	10 (6.0%)	14 (5.5%)
KETOPROFEN	3 (3.4%)	8 (4.8%)	11 (4.3%)
ACETYLSALICYLIC ACID	4 (4.6%)	6 (3.6%)	10 (3.9%)
NAPROXEN	1 (1.1%)	9 (5.4%)	10 (3.9%)
FOLIC ACID	2 (2.3%)	7 (4.2%)	9 (3.5%)
DICLOFENAC SODIUM	2 (2.3%)	6 (3.6%)	8 (3.1%)
LOXOPROFEN	1 (1.1%)	5 (3.0%)	6 (2.4%)
LOXOPROFEN SODIUM DIHYDRATE	2 (2.3%)	4 (2.4%)	6 (2.4%)
BENZYDAMINE HYDROCHLORIDE	1 (1.1%)	4 (2.4%)	5 (2.0%)
KETOROLAC	1 (1.1%)	3 (1.8%)	4 (1.6%)
KETOROLAC TROMETHAMINE	0	4 (2.4%)	4 (1.6%)
MELOXICAM	3 (3.4%)	1 (0.6%)	4 (1.6%)
MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER	1 (1.1%)	3 (1.8%)	4 (1.6%)
NIMESULIDE	1 (1.1%)	3 (1.8%)	4 (1.6%)
HEPARINOID	0	3 (1.8%)	3 (1.2%)
NAPROXEN SODIUM	0	3 (1.8%)	3 (1.2%)
ACECLOFENAC	0	2 (1.2%)	2 (0.8%)
CAMPHOR;CHLORPHENAMINE MALEATE;HEXACHLOROPHENE; LIDOCAINE HYDROCHLORIDE;MENTHOL;METHYL SALICYLATE	0	2 (1.2%)	2 (0.8%)
DEXKETOPROFEN	0	2 (1.2%)	2 (0.8%)
DEXKETOPROFEN TROMETAMOL	2 (2.3%)	0	2 (0.8%)
LOXOPROFEN SODIUM	1 (1.1%)	1 (0.6%)	2 (0.8%)
CAMPHOR;MENTHOL	0	1 (0.6%)	1 (0.4%)
CHONDROITIN SULFATE SODIUM	1 (1.1%)	0	1 (0.4%)
DICLOFENAC DIETHYLAMINE;LINUM USITATISSIMUM SEED OIL;MENTHOL;METHYL SALICYLATE	0	1 (0.6%)	1 (0.4%)
DICLOFENAC POTASSIUM	0	1 (0.6%)	1 (0.4%)
DIMETHYL SULFOXIDE	0	1 (0.6%)	1 (0.4%)
ESFLURBIPROFEN;MENTHA SPP. OIL	0	1 (0.6%)	1 (0.4%)
FELBINAC	0	1 (0.6%)	1 (0.4%)
FLURBIPROFEN SODIUM	0	1 (0.6%)	1 (0.4%)
GLUCOSAMINE	1 (1.1%)	0	1 (0.4%)
IBUPROFEN ARGININE	0	1 (0.6%)	1 (0.4%)
INDOMETACIN	0	1 (0.6%)	1 (0.4%)
KETOPROFEN LYSINE	0	1 (0.6%)	1 (0.4%)
MAGNESIUM CHLORIDE	0	1 (0.6%)	1 (0.4%)
MENTHOL;METHYL SALICYLATE	1 (1.1%)	0	1 (0.4%)
OTHER TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	1 (1.1%)	0	1 (0.4%)
VACCINIUM MACROCARPON	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE			
Total number of patients with at least one treatment	13 (14.9%)	15 (8.9%)	28 (11.0%)
Total number of treatments	16	21	37
SILYBUM MARIANUM	1 (1.1%)	2 (1.2%)	3 (1.2%)
ARTEMISIA ARGYI	0	2 (1.2%)	2 (0.8%)
GLYCYRRHIZA GLABRA EXTRACT;PAPAVER SOMNIFERUM	0	2 (1.2%)	2 (0.8%)
VITIS VINIFERA EXTRACT	0	2 (1.2%)	2 (0.8%)
ACHYRANTHES BIDENTATA ROOT;ACONITUM SPP. PROCESSED ROOT;ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER;CINNAMOMUM CASSIA BARK;CORNUS OFFICINALIS FRUIT;DIOSCOREA SPP. RHIZOME;PAEONIA X SUFFRUTICOSA ROOT BARK;PLANTAGO ASIATICA SEED; PORIA COCOS SCLEROTIUM;REHMANNIA GLUTINOSA ROOT	0	1 (0.6%)	1 (0.4%)
ACORUS CALAMUS RHIZOME;ARNICA MONTANA;MATRICARIA CHAMOMILLA;MENTHA X PIPERITA LEAF;QUERCUS SPP. BARK;SALVIA OFFICINALIS LEAF;THYMUS VULGARIS	1 (1.1%)	0	1 (0.4%)
ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER; ARTEMISIA CAPILLARIS FLOWER;ATRACTYLODES LANCEA RHIZOME;CINNAMOMUM CASSIA BARK;POLYPORUS UMBELLATUS SCLEROTIUM;PORIA COCOS SCLEROTIUM	0	1 (0.6%)	1 (0.4%)
ANGELICA ACUTILOBA ROOT;ASTRAGALUS SPP. ROOT; ATRACTYLODES LANCEA RHIZOME;CINNAMOMUM CASSIA BARK;CNIDIUM OFFICINALE RHIZOME;GLYCYRRHIZA SPP. ROOT;PAEONIA LACTIFLORA ROOT;PANAX GINSENG ROOT; PORIA COCOS SCLEROTIUM;REHMANNIA GLUTINOSA ROOT	0	1 (0.6%)	1 (0.4%)
ANGELICA ACUTILOBA ROOT;ATRACTYLODES LANCEA RHIZOME;BUPLEURUM FALCATUM ROOT;GARDENIA JASMINOIDES FRUIT;GLYCYRRHIZA SPP. ROOT;MENTHA CANADENSIS HERB;PAEONIA LACTIFLORA ROOT;PAEONIA X SUFFRUTICOSA ROOT BARK;PORIA COCOS SCLEROTIUM; ZINGIBER OFFICINALE RHIZOME	0	1 (0.6%)	1 (0.4%)
CALENDULA SPP.	0	1 (0.6%)	1 (0.4%)
CINNAMOMUM CASSIA;EPHEDRA SPP.;GLYCYRRHIZA SPP.; PAEONIA LACTIFLORA;PUERARIA MONTANA VAR. LOBATA; ZINGIBER OFFICINALE;ZIZIPHUS JUJUBA	0	1 (0.6%)	1 (0.4%)
CITRUS X PARADISI SEED	1 (1.1%)	0	1 (0.4%)
CURCUMA LONGA	1 (1.1%)	0	1 (0.4%)
CYNARA CARDUNCULUS EXTRACT	1 (1.1%)	0	1 (0.4%)
GENTIANA LUTEA ROOT;PRIMULA SPP. FLOWER;RUMEX SPP. HERB;SAMBUCUS NIGRA FLOWER;VERBENA OFFICINALIS HERB	1 (1.1%)	0	1 (0.4%)
HAMAMELIS VIRGINIANA EXTRACT	1 (1.1%)	0	1 (0.4%)
HERBAL COUGH AND COLD REMEDIES, OTHER	1 (1.1%)	0	1 (0.4%)
HERBAL EXTRACT NOS	0	1 (0.6%)	1 (0.4%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
HUMULUS LUPULUS;MELISSA OFFICINALIS LEAF; VALERIANA OFFICINALIS EXTRACT	0	1 (0.6%)	1 (0.4%)
OLEA EUROPAEA OIL	0	1 (0.6%)	1 (0.4%)
SENNA SPP.	1 (1.1%)	0	1 (0.4%)
SESAMUM INDICUM SEED OIL	1 (1.1%)	0	1 (0.4%)
THYMUS VULGARIS EXTRACT	1 (1.1%)	0	1 (0.4%)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	1 (1.1%)	0	1 (0.4%)
VACCINIUM MACROCARPON	1 (1.1%)	0	1 (0.4%)
VALERIANA OFFICINALIS	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
UROLOGICALS			
Total number of patients with at least one treatment	9 (10.3%)	32 (19.0%)	41 (16.1%)
Total number of treatments	14	63	77
SODIUM BICARBONATE	2 (2.3%)	7 (4.2%)	9 (3.5%)
LIDOCAINE	1 (1.1%)	5 (3.0%)	6 (2.4%)
DULOXETINE	0	4 (2.4%)	4 (1.6%)
HYALURONATE SODIUM	1 (1.1%)	3 (1.8%)	4 (1.6%)
LIDOCAINE HYDROCHLORIDE	2 (2.3%)	2 (1.2%)	4 (1.6%)
AMITRIPTYLINE	0	3 (1.8%)	3 (1.2%)
BUDESONIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
DROTAVERINE	1 (1.1%)	1 (0.6%)	2 (0.8%)
DROTAVERINE HYDROCHLORIDE	0	2 (1.2%)	2 (0.8%)
DULOXETINE HYDROCHLORIDE	0	2 (1.2%)	2 (0.8%)
PHENAZOPYRIDINE	0	2 (1.2%)	2 (0.8%)
SOLIFENACIN SUCCINATE	1 (1.1%)	1 (0.6%)	2 (0.8%)
ACHYRANTHES BIDENTATA ROOT;ACONITUM SPP. PROCESSED ROOT;ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER;CINNAMOMUM CASSIA BARK;CORNUS OFFICINALIS FRUIT;DIOSCOREA SPP. RHIZOME;PAEONIA X SUFFRUTICOSA ROOT BARK;PLANTAGO ASIATICA SEED; PORIA COCOS SCLEROTIUM;REHMANNIA GLUTINOSA ROOT	0	1 (0.6%)	1 (0.4%)
ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER; GELATIN;POLYPORUS UMBELLATUS SCLEROTIUM;PORIA COCOS SCLEROTIUM;TALC	0	1 (0.6%)	1 (0.4%)
AMITRIPTYLINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
BENZOCAINE	0	1 (0.6%)	1 (0.4%)
CHONDROITIN SULFATE SODIUM	1 (1.1%)	0	1 (0.4%)
DIMETHYL SULFOXIDE	0	1 (0.6%)	1 (0.4%)
DOXAZOSIN	0	1 (0.6%)	1 (0.4%)
FLAVOXATE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
HYALURONIC ACID	1 (1.1%)	0	1 (0.4%)
LIDOCAINE;PRILOCAINE	1 (1.1%)	0	1 (0.4%)
MAGNESIUM CITRATE	0	1 (0.6%)	1 (0.4%)
MIRABEGRON	0	1 (0.6%)	1 (0.4%)
OTHER UROLOGICALS	0	1 (0.6%)	1 (0.4%)
OXYBUTYNIN	1 (1.1%)	0	1 (0.4%)
OXYBUTYNIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
PENTOSAN POLYSULFATE SODIUM	0	1 (0.6%)	1 (0.4%)
PHENAZOPYRIDINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
TAMSULOSIN HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
VACCINES			
Total number of patients with at least one treatment	3 (3.4%)	10 (6.0%)	13 (5.1%)
Total number of treatments	3	17	20
INFLUENZA VACCINE	3 (3.4%)	3 (1.8%)	6 (2.4%)
COVID-19 VACCINE	0	3 (1.8%)	3 (1.2%)
TOZINAMERAN	0	3 (1.8%)	3 (1.2%)
ELASOMERAN	0	1 (0.6%)	1 (0.4%)
INFLUENZA VACCINE INACT SAG 4V	0	1 (0.6%)	1 (0.4%)
VARICELLA ZOSTER VACCINE LIVE (OKA/MERCK)	0	1 (0.6%)	1 (0.4%)
VASOPROTECTIVES			
Total number of patients with at least one treatment	73 (83.9%)	139 (82.7%)	212 (83.1%)
Total number of treatments	610	1078	1688
DEXAMETHASONE	55 (63.2%)	114 (67.9%)	169 (66.3%)
DEXAMETHASONE SODIUM PHOSPHATE	12 (13.8%)	15 (8.9%)	27 (10.6%)
HYDROCORTISONE	4 (4.6%)	11 (6.5%)	15 (5.9%)
BETAMETHASONE VALERATE	4 (4.6%)	7 (4.2%)	11 (4.3%)
HYDROCORTISONE SODIUM SUCCINATE	1 (1.1%)	8 (4.8%)	9 (3.5%)
LIDOCAINE	1 (1.1%)	5 (3.0%)	6 (2.4%)
DIOSMIN;HESPERIDIN	2 (2.3%)	3 (1.8%)	5 (2.0%)
PREDNISOLONE	2 (2.3%)	3 (1.8%)	5 (2.0%)
BETAMETHASONE BUTYRATE PROPIONATE	3 (3.4%)	1 (0.6%)	4 (1.6%)
BETAMETHASONE DIPROPIONATE	2 (2.3%)	2 (1.2%)	4 (1.6%)
HYALURONATE SODIUM	1 (1.1%)	3 (1.8%)	4 (1.6%)
LIDOCAINE HYDROCHLORIDE	2 (2.3%)	2 (1.2%)	4 (1.6%)
MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER	1 (1.1%)	3 (1.8%)	4 (1.6%)
QUERCETIN	1 (1.1%)	3 (1.8%)	4 (1.6%)
TRIAMCINOLONE ACETONIDE	0	4 (2.4%)	4 (1.6%)
FLUOROMETHOLONE	0	3 (1.8%)	3 (1.2%)
HEPARIN SODIUM	0	3 (1.8%)	3 (1.2%)
HEPARINOID	0	3 (1.8%)	3 (1.2%)
BECLOMETASONE DIPROPIONATE	0	2 (1.2%)	2 (0.8%)
DIFLUCORTOLONE VALERATE;LIDOCAINE	0	2 (1.2%)	2 (0.8%)
HEPARIN	1 (1.1%)	1 (0.6%)	2 (0.8%)
NIFEDIPINE	2 (2.3%)	0	2 (0.8%)
PROCAINE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
TRIAMCINOLONE	0	2 (1.2%)	2 (0.8%)
VITIS VINIFERA EXTRACT	0	2 (1.2%)	2 (0.8%)
ALUMINIUM ACETATE;HYDROCORTISONE ACETATE; LIDOCAINE;ZINC OXIDE	0	1 (0.6%)	1 (0.4%)
ASCORBIC ACID;HESPERIDIN METHYL CHALCONE;RUSCUS ACULEATUS	0	1 (0.6%)	1 (0.4%)
ASCORBIC ACID;RUTOSIDE	0	1 (0.6%)	1 (0.4%)
BECLOMETASONE	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
BENZOCAINE	0	1 (0.6%)	1 (0.4%)
BETAMETHASONE	0	1 (0.6%)	1 (0.4%)
BETAMETHASONE VALERATE;LIDOCAINE HYDROCHLORIDE; PHENYLEPHRINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
BISMUTH SUBGALLATE;FLUOCINOLONE ACETONIDE; LIDOCAINE HYDROCHLORIDE;MENTHOL	1 (1.1%)	0	1 (0.4%)
CARBOMER	0	1 (0.6%)	1 (0.4%)
CHONDRUS CRISPUS;LIDOCAINE;TITANIUM DIOXIDE;ZINC OXIDE	1 (1.1%)	0	1 (0.4%)
CINCHOCAINE HYDROCHLORIDE;POLICRESULEN	0	1 (0.6%)	1 (0.4%)
COUMARIN;TROXERUTIN	0	1 (0.6%)	1 (0.4%)
DIOSMIN	0	1 (0.6%)	1 (0.4%)
ESCHERICHIA COLI;HYDROCORTISONE	1 (1.1%)	0	1 (0.4%)
HAMAMELIS VIRGINIANA EXTRACT	1 (1.1%)	0	1 (0.4%)
HYALURONIC ACID	1 (1.1%)	0	1 (0.4%)
HYDROCORTISONE ACETATE	1 (1.1%)	0	1 (0.4%)
LIDOCAINE HYDROCHLORIDE;TRIAMCINOLONE ACETONIDE	1 (1.1%)	0	1 (0.4%)
LIDOCAINE;TRIBENOSIDE	0	1 (0.6%)	1 (0.4%)
LYSINE AESCINAT	1 (1.1%)	0	1 (0.4%)
PENTOSAN POLYSULFATE SODIUM	0	1 (0.6%)	1 (0.4%)
PREDNISOLONE VALEROACETATE	0	1 (0.6%)	1 (0.4%)
RUSCOGENIN;TRIMEBUTINE	0	1 (0.6%)	1 (0.4%)
STREPTODORNASE;STREPTOKINASE	1 (1.1%)	0	1 (0.4%)
THIOTRIAZOLINE	1 (1.1%)	0	1 (0.4%)
TROXERUTIN	0	1 (0.6%)	1 (0.4%)
ZINC	0	1 (0.6%)	1 (0.4%)
ZINC SULFATE	1 (1.1%)	0	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
VITAMINS			
Total number of patients with at least one treatment	15 (17.2%)	26 (15.5%)	41 (16.1%)
Total number of treatments	23	49	72
COLECALCIFEROL	7 (8.0%)	7 (4.2%)	14 (5.5%)
ASCORBIC ACID	3 (3.4%)	1 (0.6%)	4 (1.6%)
MAGNESIUM;PYRIDOXINE HYDROCHLORIDE	2 (2.3%)	2 (1.2%)	4 (1.6%)
PYRIDOXINE HYDROCHLORIDE	1 (1.1%)	3 (1.8%)	4 (1.6%)
VITAMIN D NOS	0	4 (2.4%)	4 (1.6%)
VITAMIN B COMPLEX	0	3 (1.8%)	3 (1.2%)
PYRIDOXINE	0	2 (1.2%)	2 (0.8%)
THIAMINE HYDROCHLORIDE	1 (1.1%)	1 (0.6%)	2 (0.8%)
VITAMIN B NOS	1 (1.1%)	1 (0.6%)	2 (0.8%)
VITAMINS NOS	1 (1.1%)	1 (0.6%)	2 (0.8%)
ASCORBIC ACID;CALCIUM PANTOTHENATE	0	1 (0.6%)	1 (0.4%)
ASCORBIC ACID;CYANOCOBALAMIN;FOLIC ACID;NICOTINIC ACID;PANTOTHENIC ACID;PYRIDOXINE;RIBOFLAVIN;THIAMINE;ZINC SULFATE	0	1 (0.6%)	1 (0.4%)
ASCORBIC ACID;VITAMIN B NOS	0	1 (0.6%)	1 (0.4%)
BENFOTIAMINE	0	1 (0.6%)	1 (0.4%)
CITRUS X PARADISI SEED	1 (1.1%)	0	1 (0.4%)
CYANOCOBALAMIN;DEXPANTHENOL;NICOTINAMIDE;PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN SODIUM PHOSPHATE;THIAMINE HYDROCHLORIDE	0	1 (0.6%)	1 (0.4%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN;THIAMINE MONONITRATE	1 (1.1%)	0	1 (0.4%)
DEXPANTHENOL	0	1 (0.6%)	1 (0.4%)
ELDECALCITOL	1 (1.1%)	0	1 (0.4%)
ERGOCALCIFEROL	0	1 (0.6%)	1 (0.4%)
HERBAL EXTRACT NOS;MINERALS NOS;VITAMINS NOS	0	1 (0.6%)	1 (0.4%)
MAGNESIUM LACTATE;PYRIDOXINE HYDROCHLORIDE	1 (1.1%)	0	1 (0.4%)
PANTETHINE	0	1 (0.6%)	1 (0.4%)
RETINOL;VITAMIN E NOS	0	1 (0.6%)	1 (0.4%)
THIAMINE	1 (1.1%)	0	1 (0.4%)
TOCOPHEROL	1 (1.1%)	0	1 (0.4%)
VITAMIN B1 IN COMBINATION WITH VITAMIN B6 AND/OR VITAMIN B12	0	1 (0.6%)	1 (0.4%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
Total number of patients with at least one treatment	75 (98.7%)	144 (98.6%)	219 (98.6%)
Total number of treatments	1147	2267	3414
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM			
Total number of patients with at least one treatment	14 (18.4%)	36 (24.7%)	50 (22.5%)
Total number of treatments	18	48	66
ENALAPRIL	1 (1.3%)	6 (4.1%)	7 (3.2%)
LOSARTAN	3 (3.9%)	4 (2.7%)	7 (3.2%)
LOSARTAN POTASSIUM	0	6 (4.1%)	6 (2.7%)
RAMIPRIL	1 (1.3%)	3 (2.1%)	4 (1.8%)
CAPTOPRIL	1 (1.3%)	2 (1.4%)	3 (1.4%)
PERINDOPRIL	1 (1.3%)	2 (1.4%)	3 (1.4%)
CANDESARTAN CILEXETIL	1 (1.3%)	1 (0.7%)	2 (0.9%)
HYDROCHLOROTHIAZIDE;LISINOPRIL	0	2 (1.4%)	2 (0.9%)
HYDROCHLOROTHIAZIDE;LOSARTAN POTASSIUM	1 (1.3%)	1 (0.7%)	2 (0.9%)
INDAPAMIDE;PERINDOPRIL ARGININE	1 (1.3%)	1 (0.7%)	2 (0.9%)
INDAPAMIDE;PERINDOPRIL ERBUMINE	0	2 (1.4%)	2 (0.9%)
IRBESARTAN	1 (1.3%)	1 (0.7%)	2 (0.9%)
TELMISARTAN	0	2 (1.4%)	2 (0.9%)
VALSARTAN	1 (1.3%)	1 (0.7%)	2 (0.9%)
AMLODIPINE BESILATE;HYDROCHLOROTHIAZIDE; OLMESARTAN MEDOXOMIL	0	1 (0.7%)	1 (0.5%)
AMLODIPINE BESILATE;INDAPAMIDE;PERINDOPRIL ARGININE	1 (1.3%)	0	1 (0.5%)
AMLODIPINE BESILATE;IRBESARTAN	0	1 (0.7%)	1 (0.5%)
CANDESARTAN	1 (1.3%)	0	1 (0.5%)
ENALAPRILAT	1 (1.3%)	0	1 (0.5%)
HYDROCHLOROTHIAZIDE;IRBESARTAN	0	1 (0.7%)	1 (0.5%)
HYDROCHLOROTHIAZIDE;LISINOPRIL DIHYDRATE	0	1 (0.7%)	1 (0.5%)
HYDROCHLOROTHIAZIDE;RAMIPRIL	0	1 (0.7%)	1 (0.5%)
HYDROCHLOROTHIAZIDE;TELMISARTAN	0	1 (0.7%)	1 (0.5%)
LISINOPRIL	1 (1.3%)	0	1 (0.5%)
OLMESARTAN	1 (1.3%)	0	1 (0.5%)
OLMESARTAN MEDOXOMIL	0	1 (0.7%)	1 (0.5%)
PERINDOPRIL ERBUMINE	0	1 (0.7%)	1 (0.5%)

Treatments are coded using the WHODRUG GLOBAL B3 SEPTEMBER 1, 2022. dictionary. Treatments can appear under multiple classes. The table includes medications that have temporal overlap with study drug administration. Multiple uses of a specific medication for a patient were counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a patient were counted once in the frequency for the medication class. Use of the anti-diarrheal medication Loperamide is primarily summarized in separate outputs.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out
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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ALL OTHER NON-THERAPEUTIC PRODUCTS			
Total number of patients with at least one treatment	10 (13.2%)	19 (13.0%)	29 (13.1%)
Total number of treatments	49	74	123
ASCORBIC ACID	7 (9.2%)	9 (6.2%)	16 (7.2%)
SODIUM CHLORIDE	3 (3.9%)	13 (8.9%)	16 (7.2%)
HYALURONIC ACID	1 (1.3%)	0	1 (0.5%)
MEDICAL DEVICES, WITHOUT SUBSTANCES	1 (1.3%)	0	1 (0.5%)
SODIUM CITRATE	1 (1.3%)	0	1 (0.5%)
SODIUM HYPOCHLORITE	0	1 (0.7%)	1 (0.5%)
ALL OTHER THERAPEUTIC PRODUCTS			
Total number of patients with at least one treatment	19 (25.0%)	32 (21.9%)	51 (23.0%)
Total number of treatments	36	69	105
ASCORBIC ACID	7 (9.2%)	9 (6.2%)	16 (7.2%)
ACETYLCYSTEINE	4 (5.3%)	7 (4.8%)	11 (5.0%)
CALCIUM CARBONATE	1 (1.3%)	7 (4.8%)	8 (3.6%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE HYDROCHLORIDE	2 (2.6%)	2 (1.4%)	4 (1.8%)
ALL OTHER THERAPEUTIC PRODUCTS	1 (1.3%)	1 (0.7%)	2 (0.9%)
CALCIUM;VITAMIN D NOS	1 (1.3%)	1 (0.7%)	2 (0.9%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE DISULFIDE PHOSPHATE	0	2 (1.4%)	2 (0.9%)
GLUTATHIONE	1 (1.3%)	1 (0.7%)	2 (0.9%)
MEGLUMINE SODIUM SUCCINATE	0	2 (1.4%)	2 (0.9%)
VITAMIN B12 NOS	1 (1.3%)	1 (0.7%)	2 (0.9%)
ADENOSINE	0	1 (0.7%)	1 (0.5%)
ALUMINIUM HYDROXIDE	0	1 (0.7%)	1 (0.5%)
FLUMAZENIL	0	1 (0.7%)	1 (0.5%)
IODINE	1 (1.3%)	0	1 (0.5%)
IRON	0	1 (0.7%)	1 (0.5%)
LACTOBACILLUS RHAMNOSUS	0	1 (0.7%)	1 (0.5%)
LACTOFERRIN	0	1 (0.7%)	1 (0.5%)
PYCNOGENOL	0	1 (0.7%)	1 (0.5%)
SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)
SUGAMMADEX SODIUM	0	1 (0.7%)	1 (0.5%)
ANABOLIC AGENTS FOR SYSTEMIC USE			
Total number of patients with at least one treatment	0	1 (0.7%)	1 (0.5%)
Total number of treatments	0	1	1
OXYMETHOLONE	0	1 (0.7%)	1 (0.5%)

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ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ANALGESICS			
Total number of patients with at least one treatment	51 (67.1%)	103 (70.5%)	154 (69.4%)
Total number of treatments	297	629	926
PARACETAMOL	26 (34.2%)	57 (39.0%)	83 (37.4%)
PREGABALIN	18 (23.7%)	23 (15.8%)	41 (18.5%)
TRAMADOL	5 (6.6%)	11 (7.5%)	16 (7.2%)
OXYCODONE HYDROCHLORIDE	6 (7.9%)	5 (3.4%)	11 (5.0%)
METAMIZOLE	3 (3.9%)	7 (4.8%)	10 (4.5%)
METAMIZOLE SODIUM	2 (2.6%)	8 (5.5%)	10 (4.5%)
PARACETAMOL;TRAMADOL HYDROCHLORIDE	2 (2.6%)	8 (5.5%)	10 (4.5%)
ACETYLSALICYLIC ACID	3 (3.9%)	6 (4.1%)	9 (4.1%)
GABAPENTIN	4 (5.3%)	5 (3.4%)	9 (4.1%)
MORPHINE	2 (2.6%)	7 (4.8%)	9 (4.1%)
CAFFEINE;PARACETAMOL;PROMETHAZINE METHYLENE DISALICYLATE;SALICYLAMIDE	2 (2.6%)	4 (2.7%)	6 (2.7%)
CODEINE PHOSPHATE	2 (2.6%)	4 (2.7%)	6 (2.7%)
CODEINE PHOSPHATE;IBUPROFEN;PARACETAMOL	4 (5.3%)	2 (1.4%)	6 (2.7%)
NALOXONE HYDROCHLORIDE;OXYCODONE HYDROCHLORIDE	2 (2.6%)	4 (2.7%)	6 (2.7%)
TRAMADOL HYDROCHLORIDE	1 (1.3%)	5 (3.4%)	6 (2.7%)
CODEINE PHOSPHATE;PARACETAMOL	2 (2.6%)	3 (2.1%)	5 (2.3%)
FENTANYL	1 (1.3%)	3 (2.1%)	4 (1.8%)
FENTANYL CITRATE	1 (1.3%)	3 (2.1%)	4 (1.8%)
AMITRIPTYLINE	1 (1.3%)	2 (1.4%)	3 (1.4%)
DULOXETINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
METOPROLOL	1 (1.3%)	2 (1.4%)	3 (1.4%)
MORPHINE SULFATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
OXYCODONE	1 (1.3%)	2 (1.4%)	3 (1.4%)
AMITRIPTYLINE HYDROCHLORIDE	2 (2.6%)	0	2 (0.9%)
CLONIDINE HYDROCHLORIDE	2 (2.6%)	0	2 (0.9%)
CODEINE	0	2 (1.4%)	2 (0.9%)
DULOXETINE	0	2 (1.4%)	2 (0.9%)
FENPIVERINIUM BROMIDE;METAMIZOLE SODIUM; PITOFENONE HYDROCHLORIDE	0	2 (1.4%)	2 (0.9%)
HYDROMORPHONE HYDROCHLORIDE	0	2 (1.4%)	2 (0.9%)
PENTAZOCINE	0	2 (1.4%)	2 (0.9%)
PROPRANOLOL	0	2 (1.4%)	2 (0.9%)
ACETYLSALICYLIC ACID;ALUMINIUM GLYCINATE; MAGNESIUM CARBONATE	0	1 (0.7%)	1 (0.5%)
ACETYLSALICYLIC ACID;BUTALBITAL;CAFFEINE;CODEINE PHOSPHATE;PHENACETIN	0	1 (0.7%)	1 (0.5%)
ACETYLSALICYLIC ACID;GLYCINE	0	1 (0.7%)	1 (0.5%)
ACETYLSALICYLIC ACID;MAGNESIUM HYDROXIDE	1 (1.3%)	0	1 (0.5%)
ANALGESICS	1 (1.3%)	0	1 (0.5%)
ARTEMISIA ARGYI LEAF	1 (1.3%)	0	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ASCORBIC ACID;NOSCAPINE;PARACETAMOL; PSEUDOEPHEDRINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
BUPRENORPHINE	1 (1.3%)	0	1 (0.5%)
BUPRENORPHINE HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
CAFFEINE;CODEINE PHOSPHATE;PARACETAMOL	0	1 (0.7%)	1 (0.5%)
CAFFEINE;PAPAVER SOMNIFERUM LATEX;PARACETAMOL	0	1 (0.7%)	1 (0.5%)
CAFFEINE;PARACETAMOL	0	1 (0.7%)	1 (0.5%)
CHLORPHENAMINE MALEATE;DEXTROMETHORPHAN HYDROBROMIDE;PARACETAMOL	1 (1.3%)	0	1 (0.5%)
CLOMIPRAMINE	0	1 (0.7%)	1 (0.5%)
CODEINE PHOSPHATE HEMIHYDRATE	0	1 (0.7%)	1 (0.5%)
CODEINE;PARACETAMOL	1 (1.3%)	0	1 (0.5%)
CORTICOSTEROID NOS	0	1 (0.7%)	1 (0.5%)
DICLOFENAC;PARACETAMOL	1 (1.3%)	0	1 (0.5%)
HYDROCODONE BITARTRATE;PARACETAMOL	0	1 (0.7%)	1 (0.5%)
HYDROMORPHONE	1 (1.3%)	0	1 (0.5%)
HYOSCINE;METAMIZOLE	0	1 (0.7%)	1 (0.5%)
LEVOMENTHOL	0	1 (0.7%)	1 (0.5%)
METAMIZOLE SODIUM;TRIACETONAMINE TOSILATE	0	1 (0.7%)	1 (0.5%)
METOPROLOL TARTRATE	0	1 (0.7%)	1 (0.5%)
MORPHINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
NALOXONE HYDROCHLORIDE;TILIDINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
NEFOPAM HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
OXYCODONE HYDROCHLORIDE TRIHYDRATE	1 (1.3%)	0	1 (0.5%)
PAPAVER SOMNIFERUM	0	1 (0.7%)	1 (0.5%)
PAPAVER SOMNIFERUM TINCTURE	0	1 (0.7%)	1 (0.5%)
PARACETAMOL;TRAMADOL	0	1 (0.7%)	1 (0.5%)
PLATYCODON GRANDIFLORUS ROOT	0	1 (0.7%)	1 (0.5%)
PROPACETAMOL	0	1 (0.7%)	1 (0.5%)
PROPRANOLOL HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
SALICYLIC ACID	0	1 (0.7%)	1 (0.5%)
SODIUM CHLORIDE;TRAMADOL	1 (1.3%)	0	1 (0.5%)
VALPROATE SEMISODIUM	0	1 (0.7%)	1 (0.5%)
VENLAFAXINE	0	1 (0.7%)	1 (0.5%)
VENLAFAXINE HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
ZOLMITRIPTAN	1 (1.3%)	0	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ANESTHETICS			
Total number of patients with at least one treatment	4 (5.3%)	16 (11.0%)	20 (9.0%)
Total number of treatments	5	28	33
LIDOCAINE	1 (1.3%)	4 (2.7%)	5 (2.3%)
FENTANYL	1 (1.3%)	3 (2.1%)	4 (1.8%)
FENTANYL CITRATE	1 (1.3%)	3 (2.1%)	4 (1.8%)
LIDOCAINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
EPINEPHRINE;LIDOCAINE	0	2 (1.4%)	2 (0.9%)
LIDOCAINE;PRILOCAINE	0	2 (1.4%)	2 (0.9%)
ALKONIUM BROMIDE;TRIMECAINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
CAMPHORSULFONIC ACID;PROCAINE	1 (1.3%)	0	1 (0.5%)
MEPIVACAINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
OXETACAINE	0	1 (0.7%)	1 (0.5%)
PROCAINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
PROPOFOL	0	1 (0.7%)	1 (0.5%)
REMIFENTANIL HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
ANTI-ACNE PREPARATIONS			
Total number of patients with at least one treatment	69 (90.8%)	130 (89.0%)	199 (89.6%)
Total number of treatments	733	1064	1797
DEXAMETHASONE	51 (67.1%)	100 (68.5%)	151 (68.0%)
DEXAMETHASONE SODIUM PHOSPHATE	9 (11.8%)	22 (15.1%)	31 (14.0%)
IBUPROFEN	9 (11.8%)	16 (11.0%)	25 (11.3%)
METHYLPREDNISOLONE SODIUM SUCCINATE	4 (5.3%)	10 (6.8%)	14 (6.3%)
METHYLPREDNISOLONE	3 (3.9%)	6 (4.1%)	9 (4.1%)
FLUOROMETHOLONE	3 (3.9%)	2 (1.4%)	5 (2.3%)
AZITHROMYCIN	0	4 (2.7%)	4 (1.8%)
CLINDAMYCIN	3 (3.9%)	1 (0.7%)	4 (1.8%)
CHLORHEXIDINE GLUCONATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
DIMETICONE	1 (1.3%)	2 (1.4%)	3 (1.4%)
NADIFLOXACIN	1 (1.3%)	2 (1.4%)	3 (1.4%)
CHLORAMPHENICOL	0	2 (1.4%)	2 (0.9%)
CLINDAMYCIN PHOSPHATE	0	2 (1.4%)	2 (0.9%)
ADAPALENE	0	1 (0.7%)	1 (0.5%)
CHLORHEXIDINE	0	1 (0.7%)	1 (0.5%)
DEXAMETHASONE VALERATE	0	1 (0.7%)	1 (0.5%)
ERYTHROMYCIN;ZINC ACETATE	0	1 (0.7%)	1 (0.5%)
LACTOFERRIN	0	1 (0.7%)	1 (0.5%)
SALICYLIC ACID	0	1 (0.7%)	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ANTI-PARKINSON DRUGS			
Total number of patients with at least one treatment	25 (32.9%)	47 (32.2%)	72 (32.4%)
Total number of treatments	224	256	480
DIPHENHYDRAMINE HYDROCHLORIDE	13 (17.1%)	24 (16.4%)	37 (16.7%)
DIPHENHYDRAMINE	14 (18.4%)	21 (14.4%)	35 (15.8%)
BENSERAZIDE HYDROCHLORIDE;LEVODOPA	0	1 (0.7%)	1 (0.5%)
HYDROGEN PEROXIDE	0	1 (0.7%)	1 (0.5%)
ANTIANEMIC PREPARATIONS			
Total number of patients with at least one treatment	11 (14.5%)	28 (19.2%)	39 (17.6%)
Total number of treatments	18	63	81
FERROUS SULFATE	2 (2.6%)	5 (3.4%)	7 (3.2%)
FERRIC HYDROXIDE POLYMALTOSE COMPLEX	1 (1.3%)	5 (3.4%)	6 (2.7%)
FOLIC ACID	2 (2.6%)	3 (2.1%)	5 (2.3%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE HYDROCHLORIDE	2 (2.6%)	2 (1.4%)	4 (1.8%)
DARBEPOETIN ALFA	0	4 (2.7%)	4 (1.8%)
MECOBALAMIN	2 (2.6%)	2 (1.4%)	4 (1.8%)
ASCORBIC ACID;FERROUS SULFATE	0	3 (2.1%)	3 (1.4%)
EPOETIN ALFA	0	3 (2.1%)	3 (1.4%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE DISULFIDE PHOSPHATE	0	2 (1.4%)	2 (0.9%)
VITAMIN B12 NOS	1 (1.3%)	1 (0.7%)	2 (0.9%)
ASCORBIC ACID;FOLIC ACID;IRON	1 (1.3%)	0	1 (0.5%)
CALCIUM FOLINATE;IRON SUCCINYL-PROTEIN COMPLEX	1 (1.3%)	0	1 (0.5%)
COPPER GLUCONATE;FERROUS GLUCONATE;MANGANESE GLUCONATE	0	1 (0.7%)	1 (0.5%)
CYANOCOBALAMIN	1 (1.3%)	0	1 (0.5%)
EPOETIN NOS	1 (1.3%)	0	1 (0.5%)
ERYTHROPOIETIN HUMAN	0	1 (0.7%)	1 (0.5%)
FERRIC CARBOXYMALTOSE	0	1 (0.7%)	1 (0.5%)
FERROUS GLUCONATE	1 (1.3%)	0	1 (0.5%)
FERROUS SODIUM CITRATE	0	1 (0.7%)	1 (0.5%)
IRON	0	1 (0.7%)	1 (0.5%)
IRON SUCCINYL-PROTEIN COMPLEX	0	1 (0.7%)	1 (0.5%)
LACTOFERRIN	0	1 (0.7%)	1 (0.5%)
SACCHARATED IRON OXIDE	0	1 (0.7%)	1 (0.5%)
VITAMIN B NOS	0	1 (0.7%)	1 (0.5%)
ANTIBACTERIALS FOR SYSTEMIC USE			
Total number of patients with at least one treatment	41 (53.9%)	68 (46.6%)	109 (49.1%)
Total number of treatments	88	220	308
LEVOFLOXACIN	9 (11.8%)	17 (11.6%)	26 (11.7%)

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ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
CIPROFLOXACIN	8 (10.5%)	13 (8.9%)	21 (9.5%)
AMOXICILLIN	2 (2.6%)	10 (6.8%)	12 (5.4%)
AMOXICILLIN;CLAVULANATE POTASSIUM	4 (5.3%)	8 (5.5%)	12 (5.4%)
CEFTRIAXONE	2 (2.6%)	7 (4.8%)	9 (4.1%)
METRONIDAZOLE	2 (2.6%)	7 (4.8%)	9 (4.1%)
AMOXICILLIN;CLAVULANIC ACID	4 (5.3%)	4 (2.7%)	8 (3.6%)
FOSFOMYCIN TROMETAMOL	4 (5.3%)	2 (1.4%)	6 (2.7%)
CEFDITOREN PIVOXIL	0	5 (3.4%)	5 (2.3%)
CEFUROXIME	1 (1.3%)	4 (2.7%)	5 (2.3%)
FUSIDIC ACID	3 (3.9%)	2 (1.4%)	5 (2.3%)
PIPERACILLIN SODIUM;TAZOBACTAM SODIUM	2 (2.6%)	3 (2.1%)	5 (2.3%)
SULFAMETHOXAZOLE;TRIMETHOPRIM	2 (2.6%)	3 (2.1%)	5 (2.3%)
AZITHROMYCIN	0	4 (2.7%)	4 (1.8%)
CLINDAMYCIN	3 (3.9%)	1 (0.7%)	4 (1.8%)
AMOXICILLIN TRIHYDRATE	0	3 (2.1%)	3 (1.4%)
CEFACLOR	1 (1.3%)	2 (1.4%)	3 (1.4%)
CEFADROXIL	3 (3.9%)	0	3 (1.4%)
CEFAZOLIN	1 (1.3%)	2 (1.4%)	3 (1.4%)
CEFTRIAXONE SODIUM	1 (1.3%)	2 (1.4%)	3 (1.4%)
CLARITHROMYCIN	0	3 (2.1%)	3 (1.4%)
GENTAMICIN SULFATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
MOXIFLOXACIN HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
NITROXOLINE	3 (3.9%)	0	3 (1.4%)
ANTIBIOTICS	1 (1.3%)	1 (0.7%)	2 (0.9%)
CEFAZOLIN SODIUM	0	2 (1.4%)	2 (0.9%)
CEFCAPENE PIVOXIL HYDROCHLORIDE	0	2 (1.4%)	2 (0.9%)
CEFCAPENE PIVOXIL HYDROCHLORIDE HYDRATE	2 (2.6%)	0	2 (0.9%)
CEFDINIR	1 (1.3%)	1 (0.7%)	2 (0.9%)
CEFUROXIME AXETIL	1 (1.3%)	1 (0.7%)	2 (0.9%)
CHLORAMPHENICOL	0	2 (1.4%)	2 (0.9%)
CLAVULANIC ACID	0	2 (1.4%)	2 (0.9%)
CLINDAMYCIN PHOSPHATE	0	2 (1.4%)	2 (0.9%)
FOSFOMYCIN	0	2 (1.4%)	2 (0.9%)
GATIFLOXACIN	1 (1.3%)	1 (0.7%)	2 (0.9%)
MEROPENEM	0	2 (1.4%)	2 (0.9%)
MEROPENEM TRIHYDRATE	0	2 (1.4%)	2 (0.9%)
NEOMYCIN	0	2 (1.4%)	2 (0.9%)
NEOMYCIN SULFATE	0	2 (1.4%)	2 (0.9%)
OFLOXACIN	0	2 (1.4%)	2 (0.9%)
SULFAMETHOXAZOLE	1 (1.3%)	1 (0.7%)	2 (0.9%)
TETRACYCLINE	0	2 (1.4%)	2 (0.9%)
VANCOMYCIN	0	2 (1.4%)	2 (0.9%)
AMIKACIN	0	1 (0.7%)	1 (0.5%)
AMIKACIN SULFATE	0	1 (0.7%)	1 (0.5%)
AMOXICILLIN SODIUM;CLAVULANATE POTASSIUM	0	1 (0.7%)	1 (0.5%)
AMOXICILLIN TRIHYDRATE;CLAVULANATE POTASSIUM	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
AMOXICILLIN;SULBACTAM	0	1 (0.7%)	1 (0.5%)
AMPICILLIN	0	1 (0.7%)	1 (0.5%)
ARTEMISIA ARGYI LEAF	1 (1.3%)	0	1 (0.5%)
BACAMPICILLIN HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
BENZYLPENICILLIN	0	1 (0.7%)	1 (0.5%)
CEFALEXIN	0	1 (0.7%)	1 (0.5%)
CEFEPIME HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
CEFIXIME	0	1 (0.7%)	1 (0.5%)
CEFMETAZOLE SODIUM	0	1 (0.7%)	1 (0.5%)
CEFOTIAM HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
CEFPODOXIME PROXETIL	0	1 (0.7%)	1 (0.5%)
CEFRADINE	0	1 (0.7%)	1 (0.5%)
CEFTAZIDIME	1 (1.3%)	0	1 (0.5%)
CHLORTETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
D-MANNOSE	0	1 (0.7%)	1 (0.5%)
DICLOXACILLIN	1 (1.3%)	0	1 (0.5%)
DICLOXACILLIN SODIUM MONOHYDRATE	1 (1.3%)	0	1 (0.5%)
FOSFOMYCIN CALCIUM	0	1 (0.7%)	1 (0.5%)
FURAZIDIN POTASSIUM	1 (1.3%)	0	1 (0.5%)
MOXIFLOXACIN	0	1 (0.7%)	1 (0.5%)
NITROFURANTOIN	0	1 (0.7%)	1 (0.5%)
OXACILLIN	0	1 (0.7%)	1 (0.5%)
OXYTETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
PHENOXYMETHYLPENICILLIN	1 (1.3%)	0	1 (0.5%)
PIPERACILLIN	1 (1.3%)	0	1 (0.5%)
PLATYCODON GRANDIFLORUS ROOT	0	1 (0.7%)	1 (0.5%)
PROCAINE BENZYLPENICILLIN	1 (1.3%)	0	1 (0.5%)
SULTAMICILLIN TOSILATE	0	1 (0.7%)	1 (0.5%)
TAZOBACTAM	1 (1.3%)	0	1 (0.5%)
TETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
TRIMETHOPRIM	0	1 (0.7%)	1 (0.5%)
VANCOMYCIN HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE			
Total number of patients with at least one treatment	29 (38.2%)	53 (36.3%)	82 (36.9%)
Total number of treatments	43	110	153
LEVOFLOXACIN	9 (11.8%)	17 (11.6%)	26 (11.7%)
CIPROFLOXACIN	8 (10.5%)	13 (8.9%)	21 (9.5%)
METRONIDAZOLE	2 (2.6%)	7 (4.8%)	9 (4.1%)
ACICLOVIR	0	6 (4.1%)	6 (2.7%)
FUSIDIC ACID	3 (3.9%)	2 (1.4%)	5 (2.3%)
MUPIROCIN	3 (3.9%)	1 (0.7%)	4 (1.8%)
CLARITHROMYCIN	0	3 (2.1%)	3 (1.4%)
GENTAMICIN SULFATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
NADIFLOXACIN	1 (1.3%)	2 (1.4%)	3 (1.4%)
VIDARABINE	1 (1.3%)	2 (1.4%)	3 (1.4%)
ANTIBIOTICS	1 (1.3%)	1 (0.7%)	2 (0.9%)
CHLORAMPHENICOL	0	2 (1.4%)	2 (0.9%)
LYSOZYME CHLORIDE	0	2 (1.4%)	2 (0.9%)
NEOMYCIN	0	2 (1.4%)	2 (0.9%)
NEOMYCIN SULFATE	0	2 (1.4%)	2 (0.9%)
OFLOXACIN	0	2 (1.4%)	2 (0.9%)
SULFADIAZINE SILVER	1 (1.3%)	1 (0.7%)	2 (0.9%)
TETRACYCLINE	0	2 (1.4%)	2 (0.9%)
AMIKACIN	0	1 (0.7%)	1 (0.5%)
AMIKACIN SULFATE	0	1 (0.7%)	1 (0.5%)
BACITRACIN;NEOMYCIN	0	1 (0.7%)	1 (0.5%)
BACITRACIN;NEOMYCIN SULFATE	0	1 (0.7%)	1 (0.5%)
BENZYLPENICILLIN	0	1 (0.7%)	1 (0.5%)
CHLORAMPHENICOL;METHYLURACIL	1 (1.3%)	0	1 (0.5%)
CHLORHEXIDINE GLUCONATE;METRONIDAZOLE BENZOATE	1 (1.3%)	0	1 (0.5%)
CHLORTETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
INTERFERON ALFA-2B	1 (1.3%)	0	1 (0.5%)
LACTOFERRIN	0	1 (0.7%)	1 (0.5%)
MOXIFLOXACIN	0	1 (0.7%)	1 (0.5%)
OXYTETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
PROCAINE BENZYLPENICILLIN	1 (1.3%)	0	1 (0.5%)
TETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ ANTIINFECTIVE AGENTS			
Total number of patients with at least one treatment	26 (34.2%)	75 (51.4%)	101 (45.5%)
Total number of treatments	47	183	230
HYDROCORTISONE	5 (6.6%)	13 (8.9%)	18 (8.1%)
BETAMETHASONE BUTYRATE PROPIONATE	2 (2.6%)	7 (4.8%)	9 (4.1%)
PREDNISOLONE	2 (2.6%)	7 (4.8%)	9 (4.1%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
PREDNISONE	3 (3.9%)	5 (3.4%)	8 (3.6%)
BETAMETHASONE	5 (6.6%)	2 (1.4%)	7 (3.2%)
DIOSMECTITE	1 (1.3%)	6 (4.1%)	7 (3.2%)
HYDROCORTISONE SODIUM SUCCINATE	1 (1.3%)	5 (3.4%)	6 (2.7%)
METHYLURACIL	3 (3.9%)	3 (2.1%)	6 (2.7%)
BETAMETHASONE VALERATE	1 (1.3%)	4 (2.7%)	5 (2.3%)
ATROPINE SULFATE;DIPHENOXYLATE HYDROCHLORIDE	1 (1.3%)	3 (2.1%)	4 (1.8%)
HYDROCORTISONE BUTYRATE	0	4 (2.7%)	4 (1.8%)
SACCHAROMYCES BOULARDII	0	4 (2.7%)	4 (1.8%)
BECLOMETASONE DIPROPIONATE	0	3 (2.1%)	3 (1.4%)
MICONAZOLE	0	3 (2.1%)	3 (1.4%)
ORAL REHYDRATION SALT FORMULATIONS	0	3 (2.1%)	3 (1.4%)
PROBIOTICS NOS	0	3 (2.1%)	3 (1.4%)
RACECADOTRIL	0	3 (2.1%)	3 (1.4%)
ANTIBIOTICS	1 (1.3%)	1 (0.7%)	2 (0.9%)
BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM; ENTEROCOCCUS FAECALIS	1 (1.3%)	1 (0.7%)	2 (0.9%)
BETAMETHASONE DIPROPIONATE	1 (1.3%)	1 (0.7%)	2 (0.9%)
CODEINE	0	2 (1.4%)	2 (0.9%)
NEOMYCIN	0	2 (1.4%)	2 (0.9%)
NEOMYCIN SULFATE	0	2 (1.4%)	2 (0.9%)
POLYMETHYLSILOXANE POLYHYDRATE	2 (2.6%)	0	2 (0.9%)
VANCOMYCIN	0	2 (1.4%)	2 (0.9%)
AESCULUS HIPPOCASTANUM	0	1 (0.7%)	1 (0.5%)
ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER; ATRACTYLODES SPP. RHIZOME;CINNAMOMUM CASSIA BARK; POLYPORUS UMBELLATUS SCLEROTIUM;PORIA COCOS SCLEROTIUM	0	1 (0.7%)	1 (0.5%)
AMPHOTERICIN B	0	1 (0.7%)	1 (0.5%)
ANTIBIOTICS-RESISTANT LACTIC ACID BACTERIAE	0	1 (0.7%)	1 (0.5%)
BACILLUS COAGULANS;CYANOCOBALAMIN;FOLIC ACID	0	1 (0.7%)	1 (0.5%)
BACILLUS LICHENFORMIS	0	1 (0.7%)	1 (0.5%)
BACITRACIN;NEOMYCIN	0	1 (0.7%)	1 (0.5%)
BACITRACIN;NEOMYCIN SULFATE	0	1 (0.7%)	1 (0.5%)
BERBERINE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)
BIFIDOBACTERIUM BIFIDUM;ENTEROCOCCUS FAECALIS; LACTOBACILLUS ACIDOPHILUS	0	1 (0.7%)	1 (0.5%)
BISMUTH SUBSALICYLATE	0	1 (0.7%)	1 (0.5%)
BUDESONIDE	0	1 (0.7%)	1 (0.5%)
CAMELLIA SINENSIS	0	1 (0.7%)	1 (0.5%)
CELLULOSE MICROCRYSTALLINE;HEMICELLULOSE;LIGNIN; PECTIN	0	1 (0.7%)	1 (0.5%)
CHARCOAL, ACTIVATED	0	1 (0.7%)	1 (0.5%)
CODEINE PHOSPHATE HEMIHYDRATE	0	1 (0.7%)	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
COPTIS SPP. RHIZOME;GLYCYRRHIZA SPP. ROOT;PANAX GINSENG ROOT;PINELLIA TERNATA TUBER;SCUTELLARIA BAICALENSIS ROOT;ZINGIBER OFFICINALE PROCESSED RHIZOME;ZIZIPHUS JUJUBA FRUIT	0	1 (0.7%)	1 (0.5%)
CORTICOSTEROID NOS	0	1 (0.7%)	1 (0.5%)
ENTEROCOCCUS FAECALIS	0	1 (0.7%)	1 (0.5%)
GLUCOSE;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE	0	1 (0.7%)	1 (0.5%)
LACTOBACILLUS ACIDOPHILUS	0	1 (0.7%)	1 (0.5%)
LACTOBACILLUS CASEI	0	1 (0.7%)	1 (0.5%)
LACTOBACILLUS RHAMNOSUS	0	1 (0.7%)	1 (0.5%)
LACTOMIN	0	1 (0.7%)	1 (0.5%)
LEVOMENTHOL	0	1 (0.7%)	1 (0.5%)
LOPERAMIDE	0	1 (0.7%)	1 (0.5%)
LOPERAMIDE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
NYSTATIN	1 (1.3%)	0	1 (0.5%)
PAPAVER SOMNIFERUM	0	1 (0.7%)	1 (0.5%)
PAPAVER SOMNIFERUM TINCTURE	0	1 (0.7%)	1 (0.5%)
PREDNISOLONE METASULFOBENZOATE SODIUM	1 (1.3%)	0	1 (0.5%)
SILICON DIOXIDE	0	1 (0.7%)	1 (0.5%)
VANCOMYCIN HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ANTIEMETICS AND ANTINAUSEANTS			
Total number of patients with at least one treatment	58 (76.3%)	119 (81.5%)	177 (79.7%)
Total number of treatments	719	891	1610
ONDANSETRON	38 (50.0%)	71 (48.6%)	109 (49.1%)
DIPHENHYDRAMINE HYDROCHLORIDE	13 (17.1%)	24 (16.4%)	37 (16.7%)
DIPHENHYDRAMINE	14 (18.4%)	21 (14.4%)	35 (15.8%)
METOCLOPRAMIDE HYDROCHLORIDE	5 (6.6%)	23 (15.8%)	28 (12.6%)
METOCLOPRAMIDE	8 (10.5%)	19 (13.0%)	27 (12.2%)
DIMENHYDRINATE	3 (3.9%)	7 (4.8%)	10 (4.5%)
ONDANSETRON HYDROCHLORIDE	2 (2.6%)	7 (4.8%)	9 (4.1%)
PROCHLORPERAZINE	1 (1.3%)	7 (4.8%)	8 (3.6%)
GRANISETRON	2 (2.6%)	5 (3.4%)	7 (3.2%)
DOMPERIDONE	0	5 (3.4%)	5 (2.3%)
GRANISETRON HYDROCHLORIDE	2 (2.6%)	3 (2.1%)	5 (2.3%)
PALONOSETRON HYDROCHLORIDE	1 (1.3%)	4 (2.7%)	5 (2.3%)
PROMETHAZINE	3 (3.9%)	2 (1.4%)	5 (2.3%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE HYDROCHLORIDE	2 (2.6%)	2 (1.4%)	4 (1.8%)
HYDROXYZINE	0	4 (2.7%)	4 (1.8%)
LEVOSULPIRIDE	1 (1.3%)	3 (2.1%)	4 (1.8%)
RAMOSETRON HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
ALIZAPRIDE HYDROCHLORIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE DISULFIDE PHOSPHATE	0	2 (1.4%)	2 (0.9%)
PROCHLORPERAZINE MALEATE	0	2 (1.4%)	2 (0.9%)
ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER; ATRACTYLODES SPP. RHIZOME;CINNAMOMUM CASSIA BARK; POLYPORUS UMBELLATUS SCLEROTIUM;PORIA COCOS SCLEROTIUM	0	1 (0.7%)	1 (0.5%)
DIFENIDOL	0	1 (0.7%)	1 (0.5%)
DIFENIDOL HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
FOSAPREPITANT MEGLUMINE	0	1 (0.7%)	1 (0.5%)
HYDROXYZINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
HYOSCINE HYDROBROMIDE	0	1 (0.7%)	1 (0.5%)
HYOSCINE;METAMIZOLE	0	1 (0.7%)	1 (0.5%)
MECLOZINE	0	1 (0.7%)	1 (0.5%)
TROPISETRON	0	1 (0.7%)	1 (0.5%)

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ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ANTIEPILEPTICS			
Total number of patients with at least one treatment	29 (38.2%)	40 (27.4%)	69 (31.1%)
Total number of treatments	50	100	150
PREGABALIN	18 (23.7%)	23 (15.8%)	41 (18.5%)
LORAZEPAM	4 (5.3%)	8 (5.5%)	12 (5.4%)
GABAPENTIN	4 (5.3%)	5 (3.4%)	9 (4.1%)
CLONAZEPAM	0	6 (4.1%)	6 (2.7%)
DIAZEPAM	2 (2.6%)	3 (2.1%)	5 (2.3%)
MIDAZOLAM	0	4 (2.7%)	4 (1.8%)
MAGNESIUM SULFATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
ACETAZOLAMIDE	1 (1.3%)	0	1 (0.5%)
LAMOTRIGINE	1 (1.3%)	0	1 (0.5%)
LEVETIRACETAM	1 (1.3%)	0	1 (0.5%)
MIDAZOLAM HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
VALPROATE SEMISODIUM	0	1 (0.7%)	1 (0.5%)
ANTIFUNGALS FOR DERMATOLOGICAL USE			
Total number of patients with at least one treatment	9 (11.8%)	17 (11.6%)	26 (11.7%)
Total number of treatments	12	26	38
UREA	2 (2.6%)	5 (3.4%)	7 (3.2%)
FLUCONAZOLE	2 (2.6%)	4 (2.7%)	6 (2.7%)
MICONAZOLE	0	3 (2.1%)	3 (1.4%)
ANTIBIOTICS	1 (1.3%)	1 (0.7%)	2 (0.9%)
AMOROLFINE	0	1 (0.7%)	1 (0.5%)
AMPHOTERICIN B	0	1 (0.7%)	1 (0.5%)
BUTENAFINE HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
CICLOPIROX OLAMINE	1 (1.3%)	0	1 (0.5%)
CLOTRIMAZOLE	0	1 (0.7%)	1 (0.5%)
ECONAZOLE	0	1 (0.7%)	1 (0.5%)
ECONAZOLE NITRATE	0	1 (0.7%)	1 (0.5%)
ECONAZOLE;TRIAMCINOLONE	0	1 (0.7%)	1 (0.5%)
EFINACONAZOLE	1 (1.3%)	0	1 (0.5%)
FENTICONAZOLE NITRATE	0	1 (0.7%)	1 (0.5%)
HEXETIDINE	1 (1.3%)	0	1 (0.5%)
KETOCONAZOLE	1 (1.3%)	0	1 (0.5%)
NYSTATIN	1 (1.3%)	0	1 (0.5%)
SALICYLIC ACID	0	1 (0.7%)	1 (0.5%)
SULCONAZOLE	0	1 (0.7%)	1 (0.5%)
TERBINAFINE	1 (1.3%)	0	1 (0.5%)
TIOCONAZOLE	0	1 (0.7%)	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ANTIGOUT PREPARATIONS			
Total number of patients with at least one treatment	0	4 (2.7%)	4 (1.8%)
Total number of treatments	0	4	4
ALLOPURINOL	0	3 (2.1%)	3 (1.4%)
DOCOSAHEXAENOIC ACID;EICOSAPENTAENOIC ACID	0	1 (0.7%)	1 (0.5%)
ANTIHEMORRHAGICS			
Total number of patients with at least one treatment	2 (2.6%)	10 (6.8%)	12 (5.4%)
Total number of treatments	3	16	19
TRANEXAMIC ACID	1 (1.3%)	6 (4.1%)	7 (3.2%)
CARBAZOCHROME SODIUM SULFONATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
ETAMSILATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
AMINOCAPROIC ACID	0	1 (0.7%)	1 (0.5%)
CORDYCEPS SINENSIS	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ANTIHISTAMINES FOR SYSTEMIC USE			
Total number of patients with at least one treatment	70 (92.1%)	132 (90.4%)	202 (91.0%)
Total number of treatments	756	1006	1762
CHLORPHENAMINE	15 (19.7%)	29 (19.9%)	44 (19.8%)
DIPHENHYDRAMINE HYDROCHLORIDE	13 (17.1%)	24 (16.4%)	37 (16.7%)
DIPHENHYDRAMINE	14 (18.4%)	21 (14.4%)	35 (15.8%)
DEXCHLORPHENIRAMINE MALEATE	9 (11.8%)	16 (11.0%)	25 (11.3%)
CLEMASTINE FUMARATE	5 (6.6%)	9 (6.2%)	14 (6.3%)
LEVOCETIRIZINE DIHYDROCHLORIDE	6 (7.9%)	8 (5.5%)	14 (6.3%)
CHLOROPYRAMINE HYDROCHLORIDE	5 (6.6%)	8 (5.5%)	13 (5.9%)
DEXCHLORPHENIRAMINE	3 (3.9%)	9 (6.2%)	12 (5.4%)
CLEMASTINE	2 (2.6%)	9 (6.2%)	11 (5.0%)
FEXOFENADINE HYDROCHLORIDE	3 (3.9%)	8 (5.5%)	11 (5.0%)
CHLORPHENAMINE MALEATE	5 (6.6%)	5 (3.4%)	10 (4.5%)
DIMENHYDRINATE	3 (3.9%)	7 (4.8%)	10 (4.5%)
CETIRIZINE	3 (3.9%)	5 (3.4%)	8 (3.6%)
LORATADINE	3 (3.9%)	4 (2.7%)	7 (3.2%)
BILASTINE	1 (1.3%)	4 (2.7%)	5 (2.3%)
DESLORATADINE	2 (2.6%)	3 (2.1%)	5 (2.3%)
FEXOFENADINE	1 (1.3%)	4 (2.7%)	5 (2.3%)
PROMETHAZINE	3 (3.9%)	2 (1.4%)	5 (2.3%)
BISULEPIN HYDROCHLORIDE	1 (1.3%)	3 (2.1%)	4 (1.8%)
CETIRIZINE HYDROCHLORIDE	1 (1.3%)	3 (2.1%)	4 (1.8%)
EBASTINE	2 (2.6%)	2 (1.4%)	4 (1.8%)
HYDROXYZINE	0	4 (2.7%)	4 (1.8%)
QUERCETIN	2 (2.6%)	2 (1.4%)	4 (1.8%)
DIMETINDENE	0	3 (2.1%)	3 (1.4%)
LEVOCETIRIZINE	0	3 (2.1%)	3 (1.4%)
OLOPATADINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
BEPOTASTINE BESILATE	0	2 (1.4%)	2 (0.9%)
BISULEPIN	0	2 (1.4%)	2 (0.9%)
CHLOROPYRAMINE	2 (2.6%)	0	2 (0.9%)
AZELASTINE	0	1 (0.7%)	1 (0.5%)
BEPOTASTINE SALICYLATE	0	1 (0.7%)	1 (0.5%)
BUCLIZINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
CYPROHEPTADINE HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
HYDROXYZINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
KETOTIFEN FUMARATE	0	1 (0.7%)	1 (0.5%)
MECLOZINE	0	1 (0.7%)	1 (0.5%)
OXOMEMAZINE	0	1 (0.7%)	1 (0.5%)
PIPRINHYDRINATE	0	1 (0.7%)	1 (0.5%)
RUPATADINE	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ANTIHYPERTENSIVES			
Total number of patients with at least one treatment	4 (5.3%)	4 (2.7%)	8 (3.6%)
Total number of treatments	8	5	13
MAGNESIUM SULFATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
CLONIDINE HYDROCHLORIDE	2 (2.6%)	0	2 (0.9%)
MOXONIDINE	2 (2.6%)	0	2 (0.9%)
TADALAFIL	0	1 (0.7%)	1 (0.5%)
URAPIDIL	0	1 (0.7%)	1 (0.5%)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS			
Total number of patients with at least one treatment	43 (56.6%)	66 (45.2%)	109 (49.1%)
Total number of treatments	289	496	785
IBUPROFEN	9 (11.8%)	16 (11.0%)	25 (11.3%)
ADEMETIONINE	9 (11.8%)	4 (2.7%)	13 (5.9%)
DICLOFENAC SODIUM	3 (3.9%)	7 (4.8%)	10 (4.5%)
KETOPROFEN	4 (5.3%)	5 (3.4%)	9 (4.1%)
LOXOPROFEN SODIUM DIHYDRATE	5 (6.6%)	4 (2.7%)	9 (4.1%)
NIMESULIDE	5 (6.6%)	4 (2.7%)	9 (4.1%)
DICLOFENAC	0	8 (5.5%)	8 (3.6%)
LOXOPROFEN SODIUM	3 (3.9%)	4 (2.7%)	7 (3.2%)
ACECLOFENAC	4 (5.3%)	2 (1.4%)	6 (2.7%)
CELECOXIB	3 (3.9%)	3 (2.1%)	6 (2.7%)
HEPARINOID	2 (2.6%)	4 (2.7%)	6 (2.7%)
KETOROLAC TROMETHAMINE	0	6 (4.1%)	6 (2.7%)
NAPROXEN	4 (5.3%)	2 (1.4%)	6 (2.7%)
BENZYDAMINE HYDROCHLORIDE	2 (2.6%)	3 (2.1%)	5 (2.3%)
MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER	2 (2.6%)	3 (2.1%)	5 (2.3%)
GUAIAZULENE	1 (1.3%)	3 (2.1%)	4 (1.8%)
KETOROLAC	3 (3.9%)	1 (0.7%)	4 (1.8%)
DEXKETOPROFEN TROMETAMOL	1 (1.3%)	2 (1.4%)	3 (1.4%)
ETORICOXIB	2 (2.6%)	1 (0.7%)	3 (1.4%)
LOXOPROFEN	0	3 (2.1%)	3 (1.4%)
MELOXICAM	1 (1.3%)	2 (1.4%)	3 (1.4%)
BROMFENAC SODIUM	1 (1.3%)	1 (0.7%)	2 (0.9%)
DEXKETOPROFEN	1 (1.3%)	1 (0.7%)	2 (0.9%)
ETOFENAMATE	0	2 (1.4%)	2 (0.9%)
INDOMETACIN	1 (1.3%)	1 (0.7%)	2 (0.9%)
LORNOXICAM	1 (1.3%)	1 (0.7%)	2 (0.9%)
MEFENAMIC ACID	0	2 (1.4%)	2 (0.9%)
NAPROXEN SODIUM	2 (2.6%)	0	2 (0.9%)
ASTRAGALUS SPP. ROOT;ATRACTYLODES SPP. RHIZOME; GLYCYRRHIZA SPP. ROOT;SINOMENIUM ACUTUM STEM; ZINGIBER OFFICINALE RHIZOME;ZIZIPHUS JUJUBA FRUIT	1 (1.3%)	0	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ATRACTYLODES LANCEA RHIZOME;CALCIUM SULFATE; EPHEDRA SPP. HERB;GLYCYRRHIZA SPP. ROOT;ZINGIBER OFFICINALE RHIZOME;ZIZIPHUS JUJUBA FRUIT	1 (1.3%)	0	1 (0.5%)
CURCUMIN	0	1 (0.7%)	1 (0.5%)
DICLOFENAC POTASSIUM	0	1 (0.7%)	1 (0.5%)
ESOMEPRAZOLE STRONTIUM;NAPROXEN	1 (1.3%)	0	1 (0.5%)
FISH OIL	0	1 (0.7%)	1 (0.5%)
FLURBIPROFEN AXETIL	0	1 (0.7%)	1 (0.5%)
GLUCOSAMINE	0	1 (0.7%)	1 (0.5%)
IBUPROFEN ARGININE	1 (1.3%)	0	1 (0.5%)
PELUBIPROFEN	1 (1.3%)	0	1 (0.5%)
RABBIT VACCINIA EXTRACT	1 (1.3%)	0	1 (0.5%)
ROSA CANINA	1 (1.3%)	0	1 (0.5%)
ANTIMYCOBACTERIALS			
Total number of patients with at least one treatment	1 (1.3%)	1 (0.7%)	2 (0.9%)
Total number of treatments	1	1	2
ANTIBIOTICS	1 (1.3%)	1 (0.7%)	2 (0.9%)
ANTIMYCOTICS FOR SYSTEMIC USE			
Total number of patients with at least one treatment	6 (7.9%)	6 (4.1%)	12 (5.4%)
Total number of treatments	6	10	16
FLUCONAZOLE	2 (2.6%)	4 (2.7%)	6 (2.7%)
MICONAZOLE	0	3 (2.1%)	3 (1.4%)
ANTIBIOTICS	1 (1.3%)	1 (0.7%)	2 (0.9%)
AMPHOTERICIN B	0	1 (0.7%)	1 (0.5%)
ITRACONAZOLE	1 (1.3%)	0	1 (0.5%)
KETOCONAZOLE	1 (1.3%)	0	1 (0.5%)
NYSTATIN	1 (1.3%)	0	1 (0.5%)
ANTINEOPLASTIC AGENTS			
Total number of patients with at least one treatment	4 (5.3%)	5 (3.4%)	9 (4.1%)
Total number of treatments	10	8	18
CELECOXIB	3 (3.9%)	3 (2.1%)	6 (2.7%)
PROPRANOLOL	0	2 (1.4%)	2 (0.9%)
PROPRANOLOL HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ANTIOBESITY PREPARATIONS, EXCL. DIET PRODUCTS			
Total number of patients with at least one treatment	1 (1.3%)	2 (1.4%)	3 (1.4%)
Total number of treatments	2	2	4
ASTRAGALUS SPP. ROOT;ATRACTYLODES SPP. RHIZOME; GLYCYRRHIZA SPP. ROOT;SINOMENIUM ACUTUM STEM; ZINGIBER OFFICINALE RHIZOME;ZIZIPHUS JUJUBA FRUIT	1 (1.3%)	0	1 (0.5%)
CAMELLIA SINENSIS	0	1 (0.7%)	1 (0.5%)
ORLISTAT	0	1 (0.7%)	1 (0.5%)
ANTIPROTOZOALS			
Total number of patients with at least one treatment	2 (2.6%)	13 (8.9%)	15 (6.8%)
Total number of treatments	2	15	17
METRONIDAZOLE	2 (2.6%)	7 (4.8%)	9 (4.1%)
MICONAZOLE	0	3 (2.1%)	3 (1.4%)
OFLOXACIN	0	2 (1.4%)	2 (0.9%)
CLOTRIMAZOLE	0	1 (0.7%)	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.			
Total number of patients with at least one treatment	69 (90.8%)	127 (87.0%)	196 (88.3%)
Total number of treatments	751	980	1731
CHLORPHENAMINE	15 (19.7%)	29 (19.9%)	44 (19.8%)
DIPHENHYDRAMINE HYDROCHLORIDE	13 (17.1%)	24 (16.4%)	37 (16.7%)
DIPHENHYDRAMINE	14 (18.4%)	21 (14.4%)	35 (15.8%)
DEXCHLORPHENIRAMINE MALEATE	9 (11.8%)	16 (11.0%)	25 (11.3%)
CLEMASTINE FUMARATE	5 (6.6%)	9 (6.2%)	14 (6.3%)
LEVOCETIRIZINE DIHYDROCHLORIDE	6 (7.9%)	8 (5.5%)	14 (6.3%)
CHLOROPYRAMINE HYDROCHLORIDE	5 (6.6%)	8 (5.5%)	13 (5.9%)
DEXCHLORPHENIRAMINE	3 (3.9%)	9 (6.2%)	12 (5.4%)
CLEMASTINE	2 (2.6%)	9 (6.2%)	11 (5.0%)
FEXOFENADINE HYDROCHLORIDE	3 (3.9%)	8 (5.5%)	11 (5.0%)
CHLORPHENAMINE MALEATE	5 (6.6%)	5 (3.4%)	10 (4.5%)
CETIRIZINE	3 (3.9%)	5 (3.4%)	8 (3.6%)
LORATADINE	3 (3.9%)	4 (2.7%)	7 (3.2%)
BILASTINE	1 (1.3%)	4 (2.7%)	5 (2.3%)
DESLORATADINE	2 (2.6%)	3 (2.1%)	5 (2.3%)
FEXOFENADINE	1 (1.3%)	4 (2.7%)	5 (2.3%)
LIDOCAINE	1 (1.3%)	4 (2.7%)	5 (2.3%)
PROMETHAZINE	3 (3.9%)	2 (1.4%)	5 (2.3%)
CETIRIZINE HYDROCHLORIDE	1 (1.3%)	3 (2.1%)	4 (1.8%)
EBASTINE	2 (2.6%)	2 (1.4%)	4 (1.8%)
HYDROXYZINE	0	4 (2.7%)	4 (1.8%)
CAMPHOR;CHLORPHENAMINE MALEATE;HEXACHLOROPHENE; LIDOCAINE HYDROCHLORIDE;MENTHOL;METHYL SALICYLATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
DIMETINDENE	0	3 (2.1%)	3 (1.4%)
LEVOCETIRIZINE	0	3 (2.1%)	3 (1.4%)
LIDOCAINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
OLOPATADINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
BENZOCAINE;CHLORPHENAMINE MALEATE	1 (1.3%)	1 (0.7%)	2 (0.9%)
CAMPHOR	0	2 (1.4%)	2 (0.9%)
CHLOROPYRAMINE	2 (2.6%)	0	2 (0.9%)
LIDOCAINE;PRILOCAINE	0	2 (1.4%)	2 (0.9%)
ATRACTYLODES LANCEA RHIZOME;CALCIUM SULFATE; EPHEDRA SPP. HERB;GLYCYRRHIZA SPP. ROOT;ZINGIBER OFFICINALE RHIZOME;ZIZIPHUS JUJUBA FRUIT	1 (1.3%)	0	1 (0.5%)
CALAMINE	1 (1.3%)	0	1 (0.5%)
CYPROHEPTADINE HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
DOXEPIN HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
HYDROXYZINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
KETOTIFEN FUMARATE	0	1 (0.7%)	1 (0.5%)
LEVOMENTHOL	0	1 (0.7%)	1 (0.5%)
RUPATADINE	0	1 (0.7%)	1 (0.5%)

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Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ANTISEPTICS AND DISINFECTANTS			
Total number of patients with at least one treatment	5 (6.6%)	13 (8.9%)	18 (8.1%)
Total number of treatments	6	15	21
CHLORHEXIDINE GLUCONATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
POVIDONE-IODINE	0	3 (2.1%)	3 (1.4%)
ANTIMONY POTASSIUM TARTRATE	0	2 (1.4%)	2 (0.9%)
ALKONIUM BROMIDE;TRIMECAINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
ALUMINIUM ACETATE	1 (1.3%)	0	1 (0.5%)
BENZALKONIUM CHLORIDE;BENZYL ALCOHOL; CHLORHEXIDINE GLUCONATE	0	1 (0.7%)	1 (0.5%)
CHLORHEXIDINE	0	1 (0.7%)	1 (0.5%)
DECAMETHOXINE	1 (1.3%)	0	1 (0.5%)
HYDROGEN PEROXIDE	0	1 (0.7%)	1 (0.5%)
IODINE	1 (1.3%)	0	1 (0.5%)
OCTENIDINE HYDROCHLORIDE;PHENOXYETHANOL	0	1 (0.7%)	1 (0.5%)
POLIHEXANIDE	1 (1.3%)	0	1 (0.5%)
POLIHEXANIDE;UNDECYLENAMIDOPROPYL BETAINE	1 (1.3%)	0	1 (0.5%)
SODIUM HYPOCHLORITE	0	1 (0.7%)	1 (0.5%)
THYMOL	0	1 (0.7%)	1 (0.5%)
ANTITHROMBOTIC AGENTS			
Total number of patients with at least one treatment	18 (23.7%)	35 (24.0%)	53 (23.9%)
Total number of treatments	42	51	93
ENOXAPARIN SODIUM	2 (2.6%)	10 (6.8%)	12 (5.4%)
ACETYLSALICYLIC ACID	3 (3.9%)	6 (4.1%)	9 (4.1%)
ENOXAPARIN	3 (3.9%)	5 (3.4%)	8 (3.6%)
HEPARINOID	2 (2.6%)	4 (2.7%)	6 (2.7%)
RIVAROXABAN	5 (6.6%)	1 (0.7%)	6 (2.7%)
MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER	2 (2.6%)	3 (2.1%)	5 (2.3%)
TINZAPARIN SODIUM	2 (2.6%)	2 (1.4%)	4 (1.8%)
APIXABAN	2 (2.6%)	1 (0.7%)	3 (1.4%)
CLOPIDOGREL	1 (1.3%)	1 (0.7%)	2 (0.9%)
DALTEPARIN SODIUM	1 (1.3%)	1 (0.7%)	2 (0.9%)
NADROPARIN CALCIUM	1 (1.3%)	1 (0.7%)	2 (0.9%)
ACETYLSALICYLIC ACID;ALUMINIUM GLYCINATE; MAGNESIUM CARBONATE	0	1 (0.7%)	1 (0.5%)
ACETYLSALICYLIC ACID;GLYCINE	0	1 (0.7%)	1 (0.5%)
ACETYLSALICYLIC ACID;MAGNESIUM HYDROXIDE	1 (1.3%)	0	1 (0.5%)
DABIGATRAN ETEXILATE MESILATE	0	1 (0.7%)	1 (0.5%)
FONDAPARINUX SODIUM	0	1 (0.7%)	1 (0.5%)
HEPARIN	0	1 (0.7%)	1 (0.5%)
UROKINASE	0	1 (0.7%)	1 (0.5%)

Treatments are coded using the WHODRUG GLOBAL B3 SEPTEMBER 1, 2022. dictionary. Treatments can appear under multiple classes. The table includes medications that have temporal overlap with study drug administration. Multiple uses of a specific medication for a patient were counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a patient were counted once in the frequency for the medication class. Use of the anti-diarrheal medication Loperamide is primarily summarized in separate outputs.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ANTIVIRALS FOR SYSTEMIC USE			
Total number of patients with at least one treatment	5 (6.6%)	13 (8.9%)	18 (8.1%)
Total number of treatments	6	28	34
ACICLOVIR	0	6 (4.1%)	6 (2.7%)
VALACICLOVIR	0	3 (2.1%)	3 (1.4%)
VIDARABINE	1 (1.3%)	2 (1.4%)	3 (1.4%)
LYSOZYME CHLORIDE	0	2 (1.4%)	2 (0.9%)
OSELTAMIVIR	1 (1.3%)	1 (0.7%)	2 (0.9%)
OSELTAMIVIR PHOSPHATE	0	2 (1.4%)	2 (0.9%)
VALACICLOVIR HYDROCHLORIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
AMENAMEVIR	0	1 (0.7%)	1 (0.5%)
ENTECAVIR	0	1 (0.7%)	1 (0.5%)
FAMCICLOVIR	0	1 (0.7%)	1 (0.5%)
INOSINE PRANOBEX	1 (1.3%)	0	1 (0.5%)
LAMIVUDINE	0	1 (0.7%)	1 (0.5%)
LANINAMIVIR OCTANOATE	1 (1.3%)	0	1 (0.5%)
TENOFOVIR DISOPROXIL FUMARATE	1 (1.3%)	0	1 (0.5%)
APPETITE STIMULANTS			
Total number of patients with at least one treatment	1 (1.3%)	1 (0.7%)	2 (0.9%)
Total number of treatments	2	1	3
CYPROHEPTADINE HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
MEGESTROL	0	1 (0.7%)	1 (0.5%)
BETA BLOCKING AGENTS			
Total number of patients with at least one treatment	6 (7.9%)	25 (17.1%)	31 (14.0%)
Total number of treatments	6	34	40
BISOPROLOL	1 (1.3%)	5 (3.4%)	6 (2.7%)
BISOPROLOL FUMARATE	1 (1.3%)	5 (3.4%)	6 (2.7%)
ATENOLOL	0	3 (2.1%)	3 (1.4%)
METOPROLOL	1 (1.3%)	2 (1.4%)	3 (1.4%)
CARVEDILOL	0	2 (1.4%)	2 (0.9%)
NEBIVOLOL HYDROCHLORIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
PROPRANOLOL	0	2 (1.4%)	2 (0.9%)
ATENOLOL;CHLORTALIDONE;NIFEDIPINE	0	1 (0.7%)	1 (0.5%)
BETAXOLOL HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
BISOPROLOL FUMARATE;HYDROCHLOROTHIAZIDE	0	1 (0.7%)	1 (0.5%)
HYDROCHLOROTHIAZIDE;METOPROLOL TARTRATE	1 (1.3%)	0	1 (0.5%)
HYDROCHLOROTHIAZIDE;NEBIVOLOL HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
METOPROLOL TARTRATE	0	1 (0.7%)	1 (0.5%)
NEBIVOLOL	0	1 (0.7%)	1 (0.5%)
PROPRANOLOL HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
SOTALOL	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
BILE AND LIVER THERAPY			
Total number of patients with at least one treatment	13 (17.1%)	30 (20.5%)	43 (19.4%)
Total number of treatments	86	72	158
ACETYLCYSTEINE	4 (5.3%)	7 (4.8%)	11 (5.0%)
ARGININE GLUTAMATE	6 (7.9%)	4 (2.7%)	10 (4.5%)
INOSINE;MEGLUMINE;METHIONINE;NICOTINAMIDE; SUCCINIC ACID	4 (5.3%)	2 (1.4%)	6 (2.7%)
CYNARA CARDUNCULUS EXTRACT	1 (1.3%)	4 (2.7%)	5 (2.3%)
LACTULOSE	2 (2.6%)	3 (2.1%)	5 (2.3%)
SILYBUM MARIANUM	0	5 (3.4%)	5 (2.3%)
DROTAVERINE HYDROCHLORIDE	1 (1.3%)	3 (2.1%)	4 (1.8%)
URSODEOXYCHOLIC ACID	2 (2.6%)	2 (1.4%)	4 (1.8%)
THIOTRIAZOLINE	2 (2.6%)	1 (0.7%)	3 (1.4%)
DROTAVERINE	1 (1.3%)	1 (0.7%)	2 (0.9%)
PHOSPHOLIPIDS	0	2 (1.4%)	2 (0.9%)
ARGININE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
CYNARA CARDUNCULUS	0	1 (0.7%)	1 (0.5%)
GLUTATHIONE;SILYBUM MARIANUM;VITAMIN E NOS	1 (1.3%)	0	1 (0.5%)
GLYCYRRHIZIC ACID;PHOSPHOLIPIDS	0	1 (0.7%)	1 (0.5%)
LECITHIN	1 (1.3%)	0	1 (0.5%)
ORNITHINE ASPARTATE	0	1 (0.7%)	1 (0.5%)
PHOSPHOLIPIDS SOYBEAN	1 (1.3%)	0	1 (0.5%)
ROSA CANINA	1 (1.3%)	0	1 (0.5%)
TIMONACIC	1 (1.3%)	0	1 (0.5%)
BLOOD SUBSTITUTES AND PERFUSION SOLUTIONS			
Total number of patients with at least one treatment	18 (23.7%)	47 (32.2%)	65 (29.3%)
Total number of treatments	150	228	378
SODIUM CHLORIDE	3 (3.9%)	13 (8.9%)	16 (7.2%)
POTASSIUM CHLORIDE	3 (3.9%)	10 (6.8%)	13 (5.9%)
CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE;SORBITOL	6 (7.9%)	4 (2.7%)	10 (4.5%)
CALCIUM CHLORIDE DIHYDRATE;MAGNESIUM CHLORIDE HEXAHYDRATE;POTASSIUM CHLORIDE;SODIUM CHLORIDE; SODIUM LACTATE	4 (5.3%)	3 (2.1%)	7 (3.2%)
UREA	2 (2.6%)	5 (3.4%)	7 (3.2%)
GLUCOSE	2 (2.6%)	4 (2.7%)	6 (2.7%)
CALCIUM CHLORIDE DIHYDRATE;POTASSIUM CHLORIDE; SODIUM CHLORIDE;SODIUM LACTATE	2 (2.6%)	3 (2.1%)	5 (2.3%)
CARBOHYDRATES NOS;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE	0	5 (3.4%)	5 (2.3%)
SODIUM BICARBONATE	3 (3.9%)	2 (1.4%)	5 (2.3%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
CALCIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	2 (2.6%)	2 (1.4%)	4 (1.8%)
ELECTROLYTES NOS	0	4 (2.7%)	4 (1.8%)
CHLORHEXIDINE GLUCONATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
MAGNESIUM SULFATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
VITAMINS NOS	0	3 (2.1%)	3 (1.4%)
ALBUMIN HUMAN	1 (1.3%)	1 (0.7%)	2 (0.9%)
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE HYDROCHLORIDE	0	2 (1.4%)	2 (0.9%)
CALCIUM CHLORIDE DIHYDRATE;GLUCOSE;POTASSIUM CHLORIDE;SODIUM ACETATE	0	2 (1.4%)	2 (0.9%)
CALCIUM CHLORIDE DIHYDRATE;POTASSIUM CHLORIDE; SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	0	2 (1.4%)	2 (0.9%)
CALCIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE;SORBITOL	0	2 (1.4%)	2 (0.9%)
CALCIUM GLUCONATE	0	2 (1.4%)	2 (0.9%)
GLYCEROL	1 (1.3%)	1 (0.7%)	2 (0.9%)
LYSINE	1 (1.3%)	1 (0.7%)	2 (0.9%)
NEOMYCIN	0	2 (1.4%)	2 (0.9%)
NEOMYCIN SULFATE	0	2 (1.4%)	2 (0.9%)
PHOSPHOLIPIDS	0	2 (1.4%)	2 (0.9%)
POTASSIUM CHLORIDE;SODIUM BICARBONATE;SODIUM CHLORIDE	0	2 (1.4%)	2 (0.9%)
RED BLOOD CELLS, CONCENTRATED	1 (1.3%)	1 (0.7%)	2 (0.9%)
ACETIC ACID	0	1 (0.7%)	1 (0.5%)
ACETYLCYSTEINE;ALANINE;ARGININE;ASCORBIC ACID; ASPARTIC ACID;BIOTIN;CALCIUM CHLORIDE DIHYDRATE; CYANOCOBALAMIN;FOLIC ACID;GLUCOSE;GLUTAMIC ACID; GLYCINE;HISTIDINE;ISOLEUCINE;LEUCINE;LYSINE HYDROCHLORIDE;MAGNESIUM SULFATE HEPTAHYDRATE; METHIONINE;NICOTINAMIDE;PANTHENOL;PHENYLALANINE; POTASSIUM PHOSPHATE DIBASIC;PROLINE;PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN SODIUM PHOSPHATE;SERINE; SODIUM CHLORIDE;SODIUM LACTATE;THIAMINE HYDROCHLORIDE;THREONINE;TRYPTOPHAN, L-;TYROSINE; VALINE;ZINC SULFATE HEPTAHYDRATE	0	1 (0.7%)	1 (0.5%)
ALANINE;ARGININE HYDROCHLORIDE;CALCIUM CHLORIDE DIHYDRATE;GLUCOSE;GLYCINE;HISTIDINE HYDROCHLORIDE;ISOLEUCINE;LEUCINE;LYSINE HYDROCHLORIDE;MAGNESIUM CHLORIDE;METHIONINE; PHENYLALANINE;POTASSIUM PHOSPHATE DIBASIC; PROLINE;SERINE;SODIUM ACETATE;SODIUM CHLORIDE; THREONINE;TRYPTOPHAN, L-;TYROSINE;VALINE	0	1 (0.7%)	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ALANINE;ARGININE HYDROCHLORIDE;CYSTEINE;GLYCINE; HISTIDINE HYDROCHLORIDE;ISOLEUCINE;LEUCINE;LYSINE HYDROCHLORIDE;METHIONINE;PHENYLALANINE;PROLINE; SERINE;THREONINE;TRYPTOPHAN, L-;VALINE	0	1 (0.7%)	1 (0.5%)
ALANINE;ARGININE;CALCIUM CHLORIDE;FISH OIL; GLUCOSE MONOHYDRATE;GLYCINE;GLYCINE MAX SEED OIL; HISTIDINE;ISOLEUCINE;LEUCINE;LYSINE ACETATE; MAGNESIUM SULFATE;MEDIUM-CHAIN TRIGLYCERIDES; METHIONINE;OLEA EUROPAEA OIL;PHENYLALANINE; POTASSIUM CHLORIDE;PROLINE;SERINE;SODIUM ACETATE; SODIUM GLYCEROPHOSPHATE;TAURINE;THREONINE; TRYPTOPHAN, L-;TYROSINE;VALINE;ZINC SULFATE	0	1 (0.7%)	1 (0.5%)
ALANINE;ARGININE;CYSTEINE HYDROCHLORIDE;GLYCINE; HISTIDINE;ISOLEUCINE;LEUCINE;LYSINE ACETATE; METHIONINE;PHENYLALANINE;PROLINE;SERINE; THREONINE;TRYPTOPHAN, L-;VALINE	0	1 (0.7%)	1 (0.5%)
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE	0	1 (0.7%)	1 (0.5%)
ARGININE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
BLOOD PLASMA	1 (1.3%)	0	1 (0.5%)
BLOOD, WHOLE	1 (1.3%)	0	1 (0.5%)
CALCIUM CHLORIDE DIHYDRATE;MAGNESIUM CHLORIDE HEXAHYDRATE;MALIC ACID;POTASSIUM CHLORIDE;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	1 (1.3%)	0	1 (0.5%)
CALCIUM GLUCONATE MONOHYDRATE;GLUCOSE;MAGNESIUM CHLORIDE HEXAHYDRATE;POTASSIUM CHLORIDE;SODIUM ACETATE;SODIUM CHLORIDE;SODIUM CITRATE DIHYDRATE	0	1 (0.7%)	1 (0.5%)
CHLORHEXIDINE	0	1 (0.7%)	1 (0.5%)
CHROMIC CHLORIDE;COPPER SULFATE;MANGANESE SULFATE;ZINC SULFATE	0	1 (0.7%)	1 (0.5%)
FRUCTOSE;GLYCEROL	0	1 (0.7%)	1 (0.5%)
GLUCOSE;MAGNESIUM CHLORIDE HEXAHYDRATE;POTASSIUM CHLORIDE;POTASSIUM PHOSPHATE MONOBASIC;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	0	1 (0.7%)	1 (0.5%)
GLUCOSE;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE	0	1 (0.7%)	1 (0.5%)
GLUCOSE;SODIUM CHLORIDE;SODIUM LACTATE	0	1 (0.7%)	1 (0.5%)
MAGNESIUM CITRATE	0	1 (0.7%)	1 (0.5%)
RED BLOOD CELLS	0	1 (0.7%)	1 (0.5%)
SODIUM CITRATE	1 (1.3%)	0	1 (0.5%)
SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)
SODIUM PHOSPHATE DIBASIC;SODIUM PHOSPHATE MONOBASIC (MONOHYDRATE)	0	1 (0.7%)	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
CALCIUM CHANNEL BLOCKERS			
Total number of patients with at least one treatment	3 (3.9%)	10 (6.8%)	13 (5.9%)
Total number of treatments	3	18	21
AMLODIPINE	2 (2.6%)	5 (3.4%)	7 (3.2%)
AMLODIPINE BESILATE	1 (1.3%)	3 (2.1%)	4 (1.8%)
LERCANIDIPINE	0	2 (1.4%)	2 (0.9%)
NIFEDIPINE	0	1 (0.7%)	1 (0.5%)
CALCIUM HOMEOSTASIS			
Total number of patients with at least one treatment	2 (2.6%)	2 (1.4%)	4 (1.8%)
Total number of treatments	2	2	4
CALCIFEDIOL	2 (2.6%)	2 (1.4%)	4 (1.8%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
CARDIAC THERAPY			
Total number of patients with at least one treatment	21 (27.6%)	39 (26.7%)	60 (27.0%)
Total number of treatments	156	255	411
IBUPROFEN	9 (11.8%)	16 (11.0%)	25 (11.3%)
MELDONIUM	7 (9.2%)	4 (2.7%)	11 (5.0%)
TRIMETAZIDINE HYDROCHLORIDE	3 (3.9%)	4 (2.7%)	7 (3.2%)
IVABRADINE HYDROCHLORIDE	2 (2.6%)	3 (2.1%)	5 (2.3%)
LIDOCAINE	1 (1.3%)	4 (2.7%)	5 (2.3%)
LIDOCAINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
RACECADOTRIL	0	3 (2.1%)	3 (1.4%)
THIOTRIAZOLINE	2 (2.6%)	1 (0.7%)	3 (1.4%)
CAMPHOR	0	2 (1.4%)	2 (0.9%)
INDOMETACIN	1 (1.3%)	1 (0.7%)	2 (0.9%)
ISOSORBIDE DINITRATE	0	2 (1.4%)	2 (0.9%)
ADENOSINE	0	1 (0.7%)	1 (0.5%)
AMIODARONE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
ANNONA MURICATA LEAF	0	1 (0.7%)	1 (0.5%)
ATRACTYLODES SPP. RHIZOME;CINNAMOMUM CASSIA BARK; GLYCYRRHIZA SPP. ROOT;PORIA COCOS SCLEROTIUM	1 (1.3%)	0	1 (0.5%)
CONVALLATOXIN	1 (1.3%)	0	1 (0.5%)
DOPAMINE	0	1 (0.7%)	1 (0.5%)
EMPAGLIFLOZIN	1 (1.3%)	0	1 (0.5%)
EPHEDRINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
FLECAINIDE	0	1 (0.7%)	1 (0.5%)
GLUCOSE;INSULIN;POTASSIUM	0	1 (0.7%)	1 (0.5%)
IBUPROFEN ARGININE	1 (1.3%)	0	1 (0.5%)
IPRATROPIUM BROMIDE	1 (1.3%)	0	1 (0.5%)
LEVOCARNITINE	1 (1.3%)	0	1 (0.5%)
MAGNESIUM ASPARTATE;POTASSIUM ASPARTATE	0	1 (0.7%)	1 (0.5%)
NITROUS ETHER SPIRIT	0	1 (0.7%)	1 (0.5%)
PHENYLEPHRINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
SODIUM ALGINATE	1 (1.3%)	0	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
CORTICOSTEROIDS FOR SYSTEMIC USE			
Total number of patients with at least one treatment	67 (88.2%)	136 (93.2%)	203 (91.4%)
Total number of treatments	742	997	1739
DEXAMETHASONE	51 (67.1%)	100 (68.5%)	151 (68.0%)
DEXAMETHASONE SODIUM PHOSPHATE	9 (11.8%)	22 (15.1%)	31 (14.0%)
HYDROCORTISONE	5 (6.6%)	13 (8.9%)	18 (8.1%)
METHYLPREDNISOLONE SODIUM SUCCINATE	4 (5.3%)	10 (6.8%)	14 (6.3%)
BETAMETHASONE BUTYRATE PROPIONATE	2 (2.6%)	7 (4.8%)	9 (4.1%)
METHYLPREDNISOLONE	3 (3.9%)	6 (4.1%)	9 (4.1%)
PREDNISOLONE	2 (2.6%)	7 (4.8%)	9 (4.1%)
PREDNISONE	3 (3.9%)	5 (3.4%)	8 (3.6%)
BETAMETHASONE	5 (6.6%)	2 (1.4%)	7 (3.2%)
HYDROCORTISONE SODIUM SUCCINATE	1 (1.3%)	5 (3.4%)	6 (2.7%)
BETAMETHASONE VALERATE	1 (1.3%)	4 (2.7%)	5 (2.3%)
HYDROCORTISONE BUTYRATE	0	4 (2.7%)	4 (1.8%)
BETAMETHASONE DIPROPIONATE	1 (1.3%)	1 (0.7%)	2 (0.9%)
BETAMETHASONE;DEXCHLORPHENIRAMINE MALEATE	0	2 (1.4%)	2 (0.9%)
TRIAMCINOLONE	0	2 (1.4%)	2 (0.9%)
BETAMETHASONE SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)
CORTICOSTEROID NOS	0	1 (0.7%)	1 (0.5%)
CORTISONE ACETATE	0	1 (0.7%)	1 (0.5%)
DEXAMETHASONE VALERATE	0	1 (0.7%)	1 (0.5%)
KETOCONAZOLE	1 (1.3%)	0	1 (0.5%)
PREDNISOLONE ACETATE	0	1 (0.7%)	1 (0.5%)
PREDNISOLONE METASULFOBENZOATE SODIUM	1 (1.3%)	0	1 (0.5%)
PREDNISOLONE SODIUM SUCCINATE	0	1 (0.7%)	1 (0.5%)
TRIAMCINOLONE ACETONIDE	0	1 (0.7%)	1 (0.5%)
CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS			
Total number of patients with at least one treatment	67 (88.2%)	137 (93.8%)	204 (91.9%)
Total number of treatments	760	1032	1792
DEXAMETHASONE	51 (67.1%)	100 (68.5%)	151 (68.0%)
DEXAMETHASONE SODIUM PHOSPHATE	9 (11.8%)	22 (15.1%)	31 (14.0%)
HYDROCORTISONE	5 (6.6%)	13 (8.9%)	18 (8.1%)
METHYLPREDNISOLONE SODIUM SUCCINATE	4 (5.3%)	10 (6.8%)	14 (6.3%)
BETAMETHASONE BUTYRATE PROPIONATE	2 (2.6%)	7 (4.8%)	9 (4.1%)
METHYLPREDNISOLONE	3 (3.9%)	6 (4.1%)	9 (4.1%)
PREDNISOLONE	2 (2.6%)	7 (4.8%)	9 (4.1%)
PREDNISONE	3 (3.9%)	5 (3.4%)	8 (3.6%)
BETAMETHASONE	5 (6.6%)	2 (1.4%)	7 (3.2%)
BETAMETHASONE VALERATE;GENTAMICIN SULFATE	2 (2.6%)	4 (2.7%)	6 (2.7%)
HYDROCORTISONE SODIUM SUCCINATE	1 (1.3%)	5 (3.4%)	6 (2.7%)
BETAMETHASONE VALERATE	1 (1.3%)	4 (2.7%)	5 (2.3%)
CLOBETASOL PROPIONATE	2 (2.6%)	3 (2.1%)	5 (2.3%)

Treatments are coded using the WHODRUG GLOBAL B3 SEPTEMBER 1, 2022. dictionary. Treatments can appear under multiple classes. The table includes medications that have temporal overlap with study drug administration. Multiple uses of a specific medication for a patient were counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a patient were counted once in the frequency for the medication class. Use of the anti-diarrheal medication Loperamide is primarily summarized in separate outputs.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
FLUOROMETHOLONE	3 (3.9%)	2 (1.4%)	5 (2.3%)
HYDROCORTISONE BUTYRATE	0	4 (2.7%)	4 (1.8%)
MOMETASONE FUROATE	3 (3.9%)	1 (0.7%)	4 (1.8%)
BECLOMETASONE DIPROPIONATE	0	3 (2.1%)	3 (1.4%)
METHYLPREDNISOLONE ACEPONATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
BETAMETHASONE DIPROPIONATE	1 (1.3%)	1 (0.7%)	2 (0.9%)
DESONIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
DIFLUCORTOLONE VALERATE	0	2 (1.4%)	2 (0.9%)
PREDNICARBATE	0	2 (1.4%)	2 (0.9%)
TRIAMCINOLONE	0	2 (1.4%)	2 (0.9%)
BACTERIA NOS;HYDROCORTISONE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE DIPROPIONATE;GENTAMICIN SULFATE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE SODIUM PHOSPHATE;NEOMYCIN SULFATE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE VALERATE;FUSIDIC ACID	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE VALERATE;NEOMYCIN SULFATE	1 (1.3%)	0	1 (0.5%)
BETAMETHASONE;GENTAMICIN	1 (1.3%)	0	1 (0.5%)
BUDESONIDE	0	1 (0.7%)	1 (0.5%)
CHLORHEXIDINE HYDROCHLORIDE;TRIAMCINOLONE ACETONIDE	0	1 (0.7%)	1 (0.5%)
CLOBETASONE BUTYRATE	0	1 (0.7%)	1 (0.5%)
CORTICOSTEROID NOS	0	1 (0.7%)	1 (0.5%)
DESOXIMETASONE	1 (1.3%)	0	1 (0.5%)
DEXAMETHASONE SODIUM PHOSPHATE;NEOMYCIN SULFATE	0	1 (0.7%)	1 (0.5%)
DEXAMETHASONE VALERATE	0	1 (0.7%)	1 (0.5%)
DIFLUCORTOLONE	0	1 (0.7%)	1 (0.5%)
DIFLUPREDNATE	0	1 (0.7%)	1 (0.5%)
FLUOCINOLONE ACETONIDE	1 (1.3%)	0	1 (0.5%)
FLUOCINONIDE	1 (1.3%)	0	1 (0.5%)
FLUOCINONIDE;GENTAMICIN SULFATE	1 (1.3%)	0	1 (0.5%)
FLUTICASONE	0	1 (0.7%)	1 (0.5%)
FLUTICASONE PROPIONATE	0	1 (0.7%)	1 (0.5%)
PREDNISOLONE ACETATE	0	1 (0.7%)	1 (0.5%)
PREDNISOLONE METASULFOBENZOATE SODIUM	1 (1.3%)	0	1 (0.5%)
PREDNISOLONE SODIUM SUCCINATE	0	1 (0.7%)	1 (0.5%)
TRIAMCINOLONE ACETONIDE	0	1 (0.7%)	1 (0.5%)
COUGH AND COLD PREPARATIONS			
Total number of patients with at least one treatment	19 (25.0%)	46 (31.5%)	65 (29.3%)
Total number of treatments	66	154	220
SODIUM CHLORIDE	3 (3.9%)	13 (8.9%)	16 (7.2%)
ACETYLCYSTEINE	4 (5.3%)	7 (4.8%)	11 (5.0%)
DEXTROMETHORPHAN HYDROBROMIDE	2 (2.6%)	6 (4.1%)	8 (3.6%)
AMBROXOL HYDROCHLORIDE	5 (6.6%)	2 (1.4%)	7 (3.2%)
CODEINE PHOSPHATE	2 (2.6%)	4 (2.7%)	6 (2.7%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
CARBOCISTEINE	2 (2.6%)	3 (2.1%)	5 (2.3%)
ELECTROLYTES NOS	0	4 (2.7%)	4 (1.8%)
DEXTROMETHORPHAN	1 (1.3%)	2 (1.4%)	3 (1.4%)
AMBROXOL	1 (1.3%)	1 (0.7%)	2 (0.9%)
AMMONIUM CHLORIDE;CHLORPHENAMINE MALEATE; DIHYDROCODEINE BITARTRATE;METHYLEPHEDRINE HYDROCHLORIDE-DL	1 (1.3%)	1 (0.7%)	2 (0.9%)
CAMPHOR	0	2 (1.4%)	2 (0.9%)
CINNAMOMUM CASSIA;EPHEDRA SPP.;GLYCYRRHIZA SPP.; PAEONIA LACTIFLORA;PUERARIA MONTANA VAR. LOBATA; ZINGIBER OFFICINALE;ZIZIPHUS JUJUBA	0	2 (1.4%)	2 (0.9%)
CODEINE	0	2 (1.4%)	2 (0.9%)
DEXTROMETHORPHAN HYDROBROMIDE MONOHYDRATE	2 (2.6%)	0	2 (0.9%)
DIMEMORFAN PHOSPHATE	0	2 (1.4%)	2 (0.9%)
GLYCEROL	1 (1.3%)	1 (0.7%)	2 (0.9%)
GLYCYRRHIZA GLABRA EXTRACT;PAPAVER SOMNIFERUM	1 (1.3%)	1 (0.7%)	2 (0.9%)
L-CARBOCISTEINE	1 (1.3%)	1 (0.7%)	2 (0.9%)
POTASSIUM CRESOLSULFONATE	0	2 (1.4%)	2 (0.9%)
ACETIC ACID	0	1 (0.7%)	1 (0.5%)
AESCULUS HIPPOCASTANUM	0	1 (0.7%)	1 (0.5%)
BACTERIA LYSATE NOS	1 (1.3%)	0	1 (0.5%)
BENPROPERINE	1 (1.3%)	0	1 (0.5%)
BROMHEXINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
CHLORPHENAMINE MALEATE;DEXTROMETHORPHAN HYDROBROMIDE;PARACETAMOL	1 (1.3%)	0	1 (0.5%)
CHLORPHENAMINE MALEATE;DIHYDROCODEINE BITARTRATE; GUAIFENESIN;METHYLEPHEDRINE HYDROCHLORIDE-DL	0	1 (0.7%)	1 (0.5%)
CHLORPHENAMINE MALEATE;GUAIFENESIN; METHYLEPHEDRINE HYDROCHLORIDE-DL	1 (1.3%)	0	1 (0.5%)
CHLORPHENAMINE;DEXTROMETHORPHAN	0	1 (0.7%)	1 (0.5%)
CODEINE PHOSPHATE HEMIHYDRATE	0	1 (0.7%)	1 (0.5%)
CODEINE PHOSPHATE;PROMETHAZINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
COPTIS SPP. RHIZOME;HEDERA HELIX LEAF	0	1 (0.7%)	1 (0.5%)
COUGH AND COLD PREPARATIONS	0	1 (0.7%)	1 (0.5%)
DEXTROMETHORPHAN HYDROBROMIDE;LYSOZYME CHLORIDE; POTASSIUM CRESOLSULFONATE	1 (1.3%)	0	1 (0.5%)
DEXTROMETHORPHAN HYDROBROMIDE;LYSOZYME HYDROCHLORIDE;POTASSIUM CRESOLSULFONATE	1 (1.3%)	0	1 (0.5%)
EPRAZINONE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
GLYCYRRHIZA GLABRA EXTRACT	0	1 (0.7%)	1 (0.5%)
GUAIFENESIN	0	1 (0.7%)	1 (0.5%)
IODINE	1 (1.3%)	0	1 (0.5%)
LEVOMENTHOL	0	1 (0.7%)	1 (0.5%)
NOSCAPINE	0	1 (0.7%)	1 (0.5%)
OTHER COUGH SUPPRESSANTS AND EXPECTORANTS	0	1 (0.7%)	1 (0.5%)
PAPAVER SOMNIFERUM	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
PHOLCODINE	0	1 (0.7%)	1 (0.5%)
PLATYCODON GRANDIFLORUS ROOT	0	1 (0.7%)	1 (0.5%)
ROSA CANINA	1 (1.3%)	0	1 (0.5%)
SODIUM CITRATE	1 (1.3%)	0	1 (0.5%)
TIPEPIDINE HIBENZATE	0	1 (0.7%)	1 (0.5%)
ZINC ACETATE	0	1 (0.7%)	1 (0.5%)
DIAGNOSTIC AGENTS			
Total number of patients with at least one treatment	5 (6.6%)	8 (5.5%)	13 (5.9%)
Total number of treatments	9	13	22
GLUCOSE	2 (2.6%)	4 (2.7%)	6 (2.7%)
FOLIC ACID	2 (2.6%)	3 (2.1%)	5 (2.3%)
MAGNESIUM SULFATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
DIGESTIVES, INCL. ENZYMES			
Total number of patients with at least one treatment	6 (7.9%)	13 (8.9%)	19 (8.6%)
Total number of treatments	7	15	22
ARGININE CITRATE;BETAINE;BETAINE HYDROCHLORIDE	5 (6.6%)	2 (1.4%)	7 (3.2%)
PANCREATIN	2 (2.6%)	4 (2.7%)	6 (2.7%)
SILYBUM MARIANUM	0	5 (3.4%)	5 (2.3%)
AZULENE SODIUM SULFONATE;LEVOGLUTAMIDE	0	1 (0.7%)	1 (0.5%)
LACTOFERRIN	0	1 (0.7%)	1 (0.5%)

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
DIURETICS			
Total number of patients with at least one treatment	22 (28.9%)	34 (23.3%)	56 (25.2%)
Total number of treatments	46	76	122
FUROSEMIDE	12 (15.8%)	21 (14.4%)	33 (14.9%)
SPIRONOLACTONE	9 (11.8%)	10 (6.8%)	19 (8.6%)
HYDROCHLOROTHIAZIDE	3 (3.9%)	5 (3.4%)	8 (3.6%)
TORASEMIDE	1 (1.3%)	5 (3.4%)	6 (2.7%)
AMILORIDE HYDROCHLORIDE;HYDROCHLOROTHIAZIDE	0	4 (2.7%)	4 (1.8%)
EPLERENONE	2 (2.6%)	0	2 (0.9%)
INDAPAMIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
THEOBROMINE	1 (1.3%)	1 (0.7%)	2 (0.9%)
TRICHLORMETHIAZIDE	0	2 (1.4%)	2 (0.9%)
ACETAZOLAMIDE	1 (1.3%)	0	1 (0.5%)
ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER; ATRACTYLODES SPP. RHIZOME;CINNAMOMUM CASSIA BARK; POLYPORUS UMBELLATUS SCLEROTIUM;PORIA COCOS SCLEROTIUM	0	1 (0.7%)	1 (0.5%)
AZOSEMIDE	0	1 (0.7%)	1 (0.5%)
CHLORTALIDONE	0	1 (0.7%)	1 (0.5%)
CYNARA CARDUNCULUS	0	1 (0.7%)	1 (0.5%)
LESPEDEZA BICOLOR	0	1 (0.7%)	1 (0.5%)
ROSA CANINA	1 (1.3%)	0	1 (0.5%)
DRUGS FOR ACID RELATED DISORDERS			
Total number of patients with at least one treatment	74 (97.4%)	129 (88.4%)	203 (91.4%)
Total number of treatments	807	1019	1826
RANITIDINE	30 (39.5%)	58 (39.7%)	88 (39.6%)
FAMOTIDINE	28 (36.8%)	46 (31.5%)	74 (33.3%)
RANITIDINE HYDROCHLORIDE	23 (30.3%)	34 (23.3%)	57 (25.7%)
OMEPRAZOLE	8 (10.5%)	18 (12.3%)	26 (11.7%)
PANTOPRAZOLE	1 (1.3%)	12 (8.2%)	13 (5.9%)
ESOMEPRAZOLE	4 (5.3%)	6 (4.1%)	10 (4.5%)
PANTOPRAZOLE SODIUM SESQUIHYDRATE	4 (5.3%)	5 (3.4%)	9 (4.1%)
SODIUM GUALENATE HYDRATE	2 (2.6%)	7 (4.8%)	9 (4.1%)
CALCIUM CARBONATE	1 (1.3%)	7 (4.8%)	8 (3.6%)
REBAMIPIDE	2 (2.6%)	6 (4.1%)	8 (3.6%)
LANSOPRAZOLE	6 (7.9%)	1 (0.7%)	7 (3.2%)
MAGNESIUM OXIDE	4 (5.3%)	3 (2.1%)	7 (3.2%)
SODIUM BICARBONATE	3 (3.9%)	2 (1.4%)	5 (2.3%)
TEPRENONE	2 (2.6%)	3 (2.1%)	5 (2.3%)
ANTACIDS, OTHER COMBINATIONS	1 (1.3%)	2 (1.4%)	3 (1.4%)
RABEPRAZOLE SODIUM	2 (2.6%)	1 (0.7%)	3 (1.4%)
ALMAGATE	1 (1.3%)	1 (0.7%)	2 (0.9%)
ESOMEPRAZOLE MAGNESIUM	0	2 (1.4%)	2 (0.9%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
MAGNESIUM HYDROXIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
ALTHAEA OFFICINALIS;DEXPANTHENOL;MAGNESIUM ALGINATE;PAPAVER RHOEAS;SIMETICONE;SODIUM CARBONATE MONOHYDRATE;ZINC OXIDE	0	1 (0.7%)	1 (0.5%)
ALUMINIUM HYDROXIDE	0	1 (0.7%)	1 (0.5%)
ALUMINIUM HYDROXIDE;BENZOCAINE;MAGNESIUM HYDROXIDE	1 (1.3%)	0	1 (0.5%)
ALUMINIUM HYDROXIDE;CALCIUM CARBONATE;MAGNESIUM CARBONATE	0	1 (0.7%)	1 (0.5%)
ALUMINIUM HYDROXIDE;MAGNESIUM HYDROXIDE	1 (1.3%)	0	1 (0.5%)
ARTEMISIA ARGYI LEAF	1 (1.3%)	0	1 (0.5%)
AZULENE SODIUM SULFONATE;LEVOGLUTAMIDE	0	1 (0.7%)	1 (0.5%)
BISMUTH SUBSALICYLATE	0	1 (0.7%)	1 (0.5%)
CIMETIDINE	0	1 (0.7%)	1 (0.5%)
COPTIS SPP. RHIZOME;GLYCYRRHIZA SPP. ROOT;PANAX GINSENG ROOT;PINELLIA TERNATA TUBER;SCUTELLARIA BAICALENSIS ROOT;ZINGIBER OFFICINALE PROCESSED RHIZOME;ZIZIPHUS JUJUBA FRUIT	0	1 (0.7%)	1 (0.5%)
ENOXOLONE	0	1 (0.7%)	1 (0.5%)
GLYCYRRHIZA GLABRA EXTRACT	0	1 (0.7%)	1 (0.5%)
HYDROTALCITE	1 (1.3%)	0	1 (0.5%)
LEVOGLUTAMIDE;SODIUM GUALENATE	0	1 (0.7%)	1 (0.5%)
MISOPROSTOL	0	1 (0.7%)	1 (0.5%)
OXETACAINE	0	1 (0.7%)	1 (0.5%)
SODIUM ALGINATE	1 (1.3%)	0	1 (0.5%)
SODIUM BICARBONATE;SODIUM GUALENATE HYDRATE	0	1 (0.7%)	1 (0.5%)
SODIUM CITRATE	1 (1.3%)	0	1 (0.5%)
SUCRALFATE	0	1 (0.7%)	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
DRUGS FOR CONSTIPATION			
Total number of patients with at least one treatment	18 (23.7%)	34 (23.3%)	52 (23.4%)
Total number of treatments	53	109	162
SODIUM CHLORIDE	3 (3.9%)	13 (8.9%)	16 (7.2%)
MAGNESIUM OXIDE	4 (5.3%)	3 (2.1%)	7 (3.2%)
LACTULOSE	2 (2.6%)	3 (2.1%)	5 (2.3%)
SENNOSIDE A+B	2 (2.6%)	3 (2.1%)	5 (2.3%)
SENNOSIDE A+B CALCIUM	2 (2.6%)	3 (2.1%)	5 (2.3%)
MAGNESIUM SULFATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
PROBIOTICS NOS	0	3 (2.1%)	3 (1.4%)
DOCUSATE SODIUM	0	2 (1.4%)	2 (0.9%)
ENEMAS	0	2 (1.4%)	2 (0.9%)
GLYCEROL	1 (1.3%)	1 (0.7%)	2 (0.9%)
MACROGOL	2 (2.6%)	0	2 (0.9%)
MACROGOL 3350	0	2 (1.4%)	2 (0.9%)
MAGNESIUM HYDROXIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
BISACODYL	1 (1.3%)	0	1 (0.5%)
CARMELLOSE	0	1 (0.7%)	1 (0.5%)
CARMELLOSE SODIUM	0	1 (0.7%)	1 (0.5%)
CELLULOSE MICROCRYSTALLINE;HEMICELLULOSE;LIGNIN; PECTIN	0	1 (0.7%)	1 (0.5%)
CONTACT LAXATIVES	0	1 (0.7%)	1 (0.5%)
DOCUSATE	0	1 (0.7%)	1 (0.5%)
FRUCTOSE;GLYCEROL	0	1 (0.7%)	1 (0.5%)
MAGNESIUM CITRATE	0	1 (0.7%)	1 (0.5%)
PARAFFIN	0	1 (0.7%)	1 (0.5%)
ROSA CANINA	1 (1.3%)	0	1 (0.5%)
SENNA ALEXANDRINA	1 (1.3%)	0	1 (0.5%)
SENNA SPP.	0	1 (0.7%)	1 (0.5%)
SODIUM BICARBONATE;SODIUM PHOSPHATE MONOBASIC (ANHYDROUS)	1 (1.3%)	0	1 (0.5%)
SODIUM CITRATE	1 (1.3%)	0	1 (0.5%)
SODIUM CITRATE;SODIUM LAURYL SULFOACETATE; SORBITOL	0	1 (0.7%)	1 (0.5%)
SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)
SODIUM PHOSPHATE DIBASIC;SODIUM PHOSPHATE MONOBASIC (MONOHYDRATE)	0	1 (0.7%)	1 (0.5%)
SODIUM PICOSULFATE MONOHYDRATE	1 (1.3%)	0	1 (0.5%)
STERCULIA URENS GUM	1 (1.3%)	0	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS			
Total number of patients with at least one treatment	19 (25.0%)	60 (41.1%)	79 (35.6%)
Total number of treatments	30	113	143
METOCLOPRAMIDE HYDROCHLORIDE	5 (6.6%)	23 (15.8%)	28 (12.6%)
METOCLOPRAMIDE	8 (10.5%)	19 (13.0%)	27 (12.2%)
SIMETICONE	1 (1.3%)	5 (3.4%)	6 (2.7%)
DOMPERIDONE	0	5 (3.4%)	5 (2.3%)
DROTAVERINE HYDROCHLORIDE	1 (1.3%)	3 (2.1%)	4 (1.8%)
LEVOSULPIRIDE	1 (1.3%)	3 (2.1%)	4 (1.8%)
DIMETICONE	1 (1.3%)	2 (1.4%)	3 (1.4%)
RAMOSETRON HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
ALIZAPRIDE HYDROCHLORIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
DROTAVERINE	1 (1.3%)	1 (0.7%)	2 (0.9%)
FENPIVERINIUM BROMIDE;METAMIZOLE SODIUM; PITOFENONE HYDROCHLORIDE	0	2 (1.4%)	2 (0.9%)
HYOSCINE BUTYLBROMIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
TIROPRAMIDE HYDROCHLORIDE	0	2 (1.4%)	2 (0.9%)
CLONIXIN LYSINATE;PARGEVERINE	0	1 (0.7%)	1 (0.5%)
CORYDALIS YANHUSUO TUBER;IPOMOEA NIL SEED	1 (1.3%)	0	1 (0.5%)
HYOSCINE HYDROBROMIDE	0	1 (0.7%)	1 (0.5%)
HYOSCINE;METAMIZOLE	0	1 (0.7%)	1 (0.5%)
METAMIZOLE SODIUM;PITOFENONE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
PAPAVER SOMNIFERUM	0	1 (0.7%)	1 (0.5%)
PARGEVERINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
PHLOROGLUCINOL	1 (1.3%)	0	1 (0.5%)
SILICON DIOXIDE	0	1 (0.7%)	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES			
Total number of patients with at least one treatment	63 (82.9%)	123 (84.2%)	186 (83.8%)
Total number of treatments	732	877	1609
DEXAMETHASONE	51 (67.1%)	100 (68.5%)	151 (68.0%)
DEXAMETHASONE SODIUM PHOSPHATE	9 (11.8%)	22 (15.1%)	31 (14.0%)
BETAMETHASONE	5 (6.6%)	2 (1.4%)	7 (3.2%)
BETAMETHASONE VALERATE	1 (1.3%)	4 (2.7%)	5 (2.3%)
BUDESONIDE;FORMOTEROL FUMARATE	2 (2.6%)	2 (1.4%)	4 (1.8%)
MOMETASONE FUROATE	3 (3.9%)	1 (0.7%)	4 (1.8%)
AMINOPHYLLINE	2 (2.6%)	1 (0.7%)	3 (1.4%)
BECLOMETASONE DIPROPIONATE	0	3 (2.1%)	3 (1.4%)
FLUTICASONE PROPIONATE;FORMOTEROL FUMARATE	3 (3.9%)	0	3 (1.4%)
MONTELUKAST	2 (2.6%)	1 (0.7%)	3 (1.4%)
SALBUTAMOL	1 (1.3%)	2 (1.4%)	3 (1.4%)
BETAMETHASONE DIPROPIONATE	1 (1.3%)	1 (0.7%)	2 (0.9%)
FENOTEROL HYDROBROMIDE;IPRATROPIUM BROMIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
MONTELUKAST SODIUM	1 (1.3%)	1 (0.7%)	2 (0.9%)
THEOBROMINE	1 (1.3%)	1 (0.7%)	2 (0.9%)
TRIAMCINOLONE	0	2 (1.4%)	2 (0.9%)
ARTEMISIA ARGYI LEAF	1 (1.3%)	0	1 (0.5%)
BETAMETHASONE SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)
BUDESONIDE	0	1 (0.7%)	1 (0.5%)
CORDYCEPS SINENSIS	0	1 (0.7%)	1 (0.5%)
CORTICOSTEROID NOS	0	1 (0.7%)	1 (0.5%)
EPHEDRINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
FLUTICASONE	0	1 (0.7%)	1 (0.5%)
FLUTICASONE FUROATE	1 (1.3%)	0	1 (0.5%)
FLUTICASONE PROPIONATE	0	1 (0.7%)	1 (0.5%)
IPRATROPIUM BROMIDE	1 (1.3%)	0	1 (0.5%)
OLODATEROL HYDROCHLORIDE;TIOTROPIUM BROMIDE MONOHYDRATE	1 (1.3%)	0	1 (0.5%)
PROCATEROL HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
SALBUTAMOL SULFATE	0	1 (0.7%)	1 (0.5%)
THEOPHYLLINE	1 (1.3%)	0	1 (0.5%)
TIOTROPIUM BROMIDE	1 (1.3%)	0	1 (0.5%)
TRIAMCINOLONE ACETONIDE	0	1 (0.7%)	1 (0.5%)
TULOBUTEROL	1 (1.3%)	0	1 (0.5%)

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ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
DRUGS FOR TREATMENT OF BONE DISEASES			
Total number of patients with at least one treatment	27 (35.5%)	55 (37.7%)	82 (36.9%)
Total number of treatments	66	103	169
DENOSUMAB	8 (10.5%)	26 (17.8%)	34 (15.3%)
ZOLEDRONIC ACID	14 (18.4%)	19 (13.0%)	33 (14.9%)
ZOLEDRONIC ACID MONOHYDRATE	3 (3.9%)	6 (4.1%)	9 (4.1%)
PAMIDRONATE DISODIUM	1 (1.3%)	2 (1.4%)	3 (1.4%)
IBANDRONIC ACID	1 (1.3%)	1 (0.7%)	2 (0.9%)
ALENDRONATE SODIUM	1 (1.3%)	0	1 (0.5%)
IBANDRONATE SODIUM	0	1 (0.7%)	1 (0.5%)
DRUGS USED IN DIABETES			
Total number of patients with at least one treatment	7 (9.2%)	17 (11.6%)	24 (10.8%)
Total number of treatments	13	39	52
METFORMIN	4 (5.3%)	8 (5.5%)	12 (5.4%)
METFORMIN HYDROCHLORIDE	2 (2.6%)	6 (4.1%)	8 (3.6%)
GLIBENCLAMIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
INSULIN	0	2 (1.4%)	2 (0.9%)
REPAGLINIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
ALOGLIPTIN;PIOGLITAZONE	0	1 (0.7%)	1 (0.5%)
ANAGLIPTIN	1 (1.3%)	0	1 (0.5%)
EMPAGLIFLOZIN	1 (1.3%)	0	1 (0.5%)
GEMIGLIPTIN TARTRATE	0	1 (0.7%)	1 (0.5%)
GLIMEPIRIDE	0	1 (0.7%)	1 (0.5%)
GLIPIZIDE	0	1 (0.7%)	1 (0.5%)
INSULIN ASPART	0	1 (0.7%)	1 (0.5%)
INSULIN HUMAN	0	1 (0.7%)	1 (0.5%)
INSULIN HUMAN INJECTION, ISOPHANE	0	1 (0.7%)	1 (0.5%)
LINAGLIPTIN	0	1 (0.7%)	1 (0.5%)
METFORMIN EMBONATE	1 (1.3%)	0	1 (0.5%)
MIGLITOL	0	1 (0.7%)	1 (0.5%)
PIOGLITAZONE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
PLATYCODON GRANDIFLORUS ROOT	0	1 (0.7%)	1 (0.5%)
SITAGLIPTIN	0	1 (0.7%)	1 (0.5%)
SITAGLIPTIN PHOSPHATE	1 (1.3%)	0	1 (0.5%)
TENELIGLIPTIN HYDROBROMIDE	0	1 (0.7%)	1 (0.5%)
ECTOPARASITICIDES, INCL. SCABICIDES, INSECTICIDES AND REPELLENTS			
Total number of patients with at least one treatment	1 (1.3%)	3 (2.1%)	4 (1.8%)
Total number of treatments	1	3	4
DIMETICONE	1 (1.3%)	2 (1.4%)	3 (1.4%)
ACETIC ACID	0	1 (0.7%)	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
EMOLLIENTS AND PROTECTIVES			
Total number of patients with at least one treatment	17 (22.4%)	26 (17.8%)	43 (19.4%)
Total number of treatments	134	80	214
THIOCTIC ACID	7 (9.2%)	7 (4.8%)	14 (6.3%)
UREA	2 (2.6%)	5 (3.4%)	7 (3.2%)
HEPARINOID	2 (2.6%)	4 (2.7%)	6 (2.7%)
MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER	2 (2.6%)	3 (2.1%)	5 (2.3%)
WHITE SOFT PARAFFIN	1 (1.3%)	4 (2.7%)	5 (2.3%)
DIMETICONE	1 (1.3%)	2 (1.4%)	3 (1.4%)
ZINC OXIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
GLYCEROL	1 (1.3%)	1 (0.7%)	2 (0.9%)
PETROLATUM	0	2 (1.4%)	2 (0.9%)
CAMPHOR;MENTHOL;METHYL SALICYLATE	1 (1.3%)	0	1 (0.5%)
MENTHOL;ZINC OXIDE	0	1 (0.7%)	1 (0.5%)
OTHER EMOLLIENTS AND PROTECTIVES	1 (1.3%)	0	1 (0.5%)
PARAFFIN	0	1 (0.7%)	1 (0.5%)
SALICYLIC ACID	0	1 (0.7%)	1 (0.5%)
SALICYLIC ACID;UREA	0	1 (0.7%)	1 (0.5%)
ZINC ACETATE	0	1 (0.7%)	1 (0.5%)
ENDOCRINE THERAPY			
Total number of patients with at least one treatment	2 (2.6%)	3 (2.1%)	5 (2.3%)
Total number of treatments	2	3	5
GOSERELIN	0	1 (0.7%)	1 (0.5%)
GOSERELIN ACETATE	1 (1.3%)	0	1 (0.5%)
LEUPRORELIN	0	1 (0.7%)	1 (0.5%)
MEGESTROL	0	1 (0.7%)	1 (0.5%)
TRIPTORELIN	1 (1.3%)	0	1 (0.5%)
GENERAL NUTRIENTS			
Total number of patients with at least one treatment	4 (5.3%)	8 (5.5%)	12 (5.4%)
Total number of treatments	6	10	16
GLUCOSE	2 (2.6%)	4 (2.7%)	6 (2.7%)
LYSINE	1 (1.3%)	1 (0.7%)	2 (0.9%)
ARGININE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
DOCOSAHEXAENOIC ACID;EICOSAPENTAENOIC ACID	0	1 (0.7%)	1 (0.5%)
FISH OIL	0	1 (0.7%)	1 (0.5%)
LECITHIN	1 (1.3%)	0	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
GYNECOLOGICAL ANTIINFECTIVES AND ANTISEPTICS			
Total number of patients with at least one treatment	26 (34.2%)	44 (30.1%)	70 (31.5%)
Total number of treatments	48	77	125
CIPROFLOXACIN	8 (10.5%)	13 (8.9%)	21 (9.5%)
ASCORBIC ACID	7 (9.2%)	9 (6.2%)	16 (7.2%)
METRONIDAZOLE	2 (2.6%)	7 (4.8%)	9 (4.1%)
CLINDAMYCIN	3 (3.9%)	1 (0.7%)	4 (1.8%)
CHLORHEXIDINE GLUCONATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
MICONAZOLE	0	3 (2.1%)	3 (1.4%)
POVIDONE-IODINE	0	3 (2.1%)	3 (1.4%)
ANTIBIOTICS	1 (1.3%)	1 (0.7%)	2 (0.9%)
CHLORAMPHENICOL	0	2 (1.4%)	2 (0.9%)
CLINDAMYCIN PHOSPHATE	0	2 (1.4%)	2 (0.9%)
OFLOXACIN	0	2 (1.4%)	2 (0.9%)
ACETIC ACID	0	1 (0.7%)	1 (0.5%)
AMPHOTERICIN B	0	1 (0.7%)	1 (0.5%)
BERBERINE	0	1 (0.7%)	1 (0.5%)
CHLORHEXIDINE	0	1 (0.7%)	1 (0.5%)
CHLORHEXIDINE GLUCONATE;METRONIDAZOLE BENZOATE	1 (1.3%)	0	1 (0.5%)
CICLOPIROX OLAMINE	1 (1.3%)	0	1 (0.5%)
CLOTRIMAZOLE	0	1 (0.7%)	1 (0.5%)
ECONAZOLE	0	1 (0.7%)	1 (0.5%)
ECONAZOLE NITRATE	0	1 (0.7%)	1 (0.5%)
ENTEROCOCCUS FAECALIS	0	1 (0.7%)	1 (0.5%)
FENTICONAZOLE NITRATE	0	1 (0.7%)	1 (0.5%)
HEXETIDINE	1 (1.3%)	0	1 (0.5%)
KETOCONAZOLE	1 (1.3%)	0	1 (0.5%)
LACTOBACILLUS ACIDOPHILUS	0	1 (0.7%)	1 (0.5%)
LACTOBACILLUS RHAMNOSUS	0	1 (0.7%)	1 (0.5%)
NYSTATIN	1 (1.3%)	0	1 (0.5%)
OCTENIDINE HYDROCHLORIDE;PHENOXYETHANOL	0	1 (0.7%)	1 (0.5%)
OXYTETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
TERBINAFINE	1 (1.3%)	0	1 (0.5%)
TIOCONAZOLE	0	1 (0.7%)	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
HOMEOPATHIC PREPARATION			
Total number of patients with at least one treatment	14 (18.4%)	42 (28.8%)	56 (25.2%)
Total number of treatments	73	140	213
ASCORBIC ACID	7 (9.2%)	9 (6.2%)	16 (7.2%)
SODIUM CHLORIDE	3 (3.9%)	13 (8.9%)	16 (7.2%)
POTASSIUM CHLORIDE	3 (3.9%)	10 (6.8%)	13 (5.9%)
CALCIUM CARBONATE	1 (1.3%)	7 (4.8%)	8 (3.6%)
UREA	2 (2.6%)	5 (3.4%)	7 (3.2%)
SILYBUM MARIANUM	0	5 (3.4%)	5 (2.3%)
CALCIUM PHOSPHATE	0	3 (2.1%)	3 (1.4%)
AESCULUS HIPPOCASTANUM	0	1 (0.7%)	1 (0.5%)
CHARCOAL, ACTIVATED	0	1 (0.7%)	1 (0.5%)
CORTISONE ACETATE	0	1 (0.7%)	1 (0.5%)
CYANOCOBALAMIN	1 (1.3%)	0	1 (0.5%)
CYNARA CARDUNCULUS	0	1 (0.7%)	1 (0.5%)
EUPHRASIA OFFICINALIS	0	1 (0.7%)	1 (0.5%)
GINKGO BILOBA	0	1 (0.7%)	1 (0.5%)
IODINE	1 (1.3%)	0	1 (0.5%)
IRON	0	1 (0.7%)	1 (0.5%)
ROSA CANINA	1 (1.3%)	0	1 (0.5%)
SILICON DIOXIDE	0	1 (0.7%)	1 (0.5%)
SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)
IMMUNOSTIMULANTS			
Total number of patients with at least one treatment	19 (25.0%)	24 (16.4%)	43 (19.4%)
Total number of treatments	79	161	240
FILGRASTIM	11 (14.5%)	14 (9.6%)	25 (11.3%)
METHYLURACIL	3 (3.9%)	3 (2.1%)	6 (2.7%)
LENOGRASTIM	1 (1.3%)	3 (2.1%)	4 (1.8%)
FILGRASTIM SNDZ	1 (1.3%)	2 (1.4%)	3 (1.4%)
GLUTATHIONE	1 (1.3%)	1 (0.7%)	2 (0.9%)
GRANULOCYTE COLONY STIMULATING FACTOR	1 (1.3%)	1 (0.7%)	2 (0.9%)
INTERFERON ALFA-2B	1 (1.3%)	0	1 (0.5%)
MEGLUMINE ACRIDONACETATE	1 (1.3%)	0	1 (0.5%)
IMMUNOSUPPRESSANTS			
Total number of patients with at least one treatment	0	1 (0.7%)	1 (0.5%)
Total number of treatments	0	1	1
CICLOSPORIN	0	1 (0.7%)	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
LIPID MODIFYING AGENTS			
Total number of patients with at least one treatment	12 (15.8%)	31 (21.2%)	43 (19.4%)
Total number of treatments	23	41	64
ROSUVASTATIN	3 (3.9%)	4 (2.7%)	7 (3.2%)
ATORVASTATIN	2 (2.6%)	4 (2.7%)	6 (2.7%)
FENOFIBRATE	2 (2.6%)	4 (2.7%)	6 (2.7%)
ROSUVASTATIN CALCIUM	2 (2.6%)	4 (2.7%)	6 (2.7%)
SIMVASTATIN	2 (2.6%)	3 (2.1%)	5 (2.3%)
ATORVASTATIN CALCIUM	1 (1.3%)	2 (1.4%)	3 (1.4%)
PHOSPHOLIPIDS	0	2 (1.4%)	2 (0.9%)
BERBERINE	0	1 (0.7%)	1 (0.5%)
BEZAFIBRATE	0	1 (0.7%)	1 (0.5%)
CHROMIUM PICOLINATE;FISH OIL;FOLIC ACID;MONASCUS PURPUREUS;NICOTINAMIDE;PANTOTHENIC ACID; POLICOSANOL;REYNOUTRIA JAPONICA;THIOCTIC ACID; VITAMIN B12 NOS	0	1 (0.7%)	1 (0.5%)
CIPROFIBRATE	0	1 (0.7%)	1 (0.5%)
CYNARA CARDUNCULUS	0	1 (0.7%)	1 (0.5%)
DOCOSAHEXAENOIC ACID;EICOSAPENTAENOIC ACID	0	1 (0.7%)	1 (0.5%)
EZETIMIBE	1 (1.3%)	0	1 (0.5%)
FISH OIL	0	1 (0.7%)	1 (0.5%)
FLUVASTATIN	0	1 (0.7%)	1 (0.5%)
GEMFIBROZIL	1 (1.3%)	0	1 (0.5%)
LECITHIN	1 (1.3%)	0	1 (0.5%)
LOVASTATIN	0	1 (0.7%)	1 (0.5%)
OMEGA-3 TRIGLYCERIDES	0	1 (0.7%)	1 (0.5%)
PITAVASTATIN	0	1 (0.7%)	1 (0.5%)
PRAVASTATIN	0	1 (0.7%)	1 (0.5%)
MEDICATED DRESSINGS			
Total number of patients with at least one treatment	8 (10.5%)	23 (15.8%)	31 (14.0%)
Total number of treatments	28	70	98
SODIUM CHLORIDE	3 (3.9%)	13 (8.9%)	16 (7.2%)
FUSIDIC ACID	3 (3.9%)	2 (1.4%)	5 (2.3%)
CHLORHEXIDINE GLUCONATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
POVIDONE-IODINE	0	3 (2.1%)	3 (1.4%)
ZINC OXIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
CARMELLOSE	0	1 (0.7%)	1 (0.5%)
CARMELLOSE SODIUM	0	1 (0.7%)	1 (0.5%)
CHLORHEXIDINE	0	1 (0.7%)	1 (0.5%)
PARAFFIN	0	1 (0.7%)	1 (0.5%)
SODIUM ALGINATE	1 (1.3%)	0	1 (0.5%)

Treatments are coded using the WHODRUG GLOBAL B3 SEPTEMBER 1, 2022. dictionary. Treatments can appear under multiple classes. The table includes medications that have temporal overlap with study drug administration. Multiple uses of a specific medication for a patient were counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a patient were counted once in the frequency for the medication class. Use of the anti-diarrheal medication Loperamide is primarily summarized in separate outputs.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
MINERAL SUPPLEMENTS			
Total number of patients with at least one treatment	25 (32.9%)	50 (34.2%)	75 (33.8%)
Total number of treatments	77	155	232
SODIUM CHLORIDE	3 (3.9%)	13 (8.9%)	16 (7.2%)
POTASSIUM CHLORIDE	3 (3.9%)	10 (6.8%)	13 (5.9%)
CALCIUM	6 (7.9%)	5 (3.4%)	11 (5.0%)
CALCIUM CARBONATE;COLECALCIFEROL	4 (5.3%)	6 (4.1%)	10 (4.5%)
CALCIUM CARBONATE	1 (1.3%)	7 (4.8%)	8 (3.6%)
CALCIUM CARBONATE;COLECALCIFEROL;MAGNESIUM CARBONATE	4 (5.3%)	4 (2.7%)	8 (3.6%)
MAGNESIUM OXIDE	4 (5.3%)	3 (2.1%)	7 (3.2%)
CALCIUM;COLECALCIFEROL	1 (1.3%)	3 (2.1%)	4 (1.8%)
CALCIUM PHOSPHATE	0	3 (2.1%)	3 (1.4%)
MAGNESIUM SULFATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
POTASSIUM CITRATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
ZINC OXIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
CALCIUM GLUCONATE	0	2 (1.4%)	2 (0.9%)
CALCIUM;VITAMIN D NOS	1 (1.3%)	1 (0.7%)	2 (0.9%)
MAGNESIUM	0	2 (1.4%)	2 (0.9%)
MAGNESIUM HYDROXIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
MAGNESIUM;PYRIDOXINE HYDROCHLORIDE	0	2 (1.4%)	2 (0.9%)
BORON;CALCIUM;COLECALCIFEROL;COPPER;MANGANESE;ZINC	0	1 (0.7%)	1 (0.5%)
CALCIUM CITRATE	1 (1.3%)	0	1 (0.5%)
CALCIUM CITRATE;COLECALCIFEROL	1 (1.3%)	0	1 (0.5%)
CALCIUM PHOSPHATE;COLECALCIFEROL	0	1 (0.7%)	1 (0.5%)
CALCIUM;COLECALCIFEROL;MENAQUINONE-7	0	1 (0.7%)	1 (0.5%)
CHROMIC CHLORIDE;COPPER SULFATE;MANGANESE SULFATE;ZINC SULFATE	0	1 (0.7%)	1 (0.5%)
MAGNESIUM ASPARTATE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
MAGNESIUM ASPARTATE;POTASSIUM ASPARTATE	0	1 (0.7%)	1 (0.5%)
MAGNESIUM CITRATE	0	1 (0.7%)	1 (0.5%)
MAGNESIUM LACTATE;PYRIDOXINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
SILICON DIOXIDE	0	1 (0.7%)	1 (0.5%)
SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)
SODIUM PHOSPHATE DIBASIC;SODIUM PHOSPHATE MONOBASIC (MONOHYDRATE)	0	1 (0.7%)	1 (0.5%)
ZINC ACETATE	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
MUSCLE RELAXANTS			
Total number of patients with at least one treatment	4 (5.3%)	7 (4.8%)	11 (5.0%)
Total number of treatments	4	7	11
DIAZEPAM	2 (2.6%)	3 (2.1%)	5 (2.3%)
CYCLOBENZAPRINE	0	2 (1.4%)	2 (0.9%)
BACLOFEN	1 (1.3%)	0	1 (0.5%)
CARISOPRODOL	0	1 (0.7%)	1 (0.5%)
ROCURONIUM BROMIDE	0	1 (0.7%)	1 (0.5%)
TIZANIDINE HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
N/A			
Total number of patients with at least one treatment	1 (1.3%)	7 (4.8%)	8 (3.6%)
Total number of treatments	1	11	12
DIOSMECTITE	1 (1.3%)	6 (4.1%)	7 (3.2%)
ARGININE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
NASAL PREPARATIONS			
Total number of patients with at least one treatment	64 (84.2%)	124 (84.9%)	188 (84.7%)
Total number of treatments	760	1002	1762
DEXAMETHASONE	51 (67.1%)	100 (68.5%)	151 (68.0%)
DEXAMETHASONE SODIUM PHOSPHATE	9 (11.8%)	22 (15.1%)	31 (14.0%)
SODIUM CHLORIDE	3 (3.9%)	13 (8.9%)	16 (7.2%)
ACETYLCYSTEINE	4 (5.3%)	7 (4.8%)	11 (5.0%)
PREDNISOLONE	2 (2.6%)	7 (4.8%)	9 (4.1%)
HYALURONATE SODIUM	2 (2.6%)	6 (4.1%)	8 (3.6%)
BETAMETHASONE	5 (6.6%)	2 (1.4%)	7 (3.2%)
BETAMETHASONE VALERATE	1 (1.3%)	4 (2.7%)	5 (2.3%)
SODIUM BICARBONATE	3 (3.9%)	2 (1.4%)	5 (2.3%)
CALCIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	2 (2.6%)	2 (1.4%)	4 (1.8%)
MOMETASONE FUROATE	3 (3.9%)	1 (0.7%)	4 (1.8%)
MUPIROCIN	3 (3.9%)	1 (0.7%)	4 (1.8%)
BECLOMETASONE DIPROPIONATE	0	3 (2.1%)	3 (1.4%)
OLOPATADINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
POVIDONE-IODINE	0	3 (2.1%)	3 (1.4%)
PSEUDOEPHEDRINE HYDROCHLORIDE;TRIPROLIDINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
BETAMETHASONE DIPROPIONATE	1 (1.3%)	1 (0.7%)	2 (0.9%)
SEA WATER	2 (2.6%)	0	2 (0.9%)
TRIAMCINOLONE	0	2 (1.4%)	2 (0.9%)
AZELASTINE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)
BUDESONIDE	0	1 (0.7%)	1 (0.5%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
CAMPHOR;MENTHOL;METHYL SALICYLATE	1 (1.3%)	0	1 (0.5%)
CORTICOSTEROID NOS	0	1 (0.7%)	1 (0.5%)
DEXAMETHASONE ISONICOTINATE;NEOMYCIN SULFATE; TRAMAZOLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
DEXAMETHASONE VALERATE	0	1 (0.7%)	1 (0.5%)
EBASTINE;PSEUDOEPHEDRINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
EPHEDRINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
FLUTICASONE	0	1 (0.7%)	1 (0.5%)
FLUTICASONE FUROATE	1 (1.3%)	0	1 (0.5%)
FLUTICASONE PROPIONATE	0	1 (0.7%)	1 (0.5%)
HYALURONIC ACID	1 (1.3%)	0	1 (0.5%)
IPRATROPIUM BROMIDE	1 (1.3%)	0	1 (0.5%)
KETOTIFEN FUMARATE	0	1 (0.7%)	1 (0.5%)
LEVOMENTHOL	0	1 (0.7%)	1 (0.5%)
NAPHAZOLINE	0	1 (0.7%)	1 (0.5%)
PHENYLEPHRINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
PREDNISOLONE ACETATE	0	1 (0.7%)	1 (0.5%)
PSEUDOEPHEDRINE	1 (1.3%)	0	1 (0.5%)
SODIUM HYPOCHLORITE	0	1 (0.7%)	1 (0.5%)
TETRYZOLINE	0	1 (0.7%)	1 (0.5%)
TRIAMCINOLONE ACETONIDE	0	1 (0.7%)	1 (0.5%)
XYLOMETAZOLINE	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
OPHTHALMOLOGICAL AND OTOLOGICAL PREPARATIONS			
Total number of patients with at least one treatment	64 (84.2%)	125 (85.6%)	189 (85.1%)
Total number of treatments	738	952	1690
DEXAMETHASONE	51 (67.1%)	100 (68.5%)	151 (68.0%)
DEXAMETHASONE SODIUM PHOSPHATE	9 (11.8%)	22 (15.1%)	31 (14.0%)
LEVOFLOXACIN	9 (11.8%)	17 (11.6%)	26 (11.7%)
CIPROFLOXACIN	8 (10.5%)	13 (8.9%)	21 (9.5%)
PREDNISOLONE	2 (2.6%)	7 (4.8%)	9 (4.1%)
BETAMETHASONE	5 (6.6%)	2 (1.4%)	7 (3.2%)
BETAMETHASONE VALERATE;GENTAMICIN SULFATE	2 (2.6%)	4 (2.7%)	6 (2.7%)
CHLORHEXIDINE GLUCONATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
GENTAMICIN SULFATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
CHLORAMPHENICOL	0	2 (1.4%)	2 (0.9%)
GATIFLOXACIN	1 (1.3%)	1 (0.7%)	2 (0.9%)
NEOMYCIN	0	2 (1.4%)	2 (0.9%)
NEOMYCIN SULFATE	0	2 (1.4%)	2 (0.9%)
OFLOXACIN	0	2 (1.4%)	2 (0.9%)
TETRACYCLINE	0	2 (1.4%)	2 (0.9%)
BACITRACIN;NEOMYCIN	0	1 (0.7%)	1 (0.5%)
BACITRACIN;NEOMYCIN SULFATE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE DIPROPIONATE;GENTAMICIN SULFATE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE SODIUM PHOSPHATE;NEOMYCIN SULFATE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE VALERATE;NEOMYCIN SULFATE	1 (1.3%)	0	1 (0.5%)
BETAMETHASONE;GENTAMICIN	1 (1.3%)	0	1 (0.5%)
CHLORHEXIDINE	0	1 (0.7%)	1 (0.5%)
CORTICOSTEROID NOS	0	1 (0.7%)	1 (0.5%)
DEXAMETHASONE SODIUM PHOSPHATE;NEOMYCIN SULFATE	0	1 (0.7%)	1 (0.5%)
DEXAMETHASONE VALERATE	0	1 (0.7%)	1 (0.5%)
DEXAMETHASONE;TOBRAMYCIN	0	1 (0.7%)	1 (0.5%)
PREDNISOLONE ACETATE	0	1 (0.7%)	1 (0.5%)
PREDNISOLONE METASULFOBENZOATE SODIUM	1 (1.3%)	0	1 (0.5%)
PREDNISOLONE SODIUM SUCCINATE	0	1 (0.7%)	1 (0.5%)
TETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
OPHTHALMOLOGICALS			
Total number of patients with at least one treatment	72 (94.7%)	138 (94.5%)	210 (94.6%)
Total number of treatments	929	1357	2286
DEXAMETHASONE	51 (67.1%)	100 (68.5%)	151 (68.0%)
DEXAMETHASONE SODIUM PHOSPHATE	9 (11.8%)	22 (15.1%)	31 (14.0%)
LEVOFLOXACIN	9 (11.8%)	17 (11.6%)	26 (11.7%)
CIPROFLOXACIN	8 (10.5%)	13 (8.9%)	21 (9.5%)
HYDROCORTISONE	5 (6.6%)	13 (8.9%)	18 (8.1%)
ASCORBIC ACID	7 (9.2%)	9 (6.2%)	16 (7.2%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
SODIUM CHLORIDE	3 (3.9%)	13 (8.9%)	16 (7.2%)
POTASSIUM CHLORIDE	3 (3.9%)	10 (6.8%)	13 (5.9%)
ACETYLCYSTEINE	4 (5.3%)	7 (4.8%)	11 (5.0%)
DICLOFENAC SODIUM	3 (3.9%)	7 (4.8%)	10 (4.5%)
METHYLPREDNISOLONE	3 (3.9%)	6 (4.1%)	9 (4.1%)
PREDNISOLONE	2 (2.6%)	7 (4.8%)	9 (4.1%)
SODIUM GUALENATE HYDRATE	2 (2.6%)	7 (4.8%)	9 (4.1%)
CETIRIZINE	3 (3.9%)	5 (3.4%)	8 (3.6%)
DICLOFENAC	0	8 (5.5%)	8 (3.6%)
HYALURONATE SODIUM	2 (2.6%)	6 (4.1%)	8 (3.6%)
PREDNISONE	3 (3.9%)	5 (3.4%)	8 (3.6%)
REBAMIPIDE	2 (2.6%)	6 (4.1%)	8 (3.6%)
BETAMETHASONE	5 (6.6%)	2 (1.4%)	7 (3.2%)
ACICLOVIR	0	6 (4.1%)	6 (2.7%)
BETAMETHASONE VALERATE;GENTAMICIN SULFATE	2 (2.6%)	4 (2.7%)	6 (2.7%)
FLUCONAZOLE	2 (2.6%)	4 (2.7%)	6 (2.7%)
HEPARINOID	2 (2.6%)	4 (2.7%)	6 (2.7%)
HYDROCORTISONE SODIUM SUCCINATE	1 (1.3%)	5 (3.4%)	6 (2.7%)
KETOROLAC TROMETHAMINE	0	6 (4.1%)	6 (2.7%)
NAPROXEN	4 (5.3%)	2 (1.4%)	6 (2.7%)
PANCREATIN	2 (2.6%)	4 (2.7%)	6 (2.7%)
BETAMETHASONE VALERATE	1 (1.3%)	4 (2.7%)	5 (2.3%)
BILASTINE	1 (1.3%)	4 (2.7%)	5 (2.3%)
CEFUROXIME	1 (1.3%)	4 (2.7%)	5 (2.3%)
FLUOROMETHOLONE	3 (3.9%)	2 (1.4%)	5 (2.3%)
FUSIDIC ACID	3 (3.9%)	2 (1.4%)	5 (2.3%)
LIDOCAINE	1 (1.3%)	4 (2.7%)	5 (2.3%)
MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER	2 (2.6%)	3 (2.1%)	5 (2.3%)
AZITHROMYCIN	0	4 (2.7%)	4 (1.8%)
CETIRIZINE HYDROCHLORIDE	1 (1.3%)	3 (2.1%)	4 (1.8%)
GUAIAZULENE	1 (1.3%)	3 (2.1%)	4 (1.8%)
KETOROLAC	3 (3.9%)	1 (0.7%)	4 (1.8%)
ACHYRANTHES BIDENTATA ROOT;ACONITUM SPP. PROCESSED ROOT;ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER;CINNAMOMUM CASSIA BARK;CORNUS OFFICINALIS FRUIT;DIOSCOREA SPP. RHIZOME;PAEONIA X SUFFRUTICOSA ROOT BARK;PLANTAGO ASIATICA SEED; PORIA COCOS SCLEROTIUM;REHMANNIA GLUTINOSA ROOT	1 (1.3%)	2 (1.4%)	3 (1.4%)
CHLORHEXIDINE GLUCONATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
DIMETICONE	1 (1.3%)	2 (1.4%)	3 (1.4%)
GENTAMICIN SULFATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
LIDOCAINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
MELOXICAM	1 (1.3%)	2 (1.4%)	3 (1.4%)
MOXIFLOXACIN HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
OLOPATADINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
POVIDONE-IODINE	0	3 (2.1%)	3 (1.4%)

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ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
THIOTRIAZOLINE	2 (2.6%)	1 (0.7%)	3 (1.4%)
VIDARABINE	1 (1.3%)	2 (1.4%)	3 (1.4%)
ALBUMIN HUMAN	1 (1.3%)	1 (0.7%)	2 (0.9%)
ANTIBIOTICS	1 (1.3%)	1 (0.7%)	2 (0.9%)
BEPOTASTINE BESILATE	0	2 (1.4%)	2 (0.9%)
BETAMETHASONE DIPROPIONATE	1 (1.3%)	1 (0.7%)	2 (0.9%)
BRINZOLAMIDE;TIMOLOL MALEATE	0	2 (1.4%)	2 (0.9%)
BROMFENAC SODIUM	1 (1.3%)	1 (0.7%)	2 (0.9%)
CARBOMER	0	2 (1.4%)	2 (0.9%)
CHLORAMPHENICOL	0	2 (1.4%)	2 (0.9%)
CLONIDINE HYDROCHLORIDE	2 (2.6%)	0	2 (0.9%)
DESONIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
DIQUAFOSOL TETRASODIUM	0	2 (1.4%)	2 (0.9%)
GATIFLOXACIN	1 (1.3%)	1 (0.7%)	2 (0.9%)
GLUTATHIONE	1 (1.3%)	1 (0.7%)	2 (0.9%)
GLYCEROL	1 (1.3%)	1 (0.7%)	2 (0.9%)
INDOMETACIN	1 (1.3%)	1 (0.7%)	2 (0.9%)
MACROGOL	2 (2.6%)	0	2 (0.9%)
NAPROXEN SODIUM	2 (2.6%)	0	2 (0.9%)
NEOMYCIN	0	2 (1.4%)	2 (0.9%)
NEOMYCIN SULFATE	0	2 (1.4%)	2 (0.9%)
OFLOXACIN	0	2 (1.4%)	2 (0.9%)
PIRENOXINE	1 (1.3%)	1 (0.7%)	2 (0.9%)
SEA WATER	2 (2.6%)	0	2 (0.9%)
SULFADIAZINE SILVER	1 (1.3%)	1 (0.7%)	2 (0.9%)
SULFAMETHOXAZOLE	1 (1.3%)	1 (0.7%)	2 (0.9%)
TETRACYCLINE	0	2 (1.4%)	2 (0.9%)
TRIAMCINOLONE	0	2 (1.4%)	2 (0.9%)
VANCOMYCIN	0	2 (1.4%)	2 (0.9%)
ACETAZOLAMIDE	1 (1.3%)	0	1 (0.5%)
ADENOSINE	0	1 (0.7%)	1 (0.5%)
AMIKACIN	0	1 (0.7%)	1 (0.5%)
AMIKACIN SULFATE	0	1 (0.7%)	1 (0.5%)
AMPICILLIN	0	1 (0.7%)	1 (0.5%)
AZELASTINE	0	1 (0.7%)	1 (0.5%)
BACITRACIN;NEOMYCIN	0	1 (0.7%)	1 (0.5%)
BACITRACIN;NEOMYCIN SULFATE	0	1 (0.7%)	1 (0.5%)
BENZYLPENICILLIN	0	1 (0.7%)	1 (0.5%)
BEPOTASTINE SALICYLATE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE DIPROPIONATE;GENTAMICIN SULFATE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE SODIUM PHOSPHATE;NEOMYCIN SULFATE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE VALERATE;NEOMYCIN SULFATE	1 (1.3%)	0	1 (0.5%)
BETAMETHASONE;GENTAMICIN	1 (1.3%)	0	1 (0.5%)
BETAXOLOL HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
BIMATOPROST;TIMOLOL MALEATE	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
BORIC ACID;POTASSIUM CHLORIDE;SODIUM CARBONATE ANHYDROUS;SODIUM CHLORIDE;SODIUM PHOSPHATE DIBASIC	0	1 (0.7%)	1 (0.5%)
CARMELLOSE	0	1 (0.7%)	1 (0.5%)
CARMELLOSE SODIUM	0	1 (0.7%)	1 (0.5%)
CHLORHEXIDINE	0	1 (0.7%)	1 (0.5%)
CHLORTETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
CICLOSPORIN	0	1 (0.7%)	1 (0.5%)
CLOBETASONE BUTYRATE	0	1 (0.7%)	1 (0.5%)
CLOTRIMAZOLE	0	1 (0.7%)	1 (0.5%)
CORTICOSTEROID NOS	0	1 (0.7%)	1 (0.5%)
CORTISONE ACETATE	0	1 (0.7%)	1 (0.5%)
CYANOCOBALAMIN	1 (1.3%)	0	1 (0.5%)
DECAMETHOXINE	1 (1.3%)	0	1 (0.5%)
DEXAMETHASONE SODIUM PHOSPHATE;NEOMYCIN SULFATE	0	1 (0.7%)	1 (0.5%)
DEXAMETHASONE VALERATE	0	1 (0.7%)	1 (0.5%)
DEXAMETHASONE;TOBRAMYCIN	0	1 (0.7%)	1 (0.5%)
DIFLUPREDNATE	0	1 (0.7%)	1 (0.5%)
DORZOLAMIDE HYDROCHLORIDE;TIMOLOL MALEATE	0	1 (0.7%)	1 (0.5%)
ECONAZOLE	0	1 (0.7%)	1 (0.5%)
EPHEDRINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
EUPHRASIA OFFICINALIS	0	1 (0.7%)	1 (0.5%)
FAMCICLOVIR	0	1 (0.7%)	1 (0.5%)
FLUOCINOLONE ACETONIDE	1 (1.3%)	0	1 (0.5%)
FLURBIPROFEN AXETIL	0	1 (0.7%)	1 (0.5%)
HEPARIN	0	1 (0.7%)	1 (0.5%)
HYALURONIC ACID	1 (1.3%)	0	1 (0.5%)
HYDROGEN PEROXIDE	0	1 (0.7%)	1 (0.5%)
HYOSCINE HYDROBROMIDE	0	1 (0.7%)	1 (0.5%)
INTERFERON ALFA-2B	1 (1.3%)	0	1 (0.5%)
IODINE	1 (1.3%)	0	1 (0.5%)
KETOTIFEN FUMARATE	0	1 (0.7%)	1 (0.5%)
LATANOPROST	0	1 (0.7%)	1 (0.5%)
MOXIFLOXACIN	0	1 (0.7%)	1 (0.5%)
NAPHAZOLINE	0	1 (0.7%)	1 (0.5%)
NEOSTIGMINE METILSULFATE	1 (1.3%)	0	1 (0.5%)
OXYTETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
PARAFFIN	0	1 (0.7%)	1 (0.5%)
PHENYLEPHRINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
PIRENOXINE SODIUM	1 (1.3%)	0	1 (0.5%)
PREDNISOLONE ACETATE	0	1 (0.7%)	1 (0.5%)
PREDNISOLONE METASULFOBENZOATE SODIUM	1 (1.3%)	0	1 (0.5%)
PREDNISOLONE SODIUM SUCCINATE	0	1 (0.7%)	1 (0.5%)
PROCAINE BENZYLPENICILLIN	1 (1.3%)	0	1 (0.5%)
PROCAINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
SALICYLIC ACID	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)
SODIUM PHOSPHATE DIBASIC;SODIUM PHOSPHATE MONOBASIC (MONOHYDRATE)	0	1 (0.7%)	1 (0.5%)
TETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
TETRYZOLINE	0	1 (0.7%)	1 (0.5%)
TRIAMCINOLONE ACETONIDE	0	1 (0.7%)	1 (0.5%)
VANCOMYCIN HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
XYLOMETAZOLINE	0	1 (0.7%)	1 (0.5%)
OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS			
Total number of patients with at least one treatment	16 (21.1%)	26 (17.8%)	42 (18.9%)
Total number of treatments	310	143	453
THIOCTIC ACID	7 (9.2%)	7 (4.8%)	14 (6.3%)
ADEMETIONINE	9 (11.8%)	4 (2.7%)	13 (5.9%)
ACETYLCYSTEINE	4 (5.3%)	7 (4.8%)	11 (5.0%)
CLOSTRIDIUM BUTYRICUM	2 (2.6%)	5 (3.4%)	7 (3.2%)
SODIUM BICARBONATE	3 (3.9%)	2 (1.4%)	5 (2.3%)
QUERCETIN	2 (2.6%)	2 (1.4%)	4 (1.8%)
PROBIOTICS NOS	0	3 (2.1%)	3 (1.4%)
LYSINE	1 (1.3%)	1 (0.7%)	2 (0.9%)
ADEMETIONINE 1,4-BUTANEDISULFONATE	0	1 (0.7%)	1 (0.5%)
CUCUMIS MELO;SELENIUM;THIOCTIC ACID;VITAMIN E NOS	0	1 (0.7%)	1 (0.5%)
LEVOCARNITINE	1 (1.3%)	0	1 (0.5%)
PREBIOTICS NOS;PROBIOTICS NOS	0	1 (0.7%)	1 (0.5%)
SUCRALFATE	0	1 (0.7%)	1 (0.5%)
THIOCTIC ACID;VITAMIN B NOS	1 (1.3%)	0	1 (0.5%)
ZINC ACETATE	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
OTHER DERMATOLOGICAL PREPARATIONS			
Total number of patients with at least one treatment	25 (32.9%)	51 (34.9%)	76 (34.2%)
Total number of treatments	70	251	321
IBUPROFEN	9 (11.8%)	16 (11.0%)	25 (11.3%)
ASCORBIC ACID	7 (9.2%)	9 (6.2%)	16 (7.2%)
DICLOFENAC SODIUM	3 (3.9%)	7 (4.8%)	10 (4.5%)
DICLOFENAC	0	8 (5.5%)	8 (3.6%)
HYALURONATE SODIUM	2 (2.6%)	6 (4.1%)	8 (3.6%)
TRANEXAMIC ACID	1 (1.3%)	6 (4.1%)	7 (3.2%)
PYRIDOXINE HYDROCHLORIDE	4 (5.3%)	2 (1.4%)	6 (2.7%)
SODIUM BICARBONATE	3 (3.9%)	2 (1.4%)	5 (2.3%)
CALCIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	2 (2.6%)	2 (1.4%)	4 (1.8%)
GUAIAZULENE	1 (1.3%)	3 (2.1%)	4 (1.8%)
MAGNESIUM SULFATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
POVIDONE-IODINE	0	3 (2.1%)	3 (1.4%)
THIOTRIAZOLINE	2 (2.6%)	1 (0.7%)	3 (1.4%)
CALCIUM GLUCONATE	0	2 (1.4%)	2 (0.9%)
CINNAMOMUM CASSIA;EPHEDRA SPP.;GLYCYRRHIZA SPP.; PAEONIA LACTIFLORA;PUERARIA MONTANA VAR. LOBATA; ZINGIBER OFFICINALE;ZIZIPHUS JUJUBA	0	2 (1.4%)	2 (0.9%)
PYRIDOXINE	0	2 (1.4%)	2 (0.9%)
HYALURONIC ACID	1 (1.3%)	0	1 (0.5%)
HYDROGEN PEROXIDE	0	1 (0.7%)	1 (0.5%)
LACTOFERRIN	0	1 (0.7%)	1 (0.5%)
SALICYLIC ACID	0	1 (0.7%)	1 (0.5%)
SILICON DIOXIDE	0	1 (0.7%)	1 (0.5%)
SUCRALFATE	0	1 (0.7%)	1 (0.5%)
TALC	1 (1.3%)	0	1 (0.5%)
OTHER DRUGS FOR DISORDERS OF THE MUSCULO-SKELETAL SYSTEM			
Total number of patients with at least one treatment	8 (10.5%)	9 (6.2%)	17 (7.7%)
Total number of treatments	11	12	23
HYALURONATE SODIUM	2 (2.6%)	6 (4.1%)	8 (3.6%)
CYTIDINE PHOSPHATE SODIUM;DISODIUM URIDINE MONOPHOSPHATE;URIDINE DIPHOSPHATE DISODIUM; URIDINE TRIPHOSPHATE TRISODIUM	3 (3.9%)	0	3 (1.4%)
CYTIDINE MONOPHOSPHATE DISODIUM;URIDINE TRIPHOSPHATE TRISODIUM	2 (2.6%)	0	2 (0.9%)
SERRAPEPTASE	0	2 (1.4%)	2 (0.9%)
CLOMIPRAMINE	0	1 (0.7%)	1 (0.5%)
HYALURONIC ACID	1 (1.3%)	0	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
OTHER GYNECOLOGICALS			
Total number of patients with at least one treatment	27 (35.5%)	32 (21.9%)	59 (26.6%)
Total number of treatments	47	168	215
IBUPROFEN	9 (11.8%)	16 (11.0%)	25 (11.3%)
HYALURONATE SODIUM	2 (2.6%)	6 (4.1%)	8 (3.6%)
NAPROXEN	4 (5.3%)	2 (1.4%)	6 (2.7%)
BENZYDAMINE HYDROCHLORIDE	2 (2.6%)	3 (2.1%)	5 (2.3%)
SODIUM BICARBONATE	3 (3.9%)	2 (1.4%)	5 (2.3%)
SALBUTAMOL	1 (1.3%)	2 (1.4%)	3 (1.4%)
THIOTRIAZOLINE	2 (2.6%)	1 (0.7%)	3 (1.4%)
CARBOMER	0	2 (1.4%)	2 (0.9%)
CLONIDINE HYDROCHLORIDE	2 (2.6%)	0	2 (0.9%)
GLYCEROL	1 (1.3%)	1 (0.7%)	2 (0.9%)
NAPROXEN SODIUM	2 (2.6%)	0	2 (0.9%)
ARTEMISIA ARGYI LEAF	1 (1.3%)	0	1 (0.5%)
HYALURONIC ACID	1 (1.3%)	0	1 (0.5%)
IBUPROFEN ARGININE	1 (1.3%)	0	1 (0.5%)
INTERFERON ALFA-2B	1 (1.3%)	0	1 (0.5%)
INTRAUTERINE CONTRACEPTIVE DEVICE	0	1 (0.7%)	1 (0.5%)
MISOPROSTOL	0	1 (0.7%)	1 (0.5%)
NIFEDIPINE	0	1 (0.7%)	1 (0.5%)
PAROXETINE	1 (1.3%)	0	1 (0.5%)
SALBUTAMOL SULFATE	0	1 (0.7%)	1 (0.5%)
OTHER HEMATOLOGICAL AGENTS			
Total number of patients with at least one treatment	0	1 (0.7%)	1 (0.5%)
Total number of treatments	0	1	1
BROMELAINS;CYSTEINE	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
OTHER NERVOUS SYSTEM DRUGS			
Total number of patients with at least one treatment	29 (38.2%)	41 (28.1%)	70 (31.5%)
Total number of treatments	284	182	466
THIOCTIC ACID	7 (9.2%)	7 (4.8%)	14 (6.3%)
MELDONIUM	7 (9.2%)	4 (2.7%)	11 (5.0%)
DIMENHYDRINATE	3 (3.9%)	7 (4.8%)	10 (4.5%)
GABAPENTIN	4 (5.3%)	5 (3.4%)	9 (4.1%)
TRIMETAZIDINE HYDROCHLORIDE	3 (3.9%)	4 (2.7%)	7 (3.2%)
NALOXONE HYDROCHLORIDE;OXYCODONE HYDROCHLORIDE	2 (2.6%)	4 (2.7%)	6 (2.7%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE HYDROCHLORIDE	2 (2.6%)	2 (1.4%)	4 (1.8%)
MECOBALAMIN	2 (2.6%)	2 (1.4%)	4 (1.8%)
CURCUMIN;LECITHIN;MANGIFERA INDICA;PIPER NIGRUM; PYRIDOXINE HYDROCHLORIDE;RESVERATROL;RIBOFLAVIN	0	3 (2.1%)	3 (1.4%)
BETAHISTINE MESILATE	1 (1.3%)	1 (0.7%)	2 (0.9%)
CLONIDINE HYDROCHLORIDE	2 (2.6%)	0	2 (0.9%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE DISULFIDE PHOSPHATE	0	2 (1.4%)	2 (0.9%)
CYTIDINE MONOPHOSPHATE DISODIUM;URIDINE TRIPHOSPHATE TRISODIUM	2 (2.6%)	0	2 (0.9%)
LYSINE	1 (1.3%)	1 (0.7%)	2 (0.9%)
METHYLETHYLPIRIDINOL SUCCINATE	1 (1.3%)	1 (0.7%)	2 (0.9%)
PHOSPHOLIPIDS	0	2 (1.4%)	2 (0.9%)
PROPRANOLOL	0	2 (1.4%)	2 (0.9%)
VITAMIN B12 NOS	1 (1.3%)	1 (0.7%)	2 (0.9%)
ATRACTYLODES SPP. RHIZOME;CINNAMOMUM CASSIA BARK; GLYCYRRHIZA SPP. ROOT;PORIA COCOS SCLEROTIUM	1 (1.3%)	0	1 (0.5%)
BACLOFEN	1 (1.3%)	0	1 (0.5%)
BETAHISTINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
BUPRENORPHINE	1 (1.3%)	0	1 (0.5%)
BUPRENORPHINE HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
BUPROPION HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
CHOLINE ALFOSCERATE	0	1 (0.7%)	1 (0.5%)
CYANOCOBALAMIN	1 (1.3%)	0	1 (0.5%)
CYANOCOBALAMIN;CYTIDINE PHOSPHATE;DISODIUM URIDINE MONOPHOSPHATE;FOLIC ACID	0	1 (0.7%)	1 (0.5%)
CYTIDINE MONOPHOSPHATE DISODIUM;HYDROXOCOBALAMIN ACETATE;URIDINE TRIPHOSPHATE TRISODIUM	0	1 (0.7%)	1 (0.5%)
FLUOXETINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
GINKGO BILOBA	0	1 (0.7%)	1 (0.5%)
MECLOZINE	0	1 (0.7%)	1 (0.5%)
NEOSTIGMINE METILSULFATE	1 (1.3%)	0	1 (0.5%)
PROPRANOLOL HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
TALTIRELIN TETRAHYDRATE	1 (1.3%)	0	1 (0.5%)

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
OTHER RESPIRATORY SYSTEM PRODUCTS			
Total number of patients with at least one treatment	7 (9.2%)	7 (4.8%)	14 (6.3%)
Total number of treatments	14	9	23
AMBROXOL HYDROCHLORIDE	5 (6.6%)	2 (1.4%)	7 (3.2%)
DIMETICONE	1 (1.3%)	2 (1.4%)	3 (1.4%)
AMBROXOL	1 (1.3%)	1 (0.7%)	2 (0.9%)
PHOSPHOLIPIDS	0	2 (1.4%)	2 (0.9%)
ACETAZOLAMIDE	1 (1.3%)	0	1 (0.5%)
ANEMARRHENA ASPHODELOIDES RHIZOME;CALCIUM SULFATE;CIMICIFUGA SPP. RHIZOME;ERIOBOTRYA JAPONICA LEAF;GARDENIA JASMINOIDES FRUIT;LILIUM SPP. BULB;MAGNOLIA SPP. FLOWER;OPHIOPOGON JAPONICUS TUBER;SCUTELLARIA BAICALENSIS ROOT	1 (1.3%)	0	1 (0.5%)
BACTERIA LYSATE NOS	1 (1.3%)	0	1 (0.5%)
OTOLOGICALS			
Total number of patients with at least one treatment	66 (86.8%)	130 (89.0%)	196 (88.3%)
Total number of treatments	778	1049	1827
DEXAMETHASONE	51 (67.1%)	100 (68.5%)	151 (68.0%)
DEXAMETHASONE SODIUM PHOSPHATE	9 (11.8%)	22 (15.1%)	31 (14.0%)
LEVOFLOXACIN	9 (11.8%)	17 (11.6%)	26 (11.7%)
CIPROFLOXACIN	8 (10.5%)	13 (8.9%)	21 (9.5%)
HYDROCORTISONE	5 (6.6%)	13 (8.9%)	18 (8.1%)
SODIUM CHLORIDE	3 (3.9%)	13 (8.9%)	16 (7.2%)
PREDNISOLONE	2 (2.6%)	7 (4.8%)	9 (4.1%)
BETAMETHASONE	5 (6.6%)	2 (1.4%)	7 (3.2%)
HYDROCORTISONE SODIUM SUCCINATE	1 (1.3%)	5 (3.4%)	6 (2.7%)
BETAMETHASONE VALERATE	1 (1.3%)	4 (2.7%)	5 (2.3%)
LIDOCAINE	1 (1.3%)	4 (2.7%)	5 (2.3%)
SODIUM BICARBONATE	3 (3.9%)	2 (1.4%)	5 (2.3%)
CHLORHEXIDINE GLUCONATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
GENTAMICIN SULFATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
LIDOCAINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
MICONAZOLE	0	3 (2.1%)	3 (1.4%)
BETAMETHASONE DIPROPIONATE	1 (1.3%)	1 (0.7%)	2 (0.9%)
CHLORAMPHENICOL	0	2 (1.4%)	2 (0.9%)
DOCUSATE SODIUM	0	2 (1.4%)	2 (0.9%)
GLYCEROL	1 (1.3%)	1 (0.7%)	2 (0.9%)
NEOMYCIN	0	2 (1.4%)	2 (0.9%)
NEOMYCIN SULFATE	0	2 (1.4%)	2 (0.9%)
OFLOXACIN	0	2 (1.4%)	2 (0.9%)
SEA WATER	2 (2.6%)	0	2 (0.9%)
TETRACYCLINE	0	2 (1.4%)	2 (0.9%)
ACETIC ACID	0	1 (0.7%)	1 (0.5%)

Treatments are coded using the WHODRUG GLOBAL B3 SEPTEMBER 1, 2022. dictionary. Treatments can appear under multiple classes. The table includes medications that have temporal overlap with study drug administration. Multiple uses of a specific medication for a patient were counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a patient were counted once in the frequency for the medication class. Use of the anti-diarrheal medication Loperamide is primarily summarized in separate outputs.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
BETAMETHASONE SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)
CHLORHEXIDINE	0	1 (0.7%)	1 (0.5%)
CLOTRIMAZOLE	0	1 (0.7%)	1 (0.5%)
CORTICOSTEROID NOS	0	1 (0.7%)	1 (0.5%)
DECAMETHOXINE	1 (1.3%)	0	1 (0.5%)
DEXAMETHASONE SODIUM PHOSPHATE;NEOMYCIN SULFATE	0	1 (0.7%)	1 (0.5%)
DEXAMETHASONE VALERATE	0	1 (0.7%)	1 (0.5%)
DEXAMETHASONE;TOBRAMYCIN	0	1 (0.7%)	1 (0.5%)
DOCUSATE	0	1 (0.7%)	1 (0.5%)
FLUOCINOLONE ACETONIDE	1 (1.3%)	0	1 (0.5%)
HYDROGEN PEROXIDE	0	1 (0.7%)	1 (0.5%)
OXYTETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
PREDNISOLONE ACETATE	0	1 (0.7%)	1 (0.5%)
PREDNISOLONE METASULFOBENZOATE SODIUM	1 (1.3%)	0	1 (0.5%)
PREDNISOLONE SODIUM SUCCINATE	0	1 (0.7%)	1 (0.5%)
SALICYLIC ACID	0	1 (0.7%)	1 (0.5%)
TETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
PERIPHERAL VASODILATORS			
Total number of patients with at least one treatment	2 (2.6%)	7 (4.8%)	9 (4.1%)
Total number of treatments	2	10	12
ACHYRANTHES BIDENTATA ROOT;ACONITUM SPP. PROCESSED ROOT;ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER;CINNAMOMUM CASSIA BARK;CORNUS OFFICINALIS FRUIT;DIOSCOREA SPP. RHIZOME;PAEONIA X SUFFRUTICOSA ROOT BARK;PLANTAGO ASIATICA SEED;PORIA COCOS SCLEROTIUM;REHMANNIA GLUTINOSA ROOT	1 (1.3%)	2 (1.4%)	3 (1.4%)
METHYLETHYLPIRIDINOL SUCCINATE	1 (1.3%)	1 (0.7%)	2 (0.9%)
PENTOXIFYLLINE	0	2 (1.4%)	2 (0.9%)
ACONITUM SPP. PROCESSED ROOT;ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER;CINNAMOMUM CASSIA BARK;CORNUS OFFICINALIS FRUIT;DIOSCOREA SPP. RHIZOME;PAEONIA X SUFFRUTICOSA ROOT BARK;PORIA COCOS SCLEROTIUM;REHMANNIA GLUTINOSA ROOT	0	1 (0.7%)	1 (0.5%)
BETAHISTINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
GINKGO BILOBA	0	1 (0.7%)	1 (0.5%)
PITUITARY AND HYPOTHALAMIC HORMONES AND ANALOGUES			
Total number of patients with at least one treatment	0	2 (1.4%)	2 (0.9%)
Total number of treatments	0	2	2
LEUPRORELIN	0	1 (0.7%)	1 (0.5%)
OCTREOTIDE ACETATE	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCERS			
Total number of patients with at least one treatment	11 (14.5%)	28 (19.2%)	39 (17.6%)
Total number of treatments	38	79	117
SODIUM CHLORIDE	3 (3.9%)	13 (8.9%)	16 (7.2%)
HYALURONATE SODIUM	2 (2.6%)	6 (4.1%)	8 (3.6%)
METHYLURACIL	3 (3.9%)	3 (2.1%)	6 (2.7%)
CAMPHOR;CHLORPHENAMINE MALEATE;HEXACHLOROPHENE; LIDOCAINE HYDROCHLORIDE;MENTHOL;METHYL SALICYLATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
DIMETICONE	1 (1.3%)	2 (1.4%)	3 (1.4%)
LYSINE	1 (1.3%)	1 (0.7%)	2 (0.9%)
AESCULUS HIPPOCASTANUM	0	1 (0.7%)	1 (0.5%)
CARMELLOSE	0	1 (0.7%)	1 (0.5%)
CARMELLOSE SODIUM	0	1 (0.7%)	1 (0.5%)
DEXPANTHENOL;MIRAMISTIN	1 (1.3%)	0	1 (0.5%)
ENOXOLONE	0	1 (0.7%)	1 (0.5%)
FISH OIL	0	1 (0.7%)	1 (0.5%)
HAMAMELIS VIRGINIANA;PHENAZONE;TANNIC ACID	0	1 (0.7%)	1 (0.5%)
HYALURONIC ACID	1 (1.3%)	0	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
PSYCHOANALEPTICS			
Total number of patients with at least one treatment	19 (25.0%)	23 (15.8%)	42 (18.9%)
Total number of treatments	188	86	274
ADEMETIONINE	9 (11.8%)	4 (2.7%)	13 (5.9%)
AMITRIPTYLINE	1 (1.3%)	2 (1.4%)	3 (1.4%)
DULOXETINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
MIRTAZAPINE	0	3 (2.1%)	3 (1.4%)
SERTRALINE	0	3 (2.1%)	3 (1.4%)
AMITRIPTYLINE HYDROCHLORIDE	2 (2.6%)	0	2 (0.9%)
CLONIDINE HYDROCHLORIDE	2 (2.6%)	0	2 (0.9%)
DULOXETINE	0	2 (1.4%)	2 (0.9%)
IPIDACRINE	1 (1.3%)	1 (0.7%)	2 (0.9%)
METHYLETHYLPIRIDINOL SUCCINATE	1 (1.3%)	1 (0.7%)	2 (0.9%)
ADEMETIONINE 1,4-BUTANEDISULFONATE	0	1 (0.7%)	1 (0.5%)
BUPROPION HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
CAMELLIA SINENSIS	0	1 (0.7%)	1 (0.5%)
CITALOPRAM	0	1 (0.7%)	1 (0.5%)
CITALOPRAM HYDROBROMIDE	1 (1.3%)	0	1 (0.5%)
CLOMIPRAMINE	0	1 (0.7%)	1 (0.5%)
CORDYCEPS SINENSIS	0	1 (0.7%)	1 (0.5%)
DESVENLAFAXINE	1 (1.3%)	0	1 (0.5%)
DOXEPIN HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
ESCITALOPRAM OXALATE	1 (1.3%)	0	1 (0.5%)
FLUOXETINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
GINKGO BILOBA	0	1 (0.7%)	1 (0.5%)
LAMOTRIGINE	1 (1.3%)	0	1 (0.5%)
MAGNOLIA SPP. BARK;PERILLA FRUTESCENS VAR. CRISPA HERB;PINELLIA TERNATA TUBER;PORIA COCOS SCLEROTIUM;ZINGIBER OFFICINALE RHIZOME	0	1 (0.7%)	1 (0.5%)
PAROXETINE	1 (1.3%)	0	1 (0.5%)
PIRACETAM	0	1 (0.7%)	1 (0.5%)
SERTRALINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
VENLAFAXINE	0	1 (0.7%)	1 (0.5%)
VENLAFAXINE HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
PSYCHOLEPTICS			
Total number of patients with at least one treatment	48 (63.2%)	91 (62.3%)	139 (62.6%)
Total number of treatments	292	421	713
PREGABALIN	18 (23.7%)	23 (15.8%)	41 (18.5%)
DIPHENHYDRAMINE HYDROCHLORIDE	13 (17.1%)	24 (16.4%)	37 (16.7%)
DIPHENHYDRAMINE	14 (18.4%)	21 (14.4%)	35 (15.8%)
LORAZEPAM	4 (5.3%)	8 (5.5%)	12 (5.4%)
ALPRAZOLAM	3 (3.9%)	7 (4.8%)	10 (4.5%)
PROCHLORPERAZINE	1 (1.3%)	7 (4.8%)	8 (3.6%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
ZOLPIDEM TARTRATE	1 (1.3%)	6 (4.1%)	7 (3.2%)
CLONAZEPAM	0	6 (4.1%)	6 (2.7%)
DIAZEPAM	2 (2.6%)	3 (2.1%)	5 (2.3%)
PROMETHAZINE	3 (3.9%)	2 (1.4%)	5 (2.3%)
HYDROXYZINE	0	4 (2.7%)	4 (1.8%)
LEVOSULPIRIDE	1 (1.3%)	3 (2.1%)	4 (1.8%)
MIDAZOLAM	0	4 (2.7%)	4 (1.8%)
ZOLPIDEM	1 (1.3%)	3 (2.1%)	4 (1.8%)
AMITRIPTYLINE	1 (1.3%)	2 (1.4%)	3 (1.4%)
BROMAZEPAM	1 (1.3%)	2 (1.4%)	3 (1.4%)
DULOXETINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
MELATONIN	1 (1.3%)	2 (1.4%)	3 (1.4%)
SERTRALINE	0	3 (2.1%)	3 (1.4%)
AMITRIPTYLINE HYDROCHLORIDE	2 (2.6%)	0	2 (0.9%)
DULOXETINE	0	2 (1.4%)	2 (0.9%)
ESTAZOLAM	1 (1.3%)	1 (0.7%)	2 (0.9%)
PROCHLORPERAZINE MALEATE	0	2 (1.4%)	2 (0.9%)
PROPRANOLOL	0	2 (1.4%)	2 (0.9%)
RILMAZAFONE HYDROCHLORIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
ZOPICLONE	1 (1.3%)	1 (0.7%)	2 (0.9%)
ARIPIPRAZOLE	0	1 (0.7%)	1 (0.5%)
ATRACTYLODES SPP. RHIZOME;CINNAMOMUM CASSIA BARK; GLYCYRRHIZA SPP. ROOT;PORIA COCOS SCLEROTIUM	1 (1.3%)	0	1 (0.5%)
BROTIZOLAM	1 (1.3%)	0	1 (0.5%)
CLOMIPRAMINE	0	1 (0.7%)	1 (0.5%)
DOXEPIN HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
ESCITALOPRAM OXALATE	1 (1.3%)	0	1 (0.5%)
ESZOPICLONE	0	1 (0.7%)	1 (0.5%)
FLUDIAZEPAM	0	1 (0.7%)	1 (0.5%)
FLUOXETINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
HALOPERIDOL	0	1 (0.7%)	1 (0.5%)
HYDROXYZINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
HYOSCINE HYDROBROMIDE	0	1 (0.7%)	1 (0.5%)
LORMETAZEPAM	0	1 (0.7%)	1 (0.5%)
MAGNOLIA SPP. BARK;PERILLA FRUTESCENS VAR. CRISPA HERB;PINELLIA TERNATA TUBER;PORIA COCOS SCLEROTIUM;ZINGIBER OFFICINALE RHIZOME	0	1 (0.7%)	1 (0.5%)
MIDAZOLAM HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
PAPAVER SOMNIFERUM	0	1 (0.7%)	1 (0.5%)
PAROXETINE	1 (1.3%)	0	1 (0.5%)
PLATYCODON GRANDIFLORUS ROOT	0	1 (0.7%)	1 (0.5%)
PROPRANOLOL HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
QUETIAPINE FUMARATE	0	1 (0.7%)	1 (0.5%)
SERTRALINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
THIORIDAZINE	0	1 (0.7%)	1 (0.5%)
TIAPRIDE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
VALPROATE SEMISODIUM	0	1 (0.7%)	1 (0.5%)
VENLAFAXINE	0	1 (0.7%)	1 (0.5%)
VENLAFAXINE HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM			
Total number of patients with at least one treatment	1 (1.3%)	2 (1.4%)	3 (1.4%)
Total number of treatments	1	2	3
DROSPIRENONE;ETHINYLESTRADIOL	1 (1.3%)	0	1 (0.5%)
ETHINYLESTRADIOL;GESTODENE	0	1 (0.7%)	1 (0.5%)
MEGESTROL	0	1 (0.7%)	1 (0.5%)
STOMATOLOGICAL PREPARATIONS			
Total number of patients with at least one treatment	67 (88.2%)	135 (92.5%)	202 (91.0%)
Total number of treatments	807	1101	1908
DEXAMETHASONE	51 (67.1%)	100 (68.5%)	151 (68.0%)
DEXAMETHASONE SODIUM PHOSPHATE	9 (11.8%)	22 (15.1%)	31 (14.0%)
HYDROCORTISONE	5 (6.6%)	13 (8.9%)	18 (8.1%)
SODIUM CHLORIDE	3 (3.9%)	13 (8.9%)	16 (7.2%)
DICLOFENAC SODIUM	3 (3.9%)	7 (4.8%)	10 (4.5%)
ACETYLSALICYLIC ACID	3 (3.9%)	6 (4.1%)	9 (4.1%)
KETOPROFEN	4 (5.3%)	5 (3.4%)	9 (4.1%)
METRONIDAZOLE	2 (2.6%)	7 (4.8%)	9 (4.1%)
NIMESULIDE	5 (6.6%)	4 (2.7%)	9 (4.1%)
PREDNISOLONE	2 (2.6%)	7 (4.8%)	9 (4.1%)
SODIUM GUALENATE HYDRATE	2 (2.6%)	7 (4.8%)	9 (4.1%)
DICLOFENAC	0	8 (5.5%)	8 (3.6%)
HYALURONATE SODIUM	2 (2.6%)	6 (4.1%)	8 (3.6%)
BETAMETHASONE	5 (6.6%)	2 (1.4%)	7 (3.2%)
TRANEXAMIC ACID	1 (1.3%)	6 (4.1%)	7 (3.2%)
HYDROCORTISONE SODIUM SUCCINATE	1 (1.3%)	5 (3.4%)	6 (2.7%)
NAPROXEN	4 (5.3%)	2 (1.4%)	6 (2.7%)
BENZYDAMINE HYDROCHLORIDE	2 (2.6%)	3 (2.1%)	5 (2.3%)
CLOBETASOL PROPIONATE	2 (2.6%)	3 (2.1%)	5 (2.3%)
LIDOCAINE	1 (1.3%)	4 (2.7%)	5 (2.3%)
SODIUM BICARBONATE	3 (3.9%)	2 (1.4%)	5 (2.3%)
ELECTROLYTES NOS	0	4 (2.7%)	4 (1.8%)
CHLORHEXIDINE GLUCONATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
DIMETICONE	1 (1.3%)	2 (1.4%)	3 (1.4%)
LIDOCAINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
MICONAZOLE	0	3 (2.1%)	3 (1.4%)
POVIDONE-IODINE	0	3 (2.1%)	3 (1.4%)
CARBOMER	0	2 (1.4%)	2 (0.9%)
CHLORAMPHENICOL	0	2 (1.4%)	2 (0.9%)
GLYCEROL	1 (1.3%)	1 (0.7%)	2 (0.9%)

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ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
LIDOCAINE;PRILOCAINE	0	2 (1.4%)	2 (0.9%)
NEOMYCIN	0	2 (1.4%)	2 (0.9%)
NEOMYCIN SULFATE	0	2 (1.4%)	2 (0.9%)
TETRACYCLINE	0	2 (1.4%)	2 (0.9%)
TRIAMCINOLONE	0	2 (1.4%)	2 (0.9%)
AMPHOTERICIN B	0	1 (0.7%)	1 (0.5%)
BENZOCAINE;HERBAL NOS;SALICYLIC ACID	0	1 (0.7%)	1 (0.5%)
BENZYDAMINE HYDROCHLORIDE;CETYLPYRIDINIUM CHLORIDE	0	1 (0.7%)	1 (0.5%)
BICLOTYMOL	1 (1.3%)	0	1 (0.5%)
CHLORHEXIDINE	0	1 (0.7%)	1 (0.5%)
CHLORHEXIDINE GLUCONATE;METRONIDAZOLE BENZOATE	1 (1.3%)	0	1 (0.5%)
CHLORTETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
CLOTRIMAZOLE	0	1 (0.7%)	1 (0.5%)
COPTIS SPP. RHIZOME;GLYCYRRHIZA SPP. ROOT;PANAX GINSENG ROOT;PINELLIA TERNATA TUBER;SCUTELLARIA BAICALENSIS ROOT;ZINGIBER OFFICINALE PROCESSED RHIZOME;ZIZIPHUS JUJUBA FRUIT	0	1 (0.7%)	1 (0.5%)
CORTICOSTEROID NOS	0	1 (0.7%)	1 (0.5%)
DEXAMETHASONE VALERATE	0	1 (0.7%)	1 (0.5%)
DOMIPHEN BROMIDE	0	1 (0.7%)	1 (0.5%)
ENOXOLONE	0	1 (0.7%)	1 (0.5%)
GLUCOSE OXIDASE;LACTOFERRIN;LACTOPEROXIDASE; LYSOZYME	1 (1.3%)	0	1 (0.5%)
HEXETIDINE	1 (1.3%)	0	1 (0.5%)
HYALURONIC ACID	1 (1.3%)	0	1 (0.5%)
HYDROGEN PEROXIDE	0	1 (0.7%)	1 (0.5%)
IODINE	1 (1.3%)	0	1 (0.5%)
NYSTATIN	1 (1.3%)	0	1 (0.5%)
OXYTETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
POLIHEXANIDE;UNDECYLENAMIDOPROPYL BETAINE	1 (1.3%)	0	1 (0.5%)
PREDNISOLONE ACETATE	0	1 (0.7%)	1 (0.5%)
SALICYLIC ACID	0	1 (0.7%)	1 (0.5%)
SODIUM HYPOCHLORITE	0	1 (0.7%)	1 (0.5%)
SUCRALFATE	0	1 (0.7%)	1 (0.5%)
TETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
THYMOL	0	1 (0.7%)	1 (0.5%)
TRIAMCINOLONE ACETONIDE	0	1 (0.7%)	1 (0.5%)
ZINC ACETATE	0	1 (0.7%)	1 (0.5%)

Treatments are coded using the WHODRUG GLOBAL B3 SEPTEMBER 1, 2022. dictionary. Treatments can appear under multiple classes. The table includes medications that have temporal overlap with study drug administration. Multiple uses of a specific medication for a patient were counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a patient were counted once in the frequency for the medication class. Use of the anti-diarrheal medication Loperamide is primarily summarized in separate outputs.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
THROAT PREPARATIONS			
Total number of patients with at least one treatment	26 (34.2%)	54 (37.0%)	80 (36.0%)
Total number of treatments	48	227	275
IBUPROFEN	9 (11.8%)	16 (11.0%)	25 (11.3%)
DICLOFENAC SODIUM	3 (3.9%)	7 (4.8%)	10 (4.5%)
KETOPROFEN	4 (5.3%)	5 (3.4%)	9 (4.1%)
SODIUM GUALENATE HYDRATE	2 (2.6%)	7 (4.8%)	9 (4.1%)
DICLOFENAC	0	8 (5.5%)	8 (3.6%)
AMBROXOL HYDROCHLORIDE	5 (6.6%)	2 (1.4%)	7 (3.2%)
BENZYDAMINE HYDROCHLORIDE	2 (2.6%)	3 (2.1%)	5 (2.3%)
LIDOCAINE	1 (1.3%)	4 (2.7%)	5 (2.3%)
CHLORHEXIDINE GLUCONATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
LIDOCAINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
POVIDONE-IODINE	0	3 (2.1%)	3 (1.4%)
AMBROXOL	1 (1.3%)	1 (0.7%)	2 (0.9%)
ANTIBIOTICS	1 (1.3%)	1 (0.7%)	2 (0.9%)
NEOMYCIN	0	2 (1.4%)	2 (0.9%)
NEOMYCIN SULFATE	0	2 (1.4%)	2 (0.9%)
TETRACYCLINE	0	2 (1.4%)	2 (0.9%)
BACITRACIN;NEOMYCIN	0	1 (0.7%)	1 (0.5%)
BACITRACIN;NEOMYCIN SULFATE	0	1 (0.7%)	1 (0.5%)
BENZYDAMINE HYDROCHLORIDE;CETYLPYRIDINIUM CHLORIDE	0	1 (0.7%)	1 (0.5%)
BICLOTYMOL	1 (1.3%)	0	1 (0.5%)
CETRARIA ISLANDICA;SILVER COLLOIDAL	1 (1.3%)	0	1 (0.5%)
CHLORHEXIDINE	0	1 (0.7%)	1 (0.5%)
DECAMETHOXINE	1 (1.3%)	0	1 (0.5%)
DOMIPHEN BROMIDE	0	1 (0.7%)	1 (0.5%)
HEXETIDINE	1 (1.3%)	0	1 (0.5%)
HYALURONIC ACID	1 (1.3%)	0	1 (0.5%)
IODINE	1 (1.3%)	0	1 (0.5%)
POLIHEXANIDE	1 (1.3%)	0	1 (0.5%)
SODIUM BICARBONATE;SODIUM GUALENATE HYDRATE	0	1 (0.7%)	1 (0.5%)
TETRACYCLINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
THYROID THERAPY			
Total number of patients with at least one treatment	15 (19.7%)	16 (11.0%)	31 (14.0%)
Total number of treatments	15	18	33
LEVOTHYROXINE SODIUM	10 (13.2%)	11 (7.5%)	21 (9.5%)
LEVOTHYROXINE	3 (3.9%)	3 (2.1%)	6 (2.7%)
PROPRANOLOL	0	2 (1.4%)	2 (0.9%)
IODINE	1 (1.3%)	0	1 (0.5%)
PROPRANOLOL HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
TONICS			
Total number of patients with at least one treatment	0	2 (1.4%)	2 (0.9%)
Total number of treatments	0	2	2
CURCUMIN	0	1 (0.7%)	1 (0.5%)
DIETARY SUPPLEMENT	0	1 (0.7%)	1 (0.5%)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN			
Total number of patients with at least one treatment	39 (51.3%)	70 (47.9%)	109 (49.1%)
Total number of treatments	106	437	543
IBUPROFEN	9 (11.8%)	16 (11.0%)	25 (11.3%)
DICLOFENAC SODIUM	3 (3.9%)	7 (4.8%)	10 (4.5%)
ACETYLSALICYLIC ACID	3 (3.9%)	6 (4.1%)	9 (4.1%)
KETOPROFEN	4 (5.3%)	5 (3.4%)	9 (4.1%)
LOXOPROFEN SODIUM DIHYDRATE	5 (6.6%)	4 (2.7%)	9 (4.1%)
NIMESULIDE	5 (6.6%)	4 (2.7%)	9 (4.1%)
DICLOFENAC	0	8 (5.5%)	8 (3.6%)
LOXOPROFEN SODIUM	3 (3.9%)	4 (2.7%)	7 (3.2%)
ACECLOFENAC	4 (5.3%)	2 (1.4%)	6 (2.7%)
HEPARINOID	2 (2.6%)	4 (2.7%)	6 (2.7%)
KETOROLAC TROMETHAMINE	0	6 (4.1%)	6 (2.7%)
NAPROXEN	4 (5.3%)	2 (1.4%)	6 (2.7%)
BENZYDAMINE HYDROCHLORIDE	2 (2.6%)	3 (2.1%)	5 (2.3%)
FOLIC ACID	2 (2.6%)	3 (2.1%)	5 (2.3%)
MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER	2 (2.6%)	3 (2.1%)	5 (2.3%)
KETOROLAC	3 (3.9%)	1 (0.7%)	4 (1.8%)
CAMPHOR;CHLORPHENAMINE MALEATE;HEXACHLOROPHENE; LIDOCAINE HYDROCHLORIDE;MENTHOL;METHYL SALICYLATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
DEXKETOPROFEN TROMETAMOL	1 (1.3%)	2 (1.4%)	3 (1.4%)
LOXOPROFEN	0	3 (2.1%)	3 (1.4%)
MELOXICAM	1 (1.3%)	2 (1.4%)	3 (1.4%)
CAMPHOR	0	2 (1.4%)	2 (0.9%)
DEXKETOPROFEN	1 (1.3%)	1 (0.7%)	2 (0.9%)
ETOFENAMATE	0	2 (1.4%)	2 (0.9%)
FELBINAC	2 (2.6%)	0	2 (0.9%)
INDOMETACIN	1 (1.3%)	1 (0.7%)	2 (0.9%)
NAPROXEN SODIUM	2 (2.6%)	0	2 (0.9%)
PHOSPHOLIPIDS	0	2 (1.4%)	2 (0.9%)
CAMPHOR;MENTHOL;METHYL SALICYLATE	1 (1.3%)	0	1 (0.5%)
DICLOFENAC POTASSIUM	0	1 (0.7%)	1 (0.5%)
FLURBIPROFEN AXETIL	0	1 (0.7%)	1 (0.5%)
GLUCOSAMINE	0	1 (0.7%)	1 (0.5%)
IBUPROFEN ARGININE	1 (1.3%)	0	1 (0.5%)
SALICYLIC ACID	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE			
Total number of patients with at least one treatment	10 (13.2%)	27 (18.5%)	37 (16.7%)
Total number of treatments	16	43	59
CYNARA CARDUNCULUS EXTRACT	1 (1.3%)	4 (2.7%)	5 (2.3%)
SILYBUM MARIANUM	0	5 (3.4%)	5 (2.3%)
ACHYRANTHES BIDENTATA ROOT;ACONITUM SPP. PROCESSED ROOT;ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER;CINNAMOMUM CASSIA BARK;CORNUS OFFICINALIS FRUIT;DIOSCOREA SPP. RHIZOME;PAEONIA X SUFFRUTICOSA ROOT BARK;PLANTAGO ASIATICA SEED; PORIA COCOS SCLEROTIUM;REHMANNIA GLUTINOSA ROOT	1 (1.3%)	2 (1.4%)	3 (1.4%)
CINNAMOMUM CASSIA;EPHEDRA SPP.;GLYCYRRHIZA SPP.; PAEONIA LACTIFLORA;PUERARIA MONTANA VAR. LOBATA; ZINGIBER OFFICINALE;ZIZIPHUS JUJUBA	0	2 (1.4%)	2 (0.9%)
GLYCYRRHIZA GLABRA EXTRACT;PAPAVER SOMNIFERUM	1 (1.3%)	1 (0.7%)	2 (0.9%)
ACONITUM SPP. PROCESSED ROOT	0	1 (0.7%)	1 (0.5%)
ACONITUM SPP. PROCESSED ROOT;ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER;CINNAMOMUM CASSIA BARK;CORNUS OFFICINALIS FRUIT;DIOSCOREA SPP. RHIZOME;PAEONIA X SUFFRUTICOSA ROOT BARK;PORIA COCOS SCLEROTIUM;REHMANNIA GLUTINOSA ROOT	0	1 (0.7%)	1 (0.5%)
AESCULUS HIPPOCASTANUM	0	1 (0.7%)	1 (0.5%)
AESCULUS HIPPOCASTANUM EXTRACT	0	1 (0.7%)	1 (0.5%)
ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER; ATRACTYLODES SPP. RHIZOME;CINNAMOMUM CASSIA BARK; POLYPORUS UMBELLATUS SCLEROTIUM;PORIA COCOS SCLEROTIUM	0	1 (0.7%)	1 (0.5%)
ANNONA MURICATA LEAF	0	1 (0.7%)	1 (0.5%)
ARTEMISIA ARGYI LEAF	1 (1.3%)	0	1 (0.5%)
ASTRAGALUS SPP. ROOT;ATRACTYLODES SPP. RHIZOME; GLYCYRRHIZA SPP. ROOT;SINOMENIUM ACUTUM STEM; ZINGIBER OFFICINALE RHIZOME;ZIZIPHUS JUJUBA FRUIT	1 (1.3%)	0	1 (0.5%)
ATRACTYLODES SPP. RHIZOME;CINNAMOMUM CASSIA BARK; GLYCYRRHIZA SPP. ROOT;PORIA COCOS SCLEROTIUM	1 (1.3%)	0	1 (0.5%)
CAMELLIA SINENSIS	0	1 (0.7%)	1 (0.5%)
COPTIS SPP. RHIZOME;GLYCYRRHIZA SPP. ROOT;PANAX GINSENG ROOT;PINELLIA TERNATA TUBER;SCUTELLARIA BAICALENSIS ROOT;ZINGIBER OFFICINALE PROCESSED RHIZOME;ZIZIPHUS JUJUBA FRUIT	0	1 (0.7%)	1 (0.5%)
COPTIS SPP. RHIZOME;HEDERA HELIX LEAF	0	1 (0.7%)	1 (0.5%)
CORDYCEPS SINENSIS	0	1 (0.7%)	1 (0.5%)
CORYDALIS YANHUSUO TUBER;IPOMOEA NIL SEED	1 (1.3%)	0	1 (0.5%)
CYNARA CARDUNCULUS	0	1 (0.7%)	1 (0.5%)
EUPHRASIA OFFICINALIS	0	1 (0.7%)	1 (0.5%)
GINKGO BILOBA	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
GLYCYRRHIZA GLABRA EXTRACT	0	1 (0.7%)	1 (0.5%)
GLYCYRRHIZA GLABRA FLUID EXTRACT	0	1 (0.7%)	1 (0.5%)
HAMAMELIS VIRGINIANA;PHENAZONE;TANNIC ACID	0	1 (0.7%)	1 (0.5%)
HERBAL NOS	1 (1.3%)	0	1 (0.5%)
LESPEDEZA BICOLOR	0	1 (0.7%)	1 (0.5%)
MAGNOLIA SPP. BARK;PERILLA FRUTESCENS VAR. CRISPA HERB;PINELLIA TERNATA TUBER;PORIA COCOS SCLEROTIUM;ZINGIBER OFFICINALE RHIZOME	0	1 (0.7%)	1 (0.5%)
PAPAVER SOMNIFERUM	0	1 (0.7%)	1 (0.5%)
PAPAVER SOMNIFERUM TINCTURE	0	1 (0.7%)	1 (0.5%)
PLATYCODON GRANDIFLORUS ROOT	0	1 (0.7%)	1 (0.5%)
QUERCUS SPP. BARK EXTRACT	0	1 (0.7%)	1 (0.5%)
ROSA CANINA	1 (1.3%)	0	1 (0.5%)
SENNA ALEXANDRINA	1 (1.3%)	0	1 (0.5%)
SENNA SPP.	0	1 (0.7%)	1 (0.5%)
STERCULIA URENS GUM	1 (1.3%)	0	1 (0.5%)
VITIS VINIFERA SEED	1 (1.3%)	0	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
UROLOGICALS			
Total number of patients with at least one treatment	17 (22.4%)	28 (19.2%)	45 (20.3%)
Total number of treatments	28	46	74
HYALURONATE SODIUM	2 (2.6%)	6 (4.1%)	8 (3.6%)
LIDOCAINE	1 (1.3%)	4 (2.7%)	5 (2.3%)
SODIUM BICARBONATE	3 (3.9%)	2 (1.4%)	5 (2.3%)
DROTAVERINE HYDROCHLORIDE	1 (1.3%)	3 (2.1%)	4 (1.8%)
ACHYRANTHES BIDENTATA ROOT;ACONITUM SPP. PROCESSED ROOT;ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER;CINNAMOMUM CASSIA BARK;CORNUS OFFICINALIS FRUIT;DIOSCOREA SPP. RHIZOME;PAEONIA X SUFFRUTICOSA ROOT BARK;PLANTAGO ASIATICA SEED; PORIA COCOS SCLEROTIUM;REHMANNIA GLUTINOSA ROOT	1 (1.3%)	2 (1.4%)	3 (1.4%)
AMITRIPTYLINE	1 (1.3%)	2 (1.4%)	3 (1.4%)
DULOXETINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
LIDOCAINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
POTASSIUM CITRATE	1 (1.3%)	2 (1.4%)	3 (1.4%)
AMITRIPTYLINE HYDROCHLORIDE	2 (2.6%)	0	2 (0.9%)
DROTAVERINE	1 (1.3%)	1 (0.7%)	2 (0.9%)
DULOXETINE	0	2 (1.4%)	2 (0.9%)
LIDOCAINE;PRILOCAINE	0	2 (1.4%)	2 (0.9%)
MAGNESIUM HYDROXIDE	1 (1.3%)	1 (0.7%)	2 (0.9%)
ACONITUM SPP. PROCESSED ROOT;ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER;CINNAMOMUM CASSIA BARK;CORNUS OFFICINALIS FRUIT;DIOSCOREA SPP. RHIZOME;PAEONIA X SUFFRUTICOSA ROOT BARK;PORIA COCOS SCLEROTIUM;REHMANNIA GLUTINOSA ROOT	0	1 (0.7%)	1 (0.5%)
ASTRAGALUS SPP. ROOT;ATRACTYLODES SPP. RHIZOME; GLYCYRRHIZA SPP. ROOT;SINOMENIUM ACUTUM STEM; ZINGIBER OFFICINALE RHIZOME;ZIZIPHUS JUJUBA FRUIT	1 (1.3%)	0	1 (0.5%)
ATRACTYLODES LANCEA RHIZOME;CALCIUM SULFATE; EPHEDRA SPP. HERB;GLYCYRRHIZA SPP. ROOT;ZINGIBER OFFICINALE RHIZOME;ZIZIPHUS JUJUBA FRUIT	1 (1.3%)	0	1 (0.5%)
BUDESONIDE	0	1 (0.7%)	1 (0.5%)
CLOMIPRAMINE	0	1 (0.7%)	1 (0.5%)
CORDYCEPS SINENSIS	0	1 (0.7%)	1 (0.5%)
FLAVOXATE	0	1 (0.7%)	1 (0.5%)
HYALURONIC ACID	1 (1.3%)	0	1 (0.5%)
MAGNESIUM CITRATE	0	1 (0.7%)	1 (0.5%)
SILODOSIN	1 (1.3%)	0	1 (0.5%)
SODIUM CITRATE	1 (1.3%)	0	1 (0.5%)
SOLIFENACIN	0	1 (0.7%)	1 (0.5%)
TADALAFIL	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
VACCINES			
Total number of patients with at least one treatment	4 (5.3%)	5 (3.4%)	9 (4.1%)
Total number of treatments	4	20	24
INFLUENZA VACCINE	1 (1.3%)	3 (2.1%)	4 (1.8%)
COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19)	1 (1.3%)	2 (1.4%)	3 (1.4%)
ELASOMERAN	0	3 (2.1%)	3 (1.4%)
TOZINAMERAN	1 (1.3%)	2 (1.4%)	3 (1.4%)
COVID-19 VACCINE	0	1 (0.7%)	1 (0.5%)
INFLUENZA VACCINE INACT SAG 3V	1 (1.3%)	0	1 (0.5%)
VASOPROTECTIVES			
Total number of patients with at least one treatment	63 (82.9%)	131 (89.7%)	194 (87.4%)
Total number of treatments	763	991	1754
DEXAMETHASONE	51 (67.1%)	100 (68.5%)	151 (68.0%)
DEXAMETHASONE SODIUM PHOSPHATE	9 (11.8%)	22 (15.1%)	31 (14.0%)
HYDROCORTISONE	5 (6.6%)	13 (8.9%)	18 (8.1%)
BETAMETHASONE BUTYRATE PROPIONATE	2 (2.6%)	7 (4.8%)	9 (4.1%)
PREDNISOLONE	2 (2.6%)	7 (4.8%)	9 (4.1%)
HYALURONATE SODIUM	2 (2.6%)	6 (4.1%)	8 (3.6%)
BETAMETHASONE	5 (6.6%)	2 (1.4%)	7 (3.2%)
DIOSMIN;HESPERIDIN	5 (6.6%)	1 (0.7%)	6 (2.7%)
HEPARINOID	2 (2.6%)	4 (2.7%)	6 (2.7%)
HYDROCORTISONE SODIUM SUCCINATE	1 (1.3%)	5 (3.4%)	6 (2.7%)
BETAMETHASONE VALERATE	1 (1.3%)	4 (2.7%)	5 (2.3%)
FLUOROMETHOLONE	3 (3.9%)	2 (1.4%)	5 (2.3%)
LIDOCAINE	1 (1.3%)	4 (2.7%)	5 (2.3%)
MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER	2 (2.6%)	3 (2.1%)	5 (2.3%)
QUERCETIN	2 (2.6%)	2 (1.4%)	4 (1.8%)
BECLOMETASONE DIPROPIONATE	0	3 (2.1%)	3 (1.4%)
LIDOCAINE HYDROCHLORIDE	1 (1.3%)	2 (1.4%)	3 (1.4%)
THIOTRIAZOLINE	2 (2.6%)	1 (0.7%)	3 (1.4%)
ANTIBIOTICS	1 (1.3%)	1 (0.7%)	2 (0.9%)
ASCORBIC ACID;RUTOSIDE	0	2 (1.4%)	2 (0.9%)
BETAMETHASONE DIPROPIONATE	1 (1.3%)	1 (0.7%)	2 (0.9%)
CARBOMER	0	2 (1.4%)	2 (0.9%)
ESCHERICHIA COLI;HYDROCORTISONE	0	2 (1.4%)	2 (0.9%)
ISOSORBIDE DINITRATE	0	2 (1.4%)	2 (0.9%)
TRIAMCINOLONE	0	2 (1.4%)	2 (0.9%)
AESCULUS HIPPOCASTANUM	0	1 (0.7%)	1 (0.5%)
AESCULUS HIPPOCASTANUM EXTRACT	0	1 (0.7%)	1 (0.5%)
BENZOCAINE;BISMUTH SUBNITRATE;CHLORHEXIDINE DIACETATE;ENOXOLONE;LIDOCAINE;PHENYLEPHRINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
BETAMETHASONE SODIUM PHOSPHATE	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_B_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
BETAMETHASONE VALERATE;LIDOCAINE HYDROCHLORIDE; PHENYLEPHRINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
CINCHOCAINE HYDROCHLORIDE;POLICRESULEN	0	1 (0.7%)	1 (0.5%)
CORTICOSTEROID NOS	0	1 (0.7%)	1 (0.5%)
DEXAMETHASONE VALERATE	0	1 (0.7%)	1 (0.5%)
DIFLUCORTOLONE VALERATE;LIDOCAINE	0	1 (0.7%)	1 (0.5%)
FLUOCINOLONE ACETONIDE	1 (1.3%)	0	1 (0.5%)
FLUOCINONIDE	1 (1.3%)	0	1 (0.5%)
GINKGO BILOBA;HEPTAMINOL HYDROCHLORIDE;TROXERUTIN	0	1 (0.7%)	1 (0.5%)
HEPARIN	0	1 (0.7%)	1 (0.5%)
HYALURONIC ACID	1 (1.3%)	0	1 (0.5%)
IODINE	1 (1.3%)	0	1 (0.5%)
NIFEDIPINE	0	1 (0.7%)	1 (0.5%)
OXETACAINE	0	1 (0.7%)	1 (0.5%)
PHENYLEPHRINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
PREDNISOLONE ACETATE	0	1 (0.7%)	1 (0.5%)
PREDNISOLONE METASULFOBENZOATE SODIUM	1 (1.3%)	0	1 (0.5%)
PREDNISOLONE SODIUM SUCCINATE	0	1 (0.7%)	1 (0.5%)
PROCAINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
PYCNOGENOL	0	1 (0.7%)	1 (0.5%)
SODIUM ALGINATE	1 (1.3%)	0	1 (0.5%)
TALC	1 (1.3%)	0	1 (0.5%)
TRIAMCINOLONE ACETONIDE	0	1 (0.7%)	1 (0.5%)
VITIS VINIFERA SEED	1 (1.3%)	0	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort B: HR+ /HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
VITAMINS			
Total number of patients with at least one treatment	21 (27.6%)	34 (23.3%)	55 (24.8%)
Total number of treatments	49	65	114
ASCORBIC ACID	7 (9.2%)	9 (6.2%)	16 (7.2%)
COLECALCIFEROL	5 (6.6%)	9 (6.2%)	14 (6.3%)
PYRIDOXINE HYDROCHLORIDE	4 (5.3%)	2 (1.4%)	6 (2.7%)
VITAMIN D NOS	3 (3.9%)	2 (1.4%)	5 (2.3%)
CALCIFEDIOL	2 (2.6%)	2 (1.4%)	4 (1.8%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE HYDROCHLORIDE	2 (2.6%)	2 (1.4%)	4 (1.8%)
VITAMINS NOS	0	3 (2.1%)	3 (1.4%)
CALCIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE;SORBITOL	0	2 (1.4%)	2 (0.9%)
CALCIUM PANTOTHENATE;CYANOCOBALAMIN;FOLIC ACID; NICOTINAMIDE;PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN; THIAMINE MONONITRATE;ZINC OXIDE	0	2 (1.4%)	2 (0.9%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE DISULFIDE PHOSPHATE	0	2 (1.4%)	2 (0.9%)
MAGNESIUM;PYRIDOXINE HYDROCHLORIDE	0	2 (1.4%)	2 (0.9%)
PYRIDOXINE	0	2 (1.4%)	2 (0.9%)
RETINOL;VITAMIN E NOS	2 (2.6%)	0	2 (0.9%)
ASCORBIC ACID;BETACAROTENE;BIOTIN;CALCIUM; CARBOHYDRATES NOS;CHLORIDE;CHOLINE;CHROMIUM; COPPER;CYANOCOBALAMIN;FATS NOS;FIBRE, DIETARY; FLUORINE;FOLIC ACID;IODINE;IRON;MAGNESIUM; MANGANESE;MOLYBDENUM;NICOTINAMIDE;PANTOTHENIC ACID;PHOSPHORUS;POTASSIUM;PROTEINS NOS; PYRIDOXINE;RIBOFLAVIN;SELENIUM;SODIUM;THIAMINE; VITAMIN D NOS;VITAMIN E NOS;ZINC	0	1 (0.7%)	1 (0.5%)
BENFOTIAMINE;PYRIDOXINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
CYANOCOBALAMIN;DEXPANTHENOL;NICOTINAMIDE; PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN;THIAMINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE; RIBOFLAVIN;THIAMINE DISULFIDE	0	1 (0.7%)	1 (0.5%)
FURSULTIAMINE	0	1 (0.7%)	1 (0.5%)
HYDROXOCOBALAMIN ACETATE;PYRIDOXINE HYDROCHLORIDE;THIAMINE DISULFIDE	0	1 (0.7%)	1 (0.5%)
MAGNESIUM LACTATE;PYRIDOXINE HYDROCHLORIDE	0	1 (0.7%)	1 (0.5%)
ROSA CANINA	1 (1.3%)	0	1 (0.5%)
THIAMINE HYDROCHLORIDE	1 (1.3%)	0	1 (0.5%)
VITAMIN B COMPLEX	1 (1.3%)	0	1 (0.5%)
VITAMIN B NOS	0	1 (0.7%)	1 (0.5%)
VITAMIN B1 IN COMBINATION WITH VITAMIN B6 AND/OR VITAMIN B12	0	1 (0.7%)	1 (0.5%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one treatment	102 (100%)
Total number of treatments	1763
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	
Total number of patients with at least one treatment	32 (31.4%)
Total number of treatments	36
LOSARTAN	11 (10.8%)
LISINOPRIL	3 (2.9%)
AMLODIPINE BESILATE;INDAPAMIDE;PERINDOPRIL ARGININE	2 (2.0%)
CAPTOPRIL	2 (2.0%)
AMLODIPINE BESILATE;PERINDOPRIL ARGININE	1 (1.0%)
AMLODIPINE BESILATE;VALSARTAN	1 (1.0%)
BISOPROLOL FUMARATE;PERINDOPRIL ARGININE	1 (1.0%)
CANDESARTAN	1 (1.0%)
CANDESARTAN CILEXETIL	1 (1.0%)
CAPTOPRIL;HYDROCHLOROTHIAZIDE	1 (1.0%)
ENALAPRIL	1 (1.0%)
FIMASARTAN POTASSIUM TRIHYDRATE	1 (1.0%)
HYDROCHLOROTHIAZIDE;RAMIPRIL	1 (1.0%)
IRBESARTAN	1 (1.0%)
LOSARTAN POTASSIUM	1 (1.0%)
OLMESARTAN	1 (1.0%)
PERINDOPRIL	1 (1.0%)
TELMISARTAN	1 (1.0%)
VALSARTAN	1 (1.0%)
ZOFENOPRIL CALCIUM	1 (1.0%)
ALL OTHER NON-THERAPEUTIC PRODUCTS	
Total number of patients with at least one treatment	21 (20.6%)
Total number of treatments	59
SODIUM CHLORIDE	15 (14.7%)
ASCORBIC ACID	3 (2.9%)
COCOS NUCIFERA OIL	1 (1.0%)
HYPROMELLOSE	1 (1.0%)
WATER PURIFIED	1 (1.0%)

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_C_IT.out

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
ALL OTHER THERAPEUTIC PRODUCTS	
Total number of patients with at least one treatment	21 (20.6%)
Total number of treatments	25
ACETYLCYSTEINE	3 (2.9%)
ASCORBIC ACID	3 (2.9%)
CALCIUM CARBONATE	3 (2.9%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE HYDROCHLORIDE	3 (2.9%)
IRON	3 (2.9%)
OXYGEN	2 (2.0%)
ATROPINE	1 (1.0%)
ATROPINE SULFATE	1 (1.0%)
MUCOPOLYSACCHARIDES	1 (1.0%)
NALOXONE	1 (1.0%)
POTASSIUM IODIDE	1 (1.0%)
ANALGESICS	
Total number of patients with at least one treatment	75 (73.5%)
Total number of treatments	484
PARACETAMOL	38 (37.3%)
METAMIZOLE SODIUM	19 (18.6%)
TRAMADOL	16 (15.7%)
GABAPENTIN	12 (11.8%)
PREGABALIN	8 (7.8%)
CODEINE PHOSPHATE;PARACETAMOL	7 (6.9%)
ACETYLSALICYLIC ACID	6 (5.9%)
MORPHINE	6 (5.9%)
MORPHINE SULFATE	5 (4.9%)
PARACETAMOL;TRAMADOL HYDROCHLORIDE	5 (4.9%)
CODEINE PHOSPHATE	4 (3.9%)
OXYCODONE	4 (3.9%)
AMITRIPTYLINE	3 (2.9%)
CODEINE PHOSPHATE;IBUPROFEN;PARACETAMOL	3 (2.9%)
METOPROLOL	3 (2.9%)
OXYCODONE HYDROCHLORIDE	3 (2.9%)
ACETYLSALICYLIC ACID;MAGNESIUM HYDROXIDE	2 (2.0%)
CODEINE	2 (2.0%)
CORTICOSTEROID NOS	2 (2.0%)
DULOXETINE HYDROCHLORIDE	2 (2.0%)
HYDROCODONE BITARTRATE;PARACETAMOL	2 (2.0%)
ACETYLSALICYLATE LYSINE	1 (1.0%)
ACETYLSALICYLIC ACID;ALUMINIUM GLYCINATE;MAGNESIUM CARBONATE	1 (1.0%)
ACETYLSALICYLIC ACID;CAFFEINE	1 (1.0%)
AMITRIPTYLINE HYDROCHLORIDE	1 (1.0%)
ASCORBIC ACID;PARACETAMOL;PHENIRAMINE MALEATE	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
CAFFEINE;DIHYDROERGOTAMINE MESILATE;METAMIZOLE SODIUM	1 (1.0%)
CAFFEINE;ISOMETHEPTENE;METAMIZOLE	1 (1.0%)
CAFFEINE;PAPAVER SOMNIFERUM LATEX;PARACETAMOL	1 (1.0%)
CARBAMAZEPINE	1 (1.0%)
CARBINOXAMINE;PARACETAMOL;PHENYLEPHRINE	1 (1.0%)
CETALKONIUM CHLORIDE;CHOLINE SALICYLATE	1 (1.0%)
CLONIDINE	1 (1.0%)
CODEINE;PARACETAMOL	1 (1.0%)
DEXTROMETHORPHAN HYDROBROMIDE;DOXYLAMINE SUCCINATE; PARACETAMOL	1 (1.0%)
DEXTROMETHORPHAN;PARACETAMOL;PHENYLEPHRINE	1 (1.0%)
DIPHENHYDRAMINE HYDROCHLORIDE;PARACETAMOL	1 (1.0%)
FENTANYL	1 (1.0%)
FENTANYL CITRATE	1 (1.0%)
FLUNARIZINE	1 (1.0%)
METOPROLOL SUCCINATE	1 (1.0%)
METOPROLOL TARTRATE	1 (1.0%)
NARATRIPTAN	1 (1.0%)
NEFOPAM	1 (1.0%)
OXYCODONE HYDROCHLORIDE;PARACETAMOL	1 (1.0%)
PARACETAMOL;TRAMADOL	1 (1.0%)
PETHIDINE	1 (1.0%)
PROPACETAMOL HYDROCHLORIDE	1 (1.0%)
PRUNUS CERASUS	1 (1.0%)
TOPIRAMATE	1 (1.0%)
TRAMADOL HYDROCHLORIDE	1 (1.0%)
VENLAFAXINE	1 (1.0%)
ANESTHETICS	
Total number of patients with at least one treatment	12 (11.8%)
Total number of treatments	16
LIDOCAINE	7 (6.9%)
LIDOCAINE;PRILOCAINE	2 (2.0%)
FENTANYL	1 (1.0%)
FENTANYL CITRATE	1 (1.0%)
KETAMINE	1 (1.0%)
LIDOCAINE HYDROCHLORIDE	1 (1.0%)
PROCAINE	1 (1.0%)
PROPOFOL	1 (1.0%)
ANTHELMINTICS	
Total number of patients with at least one treatment	1 (1.0%)
Total number of treatments	2
ALBENDAZOLE	1 (1.0%)
IVERMECTIN	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
ANTI-ACNE PREPARATIONS	
Total number of patients with at least one treatment	98 (96.1%)
Total number of treatments	580
DEXAMETHASONE	81 (79.4%)
IBUPROFEN	16 (15.7%)
DEXAMETHASONE SODIUM PHOSPHATE	10 (9.8%)
METHYLPREDNISOLONE	10 (9.8%)
AZITHROMYCIN	6 (5.9%)
METHYLPREDNISOLONE SODIUM SUCCINATE	6 (5.9%)
CLINDAMYCIN	4 (3.9%)
DOXYCYCLINE	3 (2.9%)
CHLORHEXIDINE	2 (2.0%)
CHLORHEXIDINE GLUCONATE	2 (2.0%)
ZINC	2 (2.0%)
CHLORAMPHENICOL	1 (1.0%)
DIMETICONE	1 (1.0%)
ANTI-PARKINSON DRUGS	
Total number of patients with at least one treatment	50 (49.0%)
Total number of treatments	251
DIPHENHYDRAMINE	33 (32.4%)
DIPHENHYDRAMINE HYDROCHLORIDE	17 (16.7%)
ORPHENADRINE	1 (1.0%)
ANTIANEMIC PREPARATIONS	
Total number of patients with at least one treatment	19 (18.6%)
Total number of treatments	29
FERRIC HYDROXIDE POLYMALTOSE COMPLEX	4 (3.9%)
FERROUS SULFATE	4 (3.9%)
FOLIC ACID	4 (3.9%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE HYDROCHLORIDE	3 (2.9%)
IRON	3 (2.9%)
EPOETIN ALFA	2 (2.0%)
VITAMIN B NOS	2 (2.0%)
CYANOCOBALAMIN	1 (1.0%)
FERRIC CARBOXYMALTOSE	1 (1.0%)
IRON SUCCINYL-PROTEIN COMPLEX	1 (1.0%)
MINERALS NOS;VITAMINS NOS	1 (1.0%)
SACCHARATED IRON OXIDE	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
ANTIBACTERIALS FOR SYSTEMIC USE	
Total number of patients with at least one treatment	53 (52.0%)
Total number of treatments	134
CIPROFLOXACIN	16 (15.7%)
AMOXICILLIN;CLAVULANATE POTASSIUM	11 (10.8%)
METRONIDAZOLE	7 (6.9%)
AZITHROMYCIN	6 (5.9%)
CEFTRIAXONE	6 (5.9%)
PIPERACILLIN SODIUM;TAZOBACTAM SODIUM	6 (5.9%)
CEFALEXIN	5 (4.9%)
AMOXICILLIN	4 (3.9%)
CLINDAMYCIN	4 (3.9%)
CEFIXIME	3 (2.9%)
CEFTRIAXONE SODIUM	3 (2.9%)
CEFUROXIME	3 (2.9%)
DOXYCYCLINE	3 (2.9%)
LEVOFLOXACIN	3 (2.9%)
PIPERACILLIN;TAZOBACTAM	3 (2.9%)
CEFAZOLIN	2 (2.0%)
CEFEPIME	2 (2.0%)
CLARITHROMYCIN	2 (2.0%)
MEROPENEM	2 (2.0%)
SULFAMETHOXAZOLE;TRIMETHOPRIM	2 (2.0%)
TRIMETHOPRIM	2 (2.0%)
AMIKACIN	1 (1.0%)
AMOXICILLIN TRIHYDRATE;CLAVULANATE POTASSIUM	1 (1.0%)
AMPICILLIN	1 (1.0%)
BACITRACIN	1 (1.0%)
CEFADROXIL	1 (1.0%)
CEFEPIME HYDROCHLORIDE	1 (1.0%)
CEFIXIME TRIHYDRATE	1 (1.0%)
CEFOTAXIME	1 (1.0%)
CEFPODOXIME PROXETIL	1 (1.0%)
CEFTRIAXONE SODIUM;SULBACTAM SODIUM	1 (1.0%)
CHLORAMPHENICOL	1 (1.0%)
CIPROFLOXACIN HYDROCHLORIDE	1 (1.0%)
FLUCLOXACILLIN	1 (1.0%)
FUSIDIC ACID	1 (1.0%)
GENTAMICIN	1 (1.0%)
MOXIFLOXACIN	1 (1.0%)
MOXIFLOXACIN HYDROCHLORIDE	1 (1.0%)
POLYMYXIN B;TRIMETHOPRIM	1 (1.0%)
PRISTINAMYCIN	1 (1.0%)
SULFAMETHOXAZOLE	1 (1.0%)
VANCOMYCIN	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE	
Total number of patients with at least one treatment	33 (32.4%)
Total number of treatments	52
CIPROFLOXACIN	16 (15.7%)
METRONIDAZOLE	7 (6.9%)
ACICLOVIR	4 (3.9%)
DOXYCYCLINE	3 (2.9%)
LEVOFLOXACIN	3 (2.9%)
MUPIROCIN	3 (2.9%)
CLARITHROMYCIN	2 (2.0%)
AMIKACIN	1 (1.0%)
BACITRACIN	1 (1.0%)
BACITRACIN ZINC;POLYMYXIN B SULFATE	1 (1.0%)
CHLORAMPHENICOL	1 (1.0%)
CIPROFLOXACIN HYDROCHLORIDE	1 (1.0%)
FUSIDIC ACID	1 (1.0%)
GENTAMICIN	1 (1.0%)
MOXIFLOXACIN	1 (1.0%)
PENCICLOVIR	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS	
Total number of patients with at least one treatment	94 (92.2%)
Total number of treatments	457
PREDNISONE	57 (55.9%)
PREDNISOLONE	30 (29.4%)
HYDROCORTISONE	12 (11.8%)
NYSTATIN	7 (6.9%)
DIOSMECTITE	6 (5.9%)
BETAMETHASONE	5 (4.9%)
LOPERAMIDE	4 (3.9%)
POLYMETHYLSILOXANE POLYHYDRATE	4 (3.9%)
ATROPINE SULFATE;DIPHENOXYLATE HYDROCHLORIDE	3 (2.9%)
HYDROCORTISONE SODIUM SUCCINATE	3 (2.9%)
BECLOMETASONE DIPROPIONATE	2 (2.0%)
CODEINE	2 (2.0%)
CORTICOSTEROID NOS	2 (2.0%)
METHYLURACIL	2 (2.0%)
ORAL REHYDRATION SALT FORMULATIONS	2 (2.0%)
PREDNISOLONE METASULFOBENZOATE SODIUM	2 (2.0%)
RACECADOTRIL	2 (2.0%)
ATROPINE;DIPHENOXYLATE	1 (1.0%)
BACILLUS CLAUSII	1 (1.0%)
BACITRACIN	1 (1.0%)
BETAMETHASONE DIPROPIONATE	1 (1.0%)
BETAMETHASONE VALERATE	1 (1.0%)
BIFIDOBACTERIUM BIFIDUM;BIFIDOBACTERIUM LACTIS; LACTOBACILLUS ACIDOPHILUS;LACTOBACILLUS CASEI;LACTOBACILLUS LACTIS	1 (1.0%)
BISMUTH SUBSALICYLATE	1 (1.0%)
BUDESONIDE	1 (1.0%)
COLESTYRAMINE	1 (1.0%)
GLUCOSE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	1 (1.0%)
HYDROCORTISONE ACETATE	1 (1.0%)
LACTOBACILLUS ACIDOPHILUS;LACTOBACILLUS RHAMNOSUS	1 (1.0%)
LACTOBACILLUS NOS	1 (1.0%)
LOPERAMIDE HYDROCHLORIDE	1 (1.0%)
MAGIC MOUTHWASH	1 (1.0%)
POLYMYXIN B;TRIMETHOPRIM	1 (1.0%)
SACCHAROMYCES BOULARDII	1 (1.0%)
SILICON DIOXIDE	1 (1.0%)
VANCOMYCIN	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_C_IT.out

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
ANTIEMETICS AND ANTINAUSEANTS	
Total number of patients with at least one treatment	96 (94.1%)
Total number of treatments	738
ONDANSETRON	57 (55.9%)
DIPHENHYDRAMINE	33 (32.4%)
DIPHENHYDRAMINE HYDROCHLORIDE	17 (16.7%)
METOCLOPRAMIDE	14 (13.7%)
PROMETHAZINE	10 (9.8%)
DIMENHYDRINATE	8 (7.8%)
GRANISETRON	7 (6.9%)
METOCLOPRAMIDE HYDROCHLORIDE	7 (6.9%)
PROCHLORPERAZINE	7 (6.9%)
HYDROXYZINE	5 (4.9%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE HYDROCHLORIDE	3 (2.9%)
ONDANSETRON HYDROCHLORIDE	3 (2.9%)
CYCLIZINE	2 (2.0%)
PROCHLORPERAZINE MALEATE	2 (2.0%)
BUTYLSCOPOLAMINE	1 (1.0%)
CHLORPROMAZINE	1 (1.0%)
DIMENHYDRINATE;FRUCTOSE;GLUCOSE;PYRIDOXINE HYDROCHLORIDE	1 (1.0%)
DIMENHYDRINATE;PYRIDOXINE	1 (1.0%)
DOMPERIDONE	1 (1.0%)
GRANISETRON HYDROCHLORIDE	1 (1.0%)
HYOSCINE	1 (1.0%)
HYOSCINE HYDROBROMIDE	1 (1.0%)
OTHER ANTIEMETICS	1 (1.0%)
PALONOSETRON HYDROCHLORIDE	1 (1.0%)
RAMOSETRON HYDROCHLORIDE	1 (1.0%)
ANTIEPILEPTICS	
Total number of patients with at least one treatment	26 (25.5%)
Total number of treatments	90
GABAPENTIN	12 (11.8%)
PREGABALIN	8 (7.8%)
LORAZEPAM	6 (5.9%)
MAGNESIUM SULFATE	6 (5.9%)
CLONAZEPAM	2 (2.0%)
MIDAZOLAM	2 (2.0%)
ACETAZOLAMIDE	1 (1.0%)
CARBAMAZEPINE	1 (1.0%)
DIAZEPAM	1 (1.0%)
LAMOTRIGINE	1 (1.0%)
TOPIRAMATE	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
ANTIFUNGALS FOR DERMATOLOGICAL USE	
Total number of patients with at least one treatment	13 (12.7%)
Total number of treatments	18
NYSTATIN	7 (6.9%)
FLUCONAZOLE	5 (4.9%)
CLOTRIMAZOLE	2 (2.0%)
KETOCONAZOLE;PYRITHIONE ZINC	1 (1.0%)
NYSTATIN;TRIAMCINOLONE	1 (1.0%)
ANTIHEMORRHAGICS	
Total number of patients with at least one treatment	2 (2.0%)
Total number of treatments	3
EPINEPHRINE	1 (1.0%)
PRUNUS CERASUS	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
ANTIHISTAMINES FOR SYSTEMIC USE	
Total number of patients with at least one treatment	99 (97.1%)
Total number of treatments	823
LORATADINE	40 (39.2%)
DIPHENHYDRAMINE	33 (32.4%)
CHLORPHENAMINE	23 (22.5%)
DEXCHLORPHENIRAMINE MALEATE	19 (18.6%)
DIPHENHYDRAMINE HYDROCHLORIDE	17 (16.7%)
CETIRIZINE	15 (14.7%)
DESLORATADINE	14 (13.7%)
PROMETHAZINE	10 (9.8%)
CLEMASTINE FUMARATE	8 (7.8%)
DIMENHYDRINATE	8 (7.8%)
CETIRIZINE HYDROCHLORIDE	6 (5.9%)
FEXOFENADINE HYDROCHLORIDE	6 (5.9%)
BILASTINE	5 (4.9%)
HYDROXYZINE	5 (4.9%)
LEVOCETIRIZINE DIHYDROCHLORIDE	5 (4.9%)
QUERCETIN	5 (4.9%)
CLEMASTINE	4 (3.9%)
CHLORPHENAMINE MALEATE	3 (2.9%)
CHLOROPYRAMINE HYDROCHLORIDE	2 (2.0%)
CYCLIZINE	2 (2.0%)
DEXCHLORPHENIRAMINE	2 (2.0%)
OLOPATADINE HYDROCHLORIDE	2 (2.0%)
AZELASTINE	1 (1.0%)
AZELASTINE HYDROCHLORIDE	1 (1.0%)
BEPOTASTINE BESILATE	1 (1.0%)
BUCLIZINE HYDROCHLORIDE	1 (1.0%)
DIMENHYDRINATE;FRUCTOSE;GLUCOSE;PYRIDOXINE HYDROCHLORIDE	1 (1.0%)
DIMENHYDRINATE;PYRIDOXINE	1 (1.0%)
DOXYLAMINE SUCCINATE	1 (1.0%)
FEXOFENADINE	1 (1.0%)
LEVOCETIRIZINE	1 (1.0%)
OXOMEMAZINE	1 (1.0%)
THIETHYLPERAZINE	1 (1.0%)
ANTIHYPERTENSIVES	
Total number of patients with at least one treatment	7 (6.9%)
Total number of treatments	8
MAGNESIUM SULFATE	6 (5.9%)
CLONIDINE	1 (1.0%)
HYDRALAZINE	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	
Total number of patients with at least one treatment	40 (39.2%)
Total number of treatments	137
IBUPROFEN	16 (15.7%)
ADEMETIONINE	7 (6.9%)
DICLOFENAC	4 (3.9%)
NIMESULIDE	4 (3.9%)
KETOPROFEN	3 (2.9%)
KETOROLAC TROMETHAMINE	3 (2.9%)
ACECLOFENAC	2 (2.0%)
BENZYDAMINE HYDROCHLORIDE	2 (2.0%)
FISH OIL	2 (2.0%)
MELOXICAM	2 (2.0%)
TENOXICAM	2 (2.0%)
CHLORPHENAMINE MALEATE;IBUPROFEN;PHENYLEPHRINE HYDROCHLORIDE	1 (1.0%)
DEXKETOPROFEN TROMETAMOL	1 (1.0%)
DICLOFENAC SODIUM	1 (1.0%)
DIPHENHYDRAMINE;IBUPROFEN	1 (1.0%)
FLURBIPROFEN	1 (1.0%)
IBUPROFEN;PSEUDOEPHEDRINE HYDROCHLORIDE	1 (1.0%)
NAPROXEN	1 (1.0%)
PALMIDROL	1 (1.0%)
PARECOXIB SODIUM	1 (1.0%)
PRUNUS CERASUS	1 (1.0%)
ANTIMYCOTICS FOR SYSTEMIC USE	
Total number of patients with at least one treatment	11 (10.8%)
Total number of treatments	13
NYSTATIN	7 (6.9%)
FLUCONAZOLE	5 (4.9%)
ANTIPROTOZOALS	
Total number of patients with at least one treatment	11 (10.8%)
Total number of treatments	13
METRONIDAZOLE	7 (6.9%)
CLOTRIMAZOLE	2 (2.0%)
HYDROXYCHLOROQUINE	2 (2.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.	
Total number of patients with at least one treatment	99 (97.1%)
Total number of treatments	799
LORATADINE	40 (39.2%)
DIPHENHYDRAMINE	33 (32.4%)
CHLORPHENAMINE	23 (22.5%)
DEXCHLORPHENIRAMINE MALEATE	19 (18.6%)
DIPHENHYDRAMINE HYDROCHLORIDE	17 (16.7%)
CETIRIZINE	15 (14.7%)
DESLORATADINE	14 (13.7%)
PROMETHAZINE	10 (9.8%)
CLEMASTINE FUMARATE	8 (7.8%)
LIDOCAINE	7 (6.9%)
CETIRIZINE HYDROCHLORIDE	6 (5.9%)
FEXOFENADINE HYDROCHLORIDE	6 (5.9%)
BILASTINE	5 (4.9%)
HYDROXYZINE	5 (4.9%)
LEVOCETIRIZINE DIHYDROCHLORIDE	5 (4.9%)
CLEMASTINE	4 (3.9%)
CHLORPHENAMINE MALEATE	3 (2.9%)
CHLOROPYRAMINE HYDROCHLORIDE	2 (2.0%)
DEXCHLORPHENIRAMINE	2 (2.0%)
LIDOCAINE;PRILOCAINE	2 (2.0%)
OLOPATADINE HYDROCHLORIDE	2 (2.0%)
ETHANOL;GLYCEROL;LIDOCAINE;MENTHOL;SALICYLIC ACID;TANNIC ACID;THYMOL	1 (1.0%)
FEXOFENADINE	1 (1.0%)
LEVOCETIRIZINE	1 (1.0%)
LIDOCAINE HYDROCHLORIDE	1 (1.0%)
ANTISEPTICS AND DISINFECTANTS	
Total number of patients with at least one treatment	10 (9.8%)
Total number of treatments	15
CHLORHEXIDINE	2 (2.0%)
CHLORHEXIDINE GLUCONATE	2 (2.0%)
CETYLPYRIDINIUM CHLORIDE	1 (1.0%)
HEXAMIDINE	1 (1.0%)
HEXAMIDINE ISETIONATE	1 (1.0%)
MIRAMISTIN	1 (1.0%)
OCTENIDINE HYDROCHLORIDE;PHENOXYETHANOL	1 (1.0%)
POVIDONE-IODINE	1 (1.0%)
THYMOL	1 (1.0%)

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ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
ANTITHROMBOTIC AGENTS	
Total number of patients with at least one treatment	24 (23.5%)
Total number of treatments	36
ENOXAPARIN	8 (7.8%)
ACETYLSALICYLIC ACID	6 (5.9%)
RIVAROXABAN	3 (2.9%)
ACETYLSALICYLIC ACID;MAGNESIUM HYDROXIDE	2 (2.0%)
ALTEPLASE	2 (2.0%)
HEPARIN	2 (2.0%)
ACETYLSALICYLATE LYSINE	1 (1.0%)
ACETYLSALICYLIC ACID;ALUMINIUM GLYCINATE;MAGNESIUM CARBONATE	1 (1.0%)
APIXABAN	1 (1.0%)
ENOXAPARIN SODIUM	1 (1.0%)
HEPARIN SODIUM	1 (1.0%)
TINZAPARIN SODIUM	1 (1.0%)
ANTIVIRALS FOR SYSTEMIC USE	
Total number of patients with at least one treatment	8 (7.8%)
Total number of treatments	11
ACICLOVIR	4 (3.9%)
OSELTAMIVIR PHOSPHATE	2 (2.0%)
VALACICLOVIR HYDROCHLORIDE	2 (2.0%)
OSELTAMIVIR	1 (1.0%)
PENCICLOVIR	1 (1.0%)
APPETITE STIMULANTS	
Total number of patients with at least one treatment	1 (1.0%)
Total number of treatments	1
MEGESTROL ACETATE	1 (1.0%)
BETA BLOCKING AGENTS	
Total number of patients with at least one treatment	16 (15.7%)
Total number of treatments	20
BISOPROLOL FUMARATE	4 (3.9%)
METOPROLOL	3 (2.9%)
BISOPROLOL	2 (2.0%)
ATENOLOL	1 (1.0%)
BISOPROLOL FUMARATE;HYDROCHLOROTHIAZIDE	1 (1.0%)
BISOPROLOL;HYDROCHLOROTHIAZIDE	1 (1.0%)
CARVEDILOL	1 (1.0%)
METOPROLOL SUCCINATE	1 (1.0%)
METOPROLOL TARTRATE	1 (1.0%)
NADOLOL	1 (1.0%)
NEBIVOLOL	1 (1.0%)
NEBIVOLOL HYDROCHLORIDE	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
BILE AND LIVER THERAPY	
Total number of patients with at least one treatment	11 (10.8%)
Total number of treatments	42
ARGININE GLUTAMATE	4 (3.9%)
ACETYLCYSTEINE	3 (2.9%)
THIOTRIAZOLINE	3 (2.9%)
CYNARA CARDUNCULUS EXTRACT	2 (2.0%)
ORNITHINE ASPARTATE	2 (2.0%)
PHOSPHOLIPIDS	2 (2.0%)
ADENINE HYDROCHLORIDE;BIFENDATE;CARNITINE OROTATE; CYANOCOBALAMIN;LIVER;PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN	1 (1.0%)
ORNITHINE	1 (1.0%)
TIMONACIC	1 (1.0%)
URSODEOXYCHOLIC ACID	1 (1.0%)

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ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
BLOOD SUBSTITUTES AND PERFUSION SOLUTIONS	
Total number of patients with at least one treatment	39 (38.2%)
Total number of treatments	128
SODIUM CHLORIDE	15 (14.7%)
POTASSIUM CHLORIDE	10 (9.8%)
SODIUM BICARBONATE	7 (6.9%)
MAGNESIUM SULFATE	6 (5.9%)
GLUCOSE	3 (2.9%)
VITAMINS NOS	3 (2.9%)
ALANINE;ARGININE;CYSTEINE HYDROCHLORIDE;GLYCINE;HISTIDINE; ISOLEUCINE;LEUCINE;LYSINE ACETATE;METHIONINE;PHENYLALANINE; PROLINE;SERINE;THREONINE;TRYPTOPHAN, L-;VALINE	2 (2.0%)
CALCIUM CHLORIDE DIHYDRATE;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE	2 (2.0%)
CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM CHLORIDE; SODIUM CHLORIDE;SODIUM LACTATE;SORBITOL	2 (2.0%)
CALCIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM LACTATE	2 (2.0%)
CHLORHEXIDINE	2 (2.0%)
CHLORHEXIDINE GLUCONATE	2 (2.0%)
PHOSPHOLIPIDS	2 (2.0%)
POTASSIUM	2 (2.0%)
ZINC	2 (2.0%)
ALANINE;ARGININE;CALCIUM CHLORIDE DIHYDRATE;FISH OIL; GLUCOSE MONOHYDRATE;GLYCINE;GLYCINE MAX OIL;HISTIDINE; ISOLEUCINE;LEUCINE;LYSINE HYDROCHLORIDE;MAGNESIUM SULFATE HEPTAHYDRATE;MEDIUM-CHAIN TRIGLYCERIDES;METHIONINE;OLEA EUROPAEA OIL;PHENYLALANINE;POTASSIUM CHLORIDE;PROLINE; SERINE;SODIUM ACETATE TRIHYDRATE;SODIUM GLYCEROPHOSPHATE; THREONINE;TRYPTOPHAN, L-;TYROSINE;VALINE;ZINC SULFATE HEPTAHYDRATE	1 (1.0%)
CALCIUM CHLORIDE DIHYDRATE;MAGNESIUM CHLORIDE HEXAHYDRATE; POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE	1 (1.0%)
CALCIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	1 (1.0%)
CALCIUM GLUCONATE	1 (1.0%)
CETYLPYRIDINIUM CHLORIDE	1 (1.0%)
GLUCOSE 1-PHOSPHATE DISODIUM	1 (1.0%)
GLUCOSE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	1 (1.0%)
MAGNESIUM CHLORIDE	1 (1.0%)
MINERALS NOS;VITAMINS NOS	1 (1.0%)
PLATELETS, CONCENTRATED	1 (1.0%)
POTASSIUM PHOSPHATE DIBASIC;POTASSIUM PHOSPHATE MONOBASIC	1 (1.0%)
POTASSIUM PHOSPHATE MONOBASIC	1 (1.0%)
RED BLOOD CELLS	1 (1.0%)
RED BLOOD CELLS, CONCENTRATED	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
CALCIUM CHANNEL BLOCKERS	
Total number of patients with at least one treatment	7 (6.9%)
Total number of treatments	8
AMLODIPINE	2 (2.0%)
AMLODIPINE BESILATE	1 (1.0%)
DILTIAZEM	1 (1.0%)
LERCANIDIPINE HYDROCHLORIDE	1 (1.0%)
NIFEDIPINE	1 (1.0%)
S AMLODIPINE NICOTINATE	1 (1.0%)
CARDIAC THERAPY	
Total number of patients with at least one treatment	31 (30.4%)
Total number of treatments	58
IBUPROFEN	16 (15.7%)
LIDOCAINE	7 (6.9%)
MELDONIUM	6 (5.9%)
THIOTRIAZOLINE	3 (2.9%)
TRIMETAZIDINE HYDROCHLORIDE	3 (2.9%)
AMIODARONE	2 (2.0%)
MAGNESIUM ASPARTATE;POTASSIUM ASPARTATE	2 (2.0%)
RACECADOTRIL	2 (2.0%)
ATROPINE	1 (1.0%)
ATROPINE SULFATE	1 (1.0%)
DOBUTAMINE	1 (1.0%)
EPINEPHRINE	1 (1.0%)
IPRATROPIUM	1 (1.0%)
IPRATROPIUM BROMIDE	1 (1.0%)
LIDOCAINE HYDROCHLORIDE	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_CNCM_NFC_C_IT.out

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
CORTICOSTEROIDS FOR SYSTEMIC USE	
Total number of patients with at least one treatment	101 (99.0%)
Total number of treatments	927
DEXAMETHASONE	81 (79.4%)
PREDNISONE	57 (55.9%)
PREDNISOLONE	30 (29.4%)
HYDROCORTISONE	12 (11.8%)
DEXAMETHASONE SODIUM PHOSPHATE	10 (9.8%)
METHYLPREDNISOLONE	10 (9.8%)
METHYLPREDNISOLONE SODIUM SUCCINATE	6 (5.9%)
BETAMETHASONE	5 (4.9%)
HYDROCORTISONE SODIUM SUCCINATE	3 (2.9%)
TRIAMCINOLONE ACETONIDE	3 (2.9%)
CORTICOSTEROID NOS	2 (2.0%)
CORTISONE	2 (2.0%)
PREDNISOLONE METASULFOBENZOATE SODIUM	2 (2.0%)
TRIAMCINOLONE	2 (2.0%)
BETAMETHASONE DIPROPIONATE	1 (1.0%)
BETAMETHASONE VALERATE	1 (1.0%)
HYDROCORTISONE ACETATE	1 (1.0%)

Treatments are coded using the WHODRUG GLOBAL B3 SEPTEMBER 1, 2022. dictionary. Treatments can appear under multiple classes. The table includes medications that have temporal overlap with study drug administration. Multiple uses of a specific medication for a patient were counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a patient were counted once in the frequency for the medication class. Use of the anti-diarrheal medication Loperamide is primarily summarized in separate outputs.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS	
Total number of patients with at least one treatment	101 (99.0%)
Total number of treatments	946
DEXAMETHASONE	81 (79.4%)
PREDNISONE	57 (55.9%)
PREDNISOLONE	30 (29.4%)
HYDROCORTISONE	12 (11.8%)
DEXAMETHASONE SODIUM PHOSPHATE	10 (9.8%)
METHYLPREDNISOLONE	10 (9.8%)
METHYLPREDNISOLONE SODIUM SUCCINATE	6 (5.9%)
BETAMETHASONE	5 (4.9%)
MOMETASONE FUROATE	4 (3.9%)
FLUTICASONE PROPIONATE	3 (2.9%)
HYDROCORTISONE SODIUM SUCCINATE	3 (2.9%)
TRIAMCINOLONE ACETONIDE	3 (2.9%)
BECLOMETASONE DIPROPIONATE	2 (2.0%)
CLOBETASOL PROPIONATE	2 (2.0%)
CORTICOSTEROID NOS	2 (2.0%)
PREDNICARBATE	2 (2.0%)
PREDNISOLONE METASULFOBENZOATE SODIUM	2 (2.0%)
TRIAMCINOLONE	2 (2.0%)
BENZALKONIUM CHLORIDE;DIMETICONE;HYDROCORTISONE;NYSTATIN	1 (1.0%)
BETAMETHASONE DIPROPIONATE	1 (1.0%)
BETAMETHASONE DIPROPIONATE;CLOTRIMAZOLE;GENTAMICIN SULFATE	1 (1.0%)
BETAMETHASONE VALERATE	1 (1.0%)
BUDESONIDE	1 (1.0%)
DIFLUCORTOLONE VALERATE	1 (1.0%)
FLUTICASONE	1 (1.0%)
HYDROCORTISONE ACETATE	1 (1.0%)
METHYLPREDNISOLONE ACEPONATE	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
COUGH AND COLD PREPARATIONS	
Total number of patients with at least one treatment	29 (28.4%)
Total number of treatments	79
SODIUM CHLORIDE	15 (14.7%)
CODEINE PHOSPHATE	4 (3.9%)
ACETYLCYSTEINE	3 (2.9%)
CODEINE	2 (2.0%)
GUAIFENESIN	2 (2.0%)
ZINC	2 (2.0%)
ACETYLCYSTEINE;AMBROXOL HYDROCHLORIDE	1 (1.0%)
AMBROXOL	1 (1.0%)
AMMONIUM CHLORIDE;CHLORPHENAMINE MALEATE;DIHYDROCODEINE BITARTRATE;METHYLEPHEDRINE HYDROCHLORIDE-DL	1 (1.0%)
BENZONATATE	1 (1.0%)
CARBOCISTEINE	1 (1.0%)
CLOPERASTINE	1 (1.0%)
COPTIS SPP. RHIZOME;HEDERA HELIX LEAF	1 (1.0%)
DEXTROMETHORPHAN HYDROBROMIDE;GUAIFENESIN	1 (1.0%)
HELICIDINE	1 (1.0%)
OXOLAMINE	1 (1.0%)
POTASSIUM IODIDE	1 (1.0%)
PRUNUS CERASUS	1 (1.0%)
DIAGNOSTIC AGENTS	
Total number of patients with at least one treatment	11 (10.8%)
Total number of treatments	13
MAGNESIUM SULFATE	6 (5.9%)
FOLIC ACID	4 (3.9%)
GLUCOSE	3 (2.9%)
DIGESTIVES, INCL. ENZYMES	
Total number of patients with at least one treatment	8 (7.8%)
Total number of treatments	11
ARGININE CITRATE;BETAINE;BETAINE HYDROCHLORIDE	5 (4.9%)
PANCREATIN	3 (2.9%)
BROMELAINS;DIMETICONE;PANCREATIN	1 (1.0%)
PRUNUS CERASUS	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
DIURETICS	
Total number of patients with at least one treatment	20 (19.6%)
Total number of treatments	31
HYDROCHLOROTHIAZIDE	7 (6.9%)
FUROSEMIDE	6 (5.9%)
TORASEMIDE	3 (2.9%)
SPIRONOLACTONE	2 (2.0%)
ACETAZOLAMIDE	1 (1.0%)
AMILORIDE HYDROCHLORIDE;HYDROCHLOROTHIAZIDE	1 (1.0%)
CHLORTALIDONE	1 (1.0%)
HYDROCHLOROTHIAZIDE;TRIAMTERENE	1 (1.0%)
INDAPAMIDE	1 (1.0%)
DRUGS FOR ACID RELATED DISORDERS	
Total number of patients with at least one treatment	94 (92.2%)
Total number of treatments	591
RANITIDINE	45 (44.1%)
FAMOTIDINE	38 (37.3%)
OMEPRAZOLE	18 (17.6%)
RANITIDINE HYDROCHLORIDE	8 (7.8%)
PANTOPRAZOLE SODIUM SESQUIHYDRATE	7 (6.9%)
SODIUM BICARBONATE	7 (6.9%)
CIMETIDINE	5 (4.9%)
LANSOPRAZOLE	5 (4.9%)
ESOMEPRAZOLE	4 (3.9%)
PANTOPRAZOLE	4 (3.9%)
ANTACIDS, OTHER COMBINATIONS	3 (2.9%)
CALCIUM CARBONATE	3 (2.9%)
RABEPRAZOLE SODIUM	2 (2.0%)
REBAMIPIDE	2 (2.0%)
ALMAGATE	1 (1.0%)
BISMUTH SUBSALICYLATE	1 (1.0%)
CALCIUM CARBONATE;SODIUM ALGINATE;SODIUM BICARBONATE	1 (1.0%)
DEXLANSOPRAZOLE	1 (1.0%)
ESOMEPRAZOLE MAGNESIUM	1 (1.0%)
LAFUTIDINE	1 (1.0%)
MAGALDRATE;SIMETICONE	1 (1.0%)
MAGNESIUM OXIDE	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
DRUGS FOR CONSTIPATION	
Total number of patients with at least one treatment	26 (25.5%)
Total number of treatments	81
SODIUM CHLORIDE	15 (14.7%)
MAGNESIUM SULFATE	6 (5.9%)
MACROGOL 3350	3 (2.9%)
BULK-FORMING LAXATIVES	2 (2.0%)
CARMELLOSE SODIUM	2 (2.0%)
CONTACT LAXATIVES	2 (2.0%)
MACROGOL 3350;POTASSIUM CHLORIDE;SODIUM BICARBONATE;SODIUM CHLORIDE	2 (2.0%)
DOCUSATE	1 (1.0%)
LACTOBACILLUS ACIDOPHILUS;LACTOBACILLUS RHAMNOSUS	1 (1.0%)
MACROGOL	1 (1.0%)
MAGNESIUM OXIDE	1 (1.0%)
NALOXEGOL OXALATE	1 (1.0%)
NALOXONE	1 (1.0%)
PARAFFIN	1 (1.0%)
POTASSIUM PHOSPHATE DIBASIC;POTASSIUM PHOSPHATE MONOBASIC	1 (1.0%)
SENNA ALEXANDRINA GLYCOSIDE EXTRACT	1 (1.0%)
SENNA SPP.	1 (1.0%)
SENNOSIDE A+B	1 (1.0%)
SODIUM CITRATE;SODIUM LAURYL SULFOACETATE;SORBITOL	1 (1.0%)
SODIUM PICOSULFATE	1 (1.0%)
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	
Total number of patients with at least one treatment	33 (32.4%)
Total number of treatments	59
METOCLOPRAMIDE	14 (13.7%)
METOCLOPRAMIDE HYDROCHLORIDE	7 (6.9%)
HYOSCINE BUTYLBROMIDE	4 (3.9%)
BROMOPRIDE	3 (2.9%)
SIMETICONE	2 (2.0%)
ALVERINE CITRATE;SIMETICONE	1 (1.0%)
ATROPINE	1 (1.0%)
ATROPINE SULFATE	1 (1.0%)
BUTYLSCOPOLAMINE	1 (1.0%)
DICYCLOVERINE HYDROCHLORIDE;PARACETAMOL	1 (1.0%)
DIMETICONE	1 (1.0%)
DOMPERIDONE	1 (1.0%)
HYOSCINE	1 (1.0%)
HYOSCINE HYDROBROMIDE	1 (1.0%)
ITOPRIDE HYDROCHLORIDE	1 (1.0%)
RAMOSETRON HYDROCHLORIDE	1 (1.0%)
SILICON DIOXIDE	1 (1.0%)
TIROPRAMIDE HYDROCHLORIDE	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	
Total number of patients with at least one treatment	94 (92.2%)
Total number of treatments	568
DEXAMETHASONE	81 (79.4%)
DEXAMETHASONE SODIUM PHOSPHATE	10 (9.8%)
SALBUTAMOL	6 (5.9%)
BETAMETHASONE	5 (4.9%)
MOMETASONE FUROATE	4 (3.9%)
FLUTICASONE PROPIONATE	3 (2.9%)
FLUTICASONE PROPIONATE;SALMETEROL XINAFOATE	3 (2.9%)
TRIAMCINOLONE ACETONIDE	3 (2.9%)
BECLOMETASONE DIPROPIONATE	2 (2.0%)
CORTICOSTEROID NOS	2 (2.0%)
SALBUTAMOL SULFATE	2 (2.0%)
TRIAMCINOLONE	2 (2.0%)
AMBROXOL ACEFYLLINATE	1 (1.0%)
BETAMETHASONE DIPROPIONATE	1 (1.0%)
BETAMETHASONE VALERATE	1 (1.0%)
BUDESONIDE	1 (1.0%)
BUDESONIDE;FORMOTEROL FUMARATE	1 (1.0%)
EPINEPHRINE	1 (1.0%)
FENOTEROL	1 (1.0%)
FENOTEROL HYDROBROMIDE	1 (1.0%)
FLUTICASONE	1 (1.0%)
IPRATROPIUM	1 (1.0%)
IPRATROPIUM BROMIDE	1 (1.0%)
MONTELUKAST	1 (1.0%)
MONTELUKAST SODIUM	1 (1.0%)
TIOTROPIUM BROMIDE	1 (1.0%)
DRUGS FOR TREATMENT OF BONE DISEASES	
Total number of patients with at least one treatment	8 (7.8%)
Total number of treatments	8
DENOSUMAB	3 (2.9%)
ZOLEDRONIC ACID	3 (2.9%)
IBANDRONATE SODIUM	1 (1.0%)
PAMIDRONATE DISODIUM	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
DRUGS USED IN DIABETES	
Total number of patients with at least one treatment	11 (10.8%)
Total number of treatments	24
METFORMIN	5 (4.9%)
INSULIN	2 (2.0%)
INSULIN LISPRO	2 (2.0%)
METFORMIN HYDROCHLORIDE	2 (2.0%)
GLIBENCLAMIDE	1 (1.0%)
GLICLAZIDE	1 (1.0%)
GLIMEPIRIDE	1 (1.0%)
INSULIN GLARGINE	1 (1.0%)
ISOPHANE INSULIN	1 (1.0%)
LINAGLIPTIN;METFORMIN HYDROCHLORIDE	1 (1.0%)
SITAGLIPTIN PHOSPHATE	1 (1.0%)
TENELIGLIPTIN HYDROBROMIDE	1 (1.0%)
ECTOPARASITICIDES, INCL. SCABICIDES, INSECTICIDES AND REPELLENTS	
Total number of patients with at least one treatment	2 (2.0%)
Total number of treatments	2
DIMETICONE	1 (1.0%)
IVERMECTIN	1 (1.0%)
EMOLLIENTS AND PROTECTIVES	
Total number of patients with at least one treatment	15 (14.7%)
Total number of treatments	64
THIOCTIC ACID	8 (7.8%)
OTHER EMOLLIENTS AND PROTECTIVES	2 (2.0%)
ZINC	2 (2.0%)
AVENA SATIVA FLUID EXTRACT	1 (1.0%)
AVOBENZONE;OCTINOXATE	1 (1.0%)
BENZYL ALCOHOL;BENZYL BENZOATE;BENZYL CINNAMATE;WOOL FAT; ZINC OXIDE	1 (1.0%)
DIMETICONE	1 (1.0%)
PARAFFIN	1 (1.0%)
PROPYLENE GLYCOL	1 (1.0%)
PRUNUS CERASUS	1 (1.0%)
ENDOCRINE THERAPY	
Total number of patients with at least one treatment	1 (1.0%)
Total number of treatments	1
MEGESTROL ACETATE	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
GENERAL NUTRIENTS	
Total number of patients with at least one treatment	8 (7.8%)
Total number of treatments	9
GLUCOSE	3 (2.9%)
FISH OIL	2 (2.0%)
ASCORBIC ACID;BIOTIN;CALCIUM CITRATE;CALCIUM PANTOTHENATE; CYANOCOBALAMIN;FERROUS SULFATE;FIBRE, DIETARY;FOLIC ACID; GLYCINE MAX SEED OIL;MAGNESIUM CARBONATE;MALTODEXTRIN; NICOTINAMIDE;POTASSIUM CITRATE;PROTEINS NOS;PYRIDOXINE HYDROCHLORIDE;RETINOL;RIBOFLAVIN;SODIUM CHLORIDE;SUCROSE; THIAMINE HYDROCHLORIDE;TOCOPHERYL ACETATE;WHEY PROTEIN;ZEA MAYS STARCH	1 (1.0%)
BETA-ALANINE	1 (1.0%)
CARBOHYDRATES NOS;LIPIDS NOS;MINERALS NOS;PROTEINS NOS	1 (1.0%)
MINERALS NOS;VITAMINS NOS	1 (1.0%)
GYNECOLOGICAL ANTIINFECTIVES AND ANTISEPTICS	
Total number of patients with at least one treatment	40 (39.2%)
Total number of treatments	62
CIPROFLOXACIN	16 (15.7%)
METRONIDAZOLE	7 (6.9%)
NYSTATIN	7 (6.9%)
CLINDAMYCIN	4 (3.9%)
ASCORBIC ACID	3 (2.9%)
CHLORHEXIDINE	2 (2.0%)
CHLORHEXIDINE GLUCONATE	2 (2.0%)
CLOTRIMAZOLE	2 (2.0%)
POTASSIUM	2 (2.0%)
CHLORAMPHENICOL	1 (1.0%)
CIPROFLOXACIN HYDROCHLORIDE	1 (1.0%)
LACTOBACILLUS NOS	1 (1.0%)
NYSTATIN;TRIAMCINOLONE	1 (1.0%)
OCTENIDINE HYDROCHLORIDE;PHENOXYETHANOL	1 (1.0%)
POVIDONE-IODINE	1 (1.0%)

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ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
HOMEOPATHIC PREPARATION	
Total number of patients with at least one treatment	27 (26.5%)
Total number of treatments	89
SODIUM CHLORIDE	15 (14.7%)
POTASSIUM CHLORIDE	10 (9.8%)
ASCORBIC ACID	3 (2.9%)
CALCIUM CARBONATE	3 (2.9%)
IRON	3 (2.9%)
CORTISONE	2 (2.0%)
POTASSIUM	2 (2.0%)
ZINC	2 (2.0%)
CYANOCOBALAMIN	1 (1.0%)
EPINEPHRINE	1 (1.0%)
SILICON DIOXIDE	1 (1.0%)
IMMUNOSTIMULANTS	
Total number of patients with at least one treatment	16 (15.7%)
Total number of treatments	90
FILGRASTIM	13 (12.7%)
METHYLURACIL	2 (2.0%)
FILGRASTIM SNDZ	1 (1.0%)
LENOGRASTIM	1 (1.0%)
TBO FILGRASTIM	1 (1.0%)
IMMUNOSUPPRESSANTS	
Total number of patients with at least one treatment	3 (2.9%)
Total number of treatments	5
HYDROXYCHLOROQUINE	2 (2.0%)
AZATHIOPRINE	1 (1.0%)
INFLIXIMAB	1 (1.0%)
LIPID MODIFYING AGENTS	
Total number of patients with at least one treatment	22 (21.6%)
Total number of treatments	27
SIMVASTATIN	6 (5.9%)
ATORVASTATIN	5 (4.9%)
ROSUVASTATIN	3 (2.9%)
EZETIMIBE	2 (2.0%)
FISH OIL	2 (2.0%)
PHOSPHOLIPIDS	2 (2.0%)
CIPROFIBRATE	1 (1.0%)
COLESTYRAMINE	1 (1.0%)
PRAVASTATIN	1 (1.0%)
ROSUVASTATIN CALCIUM	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
MEDICATED DRESSINGS	
Total number of patients with at least one treatment	24 (23.5%)
Total number of treatments	65
SODIUM CHLORIDE	15 (14.7%)
CARMELLOSE SODIUM	2 (2.0%)
CHLORHEXIDINE	2 (2.0%)
CHLORHEXIDINE GLUCONATE	2 (2.0%)
ZINC	2 (2.0%)
CETYLPYRIDINIUM CHLORIDE	1 (1.0%)
FUSIDIC ACID	1 (1.0%)
PARAFFIN	1 (1.0%)
POVIDONE-IODINE	1 (1.0%)
MINERAL SUPPLEMENTS	
Total number of patients with at least one treatment	30 (29.4%)
Total number of treatments	96
SODIUM CHLORIDE	15 (14.7%)
POTASSIUM CHLORIDE	10 (9.8%)
MAGNESIUM SULFATE	6 (5.9%)
CALCIUM CARBONATE	3 (2.9%)
CALCIUM CARBONATE;COLECALCIFEROL	3 (2.9%)
MAGNESIUM ASPARTATE;POTASSIUM ASPARTATE	2 (2.0%)
POTASSIUM	2 (2.0%)
ZINC	2 (2.0%)
CALCIUM	1 (1.0%)
CALCIUM GLUCONATE	1 (1.0%)
ECHINACEA ANGUSTIFOLIA;MAGNESIUM AMINO ACID CHELATE; MANGANESE AMINO ACID CHELATE;PYRIDOXINE HYDROCHLORIDE; RETINOL;SMILAX ARISTOLOCHIIFOLIA;ZINC AMINO ACID CHELATE	1 (1.0%)
MAGNESIUM	1 (1.0%)
MAGNESIUM CHLORIDE	1 (1.0%)
MAGNESIUM OXIDE	1 (1.0%)
MINERALS NOS;VITAMINS NOS	1 (1.0%)
POTASSIUM PHOSPHATE DIBASIC;POTASSIUM PHOSPHATE MONOBASIC	1 (1.0%)
POTASSIUM PHOSPHATE MONOBASIC	1 (1.0%)
SILICON DIOXIDE	1 (1.0%)
MUSCLE RELAXANTS	
Total number of patients with at least one treatment	5 (4.9%)
Total number of treatments	23
CAFFEINE;CARISOPRODOL;DICLOFENAC SODIUM;PARACETAMOL	2 (2.0%)
CYCLOBENZAPRINE	2 (2.0%)
CAFFEINE;METAMIZOLE SODIUM;ORPHENADRINE CITRATE	1 (1.0%)
DIAZEPAM	1 (1.0%)
ORPHENADRINE	1 (1.0%)
TOLPERISONE	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
N/A	
Total number of patients with at least one treatment	8 (7.8%)
Total number of treatments	13
DIOSMECTITE	6 (5.9%)
CETRARIA ISLANDICA;MENTHA X PIPERITA OIL	1 (1.0%)
MAGIC MOUTHWASH	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
NASAL PREPARATIONS	
Total number of patients with at least one treatment	98 (96.1%)
Total number of treatments	743
DEXAMETHASONE	81 (79.4%)
PREDNISOLONE	30 (29.4%)
SODIUM CHLORIDE	15 (14.7%)
DEXAMETHASONE SODIUM PHOSPHATE	10 (9.8%)
SODIUM BICARBONATE	7 (6.9%)
BETAMETHASONE	5 (4.9%)
MOMETASONE FUROATE	4 (3.9%)
ACETYLCYSTEINE	3 (2.9%)
FLUTICASONE PROPIONATE	3 (2.9%)
MUPIROCIN	3 (2.9%)
TRIAMCINOLONE ACETONIDE	3 (2.9%)
BECLOMETASONE DIPROPIONATE	2 (2.0%)
CORTICOSTEROID NOS	2 (2.0%)
OLOPATADINE HYDROCHLORIDE	2 (2.0%)
TRIAMCINOLONE	2 (2.0%)
ZINC	2 (2.0%)
AZELASTINE	1 (1.0%)
AZELASTINE HYDROCHLORIDE	1 (1.0%)
AZELASTINE HYDROCHLORIDE;FLUTICASONE PROPIONATE	1 (1.0%)
BETAMETHASONE DIPROPIONATE	1 (1.0%)
BETAMETHASONE VALERATE	1 (1.0%)
BUDESONIDE	1 (1.0%)
CALCIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	1 (1.0%)
CHLORHEXIDINE;TIXOCORTOL	1 (1.0%)
CHLORPHENAMINE MALEATE;IBUPROFEN;PHENYLEPHRINE HYDROCHLORIDE	1 (1.0%)
DEXPANTHENOL;MEPYRAMINE MALEATE;NAPHAZOLINE HYDROCHLORIDE	1 (1.0%)
EPINEPHRINE	1 (1.0%)
FLUTICASONE	1 (1.0%)
HEXAMIDINE	1 (1.0%)
HEXAMIDINE ISETIONATE	1 (1.0%)
HYALURONATE SODIUM	1 (1.0%)
HYPROMELLOSE	1 (1.0%)
IBUPROFEN;PSEUDOEPHEDRINE HYDROCHLORIDE	1 (1.0%)
IPRATROPIUM	1 (1.0%)
IPRATROPIUM BROMIDE	1 (1.0%)
LORATADINE;PSEUDOEPHEDRINE SULFATE	1 (1.0%)
MIRAMISTIN	1 (1.0%)
NAPHAZOLINE NITRATE;PREDNISOLONE	1 (1.0%)
POVIDONE-IODINE	1 (1.0%)
SEA WATER	1 (1.0%)
TRAMAZOLINE HYDROCHLORIDE	1 (1.0%)

Treatments are coded using the WHODRUG GLOBAL B3 SEPTEMBER 1, 2022. dictionary. Treatments can appear under multiple classes. The table includes medications that have temporal overlap with study drug administration. Multiple uses of a specific medication for a patient were counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a patient were counted once in the frequency for the medication class. Use of the anti-diarrheal medication Loperamide is primarily summarized in separate outputs.
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ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
OPHTHALMOLOGICAL AND OTOLOGICAL PREPARATIONS	
Total number of patients with at least one treatment	96 (94.1%)
Total number of treatments	667
DEXAMETHASONE	81 (79.4%)
PREDNISOLONE	30 (29.4%)
CIPROFLOXACIN	16 (15.7%)
DEXAMETHASONE SODIUM PHOSPHATE	10 (9.8%)
BETAMETHASONE	5 (4.9%)
LEVOFLOXACIN	3 (2.9%)
CHLORHEXIDINE	2 (2.0%)
CHLORHEXIDINE GLUCONATE	2 (2.0%)
CORTICOSTEROID NOS	2 (2.0%)
PREDNISOLONE METASULFOBENZOATE SODIUM	2 (2.0%)
CHLORAMPHENICOL	1 (1.0%)
CIPROFLOXACIN HYDROCHLORIDE	1 (1.0%)
GENTAMICIN	1 (1.0%)
HEXAMIDINE	1 (1.0%)
HEXAMIDINE ISETIONATE	1 (1.0%)
MIRAMISTIN	1 (1.0%)
POLYMYXIN B;TRIMETHOPRIM	1 (1.0%)
OPHTHALMOLOGICALS	
Total number of patients with at least one treatment	101 (99.0%)
Total number of treatments	1227
DEXAMETHASONE	81 (79.4%)
PREDNISONE	57 (55.9%)
PREDNISOLONE	30 (29.4%)
CIPROFLOXACIN	16 (15.7%)
CETIRIZINE	15 (14.7%)
SODIUM CHLORIDE	15 (14.7%)
HYDROCORTISONE	12 (11.8%)
DEXAMETHASONE SODIUM PHOSPHATE	10 (9.8%)
METHYLPREDNISOLONE	10 (9.8%)
POTASSIUM CHLORIDE	10 (9.8%)
LIDOCAINE	7 (6.9%)
AZITHROMYCIN	6 (5.9%)
CETIRIZINE HYDROCHLORIDE	6 (5.9%)
BETAMETHASONE	5 (4.9%)
BILASTINE	5 (4.9%)
FLUCONAZOLE	5 (4.9%)
ACICLOVIR	4 (3.9%)
DICLOFENAC	4 (3.9%)
ACETYLCYSTEINE	3 (2.9%)
ASCORBIC ACID	3 (2.9%)
CEFUROXIME	3 (2.9%)
HYDROCORTISONE SODIUM SUCCINATE	3 (2.9%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
KETOROLAC TROMETHAMINE	3 (2.9%)
LEVOFLOXACIN	3 (2.9%)
MACROGOL 400;PROPYLENE GLYCOL	3 (2.9%)
PANCREATIN	3 (2.9%)
THIOTRIAZOLINE	3 (2.9%)
TRIAMCINOLONE ACETONIDE	3 (2.9%)
ALTEPLASE	2 (2.0%)
CARMELLOSE SODIUM	2 (2.0%)
CHLORHEXIDINE	2 (2.0%)
CHLORHEXIDINE GLUCONATE	2 (2.0%)
CLOTRIMAZOLE	2 (2.0%)
CORTICOSTEROID NOS	2 (2.0%)
CORTISONE	2 (2.0%)
HEPARIN	2 (2.0%)
MELOXICAM	2 (2.0%)
OLOPATADINE HYDROCHLORIDE	2 (2.0%)
POTASSIUM	2 (2.0%)
PREDNISOLONE METASULFOBENZOATE SODIUM	2 (2.0%)
REBAMIPIDE	2 (2.0%)
TRIAMCINOLONE	2 (2.0%)
ZINC	2 (2.0%)
ACETAZOLAMIDE	1 (1.0%)
AMIKACIN	1 (1.0%)
AMPICILLIN	1 (1.0%)
ANTIINFECTIVES, OPHTHALMIC	1 (1.0%)
ATROPINE	1 (1.0%)
ATROPINE SULFATE	1 (1.0%)
AZELASTINE	1 (1.0%)
AZELASTINE HYDROCHLORIDE	1 (1.0%)
BACITRACIN	1 (1.0%)
BACITRACIN ZINC;POLYMYXIN B SULFATE	1 (1.0%)
BEPOTASTINE BESILATE	1 (1.0%)
BETAMETHASONE DIPROPIONATE	1 (1.0%)
BETAMETHASONE VALERATE	1 (1.0%)
BRIMONIDINE	1 (1.0%)
CARBOMER	1 (1.0%)
CETYLPYRIDINIUM CHLORIDE	1 (1.0%)
CHLORAMPHENICOL	1 (1.0%)
CIPROFLOXACIN HYDROCHLORIDE	1 (1.0%)
CLONIDINE	1 (1.0%)
CYANOCOBALAMIN	1 (1.0%)
DICLOFENAC SODIUM	1 (1.0%)
DIMETICONE	1 (1.0%)
DORZOLAMIDE HYDROCHLORIDE	1 (1.0%)
EPINEPHRINE	1 (1.0%)
FLURBIPROFEN	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
FUSIDIC ACID	1 (1.0%)
GENTAMICIN	1 (1.0%)
GLUCOSE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	1 (1.0%)
HEPARIN SODIUM	1 (1.0%)
HEXAMIDINE	1 (1.0%)
HEXAMIDINE ISETIONATE	1 (1.0%)
HYALURONATE SODIUM	1 (1.0%)
HYDROCORTISONE ACETATE	1 (1.0%)
HYOSCINE	1 (1.0%)
HYOSCINE HYDROBROMIDE	1 (1.0%)
HYPROMELLOSE	1 (1.0%)
LATANOPROST	1 (1.0%)
LATANOPROST;TIMOLOL MALEATE	1 (1.0%)
LIDOCAINE HYDROCHLORIDE	1 (1.0%)
MACROGOL	1 (1.0%)
MINERALS NOS;VITAMINS NOS	1 (1.0%)
MIRAMISTIN	1 (1.0%)
MOXIFLOXACIN	1 (1.0%)
MOXIFLOXACIN HYDROCHLORIDE	1 (1.0%)
NAPROXEN	1 (1.0%)
PARAFFIN	1 (1.0%)
PERFLUOROHEXYLOCTANE	1 (1.0%)
POLYMYXIN B;TRIMETHOPRIM	1 (1.0%)
POTASSIUM IODIDE	1 (1.0%)
POTASSIUM PHOSPHATE DIBASIC;POTASSIUM PHOSPHATE MONOBASIC	1 (1.0%)
POVIDONE-IODINE	1 (1.0%)
PROCAINE	1 (1.0%)
PROPYLENE GLYCOL	1 (1.0%)
SEA WATER	1 (1.0%)
SULFAMETHOXAZOLE	1 (1.0%)
TRAMAZOLINE HYDROCHLORIDE	1 (1.0%)
TRAVOPROST	1 (1.0%)
VANCOMYCIN	1 (1.0%)
WATER PURIFIED	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS	
Total number of patients with at least one treatment	20 (19.6%)
Total number of treatments	144
THIOCTIC ACID	8 (7.8%)
ADEMETIONINE	7 (6.9%)
SODIUM BICARBONATE	7 (6.9%)
QUERCETIN	5 (4.9%)
ACETYLCYSTEINE	3 (2.9%)
ZINC	2 (2.0%)
ORNITHINE	1 (1.0%)
PROTEINS NOS;VITIS VINIFERA SEED;XYLOGLUCAN; XYLOOLIGOSACCHARIDE	1 (1.0%)
OTHER DERMATOLOGICAL PREPARATIONS	
Total number of patients with at least one treatment	37 (36.3%)
Total number of treatments	63
IBUPROFEN	16 (15.7%)
SODIUM BICARBONATE	7 (6.9%)
MAGNESIUM SULFATE	6 (5.9%)
DICLOFENAC	4 (3.9%)
ASCORBIC ACID	3 (2.9%)
PYRIDOXINE	3 (2.9%)
THIOTRIAZOLINE	3 (2.9%)
OXYGEN	2 (2.0%)
PYRIDOXINE HYDROCHLORIDE	2 (2.0%)
BRIMONIDINE	1 (1.0%)
CALCIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	1 (1.0%)
CALCIUM GLUCONATE	1 (1.0%)
DICLOFENAC SODIUM	1 (1.0%)
HYALURONATE SODIUM	1 (1.0%)
IVERMECTIN	1 (1.0%)
MINERALS NOS;VITAMINS NOS	1 (1.0%)
POVIDONE-IODINE	1 (1.0%)
SILICON DIOXIDE	1 (1.0%)
OTHER DRUGS FOR DISORDERS OF THE MUSCULO-SKELETAL SYSTEM	
Total number of patients with at least one treatment	6 (5.9%)
Total number of treatments	11
CYTIDINE PHOSPHATE SODIUM;DISODIUM URIDINE MONOPHOSPHATE; URIDINE DIPHOSPHATE DISODIUM;URIDINE TRIPHOSPHATE TRISODIUM	4 (3.9%)
CYTIDINE MONOPHOSPHATE DISODIUM;URIDINE TRIPHOSPHATE TRISODIUM	2 (2.0%)
CYTIDINE MONOPHOSPHATE DISODIUM	1 (1.0%)
HYALURONATE SODIUM	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
OTHER GYNECOLOGICALS	
Total number of patients with at least one treatment	36 (35.3%)
Total number of treatments	51
IBUPROFEN	16 (15.7%)
SODIUM BICARBONATE	7 (6.9%)
SALBUTAMOL	6 (5.9%)
THIOTRIAZOLINE	3 (2.9%)
BENZYDAMINE HYDROCHLORIDE	2 (2.0%)
SALBUTAMOL SULFATE	2 (2.0%)
BETA-ALANINE	1 (1.0%)
CARBOMER	1 (1.0%)
CLONIDINE	1 (1.0%)
FENOTEROL	1 (1.0%)
FENOTEROL HYDROBROMIDE	1 (1.0%)
HYALURONATE SODIUM	1 (1.0%)
NAPROXEN	1 (1.0%)
NIFEDIPINE	1 (1.0%)
POLYCARBOPHIL;SODIUM ACETATE	1 (1.0%)
WATER PURIFIED	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
OTHER NERVOUS SYSTEM DRUGS	
Total number of patients with at least one treatment	37 (36.3%)
Total number of treatments	155
GABAPENTIN	12 (11.8%)
DIMENHYDRINATE	8 (7.8%)
THIOCTIC ACID	8 (7.8%)
MELDONIUM	6 (5.9%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE HYDROCHLORIDE	3 (2.9%)
TRIMETAZIDINE HYDROCHLORIDE	3 (2.9%)
BETAHISTINE	2 (2.0%)
CYANOCOBALAMIN;CYTIDINE PHOSPHATE;DISODIUM URIDINE MONOPHOSPHATE;FOLIC ACID	2 (2.0%)
CYTIDINE MONOPHOSPHATE DISODIUM;URIDINE TRIPHOSPHATE TRISODIUM	2 (2.0%)
FLUOXETINE	2 (2.0%)
METHYLETHYLPIRIDINOL SUCCINATE	2 (2.0%)
PHOSPHOLIPIDS	2 (2.0%)
BETAHISTINE HYDROCHLORIDE	1 (1.0%)
BORAGO OFFICINALIS SEED OIL;NICOTINIC ACID;PANTOTHENIC ACID;PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN;SELENIUM;THIOCTIC ACID;VITAMIN B1 NOS;VITAMIN E NOS	1 (1.0%)
BUPROPION HYDROCHLORIDE	1 (1.0%)
CHOLINE ALFOSCERATE	1 (1.0%)
CINNARIZINE;DIMENHYDRINATE	1 (1.0%)
CLONIDINE	1 (1.0%)
CYANOCOBALAMIN	1 (1.0%)
DIMENHYDRINATE;FRUCTOSE;GLUCOSE;PYRIDOXINE HYDROCHLORIDE	1 (1.0%)
DIMENHYDRINATE;PYRIDOXINE	1 (1.0%)
FLUNARIZINE	1 (1.0%)
NALOXONE	1 (1.0%)
OTHER RESPIRATORY SYSTEM PRODUCTS	
Total number of patients with at least one treatment	6 (5.9%)
Total number of treatments	8
PHOSPHOLIPIDS	2 (2.0%)
ACETAZOLAMIDE	1 (1.0%)
AMBROXOL	1 (1.0%)
DIMETICONE	1 (1.0%)
OTHER RESPIRATORY SYSTEM PRODUCTS	1 (1.0%)
PALMIDROL	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
OTOLOGICALS	
Total number of patients with at least one treatment	100 (98.0%)
Total number of treatments	761
DEXAMETHASONE	81 (79.4%)
PREDNISOLONE	30 (29.4%)
CIPROFLOXACIN	16 (15.7%)
SODIUM CHLORIDE	15 (14.7%)
HYDROCORTISONE	12 (11.8%)
DEXAMETHASONE SODIUM PHOSPHATE	10 (9.8%)
LIDOCAINE	7 (6.9%)
SODIUM BICARBONATE	7 (6.9%)
BETAMETHASONE	5 (4.9%)
HYDROCORTISONE SODIUM SUCCINATE	3 (2.9%)
LEVOFLOXACIN	3 (2.9%)
CHLORHEXIDINE	2 (2.0%)
CHLORHEXIDINE GLUCONATE	2 (2.0%)
CLOTRIMAZOLE	2 (2.0%)
CORTICOSTEROID NOS	2 (2.0%)
PREDNISOLONE METASULFOBENZOATE SODIUM	2 (2.0%)
BETAMETHASONE DIPROPIONATE	1 (1.0%)
BETAMETHASONE VALERATE	1 (1.0%)
CHLORAMPHENICOL	1 (1.0%)
CIPROFLOXACIN HYDROCHLORIDE	1 (1.0%)
DOCUSATE	1 (1.0%)
GENTAMICIN	1 (1.0%)
HYDROCORTISONE ACETATE	1 (1.0%)
LIDOCAINE HYDROCHLORIDE	1 (1.0%)
MIRAMISTIN	1 (1.0%)
SEA WATER	1 (1.0%)
PERIPHERAL VASODILATORS	
Total number of patients with at least one treatment	5 (4.9%)
Total number of treatments	11
BETAHISTINE	2 (2.0%)
METHYLETHYLPIRIDINOL SUCCINATE	2 (2.0%)
BETAHISTINE HYDROCHLORIDE	1 (1.0%)
FLUNARIZINE	1 (1.0%)
NICAMETATE DIHYDROGEN CITRATE	1 (1.0%)
NICERGOLINE	1 (1.0%)
PENTOXIFYLLINE	1 (1.0%)
PITUITARY AND HYPOTHALAMIC HORMONES AND ANALOGUES	
Total number of patients with at least one treatment	1 (1.0%)
Total number of treatments	1
TETRACOSACTIDE	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCERS	
Total number of patients with at least one treatment	21 (20.6%)
Total number of treatments	63
SODIUM CHLORIDE	15 (14.7%)
CARMELLOSE SODIUM	2 (2.0%)
FISH OIL	2 (2.0%)
METHYLURACIL	2 (2.0%)
BETACAROTENE;MENADIONE;RETINOL;TOCOPHEROL	1 (1.0%)
DIMETICONE	1 (1.0%)
HYALURONATE SODIUM	1 (1.0%)
PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCERS	1 (1.0%)
PSYCHOANALEPTICS	
Total number of patients with at least one treatment	26 (25.5%)
Total number of treatments	110
ADEMETIONINE	7 (6.9%)
IPIDACRINE	5 (4.9%)
MIRTAZAPINE	4 (3.9%)
AMITRIPTYLINE	3 (2.9%)
DULOXETINE HYDROCHLORIDE	2 (2.0%)
ESCITALOPRAM	2 (2.0%)
FLUOXETINE	2 (2.0%)
METHYLETHYLPIRIDINOL SUCCINATE	2 (2.0%)
TRAZODONE	2 (2.0%)
AMITRIPTYLINE HYDROCHLORIDE	1 (1.0%)
BUPROPION HYDROCHLORIDE	1 (1.0%)
CLONIDINE	1 (1.0%)
DISODIUM URIDINE MONOPHOSPHATE	1 (1.0%)
ESCITALOPRAM OXALATE	1 (1.0%)
LACTOSE;PEPTONE	1 (1.0%)
LAMOTRIGINE	1 (1.0%)
METHYLPHENIDATE HYDROCHLORIDE	1 (1.0%)
SERTRALINE	1 (1.0%)
SERTRALINE HYDROCHLORIDE	1 (1.0%)
TEMGICOLURIL	1 (1.0%)
TRAZODONE HYDROCHLORIDE	1 (1.0%)
VENLAFAXINE	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
PSYCHOLEPTICS	
Total number of patients with at least one treatment	68 (66.7%)
Total number of treatments	362
DIPHENHYDRAMINE	33 (32.4%)
DIPHENHYDRAMINE HYDROCHLORIDE	17 (16.7%)
PROMETHAZINE	10 (9.8%)
PREGABALIN	8 (7.8%)
PROCHLORPERAZINE	7 (6.9%)
LORAZEPAM	6 (5.9%)
ALPRAZOLAM	5 (4.9%)
HYDROXYZINE	5 (4.9%)
ZOLPIDEM	4 (3.9%)
AMITRIPTYLINE	3 (2.9%)
BROMAZEPAM	2 (2.0%)
CLONAZEPAM	2 (2.0%)
DULOXETINE HYDROCHLORIDE	2 (2.0%)
ESCITALOPRAM	2 (2.0%)
FLUOXETINE	2 (2.0%)
MELATONIN	2 (2.0%)
MIDAZOLAM	2 (2.0%)
OLANZAPINE	2 (2.0%)
PROCHLORPERAZINE MALEATE	2 (2.0%)
AMITRIPTYLINE HYDROCHLORIDE	1 (1.0%)
CARBAMAZEPINE	1 (1.0%)
CHLORPROMAZINE	1 (1.0%)
DIAZEPAM	1 (1.0%)
DIPHENHYDRAMINE HYDROCHLORIDE;PARACETAMOL	1 (1.0%)
DIPHENHYDRAMINE;IBUPROFEN	1 (1.0%)
DOXYLAMINE SUCCINATE	1 (1.0%)
ESCITALOPRAM OXALATE	1 (1.0%)
HYOSCINE	1 (1.0%)
HYOSCINE HYDROBROMIDE	1 (1.0%)
PRUNUS CERASUS	1 (1.0%)
QUETIAPINE FUMARATE	1 (1.0%)
SERTRALINE	1 (1.0%)
SERTRALINE HYDROCHLORIDE	1 (1.0%)
TEMAZEPAM	1 (1.0%)
TEMGICOLURIL	1 (1.0%)
VENLAFAXINE	1 (1.0%)
ZOPICLONE	1 (1.0%)
SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	
Total number of patients with at least one treatment	1 (1.0%)
Total number of treatments	1
MEGESTROL ACETATE	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
STOMATOLOGICAL PREPARATIONS	
Total number of patients with at least one treatment	100 (98.0%)
Total number of treatments	809
DEXAMETHASONE	81 (79.4%)
PREDNISOLONE	30 (29.4%)
SODIUM CHLORIDE	15 (14.7%)
HYDROCORTISONE	12 (11.8%)
DEXAMETHASONE SODIUM PHOSPHATE	10 (9.8%)
LIDOCAINE	7 (6.9%)
METRONIDAZOLE	7 (6.9%)
NYSTATIN	7 (6.9%)
SODIUM BICARBONATE	7 (6.9%)
ACETYLSALICYLIC ACID	6 (5.9%)
BETAMETHASONE	5 (4.9%)
DICLOFENAC	4 (3.9%)
NIMESULIDE	4 (3.9%)
DOXYCYCLINE	3 (2.9%)
HYDROCORTISONE SODIUM SUCCINATE	3 (2.9%)
KETOPROFEN	3 (2.9%)
TRIAMCINOLONE ACETONIDE	3 (2.9%)
BENZYDAMINE HYDROCHLORIDE	2 (2.0%)
CHLORHEXIDINE	2 (2.0%)
CHLORHEXIDINE GLUCONATE	2 (2.0%)
CLOBETASOL PROPIONATE	2 (2.0%)
CLOTRIMAZOLE	2 (2.0%)
CORTICOSTEROID NOS	2 (2.0%)
LIDOCAINE;PRILOCAINE	2 (2.0%)
OXYGEN	2 (2.0%)
POTASSIUM	2 (2.0%)
TRIAMCINOLONE	2 (2.0%)
ZINC	2 (2.0%)
CALCIUM CHLORIDE;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM PHOSPHATE DIBASIC;SODIUM PHOSPHATE MONOBASIC	1 (1.0%)
CARBOMER	1 (1.0%)
CETALKONIUM CHLORIDE;CHOLINE SALICYLATE	1 (1.0%)
CETYLPYRIDINIUM CHLORIDE	1 (1.0%)
CHLORAMPHENICOL	1 (1.0%)
CHLORHEXIDINE HYDROCHLORIDE;LIDOCAINE;TRIAMCINOLONE ACETONIDE	1 (1.0%)
CHLORHEXIDINE;TIXOCORTOL	1 (1.0%)
DICLOFENAC SODIUM	1 (1.0%)
DIMETICONE	1 (1.0%)
EPINEPHRINE	1 (1.0%)
FLURBIPROFEN	1 (1.0%)
HYALURONATE SODIUM	1 (1.0%)
HYDROCORTISONE ACETATE	1 (1.0%)

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ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
LIDOCAINE HYDROCHLORIDE	1 (1.0%)
MAGIC MOUTHWASH	1 (1.0%)
MIRAMISTIN	1 (1.0%)
NAPROXEN	1 (1.0%)
POVIDONE-IODINE	1 (1.0%)
STOMATOLOGICAL PREPARATIONS	1 (1.0%)
THYMOL	1 (1.0%)
THROAT PREPARATIONS	
Total number of patients with at least one treatment	35 (34.3%)
Total number of treatments	64
IBUPROFEN	16 (15.7%)
LIDOCAINE	7 (6.9%)
DICLOFENAC	4 (3.9%)
KETOPROFEN	3 (2.9%)
BENZYDAMINE HYDROCHLORIDE	2 (2.0%)
CHLORHEXIDINE	2 (2.0%)
CHLORHEXIDINE GLUCONATE	2 (2.0%)
AMBROXOL	1 (1.0%)
BACITRACIN	1 (1.0%)
CETYLPYRIDINIUM CHLORIDE	1 (1.0%)
CHLORHEXIDINE GLUCONATE;LIDOCAINE HYDROCHLORIDE;TYROTHRICIN	1 (1.0%)
DICLOFENAC SODIUM	1 (1.0%)
FLURBIPROFEN	1 (1.0%)
HEXAMIDINE	1 (1.0%)
HEXAMIDINE ISETIONATE	1 (1.0%)
LIDOCAINE HYDROCHLORIDE	1 (1.0%)
MIRAMISTIN	1 (1.0%)
POVIDONE-IODINE	1 (1.0%)
THYROID THERAPY	
Total number of patients with at least one treatment	17 (16.7%)
Total number of treatments	28
LEVOTHYROXINE	11 (10.8%)
LEVOTHYROXINE SODIUM	7 (6.9%)
POTASSIUM IODIDE	1 (1.0%)
TONICS	
Total number of patients with at least one treatment	2 (2.0%)
Total number of treatments	2
DIETARY SUPPLEMENT	1 (1.0%)
MINERALS NOS;VITAMINS NOS	1 (1.0%)

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	
Total number of patients with at least one treatment	40 (39.2%)
Total number of treatments	70
IBUPROFEN	16 (15.7%)
ACETYLSALICYLIC ACID	6 (5.9%)
DICLOFENAC	4 (3.9%)
FOLIC ACID	4 (3.9%)
NIMESULIDE	4 (3.9%)
KETOPROFEN	3 (2.9%)
KETOROLAC TROMETHAMINE	3 (2.9%)
ACECLOFENAC	2 (2.0%)
BENZYDAMINE HYDROCHLORIDE	2 (2.0%)
MELOXICAM	2 (2.0%)
PHOSPHOLIPIDS	2 (2.0%)
DEXKETOPROFEN TROMETAMOL	1 (1.0%)
DEXPANTHENOL;DIMETHYL SULFOXIDE;HEPARIN SODIUM	1 (1.0%)
DICLOFENAC SODIUM	1 (1.0%)
FLURBIPROFEN	1 (1.0%)
MAGNESIUM CHLORIDE	1 (1.0%)
NAPROXEN	1 (1.0%)
TOLPERISONE	1 (1.0%)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	
Total number of patients with at least one treatment	8 (7.8%)
Total number of treatments	13
CYNARA CARDUNCULUS EXTRACT	2 (2.0%)
AVENA SATIVA FLUID EXTRACT	1 (1.0%)
CETRARIA ISLANDICA;MENTHA X PIPERITA OIL	1 (1.0%)
COCOS NUCIFERA OIL	1 (1.0%)
COPTIS SPP. RHIZOME;HEDERA HELIX LEAF	1 (1.0%)
PRUNUS CERASUS	1 (1.0%)
RUSCUS ACULEATUS	1 (1.0%)
SENNA ALEXANDRINA GLYCOSIDE EXTRACT	1 (1.0%)
SENNA SPP.	1 (1.0%)
VITIS VINIFERA SEED	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
UROLOGICALS	
Total number of patients with at least one treatment	20 (19.6%)
Total number of treatments	30
LIDOCAINE	7 (6.9%)
SODIUM BICARBONATE	7 (6.9%)
AMITRIPTYLINE	3 (2.9%)
DULOXETINE HYDROCHLORIDE	2 (2.0%)
LIDOCAINE;PRILOCAINE	2 (2.0%)
AMITRIPTYLINE HYDROCHLORIDE	1 (1.0%)
BUDESONIDE	1 (1.0%)
HYALURONATE SODIUM	1 (1.0%)
LIDOCAINE HYDROCHLORIDE	1 (1.0%)
PHENAZOPYRIDINE	1 (1.0%)
POTASSIUM PHOSPHATE MONOBASIC	1 (1.0%)
VACCINES	
Total number of patients with at least one treatment	7 (6.9%)
Total number of treatments	17
COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19)	3 (2.9%)
ELASOMERAN	2 (2.0%)
COVID-19 VACCINE	1 (1.0%)
OTHER VACCINES	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
VASOPROTECTIVES	
Total number of patients with at least one treatment	100 (98.0%)
Total number of treatments	707
DEXAMETHASONE	81 (79.4%)
PREDNISOLONE	30 (29.4%)
HYDROCORTISONE	12 (11.8%)
DEXAMETHASONE SODIUM PHOSPHATE	10 (9.8%)
LIDOCAINE	7 (6.9%)
BETAMETHASONE	5 (4.9%)
QUERCETIN	5 (4.9%)
HYDROCORTISONE SODIUM SUCCINATE	3 (2.9%)
THIOTRIAZOLINE	3 (2.9%)
TRIAMCINOLONE ACETONIDE	3 (2.9%)
BECLOMETASONE DIPROPIONATE	2 (2.0%)
CORTICOSTEROID NOS	2 (2.0%)
DIOSMIN;HESPERIDIN	2 (2.0%)
HEPARIN	2 (2.0%)
PREDNISOLONE METASULFOBENZOATE SODIUM	2 (2.0%)
TRIAMCINOLONE	2 (2.0%)
ZINC	2 (2.0%)
ASCORBIC ACID;RUTOSIDE	1 (1.0%)
BENZYL BENZOATE;MYROXYLON BALSAMUM VAR. PEREIRAE BALSAM; ZINC OXIDE	1 (1.0%)
BETAMETHASONE DIPROPIONATE	1 (1.0%)
BETAMETHASONE VALERATE	1 (1.0%)
CARBOMER	1 (1.0%)
CHONDRUS CRISPUS;LIDOCAINE;TITANIUM DIOXIDE	1 (1.0%)
DEXPANTHENOL;DIMETHYL SULFOXIDE;HEPARIN SODIUM	1 (1.0%)
DILTIAZEM	1 (1.0%)
HEPARIN SODIUM	1 (1.0%)
HIDROSMIN	1 (1.0%)
HYALURONATE SODIUM	1 (1.0%)
HYDROCORTISONE ACETATE	1 (1.0%)
LIDOCAINE HYDROCHLORIDE	1 (1.0%)
NIFEDIPINE	1 (1.0%)
PROCAINE	1 (1.0%)
RUSCUS ACULEATUS	1 (1.0%)
VITIS VINIFERA SEED	1 (1.0%)

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Concomitant Medications by Medication Class and Preferred Name, Not For Cancer, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

ATC Class Level 2 Therapy	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
VITAMINS	
Total number of patients with at least one treatment	21 (20.6%)
Total number of treatments	35
COLECALCIFEROL	4 (3.9%)
ASCORBIC ACID	3 (2.9%)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE HYDROCHLORIDE	3 (2.9%)
PYRIDOXINE	3 (2.9%)
VITAMIN B COMPLEX	3 (2.9%)
VITAMIN D NOS	3 (2.9%)
VITAMINS NOS	3 (2.9%)
BIOTIN	2 (2.0%)
PYRIDOXINE HYDROCHLORIDE	2 (2.0%)
VITAMIN B NOS	2 (2.0%)
ASCORBIC ACID;BETA VULGARIS;BIOFLAVONOIDS NOS;CALCIUM AMINO ACID CHELATE;CALCIUM PANTOTHENATE;COPPER AMINO ACID CHELATE;CYSTEINE;FOLATE SODIUM;IRON AMINO ACID CHELATE; MANGANESE AMINO ACID CHELATE;MECOBALAMIN;NICOTINAMIDE;PIPER NIGRUM FRUIT;PROANTHOCYANIDIN;PYRIDOXINE HYDROCHLORIDE; RIBOFLAVIN;SELENIUM;THIAMINE HYDROCHLORIDE;TOCOPHERYL ACETATE;ZINC MONOMETHIONINE	1 (1.0%)
MINERALS NOS;VITAMINS NOS	1 (1.0%)

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Targeted Loperamide Concomitant Medications, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
Total number of patients with at least one treatment	82 (94.3%)	158 (94.0%)	240 (94.1%)
Total number of patients with at least one prophylactic loperamide	76 (87.4%)	140 (83.3%)	216 (84.7%)
Total number of patients with at least one loperamide for diarrhea	20 (23.0%)	116 (69.0%)	136 (53.3%)

Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm_lop.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_lop_A_IT.out
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	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
Total number of patients with at least one treatment	65 (85.5%)	139 (95.2%)	204 (91.9%)
Total number of patients with at least one prophylactic loperamide	59 (77.6%)	116 (79.5%)	175 (78.8%)
Total number of patients with at least one loperamide for diarrhea	18 (23.7%)	109 (74.7%)	127 (57.2%)

Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Targeted Loperamide Concomitant Medications, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one treatment	101 (99.0%)
Total number of patients with at least one prophylactic loperamide	85 (83.3%)
Total number of patients with at least one loperamide for diarrhea	70 (68.6%)

Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_cm_lop.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_cm_lop_C_IT.out
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	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Age (Years)	
n	102
Mean (SD)	54.6 (11.7)
Median	55.0
Min - Max	22 - 83
Age group (Years)	
n	102
18 - 40	13 (12.7%)
41 - 64	68 (66.7%)
>=65	21 (20.6%)
Sex	
n	102
Female	102 (100%)
Race	
n	102
American Indian or Alaska Native	5 (4.9%)
Asian	12 (11.8%)
Black or African American	9 (8.8%)
Native Hawaiian or other Pacific Islander	1 (1.0%)
White	55 (53.9%)
Multiple	5 (4.9%)
Unknown	15 (14.7%)
Ethnicity	
n	102
Hispanic or Latino	36 (35.3%)
Not Hispanic or Latino	58 (56.9%)
Not Stated	6 (5.9%)
Unknown	2 (2.0%)
BMI (kg/m2) at baseline	
n	101
Mean (SD)	27.23 (6.30)
Median	26.20
Min - Max	16.0 - 51.5
ECOG performance status	
n	102
0	61 (59.8%)
1	41 (40.2%)
Region (eCRF)	
n	102
Asia-Pacific	13 (12.7%)
Europe	38 (37.3%)
North America	13 (12.7%)
Rest of World	38 (37.3%)
Prior breast cancer radiotherapy	
n	102
Yes	36 (35.3%)
No	66 (64.7%)

The percentages are based on n. Disease Free Interval is defined as time from the final curative-intent breast surgery to the initial diagnosis of LABC/MBC. Chemotherapy Free Interval is defined as time from the last date of neoadjuvant/adjuvant chemotherapy administered to the start date of study treatment. DFI and CFI are "Not Available" for subjects having a Partial Date or Missing Date. Visceral disease is displayed as Yes or No for patients with metastatic disease, and displayed as Not Applicable for patients without metastatic disease. All recorded sites of disease except for the following are counted as visceral sites: bone, bone marrow, breast, chest, head, lymph node, neck, skin, soft tissue. Number of sites of disease in patients with mBC is displayed as Not Applicable for patients without metastatic disease. *BRCA1/2 mutation is by molecular testing and cannot distinguish between germline and somatic.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Prior anthracycline therapy	
n	102
Yes	36 (35.3%)
No	66 (64.7%)
Prior taxane therapy	
n	102
Yes	38 (37.3%)
No	64 (62.7%)
Baseline disease status	
n	102
Locally Advanced Unresectable	26 (25.5%)
Metastatic	76 (74.5%)
Disease-free interval (Years)	
n	102
< 1	4 (3.9%)
1 - 3	30 (29.4%)
> 3	6 (5.9%)
No Prior Curative Breast Surgery	58 (56.9%)
Not Available	4 (3.9%)
Chemotherapy-free interval (Years)	
n	102
1 - 3	35 (34.3%)
> 3	4 (3.9%)
No Prior Chemotherapy	60 (58.8%)
Not Available	3 (2.9%)
Visceral disease in patients with mBC	
n	102
Yes	58 (56.9%)
No	18 (17.6%)
Not Applicable	26 (25.5%)
Number of sites of disease in patients with mBC	
n	102
1 - 2	34 (33.3%)
>= 3	42 (41.2%)
Not Applicable	26 (25.5%)
Brain Metastases	
n	102
Yes	1 (1.0%)
No	101 (99.0%)
BRCA1/2 mutation status*	
n	102
Positive	17 (16.7%)
Negative	85 (83.3%)

The percentages are based on n. Disease Free Interval is defined as time from the final curative-intent breast surgery to the initial diagnosis of LABC/MBC. Chemotherapy Free Interval is defined as time from the last date of neoadjuvant/adjuvant chemotherapy administered to the start date of study treatment. DFI and CFI are "Not Available" for subjects having a Partial Date or Missing Date. Visceral disease is displayed as Yes or No for patients with metastatic disease, and displayed as Not Applicable for patients without metastatic disease. All recorded sites of disease except for the following are counted as visceral sites: bone, bone marrow, breast, chest, head, lymph node, neck, skin, soft tissue. Number of sites of disease in patients with mBC is displayed as Not Applicable for patients without metastatic disease. *BRCA1/2 mutation is by molecular testing and cannot distinguish between germline and somatic.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_dm.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_dm_C_IT.out
08MAY2023 7:32

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
PD-L1 status	
n	102
PD-L1 Positive	40 (39.2%)
PD-L1 Negative	25 (24.5%)
PD-L1 Unknown	37 (36.3%)

The percentages are based on n. Disease Free Interval is defined as time from the final curative-intent breast surgery to the initial diagnosis of LABC/MBC. Chemotherapy Free Interval is defined as time from the last date of neoadjuvant/adjuvant chemotherapy administered to the start date of study treatment. DFI and CFI are "Not Available" for subjects having a Partial Date or Missing Date. Visceral disease is displayed as Yes or No for patients with metastatic disease, and displayed as Not Applicable for patients without metastatic disease. All recorded sites of disease except for the following are counted as visceral sites: bone, bone marrow, breast, chest, head, lymph node, neck, skin, soft tissue. Number of sites of disease in patients with mBC is displayed as Not Applicable for patients without metastatic disease. *BRCA1/2 mutation is by molecular testing and cannot distinguish between germline and somatic.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Patients Withdrawn from Atezolizumab, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Reason for Treatment Discontinuation	
n	102
Adverse event	13 (12.7%)
Death	1 (1.0%)
Other	12 (11.8%)
Physician decision	6 (5.9%)
Progressive disease	63 (61.8%)
Symptomatic deterioration	3 (2.9%)
Withdrawal by subject	4 (3.9%)

Percentages are based on N in the column heading.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_atezo.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ds_atezo_C_SE.out
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Patient Status at Time of Clinical Cut Off, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
Discontinued from Study	87 (100%)	168 (100%)	255 (100%)

Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_cut.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ds_cut_A_IT.out
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Patient Status at Time of Clinical Cut Off, Cohort B: HR+/HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
Discontinued from Study	76 (100%)	146 (100%)	222 (100%)

Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_cut.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ds_cut_B_IT.out
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Patient Status at Time of Clinical Cut Off, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Discontinued from Study	102 (100%)

Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_cut.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ds_cut_C_IT.out
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Patients Withdrawn from Ipatasertib/Placebo, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)	All Patients (N=253)
Reason for Treatment Discontinuation			
n	87	166	253
Adverse event	6 (6.9%)	15 (9.0%)	21 (8.3%)
Death	0	2 (1.2%)	2 (0.8%)
Lost to follow-up	0	1 (0.6%)	1 (0.4%)
Other	6 (6.9%)	7 (4.2%)	13 (5.1%)
Physician decision	3 (3.4%)	11 (6.6%)	14 (5.5%)
Progressive disease	63 (72.4%)	109 (65.7%)	172 (68.0%)
Symptomatic deterioration	3 (3.4%)	10 (6.0%)	13 (5.1%)
Withdrawal by subject	6 (6.9%)	11 (6.6%)	17 (6.7%)

Percentages are based on N in the column heading.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_ipat.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ds_ipat_A_SE.out
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Patients Withdrawn from Ipatasertib/Placebo, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)	All Patients (N=220)
Reason for Treatment Discontinuation			
n	75	145	220
Adverse event	3 (4.0%)	16 (11.0%)	19 (8.6%)
Death	0	1 (0.7%)	1 (0.5%)
Non-compliance with study drug	0	1 (0.7%)	1 (0.5%)
Other	6 (8.0%)	2 (1.4%)	8 (3.6%)
Physician decision	6 (8.0%)	8 (5.5%)	14 (6.4%)
Progressive disease	54 (72.0%)	98 (67.6%)	152 (69.1%)
Protocol deviation	1 (1.3%)	1 (0.7%)	2 (0.9%)
Symptomatic deterioration	4 (5.3%)	7 (4.8%)	11 (5.0%)
Withdrawal by subject	1 (1.3%)	11 (7.6%)	12 (5.5%)

Percentages are based on N in the column heading.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_ipat.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ds_ipat_B_SE.out
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Patients Withdrawn from Ipatasertib, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Reason for Treatment Discontinuation	
n	102
Adverse event	11 (10.8%)
Death	1 (1.0%)
Non-compliance with study drug	1 (1.0%)
Other	12 (11.8%)
Physician decision	7 (6.9%)
Progressive disease	63 (61.8%)
Symptomatic deterioration	3 (2.9%)
Withdrawal by subject	4 (3.9%)

Percentages are based on N in the column heading.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_ipat.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ds_ipat_C_SE.out
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Patients Withdrawn from Paclitaxel, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)	All Patients (N=253)
Reason for Treatment Discontinuation			
n	87	165	252
Adverse event	14 (16.1%)	24 (14.5%)	38 (15.0%)
Death	0	2 (1.2%)	2 (0.8%)
Lost to follow-up	0	1 (0.6%)	1 (0.4%)
Other	1 (1.1%)	5 (3.0%)	6 (2.4%)
Physician decision	3 (3.4%)	10 (6.0%)	13 (5.1%)
Progressive disease	60 (69.0%)	102 (61.4%)	162 (64.0%)
Symptomatic deterioration	2 (2.3%)	10 (6.0%)	12 (4.7%)
Withdrawal by subject	7 (8.0%)	11 (6.6%)	18 (7.1%)

Percentages are based on N in the column heading.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_pac.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ds_pac_A_SE.out
08MAY2023 7:40 Page 1 of 1

Patients Withdrawn from Paclitaxel, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)	All Patients (N=220)
Reason for Treatment Discontinuation			
n	75	145	220
Adverse event	12 (16.0%)	41 (28.3%)	53 (24.1%)
Death	0	1 (0.7%)	1 (0.5%)
Non-compliance with study drug	0	1 (0.7%)	1 (0.5%)
Other	7 (9.3%)	3 (2.1%)	10 (4.5%)
Physician decision	4 (5.3%)	6 (4.1%)	10 (4.5%)
Progressive disease	47 (62.7%)	75 (51.7%)	122 (55.5%)
Protocol deviation	0	1 (0.7%)	1 (0.5%)
Symptomatic deterioration	4 (5.3%)	4 (2.8%)	8 (3.6%)
Withdrawal by subject	1 (1.3%)	13 (9.0%)	14 (6.4%)

Percentages are based on N in the column heading.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_pac.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ds_pac_B_SE.out
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Patients Withdrawn from Paclitaxel, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Reason for Treatment Discontinuation	
n	102
Adverse event	22 (21.6%)
Other	9 (8.8%)
Physician decision	8 (7.8%)
Progressive disease	56 (54.9%)
Symptomatic deterioration	3 (2.9%)
Withdrawal by subject	4 (3.9%)

Percentages are based on N in the column heading.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_ds_pac.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_ds_pac_C_SE.out
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Best Confirmed Overall Response (Investigator), Cohort C: TNBC, Measurable Disease at Baseline by Investigator, Intent-to-Treat Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Responders	54 (52.9%)
95% CI	(42.80, 62.90)
Complete Response (CR)	7 (6.9%)
95% CI	(2.80, 13.63)
Partial Response (PR)	47 (46.1%)
95% CI	(36.16, 56.23)
Stable Disease (SD)	37 (36.3%)
95% CI	(26.98, 46.39)
Progressive Disease (PD)	11 (10.8%)
95% CI	(5.51, 18.48)
Not Evaluable	0
Missing	0

95% CI for rates were constructed using Clopper-Pearson method.
Patients were classified as missing or not evaluable if no post-baseline response assessments were available or all post-baseline response assessments were not evaluable.
Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/program/t_ef_bor.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/output/t_ef_bor_BORINV_C_MDBI_IT_30OCT2021_40016.out
11MAR2022 23:47 Page 1 of 1

Clinical Benefit Rate (Investigator), Cohort C: TNBC, Measurable Disease at Baseline by Investigator, Intent-to-Treat Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Patient with clinical benefit	56 (54.9%)
95% CI	(44.74, 64.78)

95% CI for rates were constructed using Clopper-Pearson method.
Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/program/t_ef_ccb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/output/t_ef_ccb_CCBINV_C_MDBI_IT_30OCT2021_40016.out
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Time to Event Summary for Duration of Objective Response (Investigator), Cohort C: TNBC, Measurable Disease at Baseline by Investigator, Intent-to-Treat Population
Protocol: CO40016

Duration of Confirmed Response by Investigator

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Responders	54
Responders with subsequent event (%)	32 (59.3%)
Earliest contributing event	
Death	3
Disease Progression	29
Responders without subsequent event (%)	22 (40.7%)
Duration of response (Months)	
Median	8.7
95% CI	(5.7, 12.7)
25% and 75%-ile	5.4 - NE
Range	2* - 26*

* Censored observation.
The median and percentiles for duration of response are Kaplan-Meier estimates. 95% CI for median was computed using the method of Brookmeyer and Crowley.
Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/program/t_ef_dor.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/output/t_ef_dor_DORINV_C_MDBI_IT_30OCT2021_40016.out
11MAR2022 23:49

Duration of Survival Follow-up, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=168)	All Patients (N=255)
Duration of Follow-up (Months)			
n	87	168	255
Mean (SD)	17.09 (9.84)	18.50 (10.62)	18.02 (10.36)
Median	16.76	18.76	17.91
25% and 75%-ile	8.54 - 24.08	9.79 - 25.84	9.66 - 25.23
Min - Max	0.0 - 41.0	0.0 - 43.5	0.0 - 43.5

Duration of survival follow-up = time from randomization to death for patients who died, or last known alive date, for patients who were censored.
Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/program/t_ef_fudur.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/output/t_ef_fudur_A_IT_30OCT2021_40016.out
11MAR2022 23:49 Page 1 of 1

Duration of Survival Follow-up, Cohort B: HR+/HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

	Placebo + Paclitaxel (N=76)	Ipatasertib + Paclitaxel (N=146)	All Patients (N=222)
Duration of Follow-up (Months)			
n	76	146	222
Mean (SD)	22.55 (12.36)	22.41 (12.68)	22.46 (12.55)
Median	24.05	21.98	22.42
25% and 75%-ile	11.09 - 33.05	12.06 - 33.58	11.60 - 33.38
Min - Max	0.0 - 43.8	0.0 - 44.6	0.0 - 44.6

Duration of survival follow-up = time from randomization to death for patients who died, or last known alive date, for patients who were censored.
Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/program/t_ef_fudur.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/output/t_ef_fudur_B_IT_30OCT2021_40016.out
11MAR2022 23:50 Page 1 of 1

Duration of Survival Follow-up, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Duration of Follow-up (Months)	
n	102
Mean (SD)	16.69 (7.32)
Median	18.02
25% and 75%-ile	10.45 - 22.83
Min - Max	1.8 - 28.4

Duration of survival follow-up = time from treatment to death for patients who died, or last known alive date, for patients who were censored.
Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/program/t_ef_fudur.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/output/t_ef_fudur_C_IT_30OCT2021_40016.out
11MAR2022 23:50 Page 1 of 1

Time to Event Summary for Overall Survival, Cohort A: TNBC, Intent-to-Treat Population
Protocol: CO40016

Overall Survival

	Placebo + Paclitaxel (N=87)		Ipatasertib + Paclitaxel (N=168)
Patients with event (%)	39 (44.8%)		87 (51.8%)
Patients without event (%)	48 (55.2%)		81 (48.2%)
Time to Event (Months)			
Median	24.9		24.2
95% CI	(16.9, 40.4)		(19.2, 29.4)
25% and 75%-ile	12.1 - 40.4		12.7 - NE
Range	0* - 41*		0* - 44*
Stratified Analysis			
p-value (log-rank)		0.7068	
Hazard Ratio		1.08	
95% CI		(0.73, 1.58)	
Unstratified Analysis			
p-value (log-rank)		0.7855	
Hazard Ratio		1.05	
95% CI		(0.72, 1.54)	
One year duration			
Patients remaining at risk	56		114
Event Free Rate (%)	76.28		75.24
95% CI	(66.93, 85.63)		(68.40, 82.08)
Difference in Event Free Rate		-1.04	
95% CI		(-12.63, 10.54)	
p-value (Z-test)		0.8597	
Two year duration			
Patients remaining at risk	22		53
Event Free Rate (%)	52.30		50.60
95% CI	(40.48, 64.12)		(42.39, 58.81)
Difference in Event Free Rate		-1.70	
95% CI		(-16.09, 12.69)	
p-value (Z-test)		0.8168	

* Censored value. ^ Censored and event.
Summaries of OS (median, percentiles) are Kaplan-Meier estimates. 95% CI for median was computed using the method of Brookmeyer and Crowley. Stratification variables are: prior adjuvant/neoadjuvant chemotherapy (yes vs. no), tumor PIK3CA/AKT1/PTEN-alteration status (PIK3CA/AKT1-activating mutations vs. PTEN alterations with no PIK3CA/AKT1-activating mutations). Hazard ratios were estimated by Cox regression.
Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/program/t_ef_tte.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/output/t_ef_tte_OS_A_IT_30OCT2021_40016.out
11MAR2022 23:44 Page 1 of 1

Time to Event Summary for Overall Survival, Cohort B: HR+/HER2- Patients, Intent-to-Treat Population
Protocol: CO40016

Overall Survival

	Placebo + Paclitaxel (N=76)		Ipatasertib + Paclitaxel (N=146)
Patients with event (%)	43 (56.6%)		77 (52.7%)
Patients without event (%)	33 (43.4%)		69 (47.3%)
Time to Event (Months)			
Median	28.4		29.0
95% CI	(20.6, 37.3)		(22.4, 34.8)
25% and 75%-ile	14.3 - NE		14.9 - NE
Range	0* - 44*		0* - 45*
Stratified Analysis			
p-value (log-rank)		0.7562	
Hazard Ratio		0.94	
95% CI		(0.65, 1.37)	
Unstratified Analysis			
p-value (log-rank)		0.6798	
Hazard Ratio		0.92	
95% CI		(0.64, 1.34)	
One year duration			
Patients remaining at risk	54		110
Event Free Rate (%)	78.75		83.38
95% CI	(69.18, 88.31)		(77.17, 89.59)
Difference in Event Free Rate		4.63	
95% CI		(-6.77, 16.04)	
p-value (Z-test)		0.4257	
Two year duration			
Patients remaining at risk	38		68
Event Free Rate (%)	56.50		55.45
95% CI	(44.75, 68.25)		(46.92, 63.98)
Difference in Event Free Rate		-1.05	
95% CI		(-15.57, 13.47)	
p-value (Z-test)		0.8872	

* Censored value. ^ Censored and event.
Summaries of OS (median, percentiles) are Kaplan-Meier estimates. 95% CI for median was computed using the method of Brookmeyer and Crowley. Stratification variables are: prior adjuvant/neoadjuvant chemotherapy (yes vs. no), prior therapy with a phosphoinositide 3-kinase (PI3K) or mTOR inhibitor (yes vs. no). Hazard ratios were estimated by Cox regression.
Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/program/t_ef_tte.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/output/t_ef_tte_OS_B_IT_30OCT2021_40016.out
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Time to Event Summary for Overall Survival, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Overall Survival

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Patients with event (%)	49 (48.0%)
Patients without event (%)	53 (52.0%)
Time to Event (Months)	
Median	22.8
95% CI	(17.8, NE)
25% and 75%-ile	12.9 - NE
Range	2* - 28*
One year duration	
Patients remaining at risk	74
Event Free Rate (%)	79.38
95% CI	(71.31, 87.44)
Two year duration	
Patients remaining at risk	17
Event Free Rate (%)	46.58
95% CI	(35.45, 57.70)

* Censored value. ^ Censored and event.
Summaries of OS (median, percentiles) are Kaplan-Meier estimates. 95% CI for median was computed using the method of Brookmeyer and Crowley.
Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/program/t_ef_tte.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/output/t_ef_tte_OS_C_IT_30OCT2021_40016.out
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Time to Event Summary for Progression-Free Survival (Investigator), Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Earliest Contributing Event to Progression Free Survival by Investigator

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Patients with event (%)	78 (76.5%)
Earliest contributing event	
Death	6
Disease Progression	72
Patients without event (%)	24 (23.5%)
Time to Event (Months)	
Median	7.1
95% CI	(5.5, 9.1)
25% and 75%-ile	3.7 - 13.9
Range	1 - 28*
One year duration	
Patients remaining at risk	24
Event Free Rate (%)	31.17
95% CI	(21.59, 40.76)

* Censored value. ^ Censored and event.
Summaries of Progression-Free Survival (median, percentiles) are Kaplan-Meier estimates.
95% CI for median was computed using the method of Brookmeyer and Crowley.
Data Cutoff Date - 30OCT2021; Data Extraction Date - 18JAN2022.

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/program/t_ef_tte.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal/prod/output/t_ef_tte_PFSINV_C_IT_30OCT2021_40016.out
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ECG Shift Table, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Assessment: ECG Interpretation

Treatment Group	Baseline	Post-Baseline Worst Value			
		Normal	Abnormal, Not Clinically Significant	Abnormal, Clinically Significant	Missing
Placebo + Paclitaxel (N=87)	Normal	30	14	0	19
	Abnormal, Not Clinically Significant	11	6	1	6
Ipatasertib + Paclitaxel (N=166)	Normal	77	18	1	29
	Abnormal, Not Clinically Significant	16	14	0	11

Table entries provide the number of patients by baseline assessment and worst post-baseline assessment. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_eg_shift.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_eg_shift_A_SE.out
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ECG Shift Table, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Assessment: ECG Interpretation

Treatment Group	Baseline	Post-Baseline Worst Value			
		Normal	Abnormal, Not Clinically Significant	Abnormal, Clinically Significant	Missing
Placebo + Paclitaxel (N=75)	Normal	37	12	0	7
	Abnormal, Not Clinically Significant	6	5	2	5
	Missing	0	1	0	0
Ipatasertib + Paclitaxel (N=145)	Normal	56	13	1	23
	Abnormal, Not Clinically Significant	15	22	1	13
	Missing	1	0	0	0

Table entries provide the number of patients by baseline assessment and worst post-baseline assessment. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_eg_shift.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_eg_shift_B_SE.out
08MAY2023 7:44

ECG Shift Table, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Assessment: ECG Interpretation

Treatment Group	Baseline	Post-Baseline Worst Value			
		Normal	Abnormal, Not Clinically Significant	Abnormal, Clinically Significant	Missing
Ipatasertib + Atezolizumab + Paclitaxel (N=102)	Normal	34	12	2	20
	Abnormal, Not Clinically Significant	13	10	0	11

Table entries provide the number of patients by baseline assessment and worst post-baseline assessment. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_eg_shift.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_eg_shift_C_SE.out
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Enrollment by Region, Country, and Investigator Number, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Region Country Investigator Number	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
ASIA-PACIFIC	13 (12.7%)
Australia	3 (2.9%)
227560	1 (1.0%)
257127	1 (1.0%)
465720	1 (1.0%)
Korea, Republic of	6 (5.9%)
227562	2 (2.0%)
255212	1 (1.0%)
495836	1 (1.0%)
536249	1 (1.0%)
22495	1 (1.0%)
Singapore	1 (1.0%)
382354	1 (1.0%)
Taiwan	3 (2.9%)
212284	2 (2.0%)
212285	1 (1.0%)
EUROPE	38 (37.3%)
France	6 (5.9%)
241138	3 (2.9%)
382701	2 (2.0%)
250622	1 (1.0%)
United Kingdom	8 (7.8%)
392692	2 (2.0%)
399707	2 (2.0%)
466907	2 (2.0%)
23255	2 (2.0%)
Poland	10 (9.8%)
371393	5 (4.9%)
530623	3 (2.9%)
244889	2 (2.0%)
Ukraine	14 (13.7%)
12943	7 (6.9%)
18311	4 (3.9%)
532818	3 (2.9%)
NORTH AMERICA	13 (12.7%)
United States	13 (12.7%)
216710	3 (2.9%)
449208	3 (2.9%)
552947	2 (2.0%)
234346	1 (1.0%)
477174	1 (1.0%)
531913	1 (1.0%)
10637	1 (1.0%)
16447	1 (1.0%)
REST OF WORLD	38 (37.3%)
Brazil	27 (26.5%)
21576	12 (11.8%)
438899	4 (3.9%)
21771	3 (2.9%)
208920	2 (2.0%)
256840	2 (2.0%)
278999	2 (2.0%)
520337	2 (2.0%)

Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_enroll.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_enroll_C_IT.out

Enrollment by Region, Country, and Investigator Number, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Region Country Investigator Number	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Peru	11 (10.8%)
472988	6 (5.9%)
233673	2 (2.0%)
299480	1 (1.0%)
399162	1 (1.0%)
550275	1 (1.0%)

Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_enroll.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_enroll_C_IT.out
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Laboratory Test Results with Highest NCI-CTCAE v4 Grade Post-Baseline, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Direction of Abnormality	Highest NCI CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Albumin	n	86	166
Low	1	19 (22.1%)	34 (20.5%)
	2	9 (10.5%)	9 (5.4%)
	3	0	2 (1.2%)
	Any	28 (32.6%)	45 (27.1%)
Alkaline Phosphatase	n	86	166
High	1	34 (39.5%)	76 (45.8%)
	2	8 (9.3%)	12 (7.2%)
	Any	42 (48.8%)	88 (53.0%)
SGPT/ALT	n	86	166
High	1	33 (38.4%)	72 (43.4%)
	2	2 (2.3%)	11 (6.6%)
	3	3 (3.5%)	10 (6.0%)
	Any	38 (44.2%)	93 (56.0%)
SGOT/AST	n	86	166
High	1	30 (34.9%)	74 (44.6%)
	2	4 (4.7%)	10 (6.0%)
	3	3 (3.5%)	5 (3.0%)
	Any	37 (43.0%)	89 (53.6%)
Calcium	n	86	166
Low	1	14 (16.3%)	44 (26.5%)
	2	11 (12.8%)	15 (9.0%)
	3	1 (1.2%)	1 (0.6%)
	Any	26 (30.2%)	60 (36.1%)
High	1	11 (12.8%)	36 (21.7%)
	2	0	2 (1.2%)
	3	0	1 (0.6%)
	Any	11 (12.8%)	39 (23.5%)
Triglycerides, Fasting	n	74	152
High	1	32 (43.2%)	59 (38.8%)
	2	4 (5.4%)	10 (6.6%)
	3	1 (1.4%)	4 (2.6%)
	Any	37 (50.0%)	73 (48.0%)
Amylase, Fasting	n	74	153
High	1	4 (5.4%)	15 (9.8%)
	2	0	4 (2.6%)
	3	1 (1.4%)	1 (0.7%)
	Any	5 (6.8%)	20 (13.1%)

NCI CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; "n" denotes the number of patients with a post-baseline lab value. For a patient with multiple post-baseline lab abnormalities, the highest (worst) grade of these abnormalities for the given lab test is reported. "Any" is the number of patients with a post-baseline abnormality of any grade for the specified lab test.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_cb_grdmax.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_cb_grdmax_A_SE.out
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Laboratory Test Results with Highest NCI-CTCAE v4 Grade Post-Baseline, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Direction of Abnormality	Highest NCI CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Lipase, Total, Fasting	n	73	153
High	1	5 (6.8%)	25 (16.3%)
	2	1 (1.4%)	5 (3.3%)
	3	1 (1.4%)	6 (3.9%)
	4	1 (1.4%)	1 (0.7%)
	Any	8 (11.0%)	37 (24.2%)
Creatinine	n	86	166
High	1	61 (70.9%)	122 (73.5%)
	2	10 (11.6%)	16 (9.6%)
	3	1 (1.2%)	0
	Any	72 (83.7%)	138 (83.1%)
Cholesterol, Fasting	n	74	152
High	1	30 (40.5%)	72 (47.4%)
	2	4 (5.4%)	6 (3.9%)
	3	0	1 (0.7%)
	Any	34 (45.9%)	79 (52.0%)
Glucose, Fasting	n	83	162
Low	1	6 (7.2%)	22 (13.6%)
	2	0	1 (0.6%)
	Any	6 (7.2%)	23 (14.2%)
High	1	31 (37.3%)	85 (52.5%)
	2	4 (4.8%)	13 (8.0%)
	3	0	2 (1.2%)
	Any	35 (42.2%)	100 (61.7%)
Glucose	n	21	28
Low	1	0	2 (7.1%)
	Any	0	2 (7.1%)
High	3	0	2 (7.1%)
	Any	0	2 (7.1%)
Hemoglobin	n	86	166
Low	1	44 (51.2%)	100 (60.2%)
	2	21 (24.4%)	46 (27.7%)
	3	4 (4.7%)	6 (3.6%)
	Any	69 (80.2%)	152 (91.6%)
High	1	2 (2.3%)	2 (1.2%)
	2	0	1 (0.6%)
	Any	2 (2.3%)	3 (1.8%)

NCI CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; "n" denotes the number of patients with a post-baseline lab value. For a patient with multiple post-baseline lab abnormalities, the highest (worst) grade of these abnormalities for the given lab test is reported. "Any" is the number of patients with a post-baseline abnormality of any grade for the specified lab test.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_cb_grdmax.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_cb_grdmax_A_SE.out
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Laboratory Test Results with Highest NCI-CTCAE v4 Grade Post-Baseline, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Direction of Abnormality	Highest NCI CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Lymphocytes Abs	n	86	166
Low	1	21 (24.4%)	41 (24.7%)
	2	23 (26.7%)	32 (19.3%)
	3	3 (3.5%)	15 (9.0%)
	4	3 (3.5%)	4 (2.4%)
	Any	50 (58.1%)	92 (55.4%)
High	2	4 (4.7%)	4 (2.4%)
	3	1 (1.2%)	0
	Any	5 (5.8%)	4 (2.4%)
Magnesium	n	86	166
Low	1	18 (20.9%)	31 (18.7%)
	2	0	4 (2.4%)
	Any	18 (20.9%)	35 (21.1%)
High	1	14 (16.3%)	10 (6.0%)
	3	1 (1.2%)	5 (3.0%)
	Any	15 (17.4%)	15 (9.0%)
Neutrophils, Total, Abs	n	86	166
Low	1	17 (19.8%)	29 (17.5%)
	2	21 (24.4%)	31 (18.7%)
	3	8 (9.3%)	19 (11.4%)
	4	1 (1.2%)	6 (3.6%)
	Any	47 (54.7%)	85 (51.2%)
Phosphorus	n	86	166
Low	1	3 (3.5%)	6 (3.6%)
	2	13 (15.1%)	27 (16.3%)
	3	1 (1.2%)	5 (3.0%)
	4	0	1 (0.6%)
	Any	17 (19.8%)	39 (23.5%)
Platelet	n	86	166
Low	1	14 (16.3%)	20 (12.0%)
	2	1 (1.2%)	2 (1.2%)
	3	1 (1.2%)	1 (0.6%)
	Any	16 (18.6%)	23 (13.9%)
Potassium	n	86	166
Low	2	11 (12.8%)	30 (18.1%)
	3	1 (1.2%)	2 (1.2%)
	Any	12 (14.0%)	32 (19.3%)
High	1	10 (11.6%)	29 (17.5%)
	2	2 (2.3%)	9 (5.4%)
	3	2 (2.3%)	2 (1.2%)
	Any	14 (16.3%)	40 (24.1%)

NCI CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; "n" denotes the number of patients with a post-baseline lab value. For a patient with multiple post-baseline lab abnormalities, the highest (worst) grade of these abnormalities for the given lab test is reported. "Any" is the number of patients with a post-baseline abnormality of any grade for the specified lab test.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_cb_grdmax.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_cb_grdmax_A_SE.out
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Laboratory Test Results with Highest NCI-CTCAE v4 Grade Post-Baseline, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Direction of Abnormality	Highest NCI CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
International Normalized Ratio	n	62	133
High	1	27 (43.5%)	68 (51.1%)
	2	1 (1.6%)	4 (3.0%)
	3	0	2 (1.5%)
	Any	28 (45.2%)	74 (55.6%)
Activated Partial Thromboplastin Time	n	62	128
High	1	3 (4.8%)	13 (10.2%)
	2	1 (1.6%)	0
	3	1 (1.6%)	1 (0.8%)
	Any	5 (8.1%)	14 (10.9%)
Sodium	n	86	166
Low	1	16 (18.6%)	28 (16.9%)
	3	6 (7.0%)	10 (6.0%)
	Any	22 (25.6%)	38 (22.9%)
High	1	5 (5.8%)	9 (5.4%)
	2	1 (1.2%)	2 (1.2%)
	Any	6 (7.0%)	11 (6.6%)
Bilirubin	n	86	166
High	1	8 (9.3%)	21 (12.7%)
	2	6 (7.0%)	1 (0.6%)
	Any	14 (16.3%)	22 (13.3%)
Total Leukocyte Count	n	86	166
Low	1	34 (39.5%)	56 (33.7%)
	2	21 (24.4%)	38 (22.9%)
	3	3 (3.5%)	11 (6.6%)
	4	1 (1.2%)	2 (1.2%)
	Any	59 (68.6%)	107 (64.5%)
High	3	1 (1.2%)	1 (0.6%)
	Any	1 (1.2%)	1 (0.6%)

NCI CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; "n" denotes the number of patients with a post-baseline lab value. For a patient with multiple post-baseline lab abnormalities, the highest (worst) grade of these abnormalities for the given lab test is reported. "Any" is the number of patients with a post-baseline abnormality of any grade for the specified lab test.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_cb_grdmax.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_cb_grdmax_A_SE.out
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Laboratory Test Results with Highest NCI-CTCAE v4 Grade Post-Baseline, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Direction of Abnormality	Highest NCI CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Albumin	n	74	144
Low	1	25 (33.8%)	42 (29.2%)
	2	5 (6.8%)	10 (6.9%)
	3	0	1 (0.7%)
	Any	30 (40.5%)	53 (36.8%)
Alkaline Phosphatase	n	74	144
High	1	30 (40.5%)	61 (42.4%)
	2	14 (18.9%)	14 (9.7%)
	3	6 (8.1%)	8 (5.6%)
	Any	50 (67.6%)	83 (57.6%)
SGPT/ALT	n	74	144
High	1	40 (54.1%)	71 (49.3%)
	2	6 (8.1%)	9 (6.3%)
	3	6 (8.1%)	11 (7.6%)
	4	1 (1.4%)	1 (0.7%)
	Any	53 (71.6%)	92 (63.9%)
SGOT/AST	n	74	144
High	1	39 (52.7%)	75 (52.1%)
	2	5 (6.8%)	6 (4.2%)
	3	8 (10.8%)	11 (7.6%)
	4	0	1 (0.7%)
	Any	52 (70.3%)	93 (64.6%)
Calcium	n	74	144
Low	1	23 (31.1%)	38 (26.4%)
	2	4 (5.4%)	8 (5.6%)
	3	0	1 (0.7%)
	Any	27 (36.5%)	47 (32.6%)
High	1	15 (20.3%)	32 (22.2%)
	2	1 (1.4%)	0
	3	1 (1.4%)	1 (0.7%)
	4	2 (2.7%)	0
	Any	19 (25.7%)	33 (22.9%)
Triglycerides, Fasting	n	71	133
High	1	35 (49.3%)	51 (38.3%)
	2	4 (5.6%)	10 (7.5%)
	3	0	2 (1.5%)
	4	1 (1.4%)	0
	Any	40 (56.3%)	63 (47.4%)

NCI CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; "n" denotes the number of patients with a post-baseline lab value. For a patient with multiple post-baseline lab abnormalities, the highest (worst) grade of these abnormalities for the given lab test is reported. "Any" is the number of patients with a post-baseline abnormality of any grade for the specified lab test.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_cb_grdmax.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_cb_grdmax_B_SE.out
08MAY2023 7:51 Page 1 of 4

Laboratory Test Results with Highest NCI-CTCAE v4 Grade Post-Baseline, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Direction of Abnormality	Highest NCI CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Amylase, Fasting	n	70	134
High	1	9 (12.9%)	15 (11.2%)
	2	3 (4.3%)	4 (3.0%)
	3	0	1 (0.7%)
	4	0	1 (0.7%)
	Any	12 (17.1%)	21 (15.7%)
Lipase, Total, Fasting	n	66	134
High	1	10 (15.2%)	24 (17.9%)
	2	3 (4.5%)	4 (3.0%)
	3	2 (3.0%)	6 (4.5%)
	4	0	1 (0.7%)
	Any	15 (22.7%)	35 (26.1%)
Creatinine	n	75	144
High	1	50 (66.7%)	102 (70.8%)
	2	9 (12.0%)	16 (11.1%)
	3	1 (1.3%)	4 (2.8%)
	Any	60 (80.0%)	122 (84.7%)
Cholesterol, Fasting	n	71	135
High	1	32 (45.1%)	70 (51.9%)
	2	9 (12.7%)	9 (6.7%)
	Any	41 (57.7%)	79 (58.5%)
Glucose, Fasting	n	73	144
Low	1	5 (6.8%)	23 (16.0%)
	2	1 (1.4%)	0
	Any	6 (8.2%)	23 (16.0%)
High	1	39 (53.4%)	74 (51.4%)
	2	5 (6.8%)	12 (8.3%)
	3	0	2 (1.4%)
	Any	44 (60.3%)	88 (61.1%)
Glucose	n	8	32
Low	1	1 (12.5%)	1 (3.1%)
	2	0	1 (3.1%)
	Any	1 (12.5%)	2 (6.3%)
High	3	0	1 (3.1%)
	Any	0	1 (3.1%)
Hemoglobin	n	75	144
Low	1	47 (62.7%)	71 (49.3%)
	2	14 (18.7%)	53 (36.8%)
	3	4 (5.3%)	7 (4.9%)
	Any	65 (86.7%)	131 (91.0%)
High	1	4 (5.3%)	9 (6.3%)
	Any	4 (5.3%)	9 (6.3%)

NCI CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; "n" denotes the number of patients with a post-baseline lab value. For a patient with multiple post-baseline lab abnormalities, the highest (worst) grade of these abnormalities for the given lab test is reported. "Any" is the number of patients with a post-baseline abnormality of any grade for the specified lab test.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_cb_grdmax.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_cb_grdmax_B_SE.out

Laboratory Test Results with Highest NCI-CTCAE v4 Grade Post-Baseline, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Direction of Abnormality	Highest NCI CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Lymphocytes Abs	n	74	144
Low	1	17 (23.0%)	29 (20.1%)
	2	18 (24.3%)	44 (30.6%)
	3	8 (10.8%)	19 (13.2%)
	4	2 (2.7%)	5 (3.5%)
	Any	45 (60.8%)	97 (67.4%)
High	2	3 (4.1%)	4 (2.8%)
	Any	3 (4.1%)	4 (2.8%)
Magnesium	n	73	143
Low	1	8 (11.0%)	38 (26.6%)
	2	0	2 (1.4%)
	3	1 (1.4%)	1 (0.7%)
	Any	9 (12.3%)	41 (28.7%)
High	1	7 (9.6%)	12 (8.4%)
	3	4 (5.5%)	3 (2.1%)
	Any	11 (15.1%)	15 (10.5%)
Neutrophils, Total, Abs	n	74	144
Low	1	13 (17.6%)	33 (22.9%)
	2	20 (27.0%)	34 (23.6%)
	3	10 (13.5%)	18 (12.5%)
	4	2 (2.7%)	7 (4.9%)
	Any	45 (60.8%)	92 (63.9%)
Phosphorus	n	74	143
Low	1	4 (5.4%)	10 (7.0%)
	2	14 (18.9%)	27 (18.9%)
	3	3 (4.1%)	5 (3.5%)
	Any	21 (28.4%)	42 (29.4%)
Platelet	n	75	144
Low	1	13 (17.3%)	17 (11.8%)
	3	1 (1.3%)	1 (0.7%)
	Any	14 (18.7%)	18 (12.5%)
Potassium	n	75	144
Low	2	14 (18.7%)	31 (21.5%)
	3	0	4 (2.8%)
	Any	14 (18.7%)	35 (24.3%)
High	1	9 (12.0%)	24 (16.7%)
	2	9 (12.0%)	3 (2.1%)
	3	1 (1.3%)	0
	Any	19 (25.3%)	27 (18.8%)

NCI CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; "n" denotes the number of patients with a post-baseline lab value. For a patient with multiple post-baseline lab abnormalities, the highest (worst) grade of these abnormalities for the given lab test is reported. "Any" is the number of patients with a post-baseline abnormality of any grade for the specified lab test.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_cb_grdmax.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_cb_grdmax_B_SE.out
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Laboratory Test Results with Highest NCI-CTCAE v4 Grade Post-Baseline, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Direction of Abnormality	Highest NCI CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
International Normalized Ratio	n	63	110
High	1	33 (52.4%)	57 (51.8%)
	2	1 (1.6%)	2 (1.8%)
	Any	34 (54.0%)	59 (53.6%)
Activated Partial Thromboplastin Time	n	60	106
High	1	2 (3.3%)	7 (6.6%)
	2	0	2 (1.9%)
	Any	2 (3.3%)	9 (8.5%)
Sodium	n	75	144
Low	1	12 (16.0%)	37 (25.7%)
	3	3 (4.0%)	5 (3.5%)
	4	0	1 (0.7%)
	Any	15 (20.0%)	43 (29.9%)
High	1	6 (8.0%)	15 (10.4%)
	2	0	5 (3.5%)
	Any	6 (8.0%)	20 (13.9%)
Bilirubin	n	74	144
High	1	8 (10.8%)	19 (13.2%)
	2	7 (9.5%)	7 (4.9%)
	3	3 (4.1%)	2 (1.4%)
	4	0	1 (0.7%)
	Any	18 (24.3%)	29 (20.1%)
Total Leukocyte Count	n	75	144
Low	1	22 (29.3%)	51 (35.4%)
	2	25 (33.3%)	42 (29.2%)
	3	8 (10.7%)	18 (12.5%)
	4	1 (1.3%)	2 (1.4%)
	Any	56 (74.7%)	113 (78.5%)
High	Any	0	0

NCI CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; "n" denotes the number of patients with a post-baseline lab value. For a patient with multiple post-baseline lab abnormalities, the highest (worst) grade of these abnormalities for the given lab test is reported. "Any" is the number of patients with a post-baseline abnormality of any grade for the specified lab test.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_cb_grdmax.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_cb_grdmax_B_SE.out
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Laboratory Test Results with Highest NCI-CTCAE v4 Grade Post-Baseline, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Direction of Abnormality	Highest NCI CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Albumin	n	102
Low	1	14 (13.7%)
	2	16 (15.7%)
	3	1 (1.0%)
	Any	31 (30.4%)
Alkaline Phosphatase	n	102
High	1	57 (55.9%)
	2	5 (4.9%)
	3	6 (5.9%)
	Any	68 (66.7%)
SGPT/ALT	n	102
High	1	44 (43.1%)
	2	6 (5.9%)
	3	12 (11.8%)
	4	1 (1.0%)
	Any	63 (61.8%)
SGOT/AST	n	102
High	1	36 (35.3%)
	2	10 (9.8%)
	3	11 (10.8%)
	Any	57 (55.9%)
Calcium	n	102
Low	1	31 (30.4%)
	2	10 (9.8%)
	4	1 (1.0%)
	Any	42 (41.2%)
High	1	23 (22.5%)
	2	2 (2.0%)
	3	1 (1.0%)
	Any	26 (25.5%)
Triglycerides, Fasting	n	93
High	1	40 (43.0%)
	2	7 (7.5%)
	4	2 (2.2%)
	Any	49 (52.7%)
Amylase, Fasting	n	93
High	1	9 (9.7%)
	2	2 (2.2%)
	3	1 (1.1%)
	Any	12 (12.9%)

NCI CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; "n" denotes the number of patients with a post-baseline lab value. For a patient with multiple post-baseline lab abnormalities, the highest (worst) grade of these abnormalities for the given lab test is reported. "Any" is the number of patients with a post-baseline abnormality of any grade for the specified lab test.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_cb_grdmax.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_cb_grdmax_C_SE.out
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Laboratory Test Results with Highest NCI-CTCAE v4 Grade Post-Baseline, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Direction of Abnormality	Highest NCI CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Lipase, Total, Fasting	n	91
High	1	13 (14.3%)
	2	6 (6.6%)
	3	3 (3.3%)
	Any	22 (24.2%)
Creatinine	n	102
High	1	76 (74.5%)
	2	9 (8.8%)
	3	3 (2.9%)
	Any	88 (86.3%)
Cholesterol, Fasting	n	93
High	1	42 (45.2%)
	2	8 (8.6%)
	3	1 (1.1%)
	4	1 (1.1%)
	Any	52 (55.9%)
Glucose, Fasting	n	98
Low	1	12 (12.2%)
	2	3 (3.1%)
	Any	15 (15.3%)
High	1	55 (56.1%)
	2	8 (8.2%)
	3	4 (4.1%)
	Any	67 (68.4%)
Glucose	n	37
Low	1	1 (2.7%)
	2	1 (2.7%)
	4	1 (2.7%)
	Any	3 (8.1%)
High	3	1 (2.7%)
	Any	1 (2.7%)
Hemoglobin	n	102
Low	1	56 (54.9%)
	2	35 (34.3%)
	3	4 (3.9%)
	Any	95 (93.1%)
High	1	5 (4.9%)
	Any	5 (4.9%)

NCI CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; "n" denotes the number of patients with a post-baseline lab value. For a patient with multiple post-baseline lab abnormalities, the highest (worst) grade of these abnormalities for the given lab test is reported. "Any" is the number of patients with a post-baseline abnormality of any grade for the specified lab test.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_cb_grdmax.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_cb_grdmax_C_SE.out
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Laboratory Test Results with Highest NCI-CTCAE v4 Grade Post-Baseline, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Direction of Abnormality	Highest NCI CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Lymphocytes Abs	n	102
Low	1	18 (17.6%)
	2	39 (38.2%)
	3	15 (14.7%)
	4	2 (2.0%)
	Any	74 (72.5%)
High	2	6 (5.9%)
	Any	6 (5.9%)
Magnesium	n	102
Low	1	29 (28.4%)
	2	1 (1.0%)
	4	1 (1.0%)
	Any	31 (30.4%)
High	1	19 (18.6%)
	3	3 (2.9%)
	4	1 (1.0%)
	Any	23 (22.5%)
Neutrophils, Total, Abs	n	102
Low	1	21 (20.6%)
	2	28 (27.5%)
	3	8 (7.8%)
	4	3 (2.9%)
	Any	60 (58.8%)
Phosphorus	n	102
Low	1	3 (2.9%)
	2	18 (17.6%)
	3	2 (2.0%)
	4	1 (1.0%)
	Any	24 (23.5%)
Platelet	n	102
Low	1	17 (16.7%)
	2	1 (1.0%)
	3	1 (1.0%)
	Any	19 (18.6%)
Potassium	n	102
Low	2	24 (23.5%)
	3	6 (5.9%)
	Any	30 (29.4%)
High	1	15 (14.7%)
	2	9 (8.8%)
	3	1 (1.0%)
	4	1 (1.0%)
	Any	26 (25.5%)

NCI CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; "n" denotes the number of patients with a post-baseline lab value. For a patient with multiple post-baseline lab abnormalities, the highest (worst) grade of these abnormalities for the given lab test is reported. "Any" is the number of patients with a post-baseline abnormality of any grade for the specified lab test.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_cb_grdmax.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_cb_grdmax_C_SE.out
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Laboratory Test Results with Highest NCI-CTCAE v4 Grade Post-Baseline, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Direction of Abnormality	Highest NCI CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
International Normalized Ratio	n	80
High	1	40 (50.0%)
	2	2 (2.5%)
	Any	42 (52.5%)
Activated Partial Thromboplastin Time	n	77
High	1	5 (6.5%)
	Any	5 (6.5%)
Sodium	n	102
Low	1	30 (29.4%)
	3	8 (7.8%)
	4	1 (1.0%)
	Any	39 (38.2%)
High	1	13 (12.7%)
	2	1 (1.0%)
	Any	14 (13.7%)
Bilirubin	n	102
High	1	19 (18.6%)
	2	2 (2.0%)
	3	3 (2.9%)
	Any	24 (23.5%)
Total Leukocyte Count	n	102
Low	1	37 (36.3%)
	2	33 (32.4%)
	3	8 (7.8%)
	4	2 (2.0%)
	Any	80 (78.4%)
High	Any	0

NCI CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; "n" denotes the number of patients with a post-baseline lab value. For a patient with multiple post-baseline lab abnormalities, the highest (worst) grade of these abnormalities for the given lab test is reported. "Any" is the number of patients with a post-baseline abnormality of any grade for the specified lab test.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_cb_grdmax.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_cb_grdmax_C_SE.out
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Hy`s Law, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Null Report: No results could be derived for this output.

ALT = Alanine Aminotransferase, AST = Aspartate Aminotransferase, TBILI = Bilirubin, ULN = Upper Limit Normal. Patients who met Hy's Law Criteria reported at least one TBILI > 2 x ULN within 7 days after latest ALT or AST > 3 x ULN. Local lab reference ranges are used to assess Hy's Law criteria.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_hy.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_hy_A_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Alkaline Phosphatase

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	60	122
	Not High	43 (71.7%)	77 (63.1%)
	1	17 (28.3%)	40 (32.8%)
	2	0	5 (4.1%)
1	Total	21	41
	Not High	1 (4.8%)	1 (2.4%)
	1	17 (81.0%)	35 (85.4%)
	2	3 (14.3%)	5 (12.2%)
2	Total	4	2
	1	0	1 (50.0%)
	2	4 (100%)	1 (50.0%)
3	Total	1	1
	2	1 (100%)	1 (100%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_A_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

SGPT/ALT

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	74	141
	Not High	46 (62.2%)	69 (48.9%)
	1	26 (35.1%)	59 (41.8%)
	2	0	6 (4.3%)
	3	2 (2.7%)	7 (5.0%)
1	Total	10	23
	Not High	1 (10.0%)	4 (17.4%)
	1	7 (70.0%)	12 (52.2%)
	2	1 (10.0%)	4 (17.4%)
	3	1 (10.0%)	3 (13.0%)
2	Total	1	2
	Not High	1 (100%)	0
	1	0	1 (50.0%)
	2	0	1 (50.0%)
3	Total	1	0
	2	1 (100%)	0
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_A_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

SGOT/AST

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	75	135
	Not High	48 (64.0%)	74 (54.8%)
	1	24 (32.0%)	53 (39.3%)
	2	1 (1.3%)	3 (2.2%)
	3	2 (2.7%)	5 (3.7%)
1	Total	9	29
	Not High	1 (11.1%)	3 (10.3%)
	1	5 (55.6%)	20 (69.0%)
	2	2 (22.2%)	6 (20.7%)
	3	1 (11.1%)	0
2	Total	2	2
	1	1 (50.0%)	1 (50.0%)
	2	1 (50.0%)	1 (50.0%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_A_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Calcium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	81	158
	Not High	74 (91.4%)	126 (79.7%)
	1	7 (8.6%)	30 (19.0%)
	2	0	1 (0.6%)
	3	0	1 (0.6%)
1	Total	5	8
	Not High	1 (20.0%)	1 (12.5%)
	1	4 (80.0%)	6 (75.0%)
	2	0	1 (12.5%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_A_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Triglycerides, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	60	114
	Not High	37 (61.7%)	73 (64.0%)
	1	21 (35.0%)	35 (30.7%)
	2	1 (1.7%)	5 (4.4%)
	3	0	1 (0.9%)
	Missing	1 (1.7%)	0
1	Total	14	28
	Not High	0	2 (7.1%)
	1	11 (78.6%)	19 (67.9%)
	2	3 (21.4%)	5 (17.9%)
	3	0	1 (3.6%)
	Missing	0	1 (3.6%)
2	Total	1	3
	1	0	1 (33.3%)
	3	1 (100%)	2 (66.7%)
Missing	Total	12	21
	Not High	0	4 (19.0%)
	1	0	4 (19.0%)
	Missing	12 (100%)	13 (61.9%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_A_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Amylase, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	68	135
	Not High	65 (95.6%)	123 (91.1%)
	1	2 (2.9%)	11 (8.1%)
	3	0	1 (0.7%)
	Missing	1 (1.5%)	0
1	Total	4	6
	Not High	2 (50.0%)	0
	1	1 (25.0%)	3 (50.0%)
	2	0	3 (50.0%)
	3	1 (25.0%)	0
2	Total	1	2
	Not High	0	1 (50.0%)
	1	1 (100%)	0
	2	0	1 (50.0%)
Missing	Total	14	23
	Not High	2 (14.3%)	9 (39.1%)
	1	0	1 (4.3%)
	Missing	12 (85.7%)	13 (56.5%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_A_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Lipase, Total, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	64	127
	Not High	59 (92.2%)	102 (80.3%)
	1	4 (6.3%)	18 (14.2%)
	2	0	2 (1.6%)
	3	1 (1.6%)	4 (3.1%)
	4	0	1 (0.8%)
1	Total	6	11
	Not High	2 (33.3%)	3 (27.3%)
	1	1 (16.7%)	5 (45.5%)
	2	0	2 (18.2%)
	3	0	1 (9.1%)
	4	1 (16.7%)	0
	Missing	2 (33.3%)	0
2	Total	0	3
	Not High	0	3 (100%)
3	Total	0	1
	3	0	1 (100%)
Missing	Total	17	24
	Not High	4 (23.5%)	8 (33.3%)
	1	0	2 (8.3%)
	2	1 (5.9%)	1 (4.2%)
	Missing	12 (70.6%)	13 (54.2%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_A_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Creatinine

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	81	157
	Not High	14 (17.3%)	26 (16.6%)
	1	58 (71.6%)	116 (73.9%)
	2	8 (9.9%)	15 (9.6%)
	3	1 (1.2%)	0
1	Total	5	9
	Not High	0	2 (22.2%)
	1	3 (60.0%)	6 (66.7%)
	2	2 (40.0%)	1 (11.1%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_A_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Cholesterol, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	52	105
	Not High	35 (67.3%)	63 (60.0%)
	1	15 (28.8%)	36 (34.3%)
	2	1 (1.9%)	4 (3.8%)
	3	0	1 (1.0%)
	Missing	1 (1.9%)	1 (1.0%)
1	Total	22	39
	Not High	5 (22.7%)	5 (12.8%)
	1	14 (63.6%)	32 (82.1%)
	2	3 (13.6%)	2 (5.1%)
2	Total	1	1
	1	1 (100%)	1 (100%)
Missing	Total	12	21
	Not High	0	5 (23.8%)
	1	0	3 (14.3%)
	Missing	12 (100%)	13 (61.9%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_A_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Glucose, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	69	122
	Not High	47 (68.1%)	58 (47.5%)
	1	22 (31.9%)	60 (49.2%)
	2	0	4 (3.3%)
1	Total	14	34
	Not High	1 (7.1%)	2 (5.9%)
	1	9 (64.3%)	24 (70.6%)
	2	4 (28.6%)	7 (20.6%)
	3	0	1 (2.9%)
2	Total	0	2
	2	0	1 (50.0%)
	3	0	1 (50.0%)
Missing	Total	4	8
	Not High	0	2 (25.0%)
	1	0	1 (12.5%)
	2	0	1 (12.5%)
	Missing	4 (100%)	4 (50.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_A_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Glucose

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	4	10
	Not High	4 (100%)	9 (90.0%)
	3	0	1 (10.0%)
Missing	Total	83	156
	Not High	17 (20.5%)	17 (10.9%)
	3	0	1 (0.6%)
	Missing	66 (79.5%)	138 (88.5%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_A_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Magnesium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	81	161
	Not High	69 (85.2%)	147 (91.3%)
	1	11 (13.6%)	9 (5.6%)
	3	1 (1.2%)	5 (3.1%)
1	Total	5	2
	Not High	2 (40.0%)	2 (100%)
	1	3 (60.0%)	0
Missing	Total	1	3
	Not High	0	2 (66.7%)
	1	0	1 (33.3%)
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Potassium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	85	158
	Not High	72 (84.7%)	123 (77.8%)
	1	10 (11.8%)	27 (17.1%)
	2	2 (2.4%)	7 (4.4%)
	3	1 (1.2%)	1 (0.6%)
1	Total	0	5
	Not High	0	2 (40.0%)
	1	0	1 (20.0%)
	2	0	2 (40.0%)
2	Total	1	2
	Not High	0	1 (50.0%)
	1	0	1 (50.0%)
	3	1 (100%)	0
3	Total	0	1
	3	0	1 (100%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Sodium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	85	164
	Not High	79 (92.9%)	154 (93.9%)
	1	5 (5.9%)	8 (4.9%)
	2	1 (1.2%)	2 (1.2%)
1	Total	1	2
	Not High	1 (100%)	1 (50.0%)
	1	0	1 (50.0%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_A_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Bilirubin

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	80	163
	Not High	71 (88.8%)	142 (87.1%)
	1	6 (7.5%)	20 (12.3%)
	2	3 (3.8%)	1 (0.6%)
1	Total	5	2
	Not High	1 (20.0%)	2 (100%)
	1	2 (40.0%)	0
	2	2 (40.0%)	0
2	Total	1	1
	1	0	1 (100%)
	2	1 (100%)	0
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Alkaline Phosphatase

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	43	90
	Not High	22 (51.2%)	54 (60.0%)
	1	18 (41.9%)	33 (36.7%)
	2	2 (4.7%)	1 (1.1%)
	3	1 (2.3%)	2 (2.2%)
1	Total	20	44
	Not High	2 (10.0%)	7 (15.9%)
	1	12 (60.0%)	27 (61.4%)
	2	5 (25.0%)	9 (20.5%)
	3	1 (5.0%)	1 (2.3%)
2	Total	10	8
	1	0	1 (12.5%)
	2	6 (60.0%)	4 (50.0%)
	3	4 (40.0%)	3 (37.5%)
3	Total	2	2
	2	1 (50.0%)	0
	3	0	2 (100%)
	Missing	1 (50.0%)	0
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

SGPT/ALT

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	51	106
	Not High	20 (39.2%)	52 (49.1%)
	1	27 (52.9%)	48 (45.3%)
	2	1 (2.0%)	3 (2.8%)
	3	2 (3.9%)	3 (2.8%)
	Missing	1 (2.0%)	0
1	Total	22	31
	Not High	1 (4.5%)	0
	1	13 (59.1%)	23 (74.2%)
	2	5 (22.7%)	2 (6.5%)
	3	3 (13.6%)	5 (16.1%)
	4	0	1 (3.2%)
2	Total	1	7
	2	0	4 (57.1%)
	3	0	3 (42.9%)
	4	1 (100%)	0
3	Total	1	0
	3	1 (100%)	0
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

SGOT/AST

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	44	100
	Not High	21 (47.7%)	49 (49.0%)
	1	21 (47.7%)	46 (46.0%)
	2	1 (2.3%)	3 (3.0%)
	3	1 (2.3%)	2 (2.0%)
1	Total	28	36
	Not High	1 (3.6%)	2 (5.6%)
	1	18 (64.3%)	27 (75.0%)
	2	4 (14.3%)	1 (2.8%)
	3	5 (17.9%)	5 (13.9%)
	4	0	1 (2.8%)
2	Total	3	6
	1	0	1 (16.7%)
	2	0	2 (33.3%)
	3	2 (66.7%)	3 (50.0%)
	Missing	1 (33.3%)	0
3	Total	0	2
	1	0	1 (50.0%)
	3	0	1 (50.0%)
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Calcium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	69	135
	Not High	54 (78.3%)	110 (81.5%)
	1	11 (15.9%)	25 (18.5%)
	2	1 (1.4%)	0
	4	2 (2.9%)	0
	Missing	1 (1.4%)	0
1	Total	6	8
	Not High	1 (16.7%)	1 (12.5%)
	1	4 (66.7%)	6 (75.0%)
	3	1 (16.7%)	1 (12.5%)
2	Total	0	1
	1	0	1 (100%)
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Triglycerides, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	50	96
	Not High	24 (48.0%)	57 (59.4%)
	1	23 (46.0%)	34 (35.4%)
	2	2 (4.0%)	4 (4.2%)
	Missing	1 (2.0%)	1 (1.0%)
1	Total	16	27
	Not High	4 (25.0%)	8 (29.6%)
	1	9 (56.3%)	13 (48.1%)
	2	2 (12.5%)	4 (14.8%)
	4	1 (6.3%)	0
	Missing	0	2 (7.4%)
2	Total	2	3
	1	2 (100%)	0
	2	0	1 (33.3%)
	3	0	2 (66.7%)
Missing	Total	7	19
	Not High	3 (42.9%)	5 (26.3%)
	1	1 (14.3%)	4 (21.1%)
	2	0	1 (5.3%)
	Missing	3 (42.9%)	9 (47.4%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_B_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Amylase, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	62	117
	Not High	55 (88.7%)	104 (88.9%)
	1	5 (8.1%)	9 (7.7%)
	2	1 (1.6%)	2 (1.7%)
	3	0	1 (0.9%)
	4	0	1 (0.9%)
	Missing	1 (1.6%)	0
1	Total	5	7
	Not High	1 (20.0%)	2 (28.6%)
	1	3 (60.0%)	4 (57.1%)
	2	1 (20.0%)	1 (14.3%)
2	Total	1	2
	Not High	0	1 (50.0%)
	2	1 (100%)	1 (50.0%)
3	Total	1	0
	Not High	1 (100%)	0
Missing	Total	6	19
	Not High	1 (16.7%)	6 (31.6%)
	1	1 (16.7%)	2 (10.5%)
	Missing	4 (66.7%)	11 (57.9%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Lipase, Total, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	58	118
	Not High	47 (81.0%)	90 (76.3%)
	1	6 (10.3%)	17 (14.4%)
	2	0	4 (3.4%)
	3	2 (3.4%)	5 (4.2%)
	4	0	1 (0.8%)
	Missing	3 (5.2%)	1 (0.8%)
1	Total	7	2
	Not High	1 (14.3%)	2 (100%)
	1	2 (28.6%)	0
	2	3 (42.9%)	0
	Missing	1 (14.3%)	0
2	Total	1	2
	Not High	1 (100%)	0
	1	0	1 (50.0%)
	3	0	1 (50.0%)
4	Total	1	2
	Not High	0	1 (50.0%)
	1	1 (100%)	1 (50.0%)
Missing	Total	8	21
	Not High	2 (25.0%)	6 (28.6%)
	1	1 (12.5%)	5 (23.8%)
	Missing	5 (62.5%)	10 (47.6%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Creatinine

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	69	137
	Not High	13 (18.8%)	21 (15.3%)
	1	47 (68.1%)	98 (71.5%)
	2	8 (11.6%)	14 (10.2%)
	3	1 (1.4%)	4 (2.9%)
1	Total	6	7
	Not High	2 (33.3%)	1 (14.3%)
	1	3 (50.0%)	4 (57.1%)
	2	1 (16.7%)	2 (28.6%)
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Cholesterol, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	44	87
	Not High	28 (63.6%)	52 (59.8%)
	1	13 (29.5%)	31 (35.6%)
	2	2 (4.5%)	3 (3.4%)
	Missing	1 (2.3%)	1 (1.1%)
1	Total	23	37
	Not High	1 (4.3%)	2 (5.4%)
	1	15 (65.2%)	31 (83.8%)
	2	7 (30.4%)	4 (10.8%)
2	Total	2	1
	1	2 (100%)	0
	2	0	1 (100%)
Missing	Total	6	20
	Not High	1 (16.7%)	2 (10.0%)
	1	2 (33.3%)	8 (40.0%)
	2	0	1 (5.0%)
	Missing	3 (50.0%)	9 (45.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Glucose, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	53	104
	Not High	28 (52.8%)	51 (49.0%)
	1	23 (43.4%)	47 (45.2%)
	2	2 (3.8%)	5 (4.8%)
	3	0	1 (1.0%)
1	Total	17	35
	Not High	0	3 (8.6%)
	1	15 (88.2%)	24 (68.6%)
	2	2 (11.8%)	7 (20.0%)
	3	0	1 (2.9%)
2	Total	1	3
	Not High	0	2 (66.7%)
	1	0	1 (33.3%)
	2	1 (100%)	0
Missing	Total	4	3
	Not High	1 (25.0%)	0
	1	1 (25.0%)	2 (66.7%)
	Missing	2 (50.0%)	1 (33.3%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Glucose

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	4	7
	Not High	3 (75.0%)	4 (57.1%)
	Missing	1 (25.0%)	3 (42.9%)
Missing	Total	71	138
	Not High	5 (7.0%)	27 (19.6%)
	3	0	1 (0.7%)
	Missing	66 (93.0%)	110 (79.7%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Magnesium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	71	143
	Not High	61 (85.9%)	127 (88.8%)
	1	4 (5.6%)	12 (8.4%)
	3	4 (5.6%)	3 (2.1%)
	Missing	2 (2.8%)	1 (0.7%)
1	Total	3	0
	1	3 (100%)	0
Missing	Total	1	2
	Not High	1 (100%)	1 (50.0%)
	Missing	0	1 (50.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Potassium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	70	139
	Not High	56 (80.0%)	116 (83.5%)
	1	7 (10.0%)	20 (14.4%)
	2	6 (8.6%)	3 (2.2%)
	3	1 (1.4%)	0
1	Total	4	5
	Not High	0	1 (20.0%)
	1	2 (50.0%)	4 (80.0%)
	2	2 (50.0%)	0
2	Total	1	0
	2	1 (100%)	0
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Sodium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	75	144
	Not High	69 (92.0%)	124 (86.1%)
	1	6 (8.0%)	15 (10.4%)
	2	0	5 (3.5%)
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Bilirubin

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	70	136
	Not High	56 (80.0%)	115 (84.6%)
	1	6 (8.6%)	14 (10.3%)
	2	5 (7.1%)	4 (2.9%)
	3	3 (4.3%)	2 (1.5%)
	4	0	1 (0.7%)
1	Total	2	7
	1	1 (50.0%)	4 (57.1%)
	2	1 (50.0%)	3 (42.9%)
2	Total	3	1
	1	1 (33.3%)	1 (100%)
	2	1 (33.3%)	0
	Missing	1 (33.3%)	0
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Alkaline Phosphatase

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	74
	Not High	33 (44.6%)
	1	34 (45.9%)
	2	2 (2.7%)
	3	5 (6.8%)
1	Total	27
	1	23 (85.2%)
	2	3 (11.1%)
	3	1 (3.7%)
Missing	Total	1
	Not High	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

SGPT/ALT

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	86
	Not High	37 (43.0%)
	1	34 (39.5%)
	2	4 (4.7%)
	3	10 (11.6%)
	4	1 (1.2%)
1	Total	16
	Not High	2 (12.5%)
	1	10 (62.5%)
	2	2 (12.5%)
	3	2 (12.5%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

SGOT/AST

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	77
	Not High	42 (54.5%)
	1	22 (28.6%)
	2	6 (7.8%)
	3	7 (9.1%)
1	Total	25
	Not High	3 (12.0%)
	1	14 (56.0%)
	2	4 (16.0%)
	3	4 (16.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Calcium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	96
	Not High	75 (78.1%)
	1	19 (19.8%)
	2	1 (1.0%)
	3	1 (1.0%)
1	Total	5
	1	4 (80.0%)
	2	1 (20.0%)
2	Total	1
	Not High	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Triglycerides, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	71
	Not High	39 (54.9%)
	1	28 (39.4%)
	2	3 (4.2%)
	4	1 (1.4%)
1	Total	16
	Not High	3 (18.8%)
	1	9 (56.3%)
	2	3 (18.8%)
	4	1 (6.3%)
Missing	Total	15
	Not High	2 (13.3%)
	1	3 (20.0%)
	2	1 (6.7%)
	Missing	9 (60.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Amylase, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	78
	Not High	70 (89.7%)
	1	6 (7.7%)
	2	1 (1.3%)
	3	1 (1.3%)
1	Total	5
	Not High	2 (40.0%)
	1	3 (60.0%)
Missing	Total	19
	Not High	9 (47.4%)
	2	1 (5.3%)
	Missing	9 (47.4%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Lipase, Total, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	76
	Not High	59 (77.6%)
	1	9 (11.8%)
	2	5 (6.6%)
	3	3 (3.9%)
1	Total	5
	Not High	1 (20.0%)
	1	3 (60.0%)
	2	1 (20.0%)
Missing	Total	21
	Not High	9 (42.9%)
	1	1 (4.8%)
	Missing	11 (52.4%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_C_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Creatinine

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	98
	Not High	12 (12.2%)
	1	74 (75.5%)
	2	9 (9.2%)
	3	3 (3.1%)
1	Total	4
	Not High	2 (50.0%)
	1	2 (50.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_C_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Cholesterol, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	60
	Not High	36 (60.0%)
	1	20 (33.3%)
	2	3 (5.0%)
	4	1 (1.7%)
1	Total	26
	Not High	3 (11.5%)
	1	18 (69.2%)
	2	4 (15.4%)
	3	1 (3.8%)
2	Total	1
	1	1 (100%)
Missing	Total	15
	Not High	2 (13.3%)
	1	3 (20.0%)
	2	1 (6.7%)
	Missing	9 (60.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_C_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Glucose, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	65
	Not High	30 (46.2%)
	1	33 (50.8%)
	2	1 (1.5%)
	3	1 (1.5%)
1	Total	30
	Not High	1 (3.3%)
	1	19 (63.3%)
	2	7 (23.3%)
	3	3 (10.0%)
Missing	Total	7
	1	3 (42.9%)
	Missing	4 (57.1%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Glucose

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	10
	Not High	10 (100%)
Missing	Total	92
	Not High	26 (28.3%)
	3	1 (1.1%)
	Missing	65 (70.7%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_CHEM_C_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Magnesium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	96
	Not High	79 (82.3%)
	1	14 (14.6%)
	3	2 (2.1%)
	4	1 (1.0%)
1	Total	5
	1	5 (100%)
3	Total	1
	3	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Potassium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	98
	Not High	76 (77.6%)
	1	11 (11.2%)
	2	9 (9.2%)
	3	1 (1.0%)
	4	1 (1.0%)
1	Total	4
	1	4 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Sodium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	102
	Not High	88 (86.3%)
	1	13 (12.7%)
	2	1 (1.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Bilirubin

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	98
	Not High	78 (79.6%)
	1	16 (16.3%)
	2	1 (1.0%)
	3	3 (3.1%)
1	Total	4
	1	3 (75.0%)
	2	1 (25.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Coagulation,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

International Normalized Ratio

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	78	141
	Not High	33 (42.3%)	50 (35.5%)
	1	27 (34.6%)	66 (46.8%)
	2	1 (1.3%)	4 (2.8%)
	3	0	1 (0.7%)
	Missing	17 (21.8%)	20 (14.2%)
1	Total	1	10
	Not High	1 (100%)	7 (70.0%)
	1	0	2 (20.0%)
	Missing	0	1 (10.0%)
2	Total	0	2
	Not High	0	1 (50.0%)
	3	0	1 (50.0%)
Missing	Total	8	13
	Not High	0	1 (7.7%)
	Missing	8 (100%)	12 (92.3%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Coagulation,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Activated Partial Thromboplastin Time

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	72	138
	Not High	57 (79.2%)	109 (79.0%)
	1	1 (1.4%)	9 (6.5%)
	2	1 (1.4%)	0
	3	1 (1.4%)	1 (0.7%)
	Missing	12 (16.7%)	19 (13.8%)
1	Total	5	5
	Not High	0	3 (60.0%)
	1	2 (40.0%)	1 (20.0%)
	Missing	3 (60.0%)	1 (20.0%)
2	Total	0	1
	Missing	0	1 (100%)
Missing	Total	10	22
	Not High	0	2 (9.1%)
	1	0	3 (13.6%)
	Missing	10 (100%)	17 (77.3%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Coagulation,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

International Normalized Ratio

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	73	132
	Not High	29 (39.7%)	47 (35.6%)
	1	32 (43.8%)	57 (43.2%)
	2	1 (1.4%)	2 (1.5%)
	Missing	11 (15.1%)	26 (19.7%)
1	Total	2	4
	Not High	0	3 (75.0%)
	1	1 (50.0%)	0
	Missing	1 (50.0%)	1 (25.0%)
Missing	Total	0	9
	Not High	0	1 (11.1%)
	Missing	0	8 (88.9%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Coagulation,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Activated Partial Thromboplastin Time

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	69	123
	Not High	57 (82.6%)	94 (76.4%)
	1	1 (1.4%)	7 (5.7%)
	2	0	1 (0.8%)
	Missing	11 (15.9%)	21 (17.1%)
1	Total	2	2
	Not High	0	1 (50.0%)
	1	1 (50.0%)	0
	2	0	1 (50.0%)
	Missing	1 (50.0%)	0
Missing	Total	4	20
	Not High	1 (25.0%)	2 (10.0%)
	Missing	3 (75.0%)	18 (90.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Coagulation,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

International Normalized Ratio

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	91
	Not High	38 (41.8%)
	1	37 (40.7%)
	2	2 (2.2%)
	Missing	14 (15.4%)
1	Total	3
	1	3 (100%)
Missing	Total	8
	Missing	8 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_COAG_C_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Coagulation,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Activated Partial Thromboplastin Time

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	82
	Not High	69 (84.1%)
	1	3 (3.7%)
	Missing	10 (12.2%)
1	Total	6
	Not High	2 (33.3%)
	1	2 (33.3%)
	Missing	2 (33.3%)
Missing	Total	14
	Not High	1 (7.1%)
	Missing	13 (92.9%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Hematology,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Hemoglobin

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	86	166
	Not High	84 (97.7%)	163 (98.2%)
	1	2 (2.3%)	2 (1.2%)
	2	0	1 (0.6%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_HEM_A_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Hematology,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Lymphocytes Abs

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	86	166
	Not High	81 (94.2%)	162 (97.6%)
	2	4 (4.7%)	4 (2.4%)
	3	1 (1.2%)	0
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Hematology,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Total Leukocyte Count

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not High	Total	86	166
	Not High	85 (98.8%)	165 (99.4%)
	3	1 (1.2%)	1 (0.6%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Hematology,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Hemoglobin

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	75	144
	Not High	71 (94.7%)	135 (93.8%)
	1	4 (5.3%)	9 (6.3%)
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Hematology,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Lymphocytes Abs

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	75	143
	Not High	71 (94.7%)	139 (97.2%)
	2	3 (4.0%)	4 (2.8%)
	Missing	1 (1.3%)	0
3	Total	0	1
	Not High	0	1 (100%)
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Hematology,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Total Leukocyte Count

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not High	Total	75	144
	Not High	75 (100%)	144 (100%)
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_high.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_HEM_B_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Hematology,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Hemoglobin

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	102
	Not High	97 (95.1%)
	1	5 (4.9%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_HEM_C_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Hematology,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Lymphocytes Abs

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	102
	Not High	96 (94.1%)
	2	6 (5.9%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (High), Hematology,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Total Leukocyte Count

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not High	Total	102
	Not High	102 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not High" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_high_HEM_C_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Albumin

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not Low	Total	77	156
	Not Low	58 (75.3%)	121 (77.6%)
	1	15 (19.5%)	26 (16.7%)
	2	4 (5.2%)	7 (4.5%)
	3	0	2 (1.3%)
1	Total	8	10
	1	4 (50.0%)	8 (80.0%)
	2	4 (50.0%)	2 (20.0%)
2	Total	1	0
	2	1 (100%)	0
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_low_CHEM_A_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Calcium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not Low	Total	83	154
	Not Low	59 (71.1%)	105 (68.2%)
	1	14 (16.9%)	37 (24.0%)
	2	9 (10.8%)	12 (7.8%)
	3	1 (1.2%)	0
1	Total	3	11
	Not Low	1 (33.3%)	1 (9.1%)
	1	0	7 (63.6%)
	2	2 (66.7%)	2 (18.2%)
	3	0	1 (9.1%)
2	Total	0	1
	2	0	1 (100%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Glucose, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not Low	Total	83	155
	Not Low	77 (92.8%)	137 (88.4%)
	1	6 (7.2%)	17 (11.0%)
	2	0	1 (0.6%)
1	Total	0	3
	1	0	3 (100%)
Missing	Total	4	8
	Not Low	0	2 (25.0%)
	1	0	2 (25.0%)
	Missing	4 (100%)	4 (50.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Glucose

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not Low	Total	4	10
	Not Low	4 (100%)	8 (80.0%)
	1	0	2 (20.0%)
Missing	Total	83	156
	Not Low	17 (20.5%)	18 (11.5%)
	Missing	66 (79.5%)	138 (88.5%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Magnesium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not Low	Total	83	158
	Not Low	68 (81.9%)	127 (80.4%)
	1	15 (18.1%)	29 (18.4%)
	2	0	2 (1.3%)
1	Total	3	5
	Not Low	0	2 (40.0%)
	1	3 (100%)	2 (40.0%)
	2	0	1 (20.0%)
Missing	Total	1	3
	Not Low	0	2 (66.7%)
	2	0	1 (33.3%)
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Phosphorus

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not Low	Total	84	160
	Not Low	68 (81.0%)	126 (78.8%)
	1	3 (3.6%)	6 (3.8%)
	2	12 (14.3%)	23 (14.4%)
	3	1 (1.2%)	4 (2.5%)
	4	0	1 (0.6%)
2	Total	2	5
	Not Low	1 (50.0%)	0
	2	1 (50.0%)	4 (80.0%)
	3	0	1 (20.0%)
3	Total	0	1
	Not Low	0	1 (100%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Potassium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not Low	Total	83	164
	Not Low	74 (89.2%)	134 (81.7%)
	2	8 (9.6%)	28 (17.1%)
	3	1 (1.2%)	2 (1.2%)
2	Total	3	2
	2	3 (100%)	2 (100%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Sodium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not Low	Total	82	157
	Not Low	63 (76.8%)	125 (79.6%)
	1	14 (17.1%)	25 (15.9%)
	3	5 (6.1%)	7 (4.5%)
1	Total	3	6
	Not Low	1 (33.3%)	3 (50.0%)
	1	1 (33.3%)	2 (33.3%)
	3	1 (33.3%)	1 (16.7%)
3	Total	1	2
	1	1 (100%)	0
	3	0	2 (100%)
4	Total	0	1
	1	0	1 (100%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Albumin

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not Low	Total	68	129
	Not Low	44 (64.7%)	89 (69.0%)
	1	19 (27.9%)	34 (26.4%)
	2	5 (7.4%)	6 (4.7%)
1	Total	6	14
	Not Low	0	2 (14.3%)
	1	6 (100%)	7 (50.0%)
	2	0	4 (28.6%)
	3	0	1 (7.1%)
2	Total	0	1
	1	0	1 (100%)
3	Total	1	0
	Missing	1 (100%)	0
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_low_CHEM_B_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Calcium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not Low	Total	72	139
	Not Low	47 (65.3%)	96 (69.1%)
	1	20 (27.8%)	35 (25.2%)
	2	4 (5.6%)	8 (5.8%)
	Missing	1 (1.4%)	0
1	Total	3	3
	1	3 (100%)	3 (100%)
2	Total	0	2
	Not Low	0	1 (50.0%)
	3	0	1 (50.0%)
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Glucose, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not Low	Total	70	141
	Not Low	65 (92.9%)	120 (85.1%)
	1	4 (5.7%)	21 (14.9%)
	2	1 (1.4%)	0
1	Total	1	1
	1	1 (100%)	1 (100%)
Missing	Total	4	3
	Not Low	2 (50.0%)	1 (33.3%)
	1	0	1 (33.3%)
	Missing	2 (50.0%)	1 (33.3%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Glucose

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not Low	Total	4	7
	Not Low	2 (50.0%)	4 (57.1%)
	1	1 (25.0%)	0
	Missing	1 (25.0%)	3 (42.9%)
Missing	Total	71	138
	Not Low	5 (7.0%)	26 (18.8%)
	1	0	1 (0.7%)
	2	0	1 (0.7%)
	Missing	66 (93.0%)	110 (79.7%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Magnesium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not Low	Total	73	141
	Not Low	64 (87.7%)	101 (71.6%)
	1	6 (8.2%)	36 (25.5%)
	2	0	2 (1.4%)
	3	1 (1.4%)	1 (0.7%)
	Missing	2 (2.7%)	1 (0.7%)
1	Total	1	2
	1	1 (100%)	2 (100%)
Missing	Total	1	2
	Not Low	0	1 (50.0%)
	1	1 (100%)	0
	Missing	0	1 (50.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Phosphorus

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not Low	Total	71	140
	Not Low	52 (73.2%)	100 (71.4%)
	1	4 (5.6%)	10 (7.1%)
	2	12 (16.9%)	25 (17.9%)
	3	2 (2.8%)	5 (3.6%)
	Missing	1 (1.4%)	0
1	Total	1	0
	2	1 (100%)	0
2	Total	2	1
	2	1 (50.0%)	1 (100%)
	3	1 (50.0%)	0
3	Total	1	1
	Not Low	1 (100%)	0
	2	0	1 (100%)
Missing	Total	0	3
	Not Low	0	1 (33.3%)
	Missing	0	2 (66.7%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Potassium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not Low	Total	74	142
	Not Low	61 (82.4%)	109 (76.8%)
	2	13 (17.6%)	29 (20.4%)
	3	0	4 (2.8%)
2	Total	0	2
	2	0	2 (100%)
3	Total	1	0
	2	1 (100%)	0
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_low.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_low_CHEM_B_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Sodium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not Low	Total	70	138
	Not Low	59 (84.3%)	100 (72.5%)
	1	9 (12.9%)	33 (23.9%)
	3	2 (2.9%)	4 (2.9%)
	4	0	1 (0.7%)
1	Total	5	6
	Not Low	1 (20.0%)	1 (16.7%)
	1	3 (60.0%)	4 (66.7%)
	3	1 (20.0%)	1 (16.7%)
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Albumin

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not Low	Total	97
	Not Low	71 (73.2%)
	1	13 (13.4%)
	2	12 (12.4%)
	3	1 (1.0%)
1	Total	5
	1	1 (20.0%)
	2	4 (80.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Calcium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not Low	Total	98
	Not Low	60 (61.2%)
	1	29 (29.6%)
	2	8 (8.2%)
	4	1 (1.0%)
1	Total	4
	1	2 (50.0%)
	2	2 (50.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_low_CHEM_C_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Glucose, Fasting

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not Low	Total	94
	Not Low	79 (84.0%)
	1	12 (12.8%)
	2	3 (3.2%)
1	Total	1
	Not Low	1 (100%)
Missing	Total	7
	Not Low	3 (42.9%)
	Missing	4 (57.1%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Glucose

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not Low	Total	10
	Not Low	8 (80.0%)
	1	1 (10.0%)
	4	1 (10.0%)
Missing	Total	92
	Not Low	26 (28.3%)
	2	1 (1.1%)
	Missing	65 (70.7%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Magnesium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not Low	Total	100
	Not Low	71 (71.0%)
	1	27 (27.0%)
	2	1 (1.0%)
	4	1 (1.0%)
1	Total	2
	1	2 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Phosphorus

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not Low	Total	96
	Not Low	75 (78.1%)
	1	3 (3.1%)
	2	16 (16.7%)
	3	2 (2.1%)
2	Total	4
	Not Low	2 (50.0%)
	2	2 (50.0%)
3	Total	1
	4	1 (100%)
Missing	Total	1
	Not Low	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Potassium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not Low	Total	100
	Not Low	71 (71.0%)
	2	23 (23.0%)
	3	6 (6.0%)
2	Total	2
	Not Low	1 (50.0%)
	2	1 (50.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Chemistry,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Sodium

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not Low	Total	99
	Not Low	63 (63.6%)
	1	29 (29.3%)
	3	6 (6.1%)
	4	1 (1.0%)
1	Total	3
	1	1 (33.3%)
	3	2 (66.7%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Hemoglobin

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not Low	Total	62	124
	Not Low	17 (27.4%)	14 (11.3%)
	1	34 (54.8%)	84 (67.7%)
	2	11 (17.7%)	25 (20.2%)
	3	0	1 (0.8%)
1	Total	22	32
	1	10 (45.5%)	16 (50.0%)
	2	9 (40.9%)	13 (40.6%)
	3	3 (13.6%)	3 (9.4%)
2	Total	2	10
	2	1 (50.0%)	8 (80.0%)
	3	1 (50.0%)	2 (20.0%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Lymphocytes Abs

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not Low	Total	69	143
	Not Low	36 (52.2%)	73 (51.0%)
	1	16 (23.2%)	36 (25.2%)
	2	14 (20.3%)	24 (16.8%)
	3	2 (2.9%)	7 (4.9%)
	4	1 (1.4%)	3 (2.1%)
1	Total	10	13
	Not Low	0	1 (7.7%)
	1	4 (40.0%)	5 (38.5%)
	2	6 (60.0%)	4 (30.8%)
	3	0	3 (23.1%)
2	Total	5	9
	1	1 (20.0%)	0
	2	3 (60.0%)	4 (44.4%)
	3	1 (20.0%)	4 (44.4%)
	4	0	1 (11.1%)
3	Total	2	1
	3	0	1 (100%)
	4	2 (100%)	0
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Neutrophils, Total, Abs

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not Low	Total	83	160
	Not Low	39 (47.0%)	81 (50.6%)
	1	16 (19.3%)	29 (18.1%)
	2	20 (24.1%)	28 (17.5%)
	3	7 (8.4%)	16 (10.0%)
	4	1 (1.2%)	6 (3.8%)
1	Total	3	6
	1	1 (33.3%)	0
	2	1 (33.3%)	3 (50.0%)
	3	1 (33.3%)	3 (50.0%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Platelet

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not Low	Total	80	163
	Not Low	70 (87.5%)	143 (87.7%)
	1	9 (11.3%)	17 (10.4%)
	2	1 (1.3%)	2 (1.2%)
	3	0	1 (0.6%)
1	Total	6	3
	1	5 (83.3%)	3 (100%)
	3	1 (16.7%)	0
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Total Leukocyte Count

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=87)	Ipatasertib + Paclitaxel (N=166)
Not Low	Total	77	152
	Not Low	27 (35.1%)	59 (38.8%)
	1	29 (37.7%)	53 (34.9%)
	2	17 (22.1%)	30 (19.7%)
	3	3 (3.9%)	9 (5.9%)
	4	1 (1.3%)	1 (0.7%)
1	Total	9	11
	1	5 (55.6%)	3 (27.3%)
	2	4 (44.4%)	5 (45.5%)
	3	0	2 (18.2%)
	4	0	1 (9.1%)
2	Total	0	3
	2	0	3 (100%)
Missing	Total	1	0
	Missing	1 (100%)	0

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Hemoglobin

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not Low	Total	57	108
	Not Low	10 (17.5%)	13 (12.0%)
	1	41 (71.9%)	63 (58.3%)
	2	3 (5.3%)	30 (27.8%)
	3	3 (5.3%)	2 (1.9%)
1	Total	16	33
	1	6 (37.5%)	8 (24.2%)
	2	9 (56.3%)	21 (63.6%)
	3	1 (6.3%)	4 (12.1%)
2	Total	2	3
	2	2 (100%)	2 (66.7%)
	3	0	1 (33.3%)
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Lymphocytes Abs

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not Low	Total	58	105
	Not Low	29 (50.0%)	46 (43.8%)
	1	13 (22.4%)	22 (21.0%)
	2	9 (15.5%)	28 (26.7%)
	3	6 (10.3%)	8 (7.6%)
	4	1 (1.7%)	1 (1.0%)
1	Total	12	21
	Not Low	0	1 (4.8%)
	1	3 (25.0%)	6 (28.6%)
	2	8 (66.7%)	9 (42.9%)
	3	1 (8.3%)	4 (19.0%)
	4	0	1 (4.8%)
2	Total	5	13
	1	1 (20.0%)	1 (7.7%)
	2	1 (20.0%)	6 (46.2%)
	3	1 (20.0%)	6 (46.2%)
	4	1 (20.0%)	0
	Missing	1 (20.0%)	0
3	Total	0	3
	2	0	1 (33.3%)
	3	0	1 (33.3%)
	4	0	1 (33.3%)
4	Total	0	2
	4	0	2 (100%)
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Neutrophils, Total, Abs

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not Low	Total	72	144
	Not Low	29 (40.3%)	52 (36.1%)
	1	13 (18.1%)	33 (22.9%)
	2	17 (23.6%)	34 (23.6%)
	3	10 (13.9%)	18 (12.5%)
	4	2 (2.8%)	7 (4.9%)
	Missing	1 (1.4%)	0
1	Total	3	0
	2	3 (100%)	0
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Platelet

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not Low	Total	66	140
	Not Low	60 (90.9%)	126 (90.0%)
	1	5 (7.6%)	13 (9.3%)
	3	1 (1.5%)	1 (0.7%)
1	Total	9	4
	Not Low	1 (11.1%)	0
	1	8 (88.9%)	4 (100%)
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_low.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_low_HEM_B_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Total Leukocyte Count

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Placebo + Paclitaxel (N=75)	Ipatasertib + Paclitaxel (N=145)
Not Low	Total	67	134
	Not Low	19 (28.4%)	31 (23.1%)
	1	21 (31.3%)	48 (35.8%)
	2	21 (31.3%)	38 (28.4%)
	3	5 (7.5%)	15 (11.2%)
	4	1 (1.5%)	2 (1.5%)
1	Total	7	9
	1	1 (14.3%)	3 (33.3%)
	2	3 (42.9%)	4 (44.4%)
	3	3 (42.9%)	2 (22.2%)
2	Total	1	1
	2	1 (100%)	0
	3	0	1 (100%)
Missing	Total	0	1
	Missing	0	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_low.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_low_HEM_B_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Hemoglobin

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not Low	Total	80
	Not Low	7 (8.8%)
	1	47 (58.8%)
	2	24 (30.0%)
	3	2 (2.5%)
1	Total	21
	1	9 (42.9%)
	2	10 (47.6%)
	3	2 (9.5%)
2	Total	1
	2	1 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_low.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_low_HEM_C_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Lymphocytes Abs

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not Low	Total	80
	Not Low	28 (35.0%)
	1	17 (21.3%)
	2	27 (33.8%)
	3	7 (8.8%)
	4	1 (1.3%)
1	Total	13
	1	1 (7.7%)
	2	8 (61.5%)
	3	3 (23.1%)
	4	1 (7.7%)
2	Total	9
	2	4 (44.4%)
	3	5 (55.6%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_low.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_low_HEM_C_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Neutrophils, Total, Abs

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not Low	Total	97
	Not Low	42 (43.3%)
	1	20 (20.6%)
	2	27 (27.8%)
	3	6 (6.2%)
	4	2 (2.1%)
1	Total	5
	1	1 (20.0%)
	2	1 (20.0%)
	3	2 (40.0%)
	4	1 (20.0%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_low.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_low_HEM_C_SE.out
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Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Platelet

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not Low	Total	99
	Not Low	83 (83.8%)
	1	14 (14.1%)
	2	1 (1.0%)
	3	1 (1.0%)
1	Total	3
	1	3 (100%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_low.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_low_HEM_C_SE.out

Laboratory Test Shift Table: Highest NCI CTCAE v4 Grade Post-Baseline (Low), Hematology,
Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Total Leukocyte Count

Baseline NCI-CTCAE Grade	Post-baseline NCI-CTCAE Grade	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Not Low	Total	88
	Not Low	22 (25.0%)
	1	33 (37.5%)
	2	26 (29.5%)
	3	5 (5.7%)
	4	2 (2.3%)
1	Total	14
	1	4 (28.6%)
	2	7 (50.0%)
	3	3 (21.4%)

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events. Table entries provide the number of patients with the highest post-baseline NCI-CTCAE grade. "Not Low" includes Grade 0 and Grade 1-4 abnormalities in the opposite direction. Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_lb_shift_low.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_lb_shift_low_HEM_C_SE.out

Breast Cancer History, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Site of primary tumor	
n	104
LEFT	58 (56.9%)
RIGHT	46 (45.1%)
Histologic subtype	
n	101
DUCTAL	74 (73.3%)
LOBULAR	3 (3.0%)
MUCINOUS	2 (2.0%)
TUBULAR	1 (1.0%)
COMEDO	1 (1.0%)
NOS	15 (14.9%)
OTHER	12 (11.9%)
Histology Grade	
n	103
Well Differentiated - G1	2 (2.0%)
Moderately Differentiated - G2	26 (25.5%)
Poorly Differentiated - G3	62 (60.8%)
Unknown	13 (12.7%)
Initial diagnosis staging	
n	102
Stage I	5 (4.9%)
Stage II	23 (22.5%)
Stage III	31 (30.4%)
Stage IV	37 (36.3%)
Unknown	6 (5.9%)

Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_mh_bchist.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_mh_bchist_C_IT.out
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MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Total number of patients with at least one condition	77 (75.5%)
Total number of conditions	363
Blood and lymphatic system disorders	
Total number of patients with at least one condition	8 (7.8%)
Total number of conditions	8
Anaemia	5 (4.9%)
Lymph node pain	1 (1.0%)
Lymphopenia	1 (1.0%)
Splenic granuloma	1 (1.0%)
Cardiac disorders	
Total number of patients with at least one condition	9 (8.8%)
Total number of conditions	16
Arteriosclerosis coronary artery	2 (2.0%)
Cardiac failure	2 (2.0%)
Left ventricular hypertrophy	2 (2.0%)
Sinus tachycardia	2 (2.0%)
Aortic valve incompetence	1 (1.0%)
Cardiac valve disease	1 (1.0%)
Cardiomegaly	1 (1.0%)
Coronary artery disease	1 (1.0%)
Hypertensive heart disease	1 (1.0%)
Metabolic cardiomyopathy	1 (1.0%)
Myocardial ischaemia	1 (1.0%)
Pericarditis	1 (1.0%)
Congenital, familial and genetic disorders	
Total number of patients with at least one condition	3 (2.9%)
Total number of conditions	4
Ehlers-Danlos syndrome	1 (1.0%)
Factor V Leiden mutation	1 (1.0%)
Myoclonic dystonia	1 (1.0%)
Venous angioma of brain	1 (1.0%)
Ear and labyrinth disorders	
Total number of patients with at least one condition	4 (3.9%)
Total number of conditions	4
Deafness	2 (2.0%)
Deafness neurosensory	1 (1.0%)
Tinnitus	1 (1.0%)
Endocrine disorders	
Total number of patients with at least one condition	16 (15.7%)
Total number of conditions	17
Hypothyroidism	12 (11.8%)
Goitre	4 (3.9%)
Thyroid mass	1 (1.0%)

Investigator text for medical history conditions is coded using MedDRA version 25.1.
Percentages are based on N in the column headings. The table includes medical conditions that were ongoing at baseline.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_mh.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_mh_CNCR_C_IT.out

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Eye disorders	
Total number of patients with at least one condition	6 (5.9%)
Total number of conditions	6
Glaucoma	4 (3.9%)
Macular degeneration	1 (1.0%)
Myopia	1 (1.0%)
Gastrointestinal disorders	
Total number of patients with at least one condition	21 (20.6%)
Total number of conditions	24
Gastrooesophageal reflux disease	4 (3.9%)
Abdominal pain upper	3 (2.9%)
Constipation	3 (2.9%)
Haemorrhoids	2 (2.0%)
Inguinal hernia	2 (2.0%)
Irritable bowel syndrome	2 (2.0%)
Abdominal pain	1 (1.0%)
Anal fistula	1 (1.0%)
Diverticulum	1 (1.0%)
Hiatus hernia	1 (1.0%)
Nausea	1 (1.0%)
Pancreatic disorder	1 (1.0%)
Pancreatic steatosis	1 (1.0%)
Pancreatitis chronic	1 (1.0%)
General disorders and administration site conditions	
Total number of patients with at least one condition	13 (12.7%)
Total number of conditions	16
Fatigue	6 (5.9%)
Axillary pain	2 (2.0%)
Chest pain	2 (2.0%)
Oedema peripheral	2 (2.0%)
Pain	2 (2.0%)
Asthenia	1 (1.0%)
Non-cardiac chest pain	1 (1.0%)
Hepatobiliary disorders	
Total number of patients with at least one condition	10 (9.8%)
Total number of conditions	15
Cholecystitis chronic	4 (3.9%)
Hepatic cyst	3 (2.9%)
Cholelithiasis	2 (2.0%)
Hepatic steatosis	2 (2.0%)
Hepatomegaly	2 (2.0%)
Liver disorder	2 (2.0%)

Investigator text for medical history conditions is coded using MedDRA version 25.1.
Percentages are based on N in the column headings. The table includes medical conditions that were ongoing at baseline.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Immune system disorders	
Total number of patients with at least one condition	5 (4.9%)
Total number of conditions	6
Seasonal allergy	3 (2.9%)
Drug hypersensitivity	1 (1.0%)
Dust allergy	1 (1.0%)
Rubber sensitivity	1 (1.0%)
Infections and infestations	
Total number of patients with at least one condition	5 (4.9%)
Total number of conditions	6
Pyelonephritis chronic	2 (2.0%)
Bronchiolitis	1 (1.0%)
Chronic sinusitis	1 (1.0%)
Chronic tonsillitis	1 (1.0%)
Urinary tract infection	1 (1.0%)
Injury, poisoning and procedural complications	
Total number of patients with at least one condition	1 (1.0%)
Total number of conditions	1
Radiation fibrosis - lung	1 (1.0%)
Investigations	
Total number of patients with at least one condition	8 (7.8%)
Total number of conditions	12
Blood lactate dehydrogenase increased	3 (2.9%)
Activated partial thromboplastin time prolonged	1 (1.0%)
Blood cholesterol increased	1 (1.0%)
Blood urea increased	1 (1.0%)
Intraocular pressure increased	1 (1.0%)
Lymphocyte count decreased	1 (1.0%)
Monocyte count decreased	1 (1.0%)
Neutrophil count decreased	1 (1.0%)
Progesterone decreased	1 (1.0%)
White blood cell count decreased	1 (1.0%)
Metabolism and nutrition disorders	
Total number of patients with at least one condition	21 (20.6%)
Total number of conditions	27
Hyperlipidaemia	5 (4.9%)
Hyperglycaemia	4 (3.9%)
Diabetes mellitus	3 (2.9%)
Hypercholesterolaemia	3 (2.9%)
Obesity	3 (2.9%)
Type 2 diabetes mellitus	3 (2.9%)
Dyslipidaemia	2 (2.0%)
Decreased appetite	1 (1.0%)
Dehydration	1 (1.0%)
Glucose tolerance impaired	1 (1.0%)
Vitamin D deficiency	1 (1.0%)

Investigator text for medical history conditions is coded using MedDRA version 25.1.
Percentages are based on N in the column headings. The table includes medical conditions that were ongoing at baseline.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Musculoskeletal and connective tissue disorders	
Total number of patients with at least one condition	29 (28.4%)
Total number of conditions	37
Back pain	7 (6.9%)
Arthralgia	5 (4.9%)
Pain in extremity	5 (4.9%)
Osteoarthritis	4 (3.9%)
Osteopenia	3 (2.9%)
Arthritis	2 (2.0%)
Intervertebral disc protrusion	2 (2.0%)
Spinal pain	2 (2.0%)
Degenerative bone disease	1 (1.0%)
Flank pain	1 (1.0%)
Musculoskeletal chest pain	1 (1.0%)
Neck pain	1 (1.0%)
Spinal disorder	1 (1.0%)
Spinal osteoarthritis	1 (1.0%)
Tendonitis	1 (1.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Total number of patients with at least one condition	7 (6.9%)
Total number of conditions	11
Uterine leiomyoma	4 (3.9%)
Adrenal adenoma	2 (2.0%)
Cancer pain	1 (1.0%)
Fibroadenoma of breast	1 (1.0%)
Fibroma	1 (1.0%)
Haemangioma of liver	1 (1.0%)
Skin cancer	1 (1.0%)

Investigator text for medical history conditions is coded using MedDRA version 25.1.
Percentages are based on N in the column headings. The table includes medical conditions that were ongoing at baseline.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_mh.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_mh_CNCR_C_IT.out

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Nervous system disorders	
Total number of patients with at least one condition	16 (15.7%)
Total number of conditions	25
Autonomic nervous system imbalance	3 (2.9%)
Epilepsy	2 (2.0%)
Headache	2 (2.0%)
Intracranial aneurysm	2 (2.0%)
Neuropathy peripheral	2 (2.0%)
Cerebral circulatory failure	1 (1.0%)
Cognitive disorder	1 (1.0%)
Encephalopathy	1 (1.0%)
Facial paralysis	1 (1.0%)
Migraine	1 (1.0%)
Myoclonus	1 (1.0%)
Paraesthesia	1 (1.0%)
Peripheral motor neuropathy	1 (1.0%)
Presyncope	1 (1.0%)
Psychogenic seizure	1 (1.0%)
Restless legs syndrome	1 (1.0%)
Spinal meningeal cyst	1 (1.0%)
Taste disorder	1 (1.0%)
Tension headache	1 (1.0%)
Psychiatric disorders	
Total number of patients with at least one condition	19 (18.6%)
Total number of conditions	31
Anxiety	9 (8.8%)
Insomnia	9 (8.8%)
Depression	8 (7.8%)
Post-traumatic stress disorder	2 (2.0%)
Attention deficit hyperactivity disorder	1 (1.0%)
Sleep disorder	1 (1.0%)
Stress	1 (1.0%)
Renal and urinary disorders	
Total number of patients with at least one condition	9 (8.8%)
Total number of conditions	9
Renal cyst	6 (5.9%)
Calculus urinary	2 (2.0%)
Pyelocaliectasis	1 (1.0%)

Investigator text for medical history conditions is coded using MedDRA version 25.1.
Percentages are based on N in the column headings. The table includes medical conditions that were ongoing at baseline.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Reproductive system and breast disorders	
Total number of patients with at least one condition	13 (12.7%)
Total number of conditions	16
Breast pain	5 (4.9%)
Ovarian cyst	4 (3.9%)
Breast cyst	1 (1.0%)
Breast discharge	1 (1.0%)
Breast disorder	1 (1.0%)
Endometriosis	1 (1.0%)
Fibrocystic breast disease	1 (1.0%)
Menopausal symptoms	1 (1.0%)
Respiratory, thoracic and mediastinal disorders	
Total number of patients with at least one condition	13 (12.7%)
Total number of conditions	18
Asthma	4 (3.9%)
Dyspnoea	3 (2.9%)
Rhinitis allergic	3 (2.9%)
Pleural effusion	2 (2.0%)
Chronic obstructive pulmonary disease	1 (1.0%)
Cough	1 (1.0%)
Obliterative bronchiolitis	1 (1.0%)
Pulmonary fibrosis	1 (1.0%)
Pulmonary hypertension	1 (1.0%)
Pulmonary mass	1 (1.0%)
Skin and subcutaneous tissue disorders	
Total number of patients with at least one condition	7 (6.9%)
Total number of conditions	10
Alopecia areata	1 (1.0%)
Dermatitis atopic	1 (1.0%)
Dermatitis contact	1 (1.0%)
Dry skin	1 (1.0%)
Dyshidrotic eczema	1 (1.0%)
Erythema	1 (1.0%)
Lichen striatus	1 (1.0%)
Pruritus	1 (1.0%)
Psoriasis	1 (1.0%)
Urticaria	1 (1.0%)
Social circumstances	
Total number of patients with at least one condition	1 (1.0%)
Total number of conditions	1
Postmenopause	1 (1.0%)
Surgical and medical procedures	
Total number of patients with at least one condition	2 (2.0%)
Total number of conditions	2
Analgesic therapy	1 (1.0%)
Thoracic cavity drainage	1 (1.0%)

Investigator text for medical history conditions is coded using MedDRA version 25.1.
Percentages are based on N in the column headings. The table includes medical conditions that were ongoing at baseline.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_mh.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_mh_CNCR_C_IT.out

MedDRA System Organ Class MedDRA Preferred Term	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Vascular disorders	
Total number of patients with at least one condition	33 (32.4%)
Total number of conditions	41
Hypertension	29 (28.4%)
Essential hypertension	2 (2.0%)
Lymphoedema	2 (2.0%)
Aortic aneurysm	1 (1.0%)
Aortic arteriosclerosis	1 (1.0%)
Arteriosclerosis	1 (1.0%)
Hot flush	1 (1.0%)
Peripheral venous disease	1 (1.0%)
Thrombosis	1 (1.0%)
Varicose vein	1 (1.0%)

Investigator text for medical history conditions is coded using MedDRA version 25.1.
Percentages are based on N in the column headings. The table includes medical conditions that were ongoing at baseline.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_mh.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_mh_CNCR_C_IT.out

Summary of Ipatasertib Plasma Pharmacokinetic Concentrations by Nominal Time
PK Evaluable Population
Protocol: CO40016

Analyte: RO5532961 (ng/mL)

Treatment Arm Visit/Timepoint	Nominal Time (hr)	n	Number of LTRs	Mean	SD	CV % Mean	Geometric Mean	CV % Geometric Mean	Median	Minimum	Maximum
Ipatasertib + Atezolizumab + Paclitaxel (N=101)											
CYCLE 1 DAY 1/1-3 HRS POST DOSE	2	94	0	260	173	66.7	175	183.0	226	0.596	688
CYCLE 1 DAY 15/ PREDOSE	336	83	0	76.2	99.8	131.0	48.5	156.9	51.0	0.727	757
CYCLE 1 DAY 15/1-3 HRS POST DOSE	338	82	0	362	301	83.2	233	161.6	294	1.90	1710
CYCLE 3 DAY 15/ PREDOSE	1680	67	0	61.9	44.1	71.2	46.0	120.3	53.4	1.02	234
CYCLE 3 DAY 15/2-4 HRS POST DOSE	1683	62	0	324	245	75.8	207	197.6	319	1.33	1470

NE = Not Evaluable LTR: Less than reportable, SD: Standard deviation, MQC: Minimum Quantifiable Concentration, CV:Co-efficient of Variation, Min:Minimum, Max:Maximum
LTR values at nominal time 0 were set to 0 and LTR values at nominal time > 0 were dropped.
For a given treatment and sampling time point:
If one-third or fewer values were LTR, then all summary statistics are reported.
If more than one-third values were LTR, then only the median and maximum are reported and other summary statistics are displayed as NR. MQC for Plasma Ipatasertib is 0.5 ng/mL.

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/PK_Final_CSR_TLG_CohortC/prod/program/t_pkc.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/PK_Final_CSR_TLG_CohortC/prod/output/t_pkc.out
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Summary of Atezolizumab Serum Pharmacokinetic Concentrations by Nominal Time
PK Evaluable Population
Protocol: CO40016

Analyte: RO5541267 (ug/mL)

Treatment Arm Visit/Timepoint	Nominal Time (hr)	n	Number of LTRs	Mean	SD	CV % Mean	Geometric Mean	CV % Geometric Mean	Median	Minimum	Maximum
Ipatasertib + Atezolizumab + Paclitaxel (N=101)											
CYCLE 1 DAY 1/30 MIN POST DOSE	0.5	84	0	322	84.5	26.3	309	31.7	325	93.0	530
CYCLE 1 DAY 15/ PREDOSE	336	78	0	94.0	20.8	22.1	91.5	23.9	93.3	39.4	148
CYCLE 2 DAY 1/ PREDOSE	672	92	0	143	53.4	37.3	130	54.1	145	12.8	339
CYCLE 3 DAY 1/ PREDOSE	1344	84	0	214	72.2	33.7	200	41.1	215	74.2	369
CYCLE 4 DAY 1/ PREDOSE	2016	80	0	253	92.3	36.5	231	52.3	259	21.9	464
CYCLE 8 DAY 1/ PREDOSE	4704	46	0	339	93.5	27.6	327	27.6	328	179	582
CYCLE 12 DAY 1/ PREDOSE	7392	21	0	387	121	31.2	371	30.5	349	242	643
CYCLE 16 DAY 1/ PREDOSE	10080	12	0	431	161	37.3	402	42.4	454	170	772
STUDY DRUG DISCONTINUATION	99999	64	0	220	158	72.1	156	169.1	181	0.187	1000

NE = Not Evaluable LTR: Less than reportable, SD: Standard deviation, MQC: Minimum Quantifiable Concentration, CV:Co-efficient of Variation, Min:Minimum, Max:Maximum
LTR values at nominal time 0 were set to 0 and LTR values at nominal time > 0 were dropped.
For a given treatment and sampling time point:
If one-third or fewer values were LTR, then all summary statistics are reported.
If more than one-third values were LTR, then only the median and maximum are reported and other summary statistics are displayed as NR. MQC for Plasma Atezolizumab is 0.06 ug/mL.

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/PK_Final_CSR_TLG_CohortC/prod/program/t_pkc_atzo.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/PK_Final_CSR_TLG_CohortC/prod/output/t_pkc_atzo.out
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Summary of metabolite of ipatasertib (G-037720) Plasma Pharmacokinetic Concentrations by Nominal Time
PK Evaluable Population
Protocol: CO40016

Analyte: G-037720, Metabolite of RO5532961 (ng/mL)

Treatment Arm / Visit/Timepoint	Nominal Time (hr)	n	Number of LTRs	Mean	SD	CV % Mean	Geometric Mean	CV % Geometric Mean	Median	Minimum	Maximum
Ipatasertib + Atezolizumab + Paclitaxel (N=101)											
CYCLE 1 DAY 1/1-3 HRS POST DOSE	2	91	0	113	89.6	78.9	67.3	222.3	102	0.631	534
CYCLE 1 DAY 15/ PREDOSE	336	83	0	40.4	46.0	113.9	26.9	133.2	29.6	0.563	334
CYCLE 1 DAY 15/1-3 HRS POST DOSE	338	82	0	142	108	76.0	96.8	140.7	119	1.81	579
CYCLE 3 DAY 15/ PREDOSE	1680	66	0	31.5	26.0	82.6	24.5	87.0	26.5	1.29	181
CYCLE 3 DAY 15/2-4 HRS POST DOSE	1683	62	0	148	113	76.0	96.5	167.9	135	1.73	488

NE = Not Evaluable LTR: Less than reportable, SD: Standard deviation, MQC: Minimum Quantifiable Concentration, CV:Co-efficient of Variation, Min:Minimum, Max:Maximum
LTR values at nominal time 0 were set to 0 and LTR values at nominal time > 0 were dropped.
For a given treatment and sampling time point:
If one-third or fewer values were LTR, then all summary statistics are reported.
If more than one-third values were LTR, then only the median and maximum are reported and other summary statistics are displayed as NR. MQC for Plasma G-037720 is 0.5 ng/mL.

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/PK_Final_CSR_TLG_CohortC/prod/program/t_pkc_met.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/PK_Final_CSR_TLG_CohortC/prod/output/t_pkc_met.out
10JUL2023 19:54

Summary Statistics of Absolute Scores and Mean Change from Baseline by Visit for EORTC QLQ-C30: Global Health Status/Quality of Life, PRO Evaluable Population, Cohort C: TNBC
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=101)	
Visit	Value at Visit	Change from Baseline
Baseline		
n	101	
Mean (SD)	74.92 (21.26)	
95% CI	(70.72, 79.11)	
Median	83.33	
Min - Max	0.0 - 100.0	
Cycle 2 Day 1		
n	100	100
Mean (SD)	74.42 (19.58)	-0.42 (18.02)
95% CI	(70.53, 78.30)	(-3.99, 3.16)
Median	83.33	0.00
Min - Max	0.0 - 100.0	-50.0 - 41.7
Cycle 3 Day 1		
n	92	92
Mean (SD)	74.46 (14.97)	0.18 (18.32)
95% CI	(71.36, 77.56)	(-3.61, 3.98)
Median	75.00	0.00
Min - Max	41.7 - 100.0	-50.0 - 50.0
Cycle 4 Day 1		
n	84	84
Mean (SD)	71.83 (17.87)	-4.37 (22.83)
95% CI	(67.95, 75.70)	(-9.32, 0.59)
Median	75.00	0.00
Min - Max	0.0 - 100.0	-91.7 - 41.7

Baseline is defined as the last assessment prior to first dose of study treatment. PRO-Evaluable Population includes all randomized patients who have a baseline and at least 1 post-baseline assessment. An increase in scores from baseline indicates improvement.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_qs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_qs_cb_GL_C_QOL.out
08MAY2023 8:15

Summary Statistics of Absolute Scores and Mean Change from Baseline by Visit for EORTC QLQ-C30: Global Health Status/Quality of Life, PRO Evaluable Population, Cohort C: TNBC
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=101) Value at Visit	Change from Baseline
Cycle 5 Day 1		
n	65	65
Mean (SD)	70.38 (17.49)	-6.41 (20.19)
95% CI	(66.05, 74.72)	(-11.41, -1.41)
Median	66.67	0.00
Min - Max	16.7 - 100.0	-66.7 - 41.7
Cycle 6 Day 1		
n	61	61
Mean (SD)	68.99 (18.01)	-7.10 (21.24)
95% CI	(64.38, 73.60)	(-12.54, -1.66)
Median	66.67	0.00
Min - Max	8.3 - 100.0	-83.3 - 25.0
Cycle 7 Day 1		
n	54	54
Mean (SD)	72.07 (16.52)	-5.09 (18.20)
95% CI	(67.56, 76.58)	(-10.06, -0.12)
Median	70.83	0.00
Min - Max	16.7 - 100.0	-50.0 - 33.3
Cycle 8 Day 1		
n	50	50
Mean (SD)	73.33 (13.88)	-4.83 (21.24)
95% CI	(69.39, 77.28)	(-10.87, 1.20)
Median	66.67	0.00
Min - Max	33.3 - 100.0	-66.7 - 33.3

Baseline is defined as the last assessment prior to first dose of study treatment. PRO-Evaluable Population includes all randomized patients who have a baseline and at least 1 post-baseline assessment. An increase in scores from baseline indicates improvement.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_qs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_qs_cb_GL_C_QOL.out
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Summary Statistics of Absolute Scores and Mean Change from Baseline by Visit for EORTC QLQ-C30: Global Health Status/Quality of Life, PRO Evaluable Population, Cohort C: TNBC
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=101)	
	Value at Visit	Change from Baseline
Cycle 9 Day 1		
n	37	37
Mean (SD)	72.75 (15.91)	-7.66 (23.68)
95% CI	(67.44, 78.05)	(-15.55, 0.24)
Median	75.00	0.00
Min - Max	25.0 - 100.0	-75.0 - 33.3
Cycle 10 Day 1		
n	33	33
Mean (SD)	70.96 (11.62)	-7.07 (18.76)
95% CI	(66.84, 75.08)	(-13.72, -0.42)
Median	66.67	0.00
Min - Max	50.0 - 83.3	-50.0 - 16.7
Cycle 11 Day 1		
n	25	25
Mean (SD)	72.33 (12.20)	-6.00 (19.02)
95% CI	(67.30, 77.37)	(-13.85, 1.85)
Median	66.67	-8.33
Min - Max	50.0 - 100.0	-41.7 - 33.3
Cycle 12 Day 1		
n	23	23
Mean (SD)	75.72 (12.03)	-2.90 (18.57)
95% CI	(70.52, 80.93)	(-10.93, 5.13)
Median	75.00	0.00
Min - Max	58.3 - 100.0	-41.7 - 25.0

Baseline is defined as the last assessment prior to first dose of study treatment. PRO-Evaluable Population includes all randomized patients who have a baseline and at least 1 post-baseline assessment. An increase in scores from baseline indicates improvement.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_qs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_qs_cb_GL_C_QOL.out
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Summary Statistics of Absolute Scores and Mean Change from Baseline by Visit for EORTC QLQ-C30: Global Health Status/Quality of Life, PRO Evaluable Population, Cohort C: TNBC
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=101)	
	Value at Visit	Change from Baseline
Cycle 13 Day 1		
n	23	23
Mean (SD)	76.81 (12.80)	-1.45 (19.08)
95% CI	(71.28, 82.35)	(-9.70, 6.80)
Median	83.33	0.00
Min - Max	50.0 - 100.0	-50.0 - 33.3
Cycle 14 Day 1		
n	19	19
Mean (SD)	70.18 (16.97)	-7.89 (21.24)
95% CI	(62.00, 78.35)	(-18.13, 2.34)
Median	66.67	0.00
Min - Max	33.3 - 91.7	-66.7 - 16.7
Cycle 15 Day 1		
n	18	18
Mean (SD)	74.07 (19.78)	-5.09 (26.37)
95% CI	(64.24, 83.91)	(-18.21, 8.02)
Median	83.33	0.00
Min - Max	33.3 - 100.0	-66.7 - 33.3
Cycle 16 Day 1		
n	16	16
Mean (SD)	67.19 (18.12)	-11.98 (27.55)
95% CI	(57.53, 76.84)	(-26.66, 2.70)
Median	66.67	0.00
Min - Max	33.3 - 91.7	-58.3 - 33.3

Baseline is defined as the last assessment prior to first dose of study treatment. PRO-Evaluable Population includes all randomized patients who have a baseline and at least 1 post-baseline assessment. An increase in scores from baseline indicates improvement.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_qs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_qs_cb_GL_C_QOL.out
08MAY2023 8:15

Summary Statistics of Absolute Scores and Mean Change from Baseline by Visit for EORTC QLQ-C30: Global Health Status/Quality of Life, PRO Evaluable Population, Cohort C: TNBC
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=101)	
	Value at Visit	Change from Baseline
Cycle 17 Day 1		
n	13	13
Mean (SD)	67.95 (24.26)	-10.90 (32.16)
95% CI	(53.29, 82.61)	(-30.33, 8.54)
Median	75.00	-8.33
Min - Max	0.0 - 91.7	-100.0 - 33.3
Cycle 18 Day 1		
n	13	13
Mean (SD)	75.00 (15.21)	-3.85 (20.30)
95% CI	(65.81, 84.19)	(-16.12, 8.42)
Median	75.00	0.00
Min - Max	50.0 - 100.0	-41.7 - 25.0
Cycle 19 Day 1		
n	13	13
Mean (SD)	75.64 (16.12)	-3.21 (25.35)
95% CI	(65.90, 85.38)	(-18.53, 12.12)
Median	83.33	0.00
Min - Max	41.7 - 100.0	-58.3 - 33.3
Cycle 20 Day 1		
n	13	13
Mean (SD)	75.64 (15.76)	-3.21 (24.89)
95% CI	(66.12, 85.17)	(-18.25, 11.84)
Median	83.33	0.00
Min - Max	41.7 - 100.0	-58.3 - 33.3

Baseline is defined as the last assessment prior to first dose of study treatment. PRO-Evaluable Population includes all randomized patients who have a baseline and at least 1 post-baseline assessment. An increase in scores from baseline indicates improvement.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_qs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_qs_cb_GL_C_QOL.out
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Summary Statistics of Absolute Scores and Mean Change from Baseline by Visit for EORTC QLQ-C30: Global Health Status/Quality of Life, PRO Evaluable Population, Cohort C: TNBC
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=101)	
Visit	Value at Visit	Change from Baseline
Cycle 21 Day 1		
n	13	13
Mean (SD)	76.28 (15.16)	-2.56 (24.86)
95% CI	(67.12, 85.44)	(-17.59, 12.46)
Median	83.33	0.00
Min - Max	50.0 - 100.0	-50.0 - 33.3
Cycle 22 Day 1		
n	13	13
Mean (SD)	66.67 (24.30)	-12.18 (32.92)
95% CI	(51.98, 81.35)	(-32.07, 7.71)
Median	66.67	0.00
Min - Max	0.0 - 100.0	-100.0 - 33.3
Cycle 23 Day 1		
n	11	11
Mean (SD)	81.06 (12.41)	3.03 (24.23)
95% CI	(72.72, 89.40)	(-13.25, 19.31)
Median	83.33	8.33
Min - Max	58.3 - 100.0	-41.7 - 41.7
Cycle 24 Day 1		
n	11	11
Mean (SD)	81.82 (12.26)	3.79 (24.54)
95% CI	(73.58, 90.05)	(-12.70, 20.27)
Median	83.33	0.00
Min - Max	66.7 - 100.0	-33.3 - 41.7

Baseline is defined as the last assessment prior to first dose of study treatment. PRO-Evaluable Population includes all randomized patients who have a baseline and at least 1 post-baseline assessment. An increase in scores from baseline indicates improvement.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_qs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_qs_cb_GL_C_QOL.out
08MAY2023 8:15

Summary Statistics of Absolute Scores and Mean Change from Baseline by Visit for EORTC QLQ-C30: Global Health Status/Quality of Life, PRO Evaluable Population, Cohort C: TNBC
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=101)	
	Value at Visit	Change from Baseline
Cycle 25 Day 1		
n	9	9
Mean (SD)	75.00 (11.79)	-4.63 (21.29)
95% CI	(65.94, 84.06)	(-21.00, 11.74)
Median	83.33	0.00
Min - Max	50.0 - 83.3	-33.3 - 33.3
Cycle 26 Day 1		
n	10	10
Mean (SD)	78.33 (13.15)	-0.83 (19.82)
95% CI	(68.93, 87.74)	(-15.01, 13.34)
Median	83.33	0.00
Min - Max	50.0 - 100.0	-33.3 - 33.3
Cycle 27 Day 1		
n	8	8
Mean (SD)	80.21 (12.55)	2.08 (26.63)
95% CI	(69.72, 90.70)	(-20.18, 24.35)
Median	83.33	4.17
Min - Max	66.7 - 100.0	-33.3 - 41.7
Cycle 28 Day 1		
n	6	6
Mean (SD)	76.39 (11.08)	1.39 (23.81)
95% CI	(64.76, 88.01)	(-23.60, 26.38)
Median	83.33	4.17
Min - Max	58.3 - 83.3	-33.3 - 33.3

Baseline is defined as the last assessment prior to first dose of study treatment. PRO-Evaluable Population includes all randomized patients who have a baseline and at least 1 post-baseline assessment. An increase in scores from baseline indicates improvement.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_qs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_qs_cb_GL_C_QOL.out
08MAY2023 8:15

Summary Statistics of Absolute Scores and Mean Change from Baseline by Visit for EORTC QLQ-C30: Global Health Status/Quality of Life, PRO Evaluable Population, Cohort C: TNBC
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=101)	
Visit	Value at Visit	Change from Baseline
Cycle 29 Day 1		
n	7	7
Mean (SD)	76.19 (10.12)	-1.19 (28.64)
95% CI	(66.83, 85.55)	(-27.68, 25.29)
Median	75.00	0.00
Min - Max	66.7 - 91.7	-33.3 - 41.7
Cycle 30 Day 1		
n	5	5
Mean (SD)	73.33 (14.91)	3.33 (24.01)
95% CI	(54.82, 91.84)	(-26.48, 33.14)
Median	83.33	8.33
Min - Max	50.0 - 83.3	-33.3 - 33.3
Cycle 31 Day 1		
n	3	3
Mean (SD)	77.78 (9.62)	22.22 (12.73)
95% CI	(53.87, 101.68)	(-9.40, 53.84)
Median	83.33	25.00
Min - Max	66.7 - 83.3	8.3 - 33.3
Cycle 32 Day 1		
n	4	4
Mean (SD)	72.92 (18.48)	10.42 (23.94)
95% CI	(43.51, 102.32)	(-27.67, 48.50)
Median	75.00	8.33
Min - Max	50.0 - 91.7	-16.7 - 41.7

Baseline is defined as the last assessment prior to first dose of study treatment. PRO-Evaluable Population includes all randomized patients who have a baseline and at least 1 post-baseline assessment. An increase in scores from baseline indicates improvement.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_qs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_qs_cb_GL_C_QOL.out
08MAY2023 8:15

Summary Statistics of Absolute Scores and Mean Change from Baseline by Visit for EORTC QLQ-C30: Global Health Status/Quality of Life, PRO Evaluable Population, Cohort C: TNBC
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=101)	
	Value at Visit	Change from Baseline
Cycle 33 Day 1		
n	3	3
Mean (SD)	75.00 (22.05)	16.67 (22.05)
95% CI	(20.23, 129.77)	(-38.10, 71.44)
Median	83.33	8.33
Min - Max	50.0 - 91.7	0.0 - 41.7
Cycle 34 Day 1		
n	3	3
Mean (SD)	75.00 (25.00)	16.67 (30.05)
95% CI	(12.90, 137.10)	(-57.97, 91.31)
Median	75.00	8.33
Min - Max	50.0 - 100.0	-8.3 - 50.0
Cycle 35 Day 1		
n	3	3
Mean (SD)	72.22 (19.25)	13.89 (17.35)
95% CI	(24.41, 120.03)	(-29.20, 56.98)
Median	83.33	8.33
Min - Max	50.0 - 83.3	0.0 - 33.3
Cycle 36 Day 1		
n	2	2
Mean (SD)	87.50 (5.89)	20.83 (29.46)
95% CI	(34.56, 140.44)	(-243.88, 285.55)
Median	87.50	20.83
Min - Max	83.3 - 91.7	0.0 - 41.7

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_qs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_qs_cb_GL_C_QOL.out
08MAY2023 8:15

Summary Statistics of Absolute Scores and Mean Change from Baseline by Visit for EORTC QLQ-C30: Global Health Status/Quality of Life, PRO Evaluable Population, Cohort C: TNBC
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=101)	
Visit	Value at Visit	Change from Baseline
Cycle 37 Day 1		
n	2	2
Mean (SD)	83.33 (0.00)	16.67 (23.57)
95% CI	(83.33, 83.33)	(-195.10, 228.44)
Median	83.33	16.67
Min - Max	83.3 - 83.3	0.0 - 33.3
Cycle 38 Day 1		
n	2	2
Mean (SD)	83.33 (0.00)	16.67 (23.57)
95% CI	(83.33, 83.33)	(-195.10, 228.44)
Median	83.33	16.67
Min - Max	83.3 - 83.3	0.0 - 33.3
Cycle 39 Day 1		
n	2	2
Mean (SD)	91.67 (11.79)	25.00 (35.36)
95% CI	(-14.22, 197.55)	(-292.66, 342.66)
Median	91.67	25.00
Min - Max	83.3 - 100.0	0.0 - 50.0
Cycle 40 Day 1		
n	1	1
Mean (SD)	83.33 (NE)	33.33 (NE)
95% CI	NE	NE
Median	83.33	33.33
Min - Max	83.3 - 83.3	33.3 - 33.3

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_qs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_qs_cb_GL_C_QOL.out
08MAY2023 8:15

Summary Statistics of Absolute Scores and Mean Change from Baseline by Visit for EORTC QLQ-C30: Global Health Status/Quality of Life, PRO Evaluable Population, Cohort C: TNBC
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=101)	
Visit	Value at Visit	Change from Baseline
Cycle 41 Day 1		
n	1	1
Mean (SD)	100.00 (NE)	50.00 (NE)
95% CI	NE	NE
Median	100.00	50.00
Min - Max	100.0 - 100.0	50.0 - 50.0
Cycle 42 Day 1		
n	1	1
Mean (SD)	91.67 (NE)	41.67 (NE)
95% CI	NE	NE
Median	91.67	41.67
Min - Max	91.7 - 91.7	41.7 - 41.7
Cycle 43 Day 1		
n	1	1
Mean (SD)	91.67 (NE)	41.67 (NE)
95% CI	NE	NE
Median	91.67	41.67
Min - Max	91.7 - 91.7	41.7 - 41.7
Cycle 44 Day 1		
n	1	1
Mean (SD)	100.00 (NE)	50.00 (NE)
95% CI	NE	NE
Median	100.00	50.00
Min - Max	100.0 - 100.0	50.0 - 50.0

Baseline is defined as the last assessment prior to first dose of study treatment. PRO-Evaluable Population includes all randomized patients who have a baseline and at least 1 post-baseline assessment. An increase in scores from baseline indicates improvement.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_qs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_qs_cb_GL_C_QOL.out
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Summary Statistics of Absolute Scores and Mean Change from Baseline by Visit for EORTC QLQ-C30: Global Health Status/Quality of Life, PRO Evaluable Population, Cohort C: TNBC
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=101)	
Visit	Value at Visit	Change from Baseline
Study Drug Discontinuation		
n	84	84
Mean (SD)	65.08 (24.39)	-9.82 (26.26)
95% CI	(59.79, 70.37)	(-15.52, -4.12)
Median	66.67	-8.33
Min - Max	0.0 - 100.0	-83.3 - 50.0
Long Term Follow Up 3 Months		
n	50	50
Mean (SD)	68.17 (20.87)	-7.17 (24.92)
95% CI	(62.23, 74.10)	(-14.25, -0.09)
Median	66.67	-8.33
Min - Max	0.0 - 100.0	-66.7 - 58.3
Long Term Follow Up 6 Months		
n	43	43
Mean (SD)	70.54 (19.87)	-5.43 (30.09)
95% CI	(64.43, 76.66)	(-14.69, 3.84)
Median	66.67	-8.33
Min - Max	16.7 - 100.0	-83.3 - 66.7
Long Term Follow Up 9 Months		
n	38	38
Mean (SD)	69.52 (22.11)	-5.48 (24.06)
95% CI	(62.25, 76.79)	(-13.39, 2.43)
Median	75.00	-8.33
Min - Max	0.0 - 100.0	-66.7 - 58.3

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Summary Statistics of Absolute Scores and Mean Change from Baseline by Visit for EORTC QLQ-C30: Global Health Status/Quality of Life, PRO Evaluable Population, Cohort C: TNBC
Protocol: CO40016

	Ipatasertib + Atezolizumab + Paclitaxel (N=101)	
Visit	Value at Visit	Change from Baseline
Long Term Follow Up 12 Months		
n	31	31
Mean (SD)	69.89 (20.49)	-6.99 (21.42)
95% CI	(62.38, 77.41)	(-14.85, 0.87)
Median	66.67	-8.33
Min - Max	33.3 - 100.0	-41.7 - 50.0
Long Term Follow Up 15 Months		
n	18	18
Mean (SD)	79.63 (16.47)	0.93 (15.89)
95% CI	(71.44, 87.82)	(-6.97, 8.83)
Median	83.33	0.00
Min - Max	50.0 - 100.0	-16.7 - 41.7
Long Term Follow Up 18 Months		
n	12	12
Mean (SD)	83.33 (15.49)	2.08 (7.22)
95% CI	(73.49, 93.17)	(-2.50, 6.67)
Median	83.33	0.00
Min - Max	41.7 - 100.0	-8.3 - 16.7
Long Term Follow Up 21 Months		
n	2	2
Mean (SD)	91.67 (11.79)	0.00 (0.00)
95% CI	(-14.22, 197.55)	(0.00, 0.00)
Median	91.67	0.00
Min - Max	83.3 - 100.0	0.0 - 0.0

Baseline is defined as the last assessment prior to first dose of study treatment. PRO-Evaluable Population includes all randomized patients who have a baseline and at least 1 post-baseline assessment. An increase in scores from baseline indicates improvement.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Baseline	
Number of subjects expected to complete	102
All questions completed	100 (98.0%)
At least one question completed	102 (100%)
Did not complete any questions	0
Cycle 2 Day 1	
Number of subjects expected to complete	101
All questions completed	96 (95.0%)
At least one question completed	100 (99.0%)

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 2 Day 1	
Did not complete any questions	1 (1.0%)
Other	1 (100%)
Cycle 3 Day 1	
Number of subjects expected to complete	95
All questions completed	91 (95.8%)
At least one question completed	92 (96.8%)
Did not complete any questions	3 (3.2%)
Patient Refused	1 (33.3%)

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 3 Day 1	
Other	1 (33.3%)
Missing Reason	1 (33.3%)
Cycle 4 Day 1	
Number of subjects expected to complete	87
All questions completed	82 (94.3%)
At least one question completed	84 (96.6%)
Did not complete any questions	3 (3.4%)
Measure not Administered	1 (33.3%)

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 4 Day 1	
Other	2 (66.7%)
Cycle 5 Day 1	
Number of subjects expected to complete	72
All questions completed	63 (87.5%)
At least one question completed	65 (90.3%)
Did not complete any questions	7 (9.7%)
Patient Refused	1 (14.3%)
Measure not Administered	1 (14.3%)

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 5 Day 1	
Other	4 (57.1%)
Missing Reason	1 (14.3%)
Cycle 6 Day 1	
Number of subjects expected to complete	66
All questions completed	60 (90.9%)
At least one question completed	61 (92.4%)
Did not complete any questions	5 (7.6%)
Patient Refused	1 (20.0%)

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 6 Day 1	
Other	4 (80.0%)
Cycle 7 Day 1	
Number of subjects expected to complete	56
All questions completed	53 (94.6%)
At least one question completed	54 (96.4%)
Did not complete any questions	2 (3.6%)
Patient Refused	1 (50.0%)
Other	1 (50.0%)

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 8 Day 1	
Number of subjects expected to complete	52
All questions completed	49 (94.2%)
At least one question completed	50 (96.2%)
Did not complete any questions	2 (3.8%)
Measure not Administered	1 (50.0%)
Other	1 (50.0%)

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 9 Day 1	
Number of subjects expected to complete	38
All questions completed	35 (92.1%)
At least one question completed	37 (97.4%)
Did not complete any questions	1 (2.6%)
Measure not Administered	1 (100%)
Cycle 10 Day 1	
Number of subjects expected to complete	34
All questions completed	33 (97.1%)

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 10 Day 1	
At least one question completed	33 (97.1%)
Did not complete any questions	1 (2.9%)
Measure not Administered	1 (100%)
Cycle 11 Day 1	
Number of subjects expected to complete	27
All questions completed	25 (92.6%)
At least one question completed	25 (92.6%)
Did not complete any questions	2 (7.4%)

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 11 Day 1	
Patient Refused	1 (50.0%)
Other	1 (50.0%)
Cycle 12 Day 1	
Number of subjects expected to complete	25
All questions completed	22 (88.0%)
At least one question completed	23 (92.0%)
Did not complete any questions	2 (8.0%)
Other	2 (100%)

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 13 Day 1	
Number of subjects expected to complete	23
All questions completed	22 (95.7%)
At least one question completed	23 (100%)
Did not complete any questions	0
Cycle 14 Day 1	
Number of subjects expected to complete	22
All questions completed	17 (77.3%)

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 14 Day 1	
At least one question completed	19 (86.4%)
Did not complete any questions	3 (13.6%)
Measure not Administered	1 (33.3%)
Other	2 (66.7%)
Cycle 15 Day 1	
Number of subjects expected to complete	18
All questions completed	18 (100%)
At least one question completed	18 (100%)

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Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 15 Day 1	
Did not complete any questions	0
Cycle 16 Day 1	
Number of subjects expected to complete	16
All questions completed	15 (93.8%)
At least one question completed	16 (100%)
Did not complete any questions	0
Cycle 17 Day 1	
Number of subjects expected to complete	13
All questions completed	13 (100%)

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 17 Day 1	
At least one question completed	13 (100%)
Did not complete any questions	0
Cycle 18 Day 1	
Number of subjects expected to complete	13
All questions completed	13 (100%)
At least one question completed	13 (100%)
Did not complete any questions	0

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 19 Day 1	
Number of subjects expected to complete	13
All questions completed	13 (100%)
At least one question completed	13 (100%)
Did not complete any questions	0
Cycle 20 Day 1	
Number of subjects expected to complete	13
All questions completed	13 (100%)
At least one question completed	13 (100%)

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 20 Day 1	
Did not complete any questions	0
Cycle 21 Day 1	
Number of subjects expected to complete	13
All questions completed	13 (100%)
At least one question completed	13 (100%)
Did not complete any questions	0
Cycle 22 Day 1	
Number of subjects expected to complete	13

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 22 Day 1	
All questions completed	13 (100%)
At least one question completed	13 (100%)
Did not complete any questions	0
Cycle 23 Day 1	
Number of subjects expected to complete	12
All questions completed	11 (91.7%)
At least one question completed	11 (91.7%)
Did not complete any questions	1 (8.3%)

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 23 Day 1	
Other	1 (100%)
Cycle 24 Day 1	
Number of subjects expected to complete	11
All questions completed	11 (100%)
At least one question completed	11 (100%)
Did not complete any questions	0
Cycle 25 Day 1	
Number of subjects expected to complete	10
All questions completed	9 (90.0%)

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_qs_comp.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_qs_comp_C30INST_C_IT.out

Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 25 Day 1	
At least one question completed	9 (90.0%)
Did not complete any questions	1 (10.0%)
Other	1 (100%)
Cycle 26 Day 1	
Number of subjects expected to complete	10
All questions completed	10 (100%)
At least one question completed	10 (100%)
Did not complete any questions	0

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 27 Day 1	
Number of subjects expected to complete	9
All questions completed	8 (88.9%)
At least one question completed	8 (88.9%)
Did not complete any questions	1 (11.1%)
Missing Reason	1 (100%)
Cycle 28 Day 1	
Number of subjects expected to complete	7

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 28 Day 1	
All questions completed	6 (85.7%)
At least one question completed	6 (85.7%)
Did not complete any questions	1 (14.3%)
Missing Reason	1 (100%)
Cycle 29 Day 1	
Number of subjects expected to complete	7
All questions completed	7 (100%)
At least one question completed	7 (100%)

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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 29 Day 1	
Did not complete any questions	0
Cycle 30 Day 1	
Number of subjects expected to complete	5
All questions completed	5 (100%)
At least one question completed	5 (100%)
Did not complete any questions	0
Cycle 31 Day 1	
Number of subjects expected to complete	4
All questions completed	3 (75.0%)

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 31 Day 1	
At least one question completed	3 (75.0%)
Did not complete any questions	1 (25.0%)
Missing Reason	1 (100%)
Cycle 32 Day 1	
Number of subjects expected to complete	4
All questions completed	4 (100%)
At least one question completed	4 (100%)
Did not complete any questions	0

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 33 Day 1	
Number of subjects expected to complete	3
All questions completed	3 (100%)
At least one question completed	3 (100%)
Did not complete any questions	0
Cycle 34 Day 1	
Number of subjects expected to complete	3
All questions completed	3 (100%)

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 34 Day 1	
At least one question completed	3 (100%)
Did not complete any questions	0
Cycle 35 Day 1	
Number of subjects expected to complete	3
All questions completed	3 (100%)
At least one question completed	3 (100%)
Did not complete any questions	0
Cycle 36 Day 1	
Number of subjects expected to complete	2

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 36 Day 1	
All questions completed	2 (100%)
At least one question completed	2 (100%)
Did not complete any questions	0
Cycle 37 Day 1	
Number of subjects expected to complete	2
All questions completed	2 (100%)
At least one question completed	2 (100%)
Did not complete any questions	0

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 38 Day 1	
Number of subjects expected to complete	2
All questions completed	2 (100%)
At least one question completed	2 (100%)
Did not complete any questions	0
Cycle 39 Day 1	
Number of subjects expected to complete	2
All questions completed	2 (100%)

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 39 Day 1	
At least one question completed	2 (100%)
Did not complete any questions	0
Cycle 40 Day 1	
Number of subjects expected to complete	1
All questions completed	1 (100%)
At least one question completed	1 (100%)
Did not complete any questions	0
Cycle 41 Day 1	
Number of subjects expected to complete	1

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 41 Day 1	
All questions completed	1 (100%)
At least one question completed	1 (100%)
Did not complete any questions	0
Cycle 42 Day 1	
Number of subjects expected to complete	1
All questions completed	1 (100%)
At least one question completed	1 (100%)
Did not complete any questions	0

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 43 Day 1	
Number of subjects expected to complete	1
All questions completed	1 (100%)
At least one question completed	1 (100%)
Did not complete any questions	0
Cycle 44 Day 1	
Number of subjects expected to complete	1
All questions completed	1 (100%)

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Cycle 44 Day 1	
At least one question completed	1 (100%)
Did not complete any questions	0
Study Drug Discontinuation	
Number of subjects expected to complete	93
All questions completed	80 (86.0%)
At least one question completed	84 (90.3%)
Did not complete any questions	9 (9.7%)
Patient Refused	3 (33.3%)

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Study Drug Discontinuation	
Measure not Administered	3 (33.3%)
Other	3 (33.3%)
Long Term Follow Up 3 Months	
Number of subjects expected to complete	79
All questions completed	0
At least one question completed	50 (63.3%)
Did not complete any questions	29 (36.7%)
Patient Refused	8 (27.6%)

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Long Term Follow Up 3 Months	
Measure not Administered	8 (27.6%)
Other	8 (27.6%)
Missing Reason	5 (17.2%)
Long Term Follow Up 6 Months	
Number of subjects expected to complete	69
All questions completed	0
At least one question completed	43 (62.3%)
Did not complete any questions	26 (37.7%)

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Long Term Follow Up 6 Months	
Patient Refused	7 (26.9%)
Measure not Administered	5 (19.2%)
Other	10 (38.5%)
Missing Reason	4 (15.4%)
Long Term Follow Up 9 Months	
Number of subjects expected to complete	57
All questions completed	0
At least one question completed	38 (66.7%)

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Long Term Follow Up 9 Months	
Did not complete any questions	19 (33.3%)
Patient Refused	3 (15.8%)
Measure not Administered	5 (26.3%)
Other	8 (42.1%)
Missing Reason	3 (15.8%)
Long Term Follow Up 12 Months	
Number of subjects expected to complete	46
All questions completed	0

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Long Term Follow Up 12 Months	
At least one question completed	31 (67.4%)
Did not complete any questions	15 (32.6%)
Patient Refused	2 (13.3%)
Measure not Administered	4 (26.7%)
Other	7 (46.7%)
Missing Reason	2 (13.3%)
Long Term Follow Up 15 Months	
Number of subjects expected to complete	31

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Long Term Follow Up 15 Months	
All questions completed	0
At least one question completed	18 (58.1%)
Did not complete any questions	13 (41.9%)
Measure not Administered	3 (23.1%)
Other	6 (46.2%)
Missing Reason	4 (30.8%)
Long Term Follow Up 18 Months	
Number of subjects expected to complete	20

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Long Term Follow Up 18 Months	
All questions completed	0
At least one question completed	12 (60.0%)
Did not complete any questions	8 (40.0%)
Measure not Administered	2 (25.0%)
Other	2 (25.0%)
Missing Reason	4 (50.0%)
Long Term Follow Up 21 Months	
Number of subjects expected to complete	8

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Questionnaire Completion Rate by Visit for EORTC QLQ-C30 in Instrument Level, Instrument Compliance, Cohort C: TNBC, Intent-to-Treat Population
Protocol: CO40016

Visit	Ipatasertib + Atezolizumab + Paclitaxel (N=102)
Long Term Follow Up 21 Months	
All questions completed	0
At least one question completed	2 (25.0%)
Did not complete any questions	6 (75.0%)
Measure not Administered	1 (16.7%)
Other	2 (33.3%)
Missing Reason	3 (50.0%)

Baseline is defined as the last assessment prior to first dose of study treatment (i.e. Baseline assessment was Cycle 1 Day 1). The EORTC QLQ-C30 should be completed on Day 1 of each cycle and at the treatment discontinuation visit unless patient discontinued treatment due to death or lost of follow-up.
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Baseline				
n	86		164	
Mean (SD)	78.2 (9.8)		76.5 (9.3)	
Median	77.5		75.0	
Min - Max	60 - 110		54 - 105	
Cycle 1 Day 1				
PRE PAC INFUSION				
n	84	83	145	144
Mean (SD)	75.3 (9.7)	-2.7 (9.0)	75.9 (8.9)	-0.7 (8.9)
Median	76.0	-3.0	76.0	0.0
Min - Max	46 - 100	-23 - 25	54 - 96	-28 - 24
AFTER PAC INFUSION				
n	84	83	157	156
Mean (SD)	75.9 (10.4)	-2.3 (10.7)	77.1 (9.4)	0.9 (10.0)
Median	77.5	-1.0	77.0	1.0
Min - Max	51 - 100	-50 - 21	60 - 107	-26 - 37
Cycle 1 Day 8				
PRE PAC INFUSION				
n	86	85	160	158
Mean (SD)	73.7 (10.1)	-4.3 (10.2)	74.3 (9.6)	-2.3 (11.1)
Median	73.5	-4.0	75.0	-2.0
Min - Max	41 - 99	-33 - 24	50 - 124	-38 - 39
AFTER PAC INFUSION				
n	78	77	148	146
Mean (SD)	74.5 (9.3)	-3.9 (10.0)	74.8 (8.9)	-1.8 (11.3)
Median	75.0	-2.0	75.0	0.0
Min - Max	52 - 95	-27 - 16	57 - 100	-40 - 30
Cycle 1 Day 15				
PRE PAC INFUSION				
n	81	80	148	146
Mean (SD)	73.0 (8.5)	-4.7 (8.6)	74.3 (10.0)	-2.2 (10.4)
Median	73.0	-5.0	74.0	-1.0
Min - Max	53 - 93	-30 - 14	51 - 99	-35 - 26
AFTER PAC INFUSION				
n	74	73	133	132
Mean (SD)	72.8 (8.5)	-5.3 (10.5)	75.3 (9.2)	-1.3 (10.9)
Median	72.0	-4.0	77.0	-0.5
Min - Max	44 - 91	-40 - 16	50 - 100	-36 - 20
Cycle 2 Day 1				
PRE PAC INFUSION				
n	78	77	161	159
Mean (SD)	73.4 (8.3)	-4.7 (10.6)	74.6 (10.9)	-1.9 (10.7)
Median	73.5	-2.0	74.0	-1.0
Min - Max	55 - 92	-40 - 11	48 - 116	-30 - 30

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	74	73	153	152
Mean (SD)	74.9 (9.5)	-3.6 (10.0)	76.2 (10.2)	0.1 (10.9)
Median	75.0	-2.0	76.0	0.0
Min - Max	50 - 98	-37 - 19	56 - 110	-30 - 36
Cycle 2 Day 8				
PRE PAC INFUSION				
n	79	78	153	151
Mean (SD)	74.4 (9.3)	-4.0 (10.5)	73.5 (9.2)	-3.0 (11.1)
Median	75.0	-2.5	72.0	-1.0
Min - Max	52 - 100	-45 - 19	53 - 99	-37 - 24
AFTER PAC INFUSION				
n	72	71	149	147
Mean (SD)	72.0 (10.0)	-6.7 (10.7)	74.8 (9.6)	-1.8 (11.3)
Median	70.0	-5.0	74.0	0.0
Min - Max	52 - 114	-43 - 10	49 - 108	-31 - 46
Cycle 2 Day 15				
PRE PAC INFUSION				
n	77	76	148	146
Mean (SD)	73.6 (10.4)	-4.3 (11.0)	73.5 (10.7)	-2.9 (11.3)
Median	75.0	-1.5	74.0	-2.0
Min - Max	49 - 108	-36 - 15	48 - 120	-31 - 30
AFTER PAC INFUSION				
n	71	70	146	144
Mean (SD)	72.4 (8.9)	-5.2 (9.6)	73.3 (8.4)	-3.2 (10.6)
Median	73.0	-3.0	73.0	-2.5
Min - Max	53 - 96	-35 - 16	51 - 92	-40 - 20
Cycle 3 Day 1				
PRE PAC INFUSION				
n	75	74	143	141
Mean (SD)	74.0 (9.8)	-4.0 (9.8)	73.4 (9.4)	-3.0 (10.3)
Median	75.0	-3.0	72.0	-1.0
Min - Max	53 - 97	-33 - 21	52 - 95	-30 - 20
AFTER PAC INFUSION				
n	70	69	134	132
Mean (SD)	75.6 (9.6)	-3.5 (10.9)	74.4 (10.7)	-2.3 (12.1)
Median	75.0	-3.0	75.0	-1.0
Min - Max	58 - 100	-36 - 23	52 - 106	-30 - 26
Cycle 3 Day 8				
PRE PAC INFUSION				
n	73	72	140	138
Mean (SD)	73.0 (9.4)	-5.2 (9.9)	74.3 (9.5)	-2.0 (11.1)
Median	74.0	-4.5	74.5	-0.5
Min - Max	43 - 93	-30 - 18	44 - 100	-31 - 30

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	69	68	138	136
Mean (SD)	72.6 (9.5)	-5.8 (10.2)	74.2 (8.8)	-2.4 (9.8)
Median	72.0	-4.0	74.5	0.0
Min - Max	54 - 105	-38 - 12	54 - 103	-28 - 23
Cycle 3 Day 15				
PRE PAC INFUSION				
n	67	66	136	135
Mean (SD)	73.3 (8.2)	-5.2 (10.3)	73.7 (10.4)	-2.9 (11.4)
Median	73.0	-5.0	74.0	-2.0
Min - Max	57 - 98	-38 - 23	43 - 109	-45 - 35
AFTER PAC INFUSION				
n	67	66	129	128
Mean (SD)	74.1 (9.0)	-4.7 (10.1)	73.4 (9.3)	-3.3 (11.3)
Median	75.0	-3.0	75.0	-2.0
Min - Max	55 - 100	-35 - 15	52 - 104	-40 - 23
Cycle 4 Day 1				
PRE PAC INFUSION				
n	69	68	132	130
Mean (SD)	72.9 (8.5)	-5.1 (9.5)	73.8 (9.5)	-2.9 (11.3)
Median	75.0	-5.0	73.5	-2.5
Min - Max	54 - 99	-33 - 15	48 - 107	-45 - 22
AFTER PAC INFUSION				
n	65	64	122	120
Mean (SD)	72.1 (9.3)	-6.0 (9.1)	75.7 (9.3)	-0.5 (11.2)
Median	72.0	-5.5	75.0	0.0
Min - Max	48 - 99	-34 - 9	59 - 114	-30 - 44
Cycle 4 Day 8				
PRE PAC INFUSION				
n	68	67	127	126
Mean (SD)	72.7 (9.4)	-5.3 (10.6)	72.4 (8.1)	-4.4 (9.8)
Median	74.0	-4.0	70.0	-4.0
Min - Max	49 - 100	-37 - 25	54 - 92	-40 - 16
AFTER PAC INFUSION				
n	65	64	120	119
Mean (SD)	74.0 (8.9)	-4.3 (9.9)	74.3 (9.1)	-2.3 (10.6)
Median	75.0	-4.0	74.0	0.0
Min - Max	47 - 92	-37 - 15	54 - 96	-30 - 18
Cycle 4 Day 15				
PRE PAC INFUSION				
n	67	66	126	124
Mean (SD)	72.5 (12.5)	-6.2 (17.1)	72.6 (9.7)	-4.2 (11.8)
Median	74.0	-3.0	72.0	-5.0
Min - Max	7 - 107	-103 - 23	41 - 98	-37 - 28

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	66	65	115	113
Mean (SD)	72.8 (9.7)	-6.1 (11.0)	74.5 (10.5)	-1.9 (11.5)
Median	73.5	-3.0	75.0	-1.0
Min - Max	45 - 96	-40 - 19	50 - 100	-31 - 28
Cycle 5 Day 1				
PRE PAC INFUSION				
n	61	60	103	101
Mean (SD)	72.1 (9.0)	-6.9 (10.2)	74.6 (9.7)	-2.0 (10.7)
Median	74.0	-5.0	75.0	0.0
Min - Max	51 - 94	-37 - 13	54 - 103	-24 - 20
AFTER PAC INFUSION				
n	57	56	96	94
Mean (SD)	74.0 (9.7)	-5.3 (9.2)	74.9 (12.6)	-1.1 (13.6)
Median	75.0	-3.0	76.0	0.0
Min - Max	55 - 97	-31 - 19	7 - 110	-54 - 40
Cycle 5 Day 8				
PRE PAC INFUSION				
n	53	52	96	95
Mean (SD)	73.1 (7.6)	-6.0 (11.4)	73.4 (8.9)	-3.2 (11.2)
Median	73.0	-4.5	74.0	-3.0
Min - Max	57 - 90	-40 - 19	51 - 100	-35 - 20
AFTER PAC INFUSION				
n	52	51	89	88
Mean (SD)	72.2 (9.3)	-6.3 (13.0)	73.5 (9.5)	-2.7 (11.3)
Median	72.0	-4.0	73.0	-1.0
Min - Max	50 - 90	-54 - 19	51 - 102	-29 - 32
Cycle 5 Day 15				
PRE PAC INFUSION				
n	56	55	91	90
Mean (SD)	73.4 (7.9)	-5.5 (10.5)	73.2 (10.2)	-2.6 (10.9)
Median	72.0	-5.0	74.0	-2.0
Min - Max	57 - 104	-33 - 15	48 - 113	-32 - 30
AFTER PAC INFUSION				
n	52	51	78	77
Mean (SD)	73.3 (9.2)	-5.4 (12.3)	74.4 (9.9)	-1.3 (10.5)
Median	73.5	-4.0	75.5	0.0
Min - Max	54 - 95	-40 - 18	53 - 100	-33 - 30
Cycle 6 Day 1				
PRE PAC INFUSION				
n	56	55	91	90
Mean (SD)	72.1 (9.1)	-6.7 (11.1)	73.6 (9.7)	-2.1 (11.1)
Median	73.5	-4.0	75.0	-1.0
Min - Max	43 - 92	-38 - 18	50 - 105	-36 - 23

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	49	48	85	84
Mean (SD)	72.4 (11.1)	-6.8 (11.8)	75.6 (9.6)	0.5 (11.2)
Median	75.0	-3.0	74.0	0.0
Min - Max	47 - 105	-40 - 17	52 - 110	-34 - 30
Cycle 6 Day 8				
PRE PAC INFUSION				
n	49	48	87	86
Mean (SD)	73.0 (8.9)	-6.0 (10.8)	72.8 (9.1)	-3.1 (11.0)
Median	73.0	-5.0	73.0	-2.5
Min - Max	56 - 101	-39 - 17	41 - 90	-36 - 27
AFTER PAC INFUSION				
n	48	47	83	82
Mean (SD)	73.2 (11.7)	-6.0 (11.5)	73.9 (9.0)	-1.2 (11.6)
Median	70.5	-4.0	74.0	-2.0
Min - Max	49 - 105	-35 - 16	54 - 91	-25 - 26
Cycle 6 Day 15				
PRE PAC INFUSION				
n	49	48	84	83
Mean (SD)	73.0 (9.4)	-6.8 (12.3)	73.0 (8.6)	-2.3 (10.9)
Median	75.0	-6.0	74.0	-1.0
Min - Max	47 - 90	-45 - 14	49 - 100	-28 - 30
AFTER PAC INFUSION				
n	47	46	80	79
Mean (SD)	72.8 (10.1)	-6.5 (10.7)	73.5 (8.4)	-1.7 (10.4)
Median	74.0	-6.5	72.0	0.0
Min - Max	44 - 97	-31 - 17	58 - 100	-26 - 26
Cycle 7 Day 1				
PRE PAC INFUSION				
n	42	41	76	75
Mean (SD)	74.2 (10.8)	-5.6 (11.3)	74.8 (8.1)	-1.8 (10.6)
Median	73.0	-3.0	74.0	-1.0
Min - Max	45 - 102	-30 - 18	54 - 90	-25 - 21
AFTER PAC INFUSION				
n	37	36	67	66
Mean (SD)	74.0 (9.2)	-4.8 (9.9)	76.4 (10.1)	0.3 (11.9)
Median	75.0	-5.0	78.0	0.5
Min - Max	59 - 93	-32 - 12	55 - 107	-28 - 37
Cycle 7 Day 8				
PRE PAC INFUSION				
n	35	34	67	66
Mean (SD)	74.4 (10.7)	-4.6 (11.9)	74.4 (8.4)	-2.6 (11.2)
Median	74.0	-2.0	76.0	-2.0
Min - Max	58 - 110	-33 - 32	47 - 91	-27 - 20

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	34	33	63	62
Mean (SD)	73.0 (9.7)	-6.3 (11.1)	75.5 (10.0)	-0.6 (11.3)
Median	72.5	-5.0	78.0	-3.5
Min - Max	44 - 99	-35 - 15	53 - 106	-20 - 36
Cycle 7 Day 15				
PRE PAC INFUSION				
n	34	33	69	68
Mean (SD)	71.0 (9.7)	-7.6 (9.1)	74.2 (9.2)	-2.2 (10.2)
Median	72.0	-6.0	75.0	-1.0
Min - Max	51 - 98	-25 - 12	52 - 91	-28 - 20
AFTER PAC INFUSION				
n	34	33	66	65
Mean (SD)	72.4 (9.0)	-6.2 (9.4)	74.0 (9.5)	-1.7 (10.9)
Median	74.5	-4.0	73.0	-1.0
Min - Max	47 - 89	-32 - 9	55 - 100	-21 - 30
Cycle 8 Day 1				
PRE PAC INFUSION				
n	33	32	70	69
Mean (SD)	74.1 (10.0)	-6.6 (9.8)	76.0 (9.8)	-0.4 (11.3)
Median	72.0	-5.0	75.5	0.0
Min - Max	54 - 96	-26 - 13	55 - 107	-34 - 30
AFTER PAC INFUSION				
n	27	26	63	62
Mean (SD)	72.8 (9.8)	-7.4 (10.7)	76.6 (10.2)	0.2 (12.1)
Median	72.0	-5.0	76.0	0.0
Min - Max	48 - 102	-36 - 10	53 - 126	-29 - 30
Cycle 8 Day 8				
PRE PAC INFUSION				
n	29	28	64	63
Mean (SD)	72.1 (8.6)	-8.1 (10.5)	74.5 (7.7)	-2.4 (11.2)
Median	72.0	-4.5	75.0	-1.0
Min - Max	53 - 91	-35 - 7	53 - 93	-26 - 21
AFTER PAC INFUSION				
n	27	26	60	59
Mean (SD)	70.0 (11.3)	-10.0 (11.0)	75.7 (7.5)	-0.2 (9.1)
Median	70.0	-9.0	76.0	1.0
Min - Max	50 - 109	-37 - 8	60 - 90	-19 - 23
Cycle 8 Day 15				
PRE PAC INFUSION				
n	28	27	61	60
Mean (SD)	70.8 (10.1)	-9.2 (10.0)	74.4 (8.1)	-2.1 (11.6)
Median	72.0	-9.0	75.0	-1.0
Min - Max	50 - 92	-30 - 10	58 - 91	-30 - 24

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	27	26	58	57
Mean (SD)	71.5 (10.7)	-7.7 (9.4)	76.1 (8.9)	0.0 (10.7)
Median	73.0	-7.0	75.0	0.0
Min - Max	52 - 96	-34 - 10	55 - 97	-22 - 25
Cycle 9 Day 1				
PRE PAC INFUSION				
n	27	26	57	56
Mean (SD)	73.4 (10.4)	-6.3 (9.3)	74.2 (9.7)	-2.1 (9.7)
Median	75.0	-5.5	75.0	-1.0
Min - Max	48 - 97	-28 - 8	49 - 96	-25 - 20
AFTER PAC INFUSION				
n	22	21	52	51
Mean (SD)	75.4 (12.2)	-3.8 (10.8)	77.2 (10.2)	0.7 (9.2)
Median	75.0	-3.0	76.0	0.0
Min - Max	48 - 99	-28 - 19	54 - 107	-18 - 25
Cycle 9 Day 8				
PRE PAC INFUSION				
n	24	23	51	50
Mean (SD)	73.5 (11.6)	-5.3 (9.6)	75.5 (8.5)	-1.1 (11.5)
Median	75.5	-6.0	76.0	1.0
Min - Max	49 - 92	-22 - 15	57 - 90	-30 - 20
AFTER PAC INFUSION				
n	21	20	50	49
Mean (SD)	72.4 (10.1)	-5.9 (9.1)	76.0 (7.5)	0.0 (9.7)
Median	75.0	-5.0	75.0	0.0
Min - Max	55 - 92	-25 - 5	63 - 98	-21 - 28
Cycle 9 Day 15				
PRE PAC INFUSION				
n	22	21	51	50
Mean (SD)	73.1 (9.8)	-7.2 (8.4)	73.5 (8.4)	-3.6 (11.6)
Median	74.5	-6.0	75.0	-5.0
Min - Max	58 - 91	-21 - 5	48 - 90	-28 - 20
AFTER PAC INFUSION				
n	20	19	48	47
Mean (SD)	73.4 (9.6)	-6.0 (9.6)	75.6 (9.8)	-1.4 (11.5)
Median	74.0	-5.0	74.0	-1.0
Min - Max	56 - 86	-20 - 8	58 - 100	-22 - 30
Cycle 10 Day 1				
PRE PAC INFUSION				
n	22	22	55	54
Mean (SD)	74.7 (10.3)	-5.6 (10.0)	73.9 (10.8)	-2.3 (10.8)
Median	73.0	-4.5	75.0	-2.0
Min - Max	60 - 99	-28 - 10	42 - 105	-27 - 27

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	19	19	44	43
Mean (SD)	73.2 (8.0)	-5.6 (8.6)	77.0 (9.7)	0.3 (9.9)
Median	73.0	-6.0	77.5	-1.0
Min - Max	60 - 88	-20 - 11	53 - 101	-18 - 23
Cycle 10 Day 8				
PRE PAC INFUSION				
n	19	18	43	42
Mean (SD)	73.1 (8.3)	-5.9 (6.8)	75.4 (8.9)	-2.5 (10.6)
Median	73.0	-5.5	75.0	-2.5
Min - Max	60 - 90	-18 - 4	53 - 110	-20 - 30
AFTER PAC INFUSION				
n	18	17	40	39
Mean (SD)	75.1 (10.1)	-2.3 (10.2)	75.2 (9.5)	-1.9 (11.1)
Median	75.5	-4.0	73.5	-5.0
Min - Max	56 - 92	-24 - 14	56 - 100	-17 - 25
Cycle 10 Day 15				
PRE PAC INFUSION				
n	18	17	46	45
Mean (SD)	71.3 (6.8)	-7.9 (7.1)	72.5 (9.9)	-5.5 (12.8)
Median	70.0	-5.0	70.5	-4.0
Min - Max	59 - 92	-21 - 3	49 - 96	-32 - 27
AFTER PAC INFUSION				
n	16	15	41	40
Mean (SD)	69.2 (8.5)	-8.0 (9.3)	74.1 (10.3)	-3.6 (13.5)
Median	70.0	-6.0	74.0	-4.5
Min - Max	54 - 85	-28 - 7	58 - 99	-31 - 29
Cycle 11 Day 1				
PRE PAC INFUSION				
n	17	16	48	47
Mean (SD)	75.0 (10.4)	-4.4 (10.6)	73.9 (10.0)	-3.1 (12.1)
Median	75.0	-2.5	75.0	-3.0
Min - Max	49 - 94	-24 - 11	45 - 94	-34 - 21
AFTER PAC INFUSION				
n	14	13	40	39
Mean (SD)	71.1 (9.1)	-6.1 (11.5)	76.6 (10.1)	-1.1 (12.8)
Median	71.5	-1.0	75.0	0.0
Min - Max	52 - 90	-32 - 8	63 - 107	-20 - 26
Cycle 11 Day 8				
PRE PAC INFUSION				
n	15	14	36	35
Mean (SD)	74.1 (10.9)	-6.1 (13.3)	73.9 (8.6)	-3.4 (12.4)
Median	74.0	-4.0	73.0	-5.0
Min - Max	52 - 90	-25 - 12	58 - 90	-22 - 20

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	14	13	34	33
Mean (SD)	69.8 (11.9)	-8.0 (11.1)	76.3 (8.8)	-0.7 (11.7)
Median	70.5	-5.0	78.0	-1.0
Min - Max	48 - 85	-26 - 8	60 - 102	-22 - 32
Cycle 11 Day 15				
PRE PAC INFUSION				
n	17	16	39	38
Mean (SD)	71.2 (7.8)	-7.9 (13.1)	75.0 (7.9)	-2.7 (12.6)
Median	72.0	-9.0	75.0	-4.0
Min - Max	58 - 87	-36 - 16	56 - 90	-30 - 23
AFTER PAC INFUSION				
n	14	13	36	35
Mean (SD)	73.1 (6.7)	-5.1 (6.3)	75.0 (8.9)	-2.1 (12.7)
Median	72.0	-5.0	75.5	-5.0
Min - Max	60 - 87	-20 - 5	56 - 94	-33 - 20
Cycle 12 Day 1				
PRE PAC INFUSION				
n	17	17	43	43
Mean (SD)	74.0 (10.9)	-5.6 (10.7)	74.7 (8.1)	-2.5 (11.4)
Median	74.0	-4.0	75.0	-4.0
Min - Max	54 - 97	-26 - 10	59 - 97	-21 - 25
AFTER PAC INFUSION				
n	14	14	35	35
Mean (SD)	70.6 (7.6)	-6.7 (7.2)	76.7 (10.0)	-0.9 (12.8)
Median	70.0	-7.0	76.0	-2.0
Min - Max	60 - 84	-18 - 5	59 - 105	-21 - 34
Cycle 12 Day 8				
PRE PAC INFUSION				
n	16	15	33	33
Mean (SD)	71.9 (7.2)	-8.2 (12.5)	73.9 (7.8)	-4.7 (10.5)
Median	71.0	-5.0	75.0	-5.0
Min - Max	56 - 84	-38 - 9	57 - 88	-21 - 21
AFTER PAC INFUSION				
n	14	13	32	32
Mean (SD)	75.0 (8.1)	-3.2 (7.9)	75.8 (10.5)	-2.4 (12.5)
Median	74.0	-5.0	77.5	-5.0
Min - Max	63 - 89	-11 - 16	51 - 101	-28 - 31
Cycle 12 Day 15				
PRE PAC INFUSION				
n	16	15	33	33
Mean (SD)	72.9 (8.8)	-6.0 (11.2)	71.3 (9.3)	-7.2 (11.4)
Median	76.0	-3.0	72.0	-8.0
Min - Max	55 - 82	-26 - 7	47 - 85	-33 - 15

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	14	13	30	30
Mean (SD)	73.4 (9.2)	-3.6 (8.0)	74.9 (10.1)	-3.1 (12.4)
Median	71.0	-4.0	75.0	-5.0
Min - Max	60 - 88	-18 - 9	54 - 101	-25 - 31
Cycle 13 Day 1				
PRE PAC INFUSION				
n	14	13	33	33
Mean (SD)	71.9 (8.7)	-8.1 (10.1)	74.1 (10.8)	-3.2 (14.4)
Median	71.5	-6.0	74.0	-4.0
Min - Max	59 - 87	-24 - 13	53 - 91	-30 - 22
AFTER PAC INFUSION				
n	12	11	27	27
Mean (SD)	70.6 (10.3)	-8.1 (10.0)	78.9 (10.6)	0.0 (13.5)
Median	71.5	-10.0	79.0	4.0
Min - Max	51 - 89	-25 - 5	58 - 101	-21 - 31
Cycle 13 Day 8				
PRE PAC INFUSION				
n	12	11	27	27
Mean (SD)	69.5 (8.1)	-7.0 (7.7)	73.9 (10.4)	-4.6 (13.6)
Median	70.0	-5.0	76.0	-5.0
Min - Max	57 - 85	-19 - 5	51 - 90	-30 - 25
AFTER PAC INFUSION				
n	11	10	24	24
Mean (SD)	70.5 (10.5)	-6.6 (8.2)	76.4 (11.6)	-1.6 (12.0)
Median	69.0	-5.0	76.5	-5.0
Min - Max	58 - 95	-21 - 5	52 - 100	-20 - 25
Cycle 13 Day 15				
PRE PAC INFUSION				
n	12	11	27	27
Mean (SD)	70.2 (9.7)	-6.0 (8.2)	75.0 (8.0)	-3.8 (12.8)
Median	69.5	-6.0	75.0	-5.0
Min - Max	56 - 89	-17 - 8	60 - 90	-24 - 20
AFTER PAC INFUSION				
n	11	10	23	23
Mean (SD)	70.5 (9.1)	-6.1 (8.2)	76.9 (9.4)	-2.2 (13.0)
Median	70.0	-4.5	77.0	-4.0
Min - Max	58 - 91	-20 - 7	60 - 92	-24 - 22
Cycle 14 Day 1				
PRE PAC INFUSION				
n	13	12	32	32
Mean (SD)	73.5 (7.9)	-5.3 (11.7)	73.8 (11.8)	-2.3 (11.9)
Median	73.0	-2.5	73.5	-2.0
Min - Max	56 - 88	-26 - 13	45 - 103	-24 - 24

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	11	10	26	26
Mean (SD)	71.9 (7.5)	-5.3 (7.7)	75.7 (12.7)	-1.3 (14.1)
Median	72.0	-6.0	75.0	-1.5
Min - Max	61 - 85	-15 - 10	52 - 108	-37 - 29
Cycle 14 Day 8				
PRE PAC INFUSION				
n	11	10	26	26
Mean (SD)	68.6 (9.0)	-8.3 (6.0)	71.6 (12.9)	-5.5 (11.4)
Median	68.0	-9.0	74.5	-5.0
Min - Max	58 - 90	-15 - 0	20 - 84	-40 - 16
AFTER PAC INFUSION				
n	10	9	24	24
Mean (SD)	68.4 (10.7)	-9.3 (8.8)	73.6 (8.9)	-3.5 (10.7)
Median	67.0	-7.0	71.0	-3.5
Min - Max	52 - 90	-23 - 1	57 - 100	-25 - 14
Cycle 14 Day 15				
PRE PAC INFUSION				
n	11	10	26	26
Mean (SD)	71.0 (10.6)	-5.5 (9.9)	70.8 (9.5)	-6.0 (11.8)
Median	75.0	-9.5	72.5	-6.5
Min - Max	57 - 85	-18 - 9	48 - 85	-32 - 20
AFTER PAC INFUSION				
n	10	9	24	24
Mean (SD)	71.8 (11.0)	-5.4 (9.2)	74.0 (7.1)	-2.0 (10.2)
Median	70.0	-10.0	74.0	-5.0
Min - Max	60 - 89	-15 - 7	60 - 87	-23 - 20
Cycle 15 Day 1				
PRE PAC INFUSION				
n	11	11	28	28
Mean (SD)	73.4 (12.8)	-5.5 (12.5)	75.3 (8.8)	-2.1 (10.3)
Median	76.0	-5.0	74.5	0.0
Min - Max	54 - 94	-22 - 12	60 - 96	-20 - 18
AFTER PAC INFUSION				
n	10	10	22	22
Mean (SD)	72.0 (12.8)	-3.9 (11.0)	77.4 (12.2)	-1.3 (12.9)
Median	73.5	-1.0	76.5	-1.5
Min - Max	55 - 95	-21 - 17	60 - 106	-24 - 30
Cycle 15 Day 8				
PRE PAC INFUSION				
n	11	10	21	21
Mean (SD)	70.2 (10.0)	-6.3 (10.7)	71.8 (9.0)	-6.2 (10.0)
Median	73.0	-6.5	74.0	-6.0
Min - Max	55 - 85	-20 - 11	53 - 86	-24 - 19

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	10	9	18	18
Mean (SD)	70.9 (8.6)	-6.2 (6.3)	74.8 (13.5)	-2.8 (15.0)
Median	69.0	-8.0	75.5	-4.0
Min - Max	60 - 87	-13 - 6	47 - 105	-32 - 35
Cycle 15 Day 15				
PRE PAC INFUSION				
n	10	9	22	22
Mean (SD)	65.5 (8.9)	-11.3 (12.1)	72.2 (9.2)	-6.0 (9.5)
Median	66.0	-9.0	74.0	-5.5
Min - Max	48 - 77	-32 - 6	54 - 88	-23 - 10
AFTER PAC INFUSION				
n	9	8	20	20
Mean (SD)	65.1 (12.1)	-11.9 (11.5)	72.9 (9.8)	-5.3 (13.9)
Median	68.0	-15.5	75.5	-4.5
Min - Max	45 - 80	-28 - 7	42 - 85	-47 - 15
Cycle 16 Day 1				
PRE PAC INFUSION				
n	11	10	24	24
Mean (SD)	75.2 (11.2)	-4.0 (14.8)	73.5 (12.4)	-4.2 (12.1)
Median	76.0	-2.5	75.5	-4.0
Min - Max	58 - 88	-23 - 17	40 - 99	-23 - 15
AFTER PAC INFUSION				
n	10	9	20	20
Mean (SD)	70.8 (8.3)	-5.0 (11.9)	77.5 (11.3)	-0.5 (13.4)
Median	69.5	-5.0	80.5	0.0
Min - Max	59 - 86	-25 - 11	51 - 100	-38 - 20
Cycle 16 Day 8				
PRE PAC INFUSION				
n	11	10	19	19
Mean (SD)	67.5 (10.8)	-7.9 (12.0)	72.9 (11.4)	-4.7 (10.0)
Median	64.0	-10.5	75.0	-5.0
Min - Max	49 - 84	-24 - 9	50 - 99	-21 - 17
AFTER PAC INFUSION				
n	10	9	19	19
Mean (SD)	68.4 (8.9)	-8.1 (11.7)	75.9 (7.6)	-1.8 (9.2)
Median	67.5	-8.0	78.0	-3.0
Min - Max	54 - 88	-25 - 13	64 - 91	-17 - 15
Cycle 16 Day 15				
PRE PAC INFUSION				
n	10	9	21	21
Mean (SD)	71.2 (9.0)	-5.8 (10.2)	73.6 (10.1)	-4.7 (9.8)
Median	74.5	-5.0	74.0	-4.0
Min - Max	56 - 79	-19 - 8	54 - 94	-22 - 13

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	9	8	19	19
Mean (SD)	67.9 (9.8)	-9.6 (8.1)	75.2 (10.4)	-2.5 (12.0)
Median	66.0	-11.5	78.0	-4.0
Min - Max	57 - 84	-19 - 7	57 - 91	-27 - 16
Cycle 17 Day 1				
PRE PAC INFUSION				
n	8	7	23	23
Mean (SD)	75.5 (12.4)	-3.9 (10.9)	76.4 (10.3)	-2.3 (12.7)
Median	76.5	1.0	80.0	0.0
Min - Max	50 - 94	-23 - 8	55 - 96	-34 - 20
AFTER PAC INFUSION				
n	7	6	20	20
Mean (SD)	73.4 (6.3)	0.8 (6.2)	79.7 (9.1)	0.2 (13.0)
Median	76.0	2.5	80.0	0.0
Min - Max	65 - 80	-8 - 8	66 - 100	-22 - 30
Cycle 17 Day 8				
PRE PAC INFUSION				
n	6	5	18	18
Mean (SD)	70.3 (7.3)	-3.2 (8.3)	74.5 (9.3)	-4.6 (8.3)
Median	70.5	-3.0	76.5	-4.5
Min - Max	61 - 81	-12 - 6	57 - 87	-16 - 15
AFTER PAC INFUSION				
n	6	5	18	18
Mean (SD)	71.5 (4.7)	-3.2 (5.2)	77.8 (10.2)	-1.2 (12.4)
Median	72.5	-3.0	78.5	-2.0
Min - Max	64 - 76	-11 - 2	60 - 98	-20 - 28
Cycle 17 Day 15				
PRE PAC INFUSION				
n	7	6	19	19
Mean (SD)	68.7 (7.1)	-6.7 (6.7)	72.1 (7.3)	-6.6 (11.4)
Median	70.0	-4.5	71.0	-9.0
Min - Max	57 - 78	-18 - -1	56 - 85	-28 - 13
AFTER PAC INFUSION				
n	7	6	19	19
Mean (SD)	74.0 (5.0)	0.5 (5.8)	76.4 (10.4)	-2.3 (10.6)
Median	72.0	1.0	79.0	-4.0
Min - Max	67 - 80	-6 - 7	52 - 99	-19 - 15
Cycle 18 Day 1				
PRE PAC INFUSION				
n	7	7	21	21
Mean (SD)	72.0 (11.3)	-6.7 (10.0)	75.3 (11.1)	-3.2 (11.8)
Median	74.0	-3.0	77.0	-6.0
Min - Max	56 - 89	-19 - 5	53 - 102	-21 - 20

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	6	6	17	17
Mean (SD)	70.5 (9.4)	-3.3 (9.6)	79.1 (12.9)	-0.7 (16.5)
Median	68.5	-6.0	79.0	-4.0
Min - Max	57 - 84	-16 - 9	60 - 110	-28 - 25
Cycle 18 Day 8				
PRE PAC INFUSION				
n	6	6	15	15
Mean (SD)	74.3 (7.0)	0.5 (8.0)	73.1 (10.3)	-6.2 (7.8)
Median	75.0	0.0	75.0	-5.0
Min - Max	65 - 84	-10 - 13	57 - 92	-19 - 5
AFTER PAC INFUSION				
n	6	6	14	14
Mean (SD)	72.0 (5.7)	-1.8 (5.7)	78.8 (9.2)	-0.4 (14.4)
Median	72.5	-2.5	79.5	-2.0
Min - Max	63 - 79	-10 - 5	66 - 100	-18 - 39
Cycle 18 Day 15				
PRE PAC INFUSION				
n	7	6	17	17
Mean (SD)	70.0 (10.1)	-3.5 (11.1)	67.8 (13.2)	-12.0 (9.4)
Median	68.0	-1.5	65.0	-10.0
Min - Max	52 - 82	-21 - 7	41 - 91	-29 - 5
AFTER PAC INFUSION				
n	7	6	16	16
Mean (SD)	70.9 (9.7)	-2.7 (10.7)	76.4 (12.0)	-4.5 (13.8)
Median	69.0	-6.0	76.5	-6.5
Min - Max	60 - 89	-13 - 14	60 - 99	-28 - 24
Cycle 19 Day 1				
PRE PAC INFUSION				
n	7	6	18	18
Mean (SD)	76.1 (10.0)	-1.3 (13.4)	73.4 (10.5)	-3.9 (9.0)
Median	82.0	5.5	76.0	-6.0
Min - Max	60 - 85	-23 - 9	51 - 90	-24 - 10
AFTER PAC INFUSION				
n	6	5	14	14
Mean (SD)	73.5 (7.5)	0.2 (7.7)	78.0 (10.6)	-1.3 (12.2)
Median	71.5	0.0	79.0	-3.0
Min - Max	65 - 87	-8 - 12	60 - 96	-20 - 25
Cycle 19 Day 8				
PRE PAC INFUSION				
n	6	5	13	13
Mean (SD)	75.5 (9.9)	2.4 (10.7)	73.1 (11.6)	-6.3 (11.7)
Median	77.5	4.0	74.0	-5.0
Min - Max	58 - 88	-15 - 14	56 - 93	-24 - 10

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	4	12	12
Mean (SD)	69.4 (11.8)	-6.0 (12.5)	73.6 (9.5)	-6.6 (9.0)
Median	72.0	-5.0	72.0	-6.5
Min - Max	52 - 82	-21 - 7	60 - 87	-20 - 5
Cycle 19 Day 15				
PRE PAC INFUSION				
n	6	5	13	13
Mean (SD)	72.0 (11.2)	-1.4 (12.3)	72.6 (9.8)	-7.4 (7.4)
Median	73.5	5.0	70.0	-8.0
Min - Max	53 - 83	-20 - 9	59 - 91	-21 - 5
AFTER PAC INFUSION				
n	6	5	13	13
Mean (SD)	73.8 (11.3)	-2.8 (9.0)	77.8 (8.8)	-2.2 (9.3)
Median	70.5	-3.0	80.0	-4.0
Min - Max	58 - 89	-15 - 10	61 - 91	-15 - 13
Cycle 20 Day 1				
PRE PAC INFUSION				
n	6	5	16	16
Mean (SD)	78.0 (8.9)	-4.2 (17.5)	72.8 (10.3)	-5.5 (8.1)
Median	80.0	7.0	73.0	-6.0
Min - Max	62 - 88	-32 - 8	49 - 88	-21 - 10
AFTER PAC INFUSION				
n	5	4	13	13
Mean (SD)	76.0 (11.1)	0.3 (10.1)	78.1 (7.4)	-1.9 (8.5)
Median	78.0	1.5	79.0	-6.0
Min - Max	60 - 86	-13 - 11	68 - 93	-12 - 15
Cycle 20 Day 8				
PRE PAC INFUSION				
n	6	5	12	12
Mean (SD)	73.5 (10.2)	-0.6 (10.9)	72.0 (12.4)	-8.2 (13.0)
Median	75.0	3.0	74.0	-8.5
Min - Max	54 - 83	-19 - 9	56 - 90	-28 - 18
AFTER PAC INFUSION				
n	6	5	12	12
Mean (SD)	74.3 (6.0)	-0.4 (5.2)	73.7 (9.8)	-6.5 (9.8)
Median	75.5	1.0	74.0	-5.5
Min - Max	64 - 80	-9 - 4	58 - 88	-21 - 8
Cycle 20 Day 15				
PRE PAC INFUSION				
n	6	5	12	12
Mean (SD)	75.2 (8.6)	2.6 (9.1)	70.3 (8.9)	-9.2 (9.9)
Median	79.0	5.0	72.0	-10.0
Min - Max	60 - 83	-13 - 9	58 - 85	-28 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	4	11	11
Mean (SD)	75.8 (3.0)	1.8 (3.0)	72.9 (10.4)	-6.7 (12.1)
Median	76.0	1.0	74.0	-7.0
Min - Max	72 - 80	-1 - 6	61 - 90	-26 - 18
Cycle 21 Day 1				
PRE PAC INFUSION				
n	5	5	13	13
Mean (SD)	70.8 (9.2)	-9.4 (14.3)	71.3 (9.4)	-7.2 (6.3)
Median	74.0	-3.0	71.0	-5.0
Min - Max	55 - 78	-30 - 5	60 - 88	-20 - 2
AFTER PAC INFUSION				
n	3	3	11	11
Mean (SD)	75.0 (5.6)	1.7 (5.8)	73.5 (13.8)	-5.5 (13.0)
Median	76.0	5.0	76.0	-5.0
Min - Max	69 - 80	-5 - 5	57 - 97	-23 - 19
Cycle 21 Day 8				
PRE PAC INFUSION				
n	3	3	11	11
Mean (SD)	69.0 (4.4)	-4.3 (6.1)	70.2 (10.7)	-8.8 (9.0)
Median	71.0	-3.0	70.0	-8.0
Min - Max	64 - 72	-11 - 1	57 - 88	-23 - 4
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	70.5 (2.1)	-2.5 (4.9)	74.7 (10.2)	-4.4 (9.6)
Median	70.5	-2.5	76.5	-0.5
Min - Max	69 - 72	-6 - 1	59 - 89	-21 - 8
Cycle 21 Day 15				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	66.5 (7.8)	-6.5 (10.6)	68.5 (9.3)	-10.6 (11.2)
Median	66.5	-6.5	68.5	-11.5
Min - Max	61 - 72	-14 - 1	57 - 82	-27 - 5
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	65.5 (6.4)	-7.5 (9.2)	71.5 (9.1)	-7.6 (11.2)
Median	65.5	-7.5	72.0	-12.0
Min - Max	61 - 70	-14 - -1	58 - 86	-19 - 12
Cycle 22 Day 1				
PRE PAC INFUSION				
n	4	4	13	13
Mean (SD)	68.8 (6.7)	-13.3 (11.9)	74.1 (7.9)	-4.4 (9.8)
Median	67.0	-10.5	71.0	-2.0
Min - Max	63 - 78	-30 - -2	59 - 90	-19 - 15

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	11	11
Mean (SD)	70.0 (6.0)	-3.3 (7.6)	79.0 (8.4)	0.0 (11.2)
Median	70.0	-5.0	80.0	0.0
Min - Max	64 - 76	-10 - 5	68 - 94	-14 - 16
Cycle 22 Day 8				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	76.0 (2.8)	3.0 (0.0)	78.3 (8.4)	-0.8 (13.8)
Median	76.0	3.0	78.0	-9.0
Min - Max	74 - 78	3 - 3	64 - 92	-16 - 20
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	73.0 (1.4)	0.0 (4.2)	76.0 (7.8)	-3.1 (10.7)
Median	73.0	0.0	76.5	-7.0
Min - Max	72 - 74	-3 - 3	60 - 90	-15 - 20
Cycle 22 Day 15				
PRE PAC INFUSION				
n	2	2	9	9
Mean (SD)	82.0 (5.7)	9.0 (2.8)	75.4 (7.2)	-2.4 (9.0)
Median	82.0	9.0	80.0	-5.0
Min - Max	78 - 86	7 - 11	59 - 81	-15 - 10
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	73.0 (1.4)	0.0 (4.2)	77.4 (8.1)	-0.4 (10.1)
Median	73.0	0.0	80.0	0.0
Min - Max	72 - 74	-3 - 3	59 - 86	-15 - 15
Cycle 23 Day 1				
PRE PAC INFUSION				
n	3	3	12	12
Mean (SD)	72.7 (3.1)	-12.0 (17.3)	72.5 (8.0)	-5.0 (9.7)
Median	72.0	-3.0	75.0	-6.0
Min - Max	70 - 76	-32 - -1	51 - 80	-23 - 15
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	74.0 (0.0)	1.0 (2.8)	79.2 (8.8)	1.3 (9.3)
Median	74.0	1.0	77.5	0.0
Min - Max	74 - 74	-1 - 3	70 - 96	-13 - 18
Cycle 23 Day 8				
PRE PAC INFUSION				
n	2	2	9	9
Mean (SD)	75.0 (4.2)	2.0 (1.4)	68.4 (9.1)	-9.4 (10.8)
Median	75.0	2.0	70.0	-9.0
Min - Max	72 - 78	1 - 3	57 - 80	-21 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	76.0 (5.7)	3.0 (2.8)	73.4 (10.1)	-4.4 (10.5)
Median	76.0	3.0	70.0	-5.0
Min - Max	72 - 80	1 - 5	60 - 90	-15 - 18
Cycle 23 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	77.5 (3.5)	4.5 (0.7)	69.8 (9.3)	-7.9 (10.2)
Median	77.5	4.5	73.5	-8.5
Min - Max	75 - 80	4 - 5	57 - 80	-20 - 10
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	73.0 (4.2)	0.0 (1.4)	72.8 (10.0)	-4.9 (12.2)
Median	73.0	0.0	71.5	-9.5
Min - Max	70 - 76	-1 - 1	60 - 85	-16 - 15
Cycle 24 Day 1				
PRE PAC INFUSION				
n	3	3	11	11
Mean (SD)	75.3 (5.7)	-9.3 (19.1)	77.2 (9.7)	-0.1 (11.7)
Median	77.0	-2.0	79.0	1.0
Min - Max	69 - 80	-31 - 5	64 - 90	-16 - 20
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	76.0 (2.8)	3.0 (0.0)	79.0 (8.5)	1.3 (8.6)
Median	76.0	3.0	83.0	-1.0
Min - Max	74 - 78	3 - 3	70 - 92	-10 - 20
Cycle 24 Day 8				
PRE PAC INFUSION				
n	2	2	7	7
Mean (SD)	67.5 (14.8)	-5.5 (17.7)	73.9 (11.9)	-2.9 (14.0)
Median	67.5	-5.5	79.0	-3.0
Min - Max	57 - 78	-18 - 7	56 - 88	-19 - 18
AFTER PAC INFUSION				
n	2	2	7	7
Mean (SD)	73.5 (10.6)	0.5 (13.4)	75.1 (13.0)	-1.6 (12.5)
Median	73.5	0.5	74.0	4.0
Min - Max	66 - 81	-9 - 10	57 - 90	-18 - 16
Cycle 24 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	78.0 (5.7)	5.0 (8.5)	74.9 (11.7)	-2.8 (11.2)
Median	78.0	5.0	77.0	2.0
Min - Max	74 - 82	-1 - 11	57 - 90	-19 - 10

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	7	7
Mean (SD)	74.0 (5.7)	1.0 (8.5)	72.0 (10.8)	-4.7 (10.2)
Median	74.0	1.0	70.0	-5.0
Min - Max	70 - 78	-5 - 7	55 - 85	-19 - 9
Cycle 25 Day 1				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	75.0 (1.4)	2.0 (4.2)	74.7 (9.8)	-3.8 (12.0)
Median	75.0	2.0	75.5	-6.0
Min - Max	74 - 76	-1 - 5	60 - 89	-19 - 17
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	71.0 (4.2)	-2.0 (7.1)	81.1 (11.2)	1.9 (12.3)
Median	71.0	-2.0	80.0	-1.0
Min - Max	68 - 74	-7 - 3	67 - 103	-10 - 25
Cycle 25 Day 8				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	78.0 (5.7)	5.0 (2.8)	70.1 (8.9)	-7.5 (11.4)
Median	78.0	5.0	71.0	-8.0
Min - Max	74 - 82	3 - 7	58 - 86	-19 - 5
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	74.0 (5.7)	1.0 (2.8)	76.6 (12.5)	-1.0 (13.5)
Median	74.0	1.0	80.0	-1.0
Min - Max	70 - 78	-1 - 3	59 - 94	-20 - 16
Cycle 25 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	78.5 (0.7)	5.5 (2.1)	70.3 (8.2)	-7.4 (7.8)
Median	78.5	5.5	70.0	-7.5
Min - Max	78 - 79	4 - 7	55 - 80	-19 - 5
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	71.5 (6.4)	-1.5 (3.5)	72.8 (9.2)	-4.9 (10.4)
Median	71.5	-1.5	73.5	-8.0
Min - Max	67 - 76	-4 - 1	58 - 87	-16 - 15
Cycle 26 Day 1				
PRE PAC INFUSION				
n	2	2	11	11
Mean (SD)	75.0 (7.1)	2.0 (4.2)	74.7 (11.4)	-3.4 (13.9)
Median	75.0	2.0	75.0	-3.0
Min - Max	70 - 80	-1 - 5	55 - 95	-25 - 25

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	74.0 (2.8)	1.0 (0.0)	76.9 (8.0)	-2.0 (9.7)
Median	74.0	1.0	78.0	-4.0
Min - Max	72 - 76	1 - 1	63 - 90	-11 - 20
Cycle 26 Day 8				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	78.0 (5.7)	5.0 (2.8)	69.1 (7.6)	-9.0 (9.6)
Median	78.0	5.0	71.5	-12.5
Min - Max	74 - 82	3 - 7	57 - 78	-18 - 6
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	77.5 (2.1)	4.5 (0.7)	69.9 (11.7)	-8.3 (12.9)
Median	77.5	4.5	68.5	-7.5
Min - Max	76 - 79	4 - 5	55 - 84	-28 - 11
Cycle 26 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	77.0 (7.1)	4.0 (4.2)	69.6 (8.2)	-8.0 (11.3)
Median	77.0	4.0	70.0	-11.5
Min - Max	72 - 82	1 - 7	58 - 81	-22 - 9
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	77.0 (4.2)	4.0 (1.4)	73.9 (8.4)	-3.8 (11.8)
Median	77.0	4.0	74.0	-5.0
Min - Max	74 - 80	3 - 5	58 - 85	-16 - 15
Cycle 27 Day 1				
PRE PAC INFUSION				
n	1	1	8	8
Mean (SD)	74.0 (NE)	3.0 (NE)	74.9 (13.2)	-4.1 (14.2)
Median	74.0	3.0	73.5	-2.5
Min - Max	74 - 74	3 - 3	57 - 94	-23 - 24
AFTER PAC INFUSION				
n	1	1	7	7
Mean (SD)	70.0 (NE)	-1.0 (NE)	77.1 (12.6)	-3.1 (13.5)
Median	70.0	-1.0	78.0	-5.0
Min - Max	70 - 70	-1 - -1	61 - 94	-14 - 24
Cycle 27 Day 8				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	74.0 (NE)	3.0 (NE)	68.7 (12.0)	-12.0 (12.3)
Median	74.0	3.0	68.5	-18.0
Min - Max	74 - 74	3 - 3	55 - 87	-23 - 6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	74.0 (NE)	3.0 (NE)	71.2 (10.4)	-9.5 (7.9)
Median	74.0	3.0	70.0	-13.0
Min - Max	74 - 74	3 - 3	57 - 87	-17 - 1
Cycle 27 Day 15				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	74.0 (NE)	3.0 (NE)	70.7 (8.5)	-5.8 (11.8)
Median	74.0	3.0	70.5	-10.0
Min - Max	74 - 74	3 - 3	57 - 80	-17 - 15
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	70.0 (NE)	-1.0 (NE)	72.5 (9.3)	-4.0 (11.8)
Median	70.0	-1.0	73.0	-6.0
Min - Max	70 - 70	-1 - -1	58 - 84	-16 - 15
Cycle 28 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	84.0 (NE)	13.0 (NE)	69.0 (8.7)	-8.8 (10.4)
Median	84.0	13.0	70.5	-12.5
Min - Max	84 - 84	13 - 13	57 - 81	-19 - 5
AFTER PAC INFUSION				
n	1	1	5	5
Mean (SD)	77.0 (NE)	6.0 (NE)	74.2 (6.5)	-3.6 (6.0)
Median	77.0	6.0	74.0	-6.0
Min - Max	77 - 77	6 - 6	67 - 84	-10 - 5
Cycle 28 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	80.0 (NE)	9.0 (NE)	61.8 (11.3)	-19.3 (10.3)
Median	80.0	9.0	60.0	-19.0
Min - Max	80 - 80	9 - 9	50 - 77	-30 - -9
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	78.0 (NE)	7.0 (NE)	74.0 (13.4)	-7.0 (9.3)
Median	78.0	7.0	72.0	-7.0
Min - Max	78 - 78	7 - 7	62 - 90	-18 - 4
Cycle 28 Day 15				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	78.0 (NE)	7.0 (NE)	76.5 (12.3)	-1.3 (13.7)
Median	78.0	7.0	76.5	-5.0
Min - Max	78 - 78	7 - 7	58 - 92	-16 - 16

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	86.0 (NE)	15.0 (NE)	76.2 (11.6)	-1.7 (10.8)
Median	86.0	15.0	78.5	-3.0
Min - Max	86 - 86	15 - 15	58 - 93	-16 - 15
Cycle 29 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	82.0 (NE)	11.0 (NE)	70.0 (14.1)	-7.8 (9.5)
Median	82.0	11.0	69.5	-11.5
Min - Max	82 - 82	11 - 11	50 - 88	-16 - 8
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	86.0 (NE)	15.0 (NE)	68.5 (6.6)	-8.8 (5.0)
Median	86.0	15.0	69.0	-7.0
Min - Max	86 - 86	15 - 15	60 - 76	-16 - -5
Cycle 29 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	88.0 (NE)	17.0 (NE)	74.0 (11.3)	-3.3 (8.5)
Median	88.0	17.0	72.5	-3.0
Min - Max	88 - 88	17 - 17	62 - 89	-12 - 5
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	71.0 (NE)	0.0 (NE)	71.5 (9.5)	-5.8 (8.8)
Median	71.0	0.0	70.5	-7.5
Min - Max	71 - 71	0 - 0	61 - 84	-13 - 5
Cycle 29 Day 15				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	90.0 (NE)	19.0 (NE)	67.3 (11.3)	-13.8 (8.3)
Median	90.0	19.0	66.5	-12.5
Min - Max	90 - 90	19 - 19	55 - 81	-25 - -5
AFTER PAC INFUSION				
n	1	1	3	3
Mean (SD)	78.0 (NE)	7.0 (NE)	77.3 (15.9)	-4.0 (9.5)
Median	78.0	7.0	85.0	1.0
Min - Max	78 - 78	7 - 7	59 - 88	-15 - 2
Cycle 30 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	74.0 (NE)	3.0 (NE)	71.0 (12.0)	-6.8 (8.2)
Median	74.0	3.0	71.0	-6.5
Min - Max	74 - 74	3 - 3	58 - 88	-16 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	78.0 (NE)	7.0 (NE)	79.5 (8.2)	2.3 (9.3)
Median	78.0	7.0	81.5	0.0
Min - Max	78 - 78	7 - 7	68 - 87	-6 - 15
Cycle 30 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	72.0 (NE)	1.0 (NE)	69.0 (9.1)	-8.3 (9.8)
Median	72.0	1.0	70.0	-10.5
Min - Max	72 - 72	1 - 1	57 - 79	-17 - 5
AFTER PAC INFUSION				
n	1	1	3	3
Mean (SD)	82.0 (NE)	11.0 (NE)	76.7 (6.5)	-1.7 (7.0)
Median	82.0	11.0	77.0	-1.0
Min - Max	82 - 82	11 - 11	70 - 83	-9 - 5
Cycle 30 Day 15				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	70.0 (NE)	-1.0 (NE)	69.0 (7.6)	-8.3 (9.1)
Median	70.0	-1.0	71.5	-11.0
Min - Max	70 - 70	-1 - -1	58 - 75	-16 - 5
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	75.0 (NE)	4.0 (NE)	68.8 (15.5)	-8.5 (10.1)
Median	75.0	4.0	65.0	-9.5
Min - Max	75 - 75	4 - 4	55 - 90	-19 - 4
Cycle 31 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	76.0 (NE)	5.0 (NE)	68.0 (14.1)	-8.0 (11.3)
Median	76.0	5.0	68.0	-8.0
Min - Max	76 - 76	5 - 5	58 - 78	-16 - 0
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	82.0 (NE)	11.0 (NE)	60.0 (NE)	-14.0 (NE)
Median	82.0	11.0	60.0	-14.0
Min - Max	82 - 82	11 - 11	60 - 60	-14 - -14
Cycle 31 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	74.0 (NE)	3.0 (NE)	64.0 (NE)	-10.0 (NE)
Median	74.0	3.0	64.0	-10.0
Min - Max	74 - 74	3 - 3	64 - 64	-10 - -10

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	77.0 (NE)	6.0 (NE)	68.0 (NE)	-6.0 (NE)
Median	77.0	6.0	68.0	-6.0
Min - Max	77 - 77	6 - 6	68 - 68	-6 - -6
Cycle 31 Day 15				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	68.0 (12.7)	-12.0 (4.2)
Median	NE	NE	68.0	-12.0
Min - Max	NE - NE	NE - NE	59 - 77	-15 - -9
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	71.5 (17.7)	-8.5 (9.2)
Median	NE	NE	71.5	-8.5
Min - Max	NE - NE	NE - NE	59 - 84	-15 - -2
Cycle 32 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	76.0 (NE)	-2.0 (NE)
Median	NE	NE	76.0	-2.0
Min - Max	NE - NE	NE - NE	76 - 76	-2 - -2
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	77.0 (11.3)	-3.0 (2.8)
Median	NE	NE	77.0	-3.0
Min - Max	NE - NE	NE - NE	69 - 85	-5 - -1
Cycle 32 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	70.0 (NE)	-1.0 (NE)	NE (NE)	NE (NE)
Median	70.0	-1.0	NE	NE
Min - Max	70 - 70	-1 - -1	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	74.0 (NE)	3.0 (NE)	75.0 (8.5)	-5.0 (0.0)
Median	74.0	3.0	75.0	-5.0
Min - Max	74 - 74	3 - 3	69 - 81	-5 - -5
Cycle 32 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	76.0 (NE)	5.0 (NE)	NE (NE)	NE (NE)
Median	76.0	5.0	NE	NE
Min - Max	76 - 76	5 - 5	NE - NE	NE - NE

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	74.0 (NE)	3.0 (NE)	70.0 (19.8)	-10.0 (11.3)
Median	74.0	3.0	70.0	-10.0
Min - Max	74 - 74	3 - 3	56 - 84	-18 - -2
Cycle 33 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	74.0 (NE)	3.0 (NE)	69.0 (NE)	-9.0 (NE)
Median	74.0	3.0	69.0	-9.0
Min - Max	74 - 74	3 - 3	69 - 69	-9 - -9
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	79.0 (NE)	8.0 (NE)	75.0 (9.9)	-5.0 (1.4)
Median	79.0	8.0	75.0	-5.0
Min - Max	79 - 79	8 - 8	68 - 82	-6 - -4
Cycle 33 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	78.0 (NE)	7.0 (NE)	NE (NE)	NE (NE)
Median	78.0	7.0	NE	NE
Min - Max	78 - 78	7 - 7	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	74.0 (NE)	3.0 (NE)	68.0 (17.0)	-12.0 (8.5)
Median	74.0	3.0	68.0	-12.0
Min - Max	74 - 74	3 - 3	56 - 80	-18 - -6
Cycle 33 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	70.0 (NE)	-1.0 (NE)	NE (NE)	NE (NE)
Median	70.0	-1.0	NE	NE
Min - Max	70 - 70	-1 - -1	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	82.0 (NE)	11.0 (NE)	67.5 (13.4)	-12.5 (4.9)
Median	82.0	11.0	67.5	-12.5
Min - Max	82 - 82	11 - 11	58 - 77	-16 - -9
Cycle 34 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	76.0 (NE)	5.0 (NE)	83.0 (NE)	5.0 (NE)
Median	76.0	5.0	83.0	5.0
Min - Max	76 - 76	5 - 5	83 - 83	5 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	72.0 (NE)	1.0 (NE)	60.0 (NE)	-14.0 (NE)
Median	72.0	1.0	60.0	-14.0
Min - Max	72 - 72	1 - 1	60 - 60	-14 - -14
Cycle 34 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	80.0 (NE)	9.0 (NE)	NE (NE)	NE (NE)
Median	80.0	9.0	NE	NE
Min - Max	80 - 80	9 - 9	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	76.0 (NE)	5.0 (NE)	55.0 (NE)	-19.0 (NE)
Median	76.0	5.0	55.0	-19.0
Min - Max	76 - 76	5 - 5	55 - 55	-19 - -19
Cycle 34 Day 15				
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	75.0 (NE)	4.0 (NE)	53.0 (NE)	-21.0 (NE)
Median	75.0	4.0	53.0	-21.0
Min - Max	75 - 75	4 - 4	53 - 53	-21 - -21
Cycle 35 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	76.0 (NE)	5.0 (NE)	58.0 (NE)	-20.0 (NE)
Median	76.0	5.0	58.0	-20.0
Min - Max	76 - 76	5 - 5	58 - 58	-20 - -20
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	74.0 (NE)	3.0 (NE)	55.0 (NE)	-19.0 (NE)
Median	74.0	3.0	55.0	-19.0
Min - Max	74 - 74	3 - 3	55 - 55	-19 - -19
Cycle 35 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	72.0 (NE)	1.0 (NE)	NE (NE)	NE (NE)
Median	72.0	1.0	NE	NE
Min - Max	72 - 72	1 - 1	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	70.0 (NE)	-1.0 (NE)	58.0 (NE)	-16.0 (NE)
Median	70.0	-1.0	58.0	-16.0
Min - Max	70 - 70	-1 - -1	58 - 58	-16 - -16

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 35 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	81.0 (NE)	10.0 (NE)	NE (NE)	NE (NE)
Median	81.0	10.0	NE	NE
Min - Max	81 - 81	10 - 10	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	70.0 (NE)	-1.0 (NE)	56.0 (NE)	-18.0 (NE)
Median	70.0	-1.0	56.0	-18.0
Min - Max	70 - 70	-1 - -1	56 - 56	-18 - -18
Cycle 36 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	81.0 (NE)	10.0 (NE)	67.0 (NE)	-11.0 (NE)
Median	81.0	10.0	67.0	-11.0
Min - Max	81 - 81	10 - 10	67 - 67	-11 - -11
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	70.0 (NE)	-1.0 (NE)	57.0 (NE)	-17.0 (NE)
Median	70.0	-1.0	57.0	-17.0
Min - Max	70 - 70	-1 - -1	57 - 57	-17 - -17
Cycle 36 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	3.0 (NE)	NE (NE)	NE (NE)
Median	74.0	3.0	NE	NE
Min - Max	74 - 74	3 - 3	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	72.0 (NE)	1.0 (NE)	56.0 (NE)	-18.0 (NE)
Median	72.0	1.0	56.0	-18.0
Min - Max	72 - 72	1 - 1	56 - 56	-18 - -18
Cycle 36 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	71.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	71.0	0.0	NE	NE
Min - Max	71 - 71	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	72.0 (NE)	1.0 (NE)	63.0 (NE)	-11.0 (NE)
Median	72.0	1.0	63.0	-11.0
Min - Max	72 - 72	1 - 1	63 - 63	-11 - -11

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 37 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	74.0 (NE)	3.0 (NE)	71.0 (NE)	-7.0 (NE)
Median	74.0	3.0	71.0	-7.0
Min - Max	74 - 74	3 - 3	71 - 71	-7 - -7
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	72.0 (NE)	1.0 (NE)	58.0 (NE)	-16.0 (NE)
Median	72.0	1.0	58.0	-16.0
Min - Max	72 - 72	1 - 1	58 - 58	-16 - -16
Cycle 37 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	82.0 (NE)	11.0 (NE)	NE (NE)	NE (NE)
Median	82.0	11.0	NE	NE
Min - Max	82 - 82	11 - 11	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	74.0 (NE)	3.0 (NE)	56.0 (NE)	-18.0 (NE)
Median	74.0	3.0	56.0	-18.0
Min - Max	74 - 74	3 - 3	56 - 56	-18 - -18
Cycle 37 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	76.0 (NE)	5.0 (NE)	NE (NE)	NE (NE)
Median	76.0	5.0	NE	NE
Min - Max	76 - 76	5 - 5	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	76.0 (NE)	5.0 (NE)	56.0 (NE)	-18.0 (NE)
Median	76.0	5.0	56.0	-18.0
Min - Max	76 - 76	5 - 5	56 - 56	-18 - -18
Cycle 38 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	79.0 (NE)	8.0 (NE)	61.0 (NE)	-17.0 (NE)
Median	79.0	8.0	61.0	-17.0
Min - Max	79 - 79	8 - 8	61 - 61	-17 - -17
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	84.0 (NE)	13.0 (NE)	59.0 (NE)	-15.0 (NE)
Median	84.0	13.0	59.0	-15.0
Min - Max	84 - 84	13 - 13	59 - 59	-15 - -15

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 38 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	3.0 (NE)	NE (NE)	NE (NE)
Median	74.0	3.0	NE	NE
Min - Max	74 - 74	3 - 3	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	82.0 (NE)	11.0 (NE)	59.0 (NE)	-15.0 (NE)
Median	82.0	11.0	59.0	-15.0
Min - Max	82 - 82	11 - 11	59 - 59	-15 - -15
Cycle 38 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	78.0 (NE)	7.0 (NE)	NE (NE)	NE (NE)
Median	78.0	7.0	NE	NE
Min - Max	78 - 78	7 - 7	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	78.0 (NE)	7.0 (NE)	55.0 (NE)	-19.0 (NE)
Median	78.0	7.0	55.0	-19.0
Min - Max	78 - 78	7 - 7	55 - 55	-19 - -19
Cycle 39 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	74.0 (NE)	3.0 (NE)	74.0 (NE)	-4.0 (NE)
Median	74.0	3.0	74.0	-4.0
Min - Max	74 - 74	3 - 3	74 - 74	-4 - -4
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	79.0 (NE)	8.0 (NE)	NE (NE)	NE (NE)
Median	79.0	8.0	NE	NE
Min - Max	79 - 79	8 - 8	NE - NE	NE - NE
Cycle 39 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	70.0 (NE)	-1.0 (NE)	57.0 (NE)	-17.0 (NE)
Median	70.0	-1.0	57.0	-17.0
Min - Max	70 - 70	-1 - -1	57 - 57	-17 - -17
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	3.0 (NE)	NE (NE)	NE (NE)
Median	74.0	3.0	NE	NE
Min - Max	74 - 74	3 - 3	NE - NE	NE - NE

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 39 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	85.0 (NE)	14.0 (NE)	59.0 (NE)	-15.0 (NE)
Median	85.0	14.0	59.0	-15.0
Min - Max	85 - 85	14 - 14	59 - 59	-15 - -15
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	72.0 (NE)	1.0 (NE)	NE (NE)	NE (NE)
Median	72.0	1.0	NE	NE
Min - Max	72 - 72	1 - 1	NE - NE	NE - NE
Cycle 40 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	86.0 (NE)	15.0 (NE)	69.5 (12.0)	-6.5 (9.2)
Median	86.0	15.0	69.5	-6.5
Min - Max	86 - 86	15 - 15	61 - 78	-13 - 0
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	76.0 (NE)	5.0 (NE)	NE (NE)	NE (NE)
Median	76.0	5.0	NE	NE
Min - Max	76 - 76	5 - 5	NE - NE	NE - NE
Cycle 40 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	82.0 (NE)	11.0 (NE)	55.0 (NE)	-19.0 (NE)
Median	82.0	11.0	55.0	-19.0
Min - Max	82 - 82	11 - 11	55 - 55	-19 - -19
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	3.0 (NE)	NE (NE)	NE (NE)
Median	74.0	3.0	NE	NE
Min - Max	74 - 74	3 - 3	NE - NE	NE - NE
Cycle 40 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	88.0 (NE)	17.0 (NE)	55.0 (NE)	-19.0 (NE)
Median	88.0	17.0	55.0	-19.0
Min - Max	88 - 88	17 - 17	55 - 55	-19 - -19
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	80.0 (NE)	9.0 (NE)	NE (NE)	NE (NE)
Median	80.0	9.0	NE	NE
Min - Max	80 - 80	9 - 9	NE - NE	NE - NE

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 41 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	76.0 (NE)	5.0 (NE)	65.0 (9.9)	-11.0 (7.1)
Median	76.0	5.0	65.0	-11.0
Min - Max	76 - 76	5 - 5	58 - 72	-16 - -6
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	72.0 (NE)	1.0 (NE)	NE (NE)	NE (NE)
Median	72.0	1.0	NE	NE
Min - Max	72 - 72	1 - 1	NE - NE	NE - NE
Cycle 41 Day 8				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	79.0 (NE)	5.0 (NE)
Median	NE	NE	79.0	5.0
Min - Max	NE - NE	NE - NE	79 - 79	5 - 5
Cycle 41 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	75.0 (NE)	4.0 (NE)	55.0 (NE)	-19.0 (NE)
Median	75.0	4.0	55.0	-19.0
Min - Max	75 - 75	4 - 4	55 - 55	-19 - -19
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	76.0 (NE)	5.0 (NE)	NE (NE)	NE (NE)
Median	76.0	5.0	NE	NE
Min - Max	76 - 76	5 - 5	NE - NE	NE - NE
Cycle 42 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	89.0 (NE)	18.0 (NE)	77.0 (NE)	-1.0 (NE)
Median	89.0	18.0	77.0	-1.0
Min - Max	89 - 89	18 - 18	77 - 77	-1 - -1
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	81.0 (NE)	10.0 (NE)	NE (NE)	NE (NE)
Median	81.0	10.0	NE	NE
Min - Max	81 - 81	10 - 10	NE - NE	NE - NE
Cycle 42 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	77.0 (NE)	6.0 (NE)	NE (NE)	NE (NE)
Median	77.0	6.0	NE	NE
Min - Max	77 - 77	6 - 6	NE - NE	NE - NE

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	79.0 (NE)	8.0 (NE)	NE (NE)	NE (NE)
Median	79.0	8.0	NE	NE
Min - Max	79 - 79	8 - 8	NE - NE	NE - NE
Cycle 42 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	78.0 (NE)	7.0 (NE)	NE (NE)	NE (NE)
Median	78.0	7.0	NE	NE
Min - Max	78 - 78	7 - 7	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	70.0 (NE)	-1.0 (NE)	NE (NE)	NE (NE)
Median	70.0	-1.0	NE	NE
Min - Max	70 - 70	-1 - -1	NE - NE	NE - NE
Cycle 43 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	82.0 (NE)	11.0 (NE)	85.0 (NE)	7.0 (NE)
Median	82.0	11.0	85.0	7.0
Min - Max	82 - 82	11 - 11	85 - 85	7 - 7
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	3.0 (NE)	NE (NE)	NE (NE)
Median	74.0	3.0	NE	NE
Min - Max	74 - 74	3 - 3	NE - NE	NE - NE
Cycle 43 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	76.0 (NE)	5.0 (NE)	NE (NE)	NE (NE)
Median	76.0	5.0	NE	NE
Min - Max	76 - 76	5 - 5	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	76.0 (NE)	5.0 (NE)	NE (NE)	NE (NE)
Median	76.0	5.0	NE	NE
Min - Max	76 - 76	5 - 5	NE - NE	NE - NE
Cycle 43 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	3.0 (NE)	NE (NE)	NE (NE)
Median	74.0	3.0	NE	NE
Min - Max	74 - 74	3 - 3	NE - NE	NE - NE

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	82.0 (NE)	11.0 (NE)	NE (NE)	NE (NE)
Median	82.0	11.0	NE	NE
Min - Max	82 - 82	11 - 11	NE - NE	NE - NE
Cycle 44 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	71.0 (NE)	-7.0 (NE)
Median	NE	NE	71.0	-7.0
Min - Max	NE - NE	NE - NE	71 - 71	-7 - -7
Cycle 45 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	65.0 (NE)	-13.0 (NE)
Median	NE	NE	65.0	-13.0
Min - Max	NE - NE	NE - NE	65 - 65	-13 - -13
Cycle 46 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	75.0 (NE)	-3.0 (NE)
Median	NE	NE	75.0	-3.0
Min - Max	NE - NE	NE - NE	75 - 75	-3 - -3
Study Drug Discontinuation				
n	75	74	140	139
Mean (SD)	76.8 (8.7)	-2.1 (10.3)	75.9 (10.1)	-0.9 (10.3)
Median	76.0	-1.5	76.5	0.0
Min - Max	60 - 106	-31 - 17	51 - 115	-27 - 30
Post-Baseline Last				
n	79	79	138	138
Mean (SD)	76.6 (8.9)	-2.2 (10.3)	75.9 (10.2)	-1.1 (10.3)
Median	76.0	-2.0	76.0	0.0
Min - Max	60 - 106	-31 - 17	51 - 115	-27 - 30
PRE PAC INFUSION				
n	1	1	5	5
Mean (SD)	41.0 (NE)	-33.0 (NE)	76.0 (7.0)	2.8 (9.8)
Median	41.0	-33.0	78.0	-4.0
Min - Max	41 - 41	-33 - -33	65 - 83	-5 - 14
AFTER PAC INFUSION				
n	6	6	21	21
Mean (SD)	75.0 (7.8)	3.2 (8.1)	72.6 (8.3)	-1.4 (9.3)
Median	72.5	4.5	70.0	-1.0
Min - Max	67 - 88	-11 - 11	60 - 88	-20 - 15

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Post-Baseline Minimum				
n	2	2	7	7
Mean (SD)	60.0 (0.0)	-15.0 (7.1)	58.9 (12.1)	-15.7 (10.7)
Median	60.0	-15.0	65.0	-14.0
Min - Max	60 - 60	-20 - -10	35 - 70	-34 - -2
PRE PAC INFUSION				
n	44	44	100	100
Mean (SD)	58.8 (13.0)	-19.3 (18.1)	60.7 (9.4)	-15.1 (10.6)
Median	60.0	-14.0	60.0	-14.0
Min - Max	7 - 76	-103 - 1	20 - 84	-45 - 10
AFTER PAC INFUSION				
n	40	40	57	57
Mean (SD)	59.7 (7.6)	-18.7 (9.5)	60.9 (9.7)	-17.0 (11.9)
Median	60.0	-18.5	60.0	-16.0
Min - Max	44 - 80	-54 - -5	7 - 75	-54 - 3
Post-Baseline Maximum				
n	10	10	13	13
Mean (SD)	86.8 (6.4)	11.4 (5.2)	88.2 (9.4)	10.5 (8.5)
Median	87.5	12.5	85.0	10.0
Min - Max	77 - 96	3 - 17	77 - 106	0 - 29
PRE PAC INFUSION				
n	43	43	81	81
Mean (SD)	87.1 (8.2)	9.7 (9.7)	89.7 (10.1)	12.8 (11.0)
Median	86.0	10.0	90.0	12.0
Min - Max	70 - 110	-11 - 32	70 - 124	-13 - 39
AFTER PAC INFUSION				
n	33	33	70	70
Mean (SD)	88.0 (9.8)	8.1 (7.8)	89.4 (10.8)	13.8 (11.9)
Median	88.0	10.0	90.0	10.0
Min - Max	61 - 114	-13 - 22	73 - 126	-10 - 46

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Baseline				
n	86		164	
Mean (SD)	125.3 (15.1)		125.2 (15.3)	
Median	125.0		125.0	
Min - Max	90 - 189		90 - 180	
Cycle 1 Day 1				
PRE PAC INFUSION				
n	84	83	145	144
Mean (SD)	121.8 (15.5)	-3.2 (12.8)	123.0 (15.4)	-2.6 (15.0)
Median	120.5	-1.0	122.0	-1.0
Min - Max	83 - 175	-48 - 25	88 - 182	-46 - 58
AFTER PAC INFUSION				
n	84	83	157	156
Mean (SD)	124.0 (17.1)	-1.5 (13.1)	125.5 (16.2)	1.0 (14.6)
Median	120.5	0.0	125.0	0.0
Min - Max	90 - 187	-29 - 30	95 - 181	-40 - 56
Cycle 1 Day 8				
PRE PAC INFUSION				
n	86	85	160	158
Mean (SD)	118.2 (14.6)	-7.1 (15.4)	118.6 (13.8)	-6.6 (16.6)
Median	119.0	-5.0	120.0	-3.5
Min - Max	74 - 157	-56 - 28	86 - 160	-54 - 32
AFTER PAC INFUSION				
n	78	77	148	146
Mean (SD)	121.0 (13.1)	-4.6 (12.2)	121.4 (13.3)	-2.9 (15.4)
Median	121.0	-5.0	120.0	0.0
Min - Max	85 - 158	-32 - 22	90 - 158	-46 - 33
Cycle 1 Day 15				
PRE PAC INFUSION				
n	81	80	148	146
Mean (SD)	117.9 (13.1)	-7.4 (14.5)	120.5 (15.4)	-3.8 (16.3)
Median	118.0	-7.0	120.0	-4.0
Min - Max	85 - 150	-61 - 23	85 - 163	-48 - 40
AFTER PAC INFUSION				
n	74	73	133	132
Mean (SD)	117.8 (12.7)	-7.6 (15.3)	123.2 (15.0)	-0.9 (16.3)
Median	117.5	-5.0	122.0	0.0
Min - Max	90 - 152	-54 - 25	90 - 179	-61 - 45
Cycle 2 Day 1				
PRE PAC INFUSION				
n	78	77	161	159
Mean (SD)	118.3 (12.3)	-6.4 (14.0)	121.0 (16.5)	-4.1 (15.0)
Median	117.5	-5.0	120.0	-4.0
Min - Max	90 - 142	-59 - 19	79 - 179	-47 - 50

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	74	73	153	152
Mean (SD)	120.3 (14.7)	-5.0 (13.2)	123.4 (16.7)	-1.5 (16.3)
Median	120.0	-3.0	120.0	-2.0
Min - Max	92 - 169	-46 - 20	90 - 180	-50 - 90
Cycle 2 Day 8				
PRE PAC INFUSION				
n	79	78	153	151
Mean (SD)	120.3 (12.8)	-4.9 (15.3)	120.2 (16.4)	-4.7 (15.5)
Median	120.0	-3.0	120.0	-3.0
Min - Max	90 - 160	-81 - 28	83 - 180	-50 - 40
AFTER PAC INFUSION				
n	72	71	149	147
Mean (SD)	117.7 (13.3)	-8.1 (16.1)	121.4 (16.8)	-3.0 (16.7)
Median	118.5	-10.0	120.0	-1.0
Min - Max	88 - 167	-57 - 31	80 - 196	-50 - 73
Cycle 2 Day 15				
PRE PAC INFUSION				
n	77	76	148	146
Mean (SD)	117.6 (13.0)	-7.6 (16.3)	119.6 (16.5)	-5.0 (16.1)
Median	116.0	-6.0	120.0	-4.5
Min - Max	94 - 161	-63 - 24	85 - 180	-50 - 60
AFTER PAC INFUSION				
n	71	70	146	144
Mean (SD)	117.9 (14.8)	-7.5 (13.8)	121.6 (14.8)	-3.2 (16.1)
Median	118.0	-5.5	120.0	-3.0
Min - Max	89 - 157	-47 - 30	87 - 170	-52 - 60
Cycle 3 Day 1				
PRE PAC INFUSION				
n	75	74	143	141
Mean (SD)	121.5 (16.0)	-3.4 (17.3)	121.2 (16.3)	-3.7 (17.1)
Median	120.0	-3.5	120.0	-2.0
Min - Max	87 - 201	-74 - 41	80 - 163	-53 - 50
AFTER PAC INFUSION				
n	70	69	134	132
Mean (SD)	119.9 (14.3)	-5.4 (16.0)	122.1 (16.4)	-2.8 (17.3)
Median	120.0	-4.0	120.0	0.0
Min - Max	92 - 160	-62 - 36	75 - 170	-51 - 58
Cycle 3 Day 8				
PRE PAC INFUSION				
n	73	72	140	138
Mean (SD)	117.6 (13.5)	-7.8 (14.9)	120.8 (15.3)	-3.9 (16.3)
Median	118.0	-5.0	121.0	-3.0
Min - Max	84 - 165	-72 - 20	86 - 185	-53 - 62

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	69	68	138	136
Mean (SD)	117.6 (12.0)	-7.6 (14.8)	121.8 (15.3)	-3.5 (14.9)
Median	119.0	-6.0	120.5	-2.0
Min - Max	90 - 143	-71 - 20	80 - 170	-50 - 47
Cycle 3 Day 15				
PRE PAC INFUSION				
n	67	66	136	135
Mean (SD)	116.8 (11.2)	-8.5 (14.9)	119.1 (14.4)	-5.5 (15.2)
Median	118.0	-9.0	120.0	-5.0
Min - Max	95 - 141	-74 - 21	89 - 170	-44 - 45
AFTER PAC INFUSION				
n	67	66	129	128
Mean (SD)	119.1 (11.5)	-6.4 (13.1)	120.4 (14.7)	-3.7 (16.3)
Median	119.0	-3.0	120.0	-2.0
Min - Max	92 - 157	-67 - 11	90 - 162	-63 - 56
Cycle 4 Day 1				
PRE PAC INFUSION				
n	69	68	132	130
Mean (SD)	118.7 (13.9)	-6.5 (15.4)	121.6 (16.0)	-3.8 (15.9)
Median	120.0	-5.0	120.5	-3.5
Min - Max	90 - 151	-68 - 30	90 - 168	-40 - 60
AFTER PAC INFUSION				
n	65	64	122	120
Mean (SD)	117.9 (13.6)	-7.3 (13.7)	123.2 (15.7)	-0.9 (15.2)
Median	118.0	-4.5	122.5	0.0
Min - Max	88 - 160	-77 - 19	94 - 180	-40 - 56
Cycle 4 Day 8				
PRE PAC INFUSION				
n	68	67	127	126
Mean (SD)	116.9 (13.5)	-8.4 (15.7)	117.4 (14.1)	-7.3 (13.3)
Median	117.0	-9.0	118.0	-8.0
Min - Max	90 - 148	-66 - 30	86 - 170	-35 - 40
AFTER PAC INFUSION				
n	65	64	120	119
Mean (SD)	117.6 (13.9)	-7.3 (13.1)	119.8 (13.3)	-4.5 (14.4)
Median	114.0	-7.0	120.0	-3.0
Min - Max	90 - 154	-58 - 30	91 - 155	-44 - 40
Cycle 4 Day 15				
PRE PAC INFUSION				
n	67	66	126	124
Mean (SD)	116.1 (12.3)	-9.8 (17.4)	117.7 (13.7)	-7.5 (15.8)
Median	117.0	-9.0	119.0	-10.0
Min - Max	88 - 147	-74 - 33	90 - 150	-54 - 50

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	66	65	115	113
Mean (SD)	118.1 (13.3)	-8.0 (13.8)	120.8 (15.8)	-3.7 (16.4)
Median	120.0	-6.0	120.0	-4.0
Min - Max	90 - 152	-58 - 15	90 - 162	-45 - 45
Cycle 5 Day 1				
PRE PAC INFUSION				
n	61	60	103	101
Mean (SD)	119.1 (14.3)	-8.2 (14.9)	121.3 (14.8)	-4.0 (14.3)
Median	117.0	-8.0	120.0	-4.0
Min - Max	94 - 173	-44 - 28	92 - 169	-41 - 40
AFTER PAC INFUSION				
n	57	56	96	94
Mean (SD)	119.9 (16.6)	-7.0 (12.8)	124.2 (15.6)	-0.7 (15.6)
Median	118.0	-8.5	121.0	0.0
Min - Max	90 - 171	-41 - 19	90 - 173	-42 - 50
Cycle 5 Day 8				
PRE PAC INFUSION				
n	53	52	96	95
Mean (SD)	115.5 (12.7)	-11.4 (16.6)	120.6 (14.2)	-4.9 (15.9)
Median	115.0	-10.0	120.0	-4.0
Min - Max	90 - 152	-67 - 15	90 - 180	-45 - 47
AFTER PAC INFUSION				
n	52	51	89	88
Mean (SD)	116.2 (13.1)	-10.2 (13.6)	120.6 (13.8)	-4.1 (16.3)
Median	118.0	-9.0	120.0	-2.0
Min - Max	88 - 146	-59 - 21	83 - 162	-66 - 32
Cycle 5 Day 15				
PRE PAC INFUSION				
n	56	55	91	90
Mean (SD)	118.4 (12.9)	-8.7 (17.5)	118.5 (14.4)	-6.3 (15.5)
Median	117.0	-8.0	120.0	-5.0
Min - Max	96 - 159	-76 - 35	87 - 171	-60 - 40
AFTER PAC INFUSION				
n	52	51	78	77
Mean (SD)	119.6 (14.2)	-7.6 (15.5)	120.4 (14.4)	-3.5 (13.7)
Median	120.0	-7.0	120.5	0.0
Min - Max	92 - 147	-61 - 26	86 - 160	-40 - 20
Cycle 6 Day 1				
PRE PAC INFUSION				
n	56	55	91	90
Mean (SD)	116.8 (13.2)	-10.4 (15.9)	120.6 (14.9)	-4.3 (16.4)
Median	116.5	-9.0	120.0	-4.0
Min - Max	90 - 145	-48 - 33	90 - 170	-52 - 47

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	Placebo + Paclitaxel (N=87) Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	Ipatasertib + Paclitaxel (N=166) Change from Baseline
AFTER PAC INFUSION				
n	49	48	85	84
Mean (SD)	119.0 (15.6)	-7.7 (14.1)	123.9 (15.0)	-0.4 (16.7)
Median	120.0	-8.0	122.0	0.0
Min - Max	85 - 158	-50 - 28	90 - 172	-48 - 42
Cycle 6 Day 8				
PRE PAC INFUSION				
n	49	48	87	86
Mean (SD)	117.7 (13.9)	-9.8 (16.8)	119.1 (13.6)	-6.1 (15.9)
Median	116.0	-9.0	120.0	-5.0
Min - Max	89 - 154	-82 - 29	88 - 165	-54 - 37
AFTER PAC INFUSION				
n	48	47	83	82
Mean (SD)	117.9 (15.9)	-10.0 (13.9)	120.7 (15.2)	-3.9 (17.7)
Median	118.5	-9.0	120.0	-4.0
Min - Max	91 - 158	-63 - 23	95 - 180	-50 - 56
Cycle 6 Day 15				
PRE PAC INFUSION				
n	49	48	84	83
Mean (SD)	117.7 (13.1)	-9.7 (16.6)	118.3 (14.4)	-6.4 (17.4)
Median	118.0	-8.0	120.0	-3.0
Min - Max	82 - 152	-70 - 23	86 - 154	-48 - 53
AFTER PAC INFUSION				
n	47	46	80	79
Mean (SD)	117.9 (14.4)	-9.2 (13.4)	121.2 (15.1)	-3.6 (16.2)
Median	119.0	-10.0	120.0	0.0
Min - Max	83 - 151	-55 - 17	83 - 162	-36 - 52
Cycle 7 Day 1				
PRE PAC INFUSION				
n	42	41	76	75
Mean (SD)	119.1 (14.3)	-8.3 (14.3)	122.6 (14.9)	-2.4 (14.3)
Median	119.5	-6.0	124.0	-2.0
Min - Max	88 - 154	-47 - 28	88 - 161	-35 - 43
AFTER PAC INFUSION				
n	37	36	67	66
Mean (SD)	118.8 (14.7)	-7.7 (12.0)	124.5 (15.6)	0.6 (15.6)
Median	120.0	-8.0	125.0	0.0
Min - Max	92 - 161	-34 - 27	97 - 170	-40 - 46
Cycle 7 Day 8				
PRE PAC INFUSION				
n	35	34	67	66
Mean (SD)	118.1 (15.9)	-9.9 (20.6)	119.7 (16.2)	-5.4 (16.4)
Median	118.0	-10.0	120.0	-5.0
Min - Max	90 - 180	-70 - 64	93 - 178	-40 - 50

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	34	33	63	62
Mean (SD)	116.9 (13.7)	-10.9 (14.8)	122.4 (15.9)	-1.7 (16.3)
Median	117.0	-10.0	120.0	-1.0
Min - Max	90 - 155	-64 - 15	90 - 178	-35 - 40
Cycle 7 Day 15				
PRE PAC INFUSION				
n	34	33	69	68
Mean (SD)	115.8 (13.1)	-10.1 (12.9)	119.6 (14.4)	-5.1 (14.7)
Median	115.5	-9.0	120.0	-5.5
Min - Max	91 - 148	-39 - 14	86 - 160	-40 - 43
AFTER PAC INFUSION				
n	34	33	66	65
Mean (SD)	117.6 (14.6)	-8.4 (11.1)	121.7 (15.4)	-3.0 (17.1)
Median	117.0	-10.0	120.5	-2.0
Min - Max	93 - 163	-31 - 13	83 - 173	-50 - 49
Cycle 8 Day 1				
PRE PAC INFUSION				
n	33	32	70	69
Mean (SD)	116.8 (15.3)	-13.0 (14.1)	124.0 (15.9)	-1.1 (15.8)
Median	115.0	-10.5	122.0	0.0
Min - Max	91 - 167	-58 - 14	90 - 174	-40 - 45
AFTER PAC INFUSION				
n	27	26	63	62
Mean (SD)	120.3 (15.2)	-8.1 (16.0)	124.6 (17.3)	0.5 (17.2)
Median	121.0	-7.5	125.0	0.0
Min - Max	89 - 162	-65 - 20	99 - 186	-50 - 44
Cycle 8 Day 8				
PRE PAC INFUSION				
n	29	28	64	63
Mean (SD)	116.8 (14.9)	-12.0 (18.5)	121.2 (13.8)	-4.2 (15.4)
Median	117.0	-7.0	120.0	-4.0
Min - Max	88 - 146	-82 - 8	90 - 178	-42 - 35
AFTER PAC INFUSION				
n	27	26	60	59
Mean (SD)	118.2 (18.1)	-10.1 (16.5)	122.4 (14.9)	-1.9 (16.4)
Median	117.0	-6.5	121.5	0.0
Min - Max	85 - 170	-67 - 25	90 - 166	-50 - 40
Cycle 8 Day 15				
PRE PAC INFUSION				
n	29	28	61	60
Mean (SD)	116.6 (14.1)	-11.4 (15.1)	120.0 (14.2)	-5.0 (15.3)
Median	118.0	-10.0	120.0	-4.5
Min - Max	92 - 147	-70 - 9	86 - 151	-37 - 40

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	27	26	58	57
Mean (SD)	117.0 (15.7)	-10.4 (17.1)	124.8 (16.9)	0.1 (18.0)
Median	117.0	-7.0	121.0	0.0
Min - Max	85 - 149	-76 - 15	96 - 173	-53 - 47
Cycle 9 Day 1				
PRE PAC INFUSION				
n	27	26	57	56
Mean (SD)	118.5 (11.2)	-9.1 (12.4)	121.6 (14.7)	-3.8 (14.6)
Median	120.0	-11.0	121.0	-4.5
Min - Max	100 - 140	-37 - 14	79 - 160	-38 - 35
AFTER PAC INFUSION				
n	22	21	52	51
Mean (SD)	118.5 (16.3)	-7.5 (12.6)	126.8 (16.4)	1.9 (16.9)
Median	117.5	-9.0	122.5	0.0
Min - Max	89 - 152	-37 - 15	90 - 170	-40 - 50
Cycle 9 Day 8				
PRE PAC INFUSION				
n	24	23	51	50
Mean (SD)	119.0 (15.4)	-6.1 (12.4)	120.1 (14.6)	-5.0 (16.9)
Median	121.5	-9.0	120.0	-4.0
Min - Max	84 - 140	-30 - 20	91 - 149	-50 - 35
AFTER PAC INFUSION				
n	21	20	50	49
Mean (SD)	119.0 (12.7)	-7.5 (9.4)	122.7 (13.6)	-2.0 (15.4)
Median	119.0	-8.5	121.5	1.0
Min - Max	98 - 147	-25 - 14	92 - 153	-41 - 29
Cycle 9 Day 15				
PRE PAC INFUSION				
n	22	21	51	50
Mean (SD)	117.5 (11.8)	-9.3 (12.0)	119.8 (13.2)	-4.7 (15.9)
Median	118.0	-12.0	120.0	-5.5
Min - Max	96 - 143	-27 - 22	87 - 147	-40 - 35
AFTER PAC INFUSION				
n	20	19	48	47
Mean (SD)	120.0 (12.3)	-6.7 (10.3)	122.7 (14.9)	-1.8 (14.0)
Median	120.0	-5.0	123.5	0.0
Min - Max	98 - 151	-21 - 13	91 - 149	-40 - 30
Cycle 10 Day 1				
PRE PAC INFUSION				
n	22	22	55	54
Mean (SD)	116.7 (10.7)	-10.0 (9.5)	121.0 (15.7)	-3.7 (14.4)
Median	114.0	-11.0	120.0	-4.0
Min - Max	100 - 136	-27 - 5	91 - 164	-47 - 25

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	19	19	44	43
Mean (SD)	114.4 (11.4)	-11.3 (8.3)	126.0 (16.2)	2.5 (15.3)
Median	112.0	-10.0	126.0	3.0
Min - Max	100 - 137	-30 - -1	95 - 174	-31 - 40
Cycle 10 Day 8				
PRE PAC INFUSION				
n	19	18	43	42
Mean (SD)	116.9 (11.9)	-8.0 (9.8)	118.7 (13.4)	-6.5 (16.2)
Median	118.0	-9.0	117.0	-5.5
Min - Max	98 - 145	-24 - 13	91 - 170	-40 - 50
AFTER PAC INFUSION				
n	18	17	40	39
Mean (SD)	117.2 (10.0)	-8.3 (7.9)	120.7 (15.3)	-3.1 (17.3)
Median	119.5	-10.0	120.0	-6.0
Min - Max	99 - 139	-20 - 13	92 - 160	-40 - 40
Cycle 10 Day 15				
PRE PAC INFUSION				
n	18	17	46	45
Mean (SD)	120.0 (12.7)	-4.9 (10.9)	116.8 (13.7)	-9.2 (14.5)
Median	122.0	-7.0	118.0	-10.0
Min - Max	104 - 153	-22 - 13	83 - 146	-49 - 21
AFTER PAC INFUSION				
n	16	15	41	40
Mean (SD)	114.9 (11.8)	-10.3 (11.1)	120.1 (15.4)	-5.3 (17.2)
Median	113.0	-11.0	120.0	-5.5
Min - Max	97 - 133	-30 - 12	87 - 150	-33 - 49
Cycle 11 Day 1				
PRE PAC INFUSION				
n	17	16	48	47
Mean (SD)	117.6 (14.2)	-6.9 (13.2)	119.3 (17.1)	-7.4 (16.0)
Median	114.0	-4.5	116.0	-7.0
Min - Max	99 - 155	-27 - 22	81 - 163	-39 - 31
AFTER PAC INFUSION				
n	14	13	40	39
Mean (SD)	114.4 (11.8)	-11.1 (15.0)	124.3 (18.8)	-1.1 (18.7)
Median	119.0	-10.0	121.0	0.0
Min - Max	91 - 130	-43 - 11	95 - 170	-38 - 37
Cycle 11 Day 8				
PRE PAC INFUSION				
n	15	14	36	35
Mean (SD)	119.3 (16.0)	-6.4 (14.6)	118.1 (16.3)	-8.0 (15.1)
Median	118.0	-8.5	117.0	-15.0
Min - Max	97 - 151	-29 - 16	89 - 160	-35 - 27

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	14	13	34	33
Mean (SD)	115.1 (15.1)	-12.0 (12.1)	123.0 (15.0)	-2.6 (17.0)
Median	114.5	-11.0	123.0	-5.0
Min - Max	93 - 143	-28 - 15	94 - 160	-34 - 46
Cycle 11 Day 15				
PRE PAC INFUSION				
n	17	16	39	38
Mean (SD)	115.9 (11.6)	-9.4 (12.7)	119.4 (14.2)	-7.0 (17.2)
Median	113.0	-11.5	120.0	-6.0
Min - Max	96 - 136	-34 - 19	90 - 156	-50 - 35
AFTER PAC INFUSION				
n	14	13	36	35
Mean (SD)	117.0 (12.2)	-7.6 (9.4)	123.3 (14.5)	-2.6 (16.8)
Median	118.0	-10.0	124.0	0.0
Min - Max	96 - 137	-27 - 7	92 - 155	-31 - 37
Cycle 12 Day 1				
PRE PAC INFUSION				
n	17	17	43	43
Mean (SD)	119.4 (16.4)	-4.6 (10.8)	124.0 (16.4)	-4.0 (15.2)
Median	113.0	-6.0	122.0	-5.0
Min - Max	103 - 153	-21 - 16	92 - 164	-37 - 33
AFTER PAC INFUSION				
n	14	14	35	35
Mean (SD)	113.9 (13.1)	-7.8 (11.4)	126.7 (15.7)	0.5 (14.4)
Median	110.5	-9.5	122.0	0.0
Min - Max	90 - 138	-25 - 14	101 - 168	-24 - 32
Cycle 12 Day 8				
PRE PAC INFUSION				
n	16	15	33	33
Mean (SD)	120.8 (12.7)	-4.7 (11.3)	118.3 (14.9)	-8.9 (14.5)
Median	119.0	-6.0	120.0	-10.0
Min - Max	104 - 151	-25 - 14	86 - 140	-41 - 18
AFTER PAC INFUSION				
n	14	13	32	32
Mean (SD)	121.2 (13.8)	-4.2 (14.5)	123.2 (15.1)	-3.6 (14.8)
Median	118.0	-9.0	124.5	-4.5
Min - Max	101 - 152	-30 - 22	96 - 147	-33 - 24
Cycle 12 Day 15				
PRE PAC INFUSION				
n	16	15	33	33
Mean (SD)	118.9 (15.9)	-5.8 (17.0)	117.8 (13.1)	-9.5 (12.7)
Median	121.5	-7.0	115.0	-7.0
Min - Max	95 - 141	-35 - 27	93 - 143	-39 - 20

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	14	13	30	30
Mean (SD)	119.4 (12.9)	-5.1 (14.4)	121.7 (15.0)	-5.0 (13.4)
Median	120.0	-5.0	124.0	-8.0
Min - Max	99 - 140	-27 - 22	95 - 147	-32 - 17
Cycle 13 Day 1				
PRE PAC INFUSION				
n	14	13	33	33
Mean (SD)	118.8 (16.1)	-7.2 (10.9)	121.3 (14.2)	-8.2 (13.8)
Median	113.0	-10.0	124.0	-11.0
Min - Max	97 - 141	-23 - 13	90 - 150	-37 - 20
AFTER PAC INFUSION				
n	12	11	27	27
Mean (SD)	116.1 (11.6)	-8.5 (12.1)	129.3 (17.7)	1.3 (13.5)
Median	117.0	-4.0	129.0	0.0
Min - Max	100 - 136	-26 - 11	100 - 168	-20 - 28
Cycle 13 Day 8				
PRE PAC INFUSION				
n	12	11	27	27
Mean (SD)	116.2 (12.9)	-6.7 (11.7)	121.7 (14.8)	-5.6 (15.4)
Median	115.0	-11.0	124.0	-5.0
Min - Max	98 - 142	-19 - 18	90 - 142	-30 - 26
AFTER PAC INFUSION				
n	11	10	24	24
Mean (SD)	117.5 (13.1)	-7.0 (16.6)	125.3 (16.2)	-2.3 (16.0)
Median	114.0	-8.5	128.0	-0.5
Min - Max	100 - 142	-32 - 19	92 - 151	-30 - 27
Cycle 13 Day 15				
PRE PAC INFUSION				
n	12	11	27	27
Mean (SD)	116.7 (12.5)	-6.0 (6.1)	121.9 (13.8)	-6.1 (12.4)
Median	113.5	-6.0	120.0	-1.0
Min - Max	101 - 134	-17 - 4	94 - 149	-31 - 18
AFTER PAC INFUSION				
n	11	10	23	23
Mean (SD)	115.6 (11.3)	-8.1 (13.9)	122.7 (13.2)	-6.4 (13.3)
Median	119.0	-12.0	125.0	-10.0
Min - Max	100 - 131	-26 - 17	100 - 143	-28 - 19
Cycle 14 Day 1				
PRE PAC INFUSION				
n	13	12	32	32
Mean (SD)	119.6 (13.0)	-5.9 (11.8)	123.8 (15.8)	-4.0 (10.2)
Median	119.0	-10.0	124.0	-5.5
Min - Max	100 - 140	-20 - 22	91 - 166	-22 - 22

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
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Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	Placebo + Paclitaxel (N=87) Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	Ipatasertib + Paclitaxel (N=166) Change from Baseline
AFTER PAC INFUSION				
n	11	10	26	26
Mean (SD)	117.1 (13.8)	-6.6 (11.7)	127.9 (17.8)	1.2 (14.6)
Median	117.0	-8.0	125.5	-0.5
Min - Max	98 - 142	-23 - 18	95 - 166	-30 - 24
Cycle 14 Day 8				
PRE PAC INFUSION				
n	11	10	26	26
Mean (SD)	112.5 (11.1)	-8.6 (7.3)	121.2 (14.3)	-5.2 (14.1)
Median	109.0	-8.0	121.0	-6.0
Min - Max	101 - 128	-21 - 3	90 - 141	-33 - 23
AFTER PAC INFUSION				
n	10	9	24	24
Mean (SD)	115.5 (13.4)	-7.2 (15.2)	125.6 (16.6)	-1.5 (12.4)
Median	110.5	-10.0	125.5	-0.5
Min - Max	100 - 136	-33 - 23	95 - 161	-32 - 22
Cycle 14 Day 15				
PRE PAC INFUSION				
n	11	10	26	26
Mean (SD)	117.7 (14.9)	-6.3 (12.8)	118.5 (9.8)	-6.6 (12.8)
Median	119.0	-7.0	120.0	-5.5
Min - Max	93 - 143	-22 - 18	99 - 140	-37 - 20
AFTER PAC INFUSION				
n	10	9	24	24
Mean (SD)	117.8 (13.4)	-8.2 (11.2)	120.7 (13.1)	-4.5 (15.3)
Median	115.5	-6.0	123.0	-4.5
Min - Max	98 - 141	-23 - 13	89 - 145	-39 - 22
Cycle 15 Day 1				
PRE PAC INFUSION				
n	11	11	28	28
Mean (SD)	119.0 (10.8)	-4.9 (12.6)	122.5 (14.0)	-5.6 (12.8)
Median	118.0	-8.0	124.5	-2.0
Min - Max	99 - 134	-27 - 14	91 - 147	-30 - 16
AFTER PAC INFUSION				
n	10	10	22	22
Mean (SD)	118.7 (12.8)	-2.8 (13.3)	125.4 (18.4)	-1.4 (12.7)
Median	119.5	-2.0	125.5	0.5
Min - Max	99 - 138	-27 - 18	98 - 169	-20 - 17
Cycle 15 Day 8				
PRE PAC INFUSION				
n	11	10	21	21
Mean (SD)	115.9 (15.5)	-7.1 (11.5)	118.9 (11.4)	-8.1 (12.4)
Median	119.0	-7.0	122.0	-5.0
Min - Max	93 - 136	-23 - 18	100 - 136	-35 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	10	9	18	18
Mean (SD)	120.1 (13.2)	-5.6 (14.5)	121.5 (19.3)	-4.3 (17.9)
Median	122.0	-7.0	120.5	-10.0
Min - Max	99 - 140	-30 - 25	94 - 172	-35 - 42
Cycle 15 Day 15				
PRE PAC INFUSION				
n	10	9	22	22
Mean (SD)	113.8 (14.5)	-6.9 (17.0)	117.8 (9.8)	-10.0 (14.2)
Median	112.0	-11.0	120.0	-8.5
Min - Max	96 - 142	-38 - 21	91 - 133	-48 - 13
AFTER PAC INFUSION				
n	9	8	20	20
Mean (SD)	113.0 (13.4)	-8.9 (15.9)	121.1 (14.3)	-6.3 (16.4)
Median	113.0	-11.5	123.0	-10.0
Min - Max	96 - 136	-27 - 23	98 - 153	-38 - 29
Cycle 16 Day 1				
PRE PAC INFUSION				
n	11	10	24	24
Mean (SD)	120.0 (15.2)	-6.9 (14.5)	124.5 (15.9)	-2.7 (12.8)
Median	124.0	-11.5	128.0	0.0
Min - Max	98 - 137	-27 - 23	83 - 157	-30 - 20
AFTER PAC INFUSION				
n	10	9	20	20
Mean (SD)	117.4 (14.4)	-6.4 (17.1)	128.6 (19.0)	2.2 (16.5)
Median	119.5	-11.0	131.0	0.0
Min - Max	93 - 139	-22 - 24	95 - 167	-24 - 43
Cycle 16 Day 8				
PRE PAC INFUSION				
n	11	10	19	19
Mean (SD)	112.5 (12.9)	-8.8 (13.8)	118.6 (11.9)	-7.7 (14.1)
Median	111.0	-10.0	118.0	-7.0
Min - Max	98 - 135	-28 - 19	96 - 140	-35 - 20
AFTER PAC INFUSION				
n	10	9	19	19
Mean (SD)	116.7 (13.6)	-6.8 (18.7)	129.7 (16.5)	3.4 (17.5)
Median	116.0	-9.0	130.0	2.0
Min - Max	98 - 138	-28 - 31	90 - 167	-20 - 43
Cycle 16 Day 15				
PRE PAC INFUSION				
n	10	9	21	21
Mean (SD)	118.4 (14.8)	-4.0 (16.0)	119.7 (10.6)	-7.0 (12.2)
Median	116.5	-6.0	123.0	-5.0
Min - Max	99 - 143	-27 - 25	96 - 133	-28 - 19

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	9	8	19	19
Mean (SD)	114.2 (16.9)	-9.8 (15.7)	129.0 (13.7)	2.6 (10.8)
Median	110.0	-11.5	130.0	0.0
Min - Max	97 - 147	-30 - 14	93 - 150	-17 - 26
Cycle 17 Day 1				
PRE PAC INFUSION				
n	8	7	23	23
Mean (SD)	124.8 (18.5)	-4.4 (9.0)	121.7 (11.5)	-7.8 (12.4)
Median	126.0	-3.0	123.0	-10.0
Min - Max	95 - 151	-15 - 8	87 - 140	-31 - 17
AFTER PAC INFUSION				
n	7	6	20	20
Mean (SD)	118.0 (10.2)	-4.8 (15.0)	131.4 (16.1)	2.1 (15.8)
Median	117.0	-4.0	130.0	2.5
Min - Max	106 - 138	-27 - 11	105 - 168	-30 - 44
Cycle 17 Day 8				
PRE PAC INFUSION				
n	6	5	18	18
Mean (SD)	121.3 (13.2)	1.0 (6.7)	123.1 (12.9)	-6.1 (13.3)
Median	120.5	0.0	124.5	-3.0
Min - Max	105 - 140	-8 - 9	91 - 141	-30 - 19
AFTER PAC INFUSION				
n	6	5	18	18
Mean (SD)	120.0 (8.9)	-0.6 (12.7)	129.4 (16.8)	0.2 (16.1)
Median	118.0	3.0	129.0	-1.5
Min - Max	110 - 136	-21 - 10	100 - 160	-30 - 31
Cycle 17 Day 15				
PRE PAC INFUSION				
n	7	6	19	19
Mean (SD)	121.6 (14.5)	-3.0 (7.7)	121.6 (9.7)	-7.2 (15.7)
Median	124.0	-1.5	123.0	-7.0
Min - Max	105 - 140	-16 - 5	96 - 137	-40 - 18
AFTER PAC INFUSION				
n	7	6	19	19
Mean (SD)	120.7 (9.1)	-3.2 (11.2)	128.7 (12.3)	-0.2 (11.3)
Median	125.0	-7.5	129.0	0.0
Min - Max	106 - 130	-15 - 14	96 - 157	-22 - 16
Cycle 18 Day 1				
PRE PAC INFUSION				
n	7	7	21	21
Mean (SD)	121.3 (18.4)	-5.3 (10.1)	124.4 (18.3)	-5.5 (15.7)
Median	120.0	-3.0	121.0	-9.0
Min - Max	95 - 150	-18 - 11	89 - 160	-39 - 30

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	6	6	17	17
Mean (SD)	121.8 (9.0)	-1.2 (18.2)	127.6 (22.7)	-2.5 (23.2)
Median	120.0	3.0	122.0	-3.0
Min - Max	112 - 139	-28 - 20	100 - 180	-60 - 36
Cycle 18 Day 8				
PRE PAC INFUSION				
n	6	6	15	15
Mean (SD)	126.0 (11.1)	3.0 (10.0)	124.3 (11.9)	-5.9 (13.1)
Median	123.5	2.5	125.0	-6.0
Min - Max	115 - 139	-12 - 18	99 - 146	-30 - 17
AFTER PAC INFUSION				
n	6	6	14	14
Mean (SD)	123.7 (12.1)	0.7 (11.1)	128.4 (19.4)	-1.8 (18.1)
Median	123.0	1.5	128.5	-3.0
Min - Max	108 - 142	-14 - 19	97 - 170	-21 - 46
Cycle 18 Day 15				
PRE PAC INFUSION				
n	7	6	17	17
Mean (SD)	117.9 (17.9)	-6.7 (11.6)	116.9 (14.7)	-13.3 (16.7)
Median	121.0	-5.0	118.0	-14.0
Min - Max	86 - 139	-21 - 9	95 - 145	-40 - 14
AFTER PAC INFUSION				
n	7	6	16	16
Mean (SD)	122.0 (9.1)	-0.8 (15.1)	124.0 (17.1)	-6.6 (16.3)
Median	119.0	3.0	124.0	-6.0
Min - Max	114 - 139	-26 - 17	100 - 154	-40 - 24
Cycle 19 Day 1				
PRE PAC INFUSION				
n	7	6	18	18
Mean (SD)	123.6 (11.1)	-5.0 (9.7)	122.2 (19.1)	-7.1 (14.9)
Median	127.0	-5.0	123.5	-7.5
Min - Max	104 - 135	-18 - 8	95 - 170	-30 - 20
AFTER PAC INFUSION				
n	6	5	14	14
Mean (SD)	123.5 (14.1)	-3.8 (8.3)	129.5 (17.2)	0.3 (12.9)
Median	126.5	0.0	125.0	-4.5
Min - Max	102 - 140	-15 - 5	100 - 156	-17 - 23
Cycle 19 Day 8				
PRE PAC INFUSION				
n	6	5	13	13
Mean (SD)	125.8 (16.2)	-2.4 (8.8)	123.2 (15.2)	-5.5 (14.5)
Median	127.5	-1.0	122.0	-10.0
Min - Max	106 - 145	-12 - 7	91 - 146	-27 - 16

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	4	12	12
Mean (SD)	121.2 (18.2)	-3.0 (17.5)	120.6 (18.2)	-8.0 (16.3)
Median	111.0	4.0	121.5	-6.5
Min - Max	105 - 149	-29 - 9	86 - 148	-32 - 20
Cycle 19 Day 15				
PRE PAC INFUSION				
n	6	5	13	13
Mean (SD)	123.7 (19.6)	-4.6 (14.1)	120.9 (16.4)	-8.2 (13.5)
Median	126.5	0.0	121.0	-15.0
Min - Max	96 - 143	-26 - 9	87 - 140	-31 - 13
AFTER PAC INFUSION				
n	6	5	13	13
Mean (SD)	124.2 (17.3)	-5.0 (12.1)	127.2 (15.6)	-1.9 (13.7)
Median	121.5	-3.0	127.0	-8.0
Min - Max	104 - 145	-19 - 8	104 - 168	-20 - 32
Cycle 20 Day 1				
PRE PAC INFUSION				
n	6	5	16	16
Mean (SD)	128.7 (14.4)	-1.8 (19.4)	121.7 (13.0)	-7.6 (14.8)
Median	128.5	2.0	122.0	-4.5
Min - Max	110 - 147	-32 - 19	92 - 143	-40 - 14
AFTER PAC INFUSION				
n	5	4	13	13
Mean (SD)	121.2 (19.4)	-3.8 (9.7)	128.2 (12.1)	-1.0 (12.0)
Median	122.0	-2.0	130.0	0.0
Min - Max	100 - 145	-16 - 5	105 - 151	-30 - 20
Cycle 20 Day 8				
PRE PAC INFUSION				
n	6	5	12	12
Mean (SD)	124.7 (13.9)	-3.8 (8.4)	119.3 (13.2)	-9.3 (16.8)
Median	128.0	-3.0	125.0	-5.0
Min - Max	108 - 141	-14 - 7	86 - 132	-40 - 13
AFTER PAC INFUSION				
n	6	5	12	12
Mean (SD)	125.8 (11.5)	-1.0 (12.3)	123.7 (11.9)	-4.9 (16.4)
Median	125.5	2.0	122.0	-4.0
Min - Max	110 - 142	-18 - 11	100 - 145	-40 - 15
Cycle 20 Day 15				
PRE PAC INFUSION				
n	6	5	12	12
Mean (SD)	126.8 (14.7)	0.8 (10.0)	117.1 (9.7)	-12.5 (14.1)
Median	127.5	3.0	119.5	-11.5
Min - Max	110 - 146	-16 - 10	94 - 130	-40 - 13

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	4	11	11
Mean (SD)	128.0 (13.5)	-4.3 (8.1)	121.0 (11.9)	-8.0 (14.8)
Median	128.0	-5.0	125.0	-7.0
Min - Max	106 - 140	-12 - 5	94 - 136	-40 - 19
Cycle 21 Day 1				
PRE PAC INFUSION				
n	5	5	13	13
Mean (SD)	124.4 (14.9)	-2.4 (15.4)	122.2 (11.8)	-4.9 (11.4)
Median	120.0	4.0	121.0	-5.0
Min - Max	111 - 146	-28 - 11	92 - 143	-26 - 11
AFTER PAC INFUSION				
n	3	3	11	11
Mean (SD)	129.0 (19.0)	2.7 (10.1)	121.5 (14.0)	-4.5 (12.6)
Median	129.0	8.0	123.0	-7.0
Min - Max	110 - 148	-9 - 9	93 - 140	-25 - 20
Cycle 21 Day 8				
PRE PAC INFUSION				
n	3	3	11	11
Mean (SD)	121.7 (6.7)	-4.7 (17.9)	116.5 (12.6)	-9.5 (15.9)
Median	120.0	-9.0	120.0	-10.0
Min - Max	116 - 129	-20 - 15	89 - 134	-34 - 10
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	117.0 (15.6)	-3.5 (12.0)	119.0 (10.9)	-6.0 (11.2)
Median	117.0	-3.5	120.0	-3.5
Min - Max	106 - 128	-12 - 5	104 - 134	-24 - 10
Cycle 21 Day 15				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	118.5 (12.0)	-2.0 (15.6)	113.4 (11.2)	-11.6 (13.4)
Median	118.5	-2.0	114.0	-10.5
Min - Max	110 - 127	-13 - 9	87 - 125	-31 - 6
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	119.0 (15.6)	-1.5 (12.0)	117.5 (13.5)	-7.5 (11.4)
Median	119.0	-1.5	119.5	-7.0
Min - Max	108 - 130	-10 - 7	94 - 133	-24 - 13
Cycle 22 Day 1				
PRE PAC INFUSION				
n	4	4	13	13
Mean (SD)	119.3 (14.6)	-12.5 (18.7)	121.1 (10.7)	-6.0 (10.7)
Median	114.5	-14.0	125.0	-3.0
Min - Max	108 - 140	-29 - 7	99 - 134	-24 - 14

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	11	11
Mean (SD)	115.7 (19.3)	-10.7 (20.4)	126.2 (14.6)	0.2 (11.8)
Median	105.0	-2.0	125.0	-4.0
Min - Max	104 - 138	-34 - 4	103 - 154	-15 - 18
Cycle 22 Day 8				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	125.0 (21.2)	4.5 (6.4)	120.7 (7.4)	-4.3 (8.7)
Median	125.0	4.5	120.5	-7.5
Min - Max	110 - 140	0 - 9	108 - 130	-12 - 12
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	120.0 (25.5)	-0.5 (2.1)	123.9 (8.1)	-1.1 (9.0)
Median	120.0	-0.5	121.0	-3.0
Min - Max	102 - 138	-2 - 1	112 - 138	-10 - 17
Cycle 22 Day 15				
PRE PAC INFUSION				
n	2	2	9	9
Mean (SD)	128.0 (25.5)	7.5 (2.1)	120.4 (10.0)	-3.8 (10.7)
Median	128.0	7.5	120.0	-9.0
Min - Max	110 - 146	6 - 9	105 - 133	-18 - 13
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	118.0 (17.0)	-2.5 (10.6)	127.0 (9.0)	2.8 (12.5)
Median	118.0	-2.5	129.0	-2.0
Min - Max	106 - 130	-10 - 5	110 - 139	-13 - 20
Cycle 23 Day 1				
PRE PAC INFUSION				
n	3	3	12	12
Mean (SD)	126.3 (12.7)	-3.3 (19.2)	117.9 (12.8)	-8.8 (13.8)
Median	124.0	0.0	118.0	-7.5
Min - Max	115 - 140	-24 - 14	94 - 135	-38 - 17
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	123.0 (18.4)	2.5 (9.2)	128.8 (20.0)	3.4 (16.5)
Median	123.0	2.5	126.5	1.0
Min - Max	110 - 136	-4 - 9	106 - 177	-13 - 41
Cycle 23 Day 8				
PRE PAC INFUSION				
n	2	2	9	9
Mean (SD)	128.0 (25.5)	7.5 (2.1)	113.4 (9.4)	-10.8 (10.8)
Median	128.0	7.5	116.0	-13.0
Min - Max	110 - 146	6 - 9	97 - 124	-21 - 10

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	124.0 (22.6)	3.5 (4.9)	117.0 (12.3)	-7.2 (10.7)
Median	124.0	3.5	120.0	-10.0
Min - Max	108 - 140	0 - 7	99 - 135	-19 - 18
Cycle 23 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	121.0 (24.0)	0.5 (3.5)	113.6 (10.8)	-9.9 (11.2)
Median	121.0	0.5	115.5	-8.5
Min - Max	104 - 138	-2 - 3	91 - 126	-27 - 3
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	126.0 (22.6)	5.5 (4.9)	121.4 (17.4)	-2.1 (14.5)
Median	126.0	5.5	126.0	0.5
Min - Max	110 - 142	2 - 9	84 - 138	-34 - 12
Cycle 24 Day 1				
PRE PAC INFUSION				
n	3	3	11	11
Mean (SD)	128.0 (18.2)	-1.7 (24.8)	124.3 (13.1)	-2.1 (12.2)
Median	118.0	9.0	129.0	-3.0
Min - Max	117 - 149	-30 - 16	95 - 144	-23 - 17
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	131.5 (17.7)	11.0 (9.9)	128.7 (14.0)	3.8 (9.6)
Median	131.5	11.0	130.0	5.0
Min - Max	119 - 144	4 - 18	105 - 142	-13 - 22
Cycle 24 Day 8				
PRE PAC INFUSION				
n	2	2	7	7
Mean (SD)	119.5 (14.8)	-1.0 (12.7)	116.7 (12.3)	-4.9 (10.8)
Median	119.5	-1.0	118.0	-6.0
Min - Max	109 - 130	-10 - 8	100 - 134	-16 - 14
AFTER PAC INFUSION				
n	2	2	7	7
Mean (SD)	127.0 (21.2)	6.5 (6.4)	121.7 (18.0)	0.1 (19.1)
Median	127.0	6.5	126.0	2.0
Min - Max	112 - 142	2 - 11	96 - 145	-36 - 17
Cycle 24 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	130.5 (23.3)	10.0 (4.2)	120.8 (14.7)	-2.8 (13.6)
Median	130.5	10.0	122.5	-1.0
Min - Max	114 - 147	7 - 13	96 - 138	-22 - 15

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	7	7
Mean (SD)	121.0 (15.6)	0.5 (12.0)	119.4 (12.7)	-2.1 (12.1)
Median	121.0	0.5	122.0	0.0
Min - Max	110 - 132	-8 - 9	101 - 139	-20 - 11
Cycle 25 Day 1				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	125.5 (19.1)	5.0 (8.5)	121.3 (12.4)	-6.7 (14.7)
Median	125.5	5.0	123.5	-9.5
Min - Max	112 - 139	-1 - 11	99 - 140	-23 - 20
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	124.0 (19.8)	3.5 (7.8)	131.4 (16.2)	4.6 (14.1)
Median	124.0	3.5	132.0	2.5
Min - Max	110 - 138	-2 - 9	108 - 160	-10 - 25
Cycle 25 Day 8				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	129.5 (20.5)	9.0 (7.1)	116.4 (10.9)	-7.1 (12.7)
Median	129.5	9.0	116.0	-8.0
Min - Max	115 - 144	4 - 14	100 - 135	-23 - 18
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	123.5 (21.9)	3.0 (5.7)	125.9 (12.6)	2.4 (11.5)
Median	123.5	3.0	129.5	4.0
Min - Max	108 - 139	-1 - 7	100 - 138	-18 - 18
Cycle 25 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	129.0 (15.6)	8.5 (12.0)	111.8 (11.0)	-11.8 (11.7)
Median	129.0	8.5	111.0	-10.0
Min - Max	118 - 140	0 - 17	97 - 128	-35 - 0
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	124.0 (19.8)	3.5 (7.8)	115.4 (18.9)	-8.1 (18.5)
Median	124.0	3.5	108.0	-13.0
Min - Max	110 - 138	-2 - 9	96 - 144	-26 - 26
Cycle 26 Day 1				
PRE PAC INFUSION				
n	2	2	11	11
Mean (SD)	125.0 (24.0)	4.5 (3.5)	121.3 (14.6)	-4.7 (13.2)
Median	125.0	4.5	124.0	-8.0
Min - Max	108 - 142	2 - 7	93 - 140	-25 - 20

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	123.5 (17.7)	3.0 (9.9)	123.2 (9.4)	-2.4 (8.4)
Median	123.5	3.0	125.0	-4.5
Min - Max	111 - 136	-4 - 10	107 - 135	-11 - 15
Cycle 26 Day 8				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	124.5 (24.7)	4.0 (2.8)	113.6 (14.2)	-10.9 (13.4)
Median	124.5	4.0	116.0	-11.0
Min - Max	107 - 142	2 - 6	92 - 129	-30 - 12
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	124.0 (19.8)	3.5 (7.8)	115.3 (16.4)	-9.3 (18.9)
Median	124.0	3.5	113.0	-8.5
Min - Max	110 - 138	-2 - 9	92 - 145	-45 - 15
Cycle 26 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	126.0 (22.6)	5.5 (4.9)	111.1 (11.7)	-12.4 (15.8)
Median	126.0	5.5	112.5	-17.0
Min - Max	110 - 142	2 - 9	87 - 122	-31 - 10
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	121.0 (24.0)	0.5 (3.5)	120.3 (9.8)	-3.3 (7.0)
Median	121.0	0.5	120.0	-1.0
Min - Max	104 - 138	-2 - 3	106 - 135	-15 - 5
Cycle 27 Day 1				
PRE PAC INFUSION				
n	1	1	8	8
Mean (SD)	112.0 (NE)	11.0 (NE)	119.9 (13.4)	-8.5 (15.0)
Median	112.0	11.0	117.5	-16.0
Min - Max	112 - 112	11 - 11	100 - 143	-20 - 23
AFTER PAC INFUSION				
n	1	1	7	7
Mean (SD)	122.0 (NE)	21.0 (NE)	127.0 (9.4)	-1.1 (10.7)
Median	122.0	21.0	125.0	0.0
Min - Max	122 - 122	21 - 21	118 - 144	-17 - 13
Cycle 27 Day 8				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	124.0 (NE)	23.0 (NE)	117.2 (14.3)	-9.7 (14.6)
Median	124.0	23.0	121.5	-10.0
Min - Max	124 - 124	23 - 23	95 - 133	-27 - 13

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	116.0 (NE)	15.0 (NE)	120.3 (14.5)	-6.5 (16.1)
Median	116.0	15.0	126.0	-7.0
Min - Max	116 - 116	15 - 15	102 - 138	-29 - 18
Cycle 27 Day 15				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	118.0 (NE)	17.0 (NE)	113.3 (7.9)	-10.2 (8.8)
Median	118.0	17.0	112.0	-11.5
Min - Max	118 - 118	17 - 17	102 - 124	-22 - 0
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	112.0 (NE)	11.0 (NE)	123.7 (16.0)	0.2 (16.4)
Median	112.0	11.0	125.0	4.5
Min - Max	112 - 112	11 - 11	102 - 144	-22 - 20
Cycle 28 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	122.0 (NE)	21.0 (NE)	113.5 (16.3)	-12.7 (11.9)
Median	122.0	21.0	110.0	-17.0
Min - Max	122 - 122	21 - 21	94 - 141	-24 - 4
AFTER PAC INFUSION				
n	1	1	5	5
Mean (SD)	116.0 (NE)	15.0 (NE)	122.8 (10.7)	-1.4 (12.6)
Median	116.0	15.0	129.0	-8.0
Min - Max	116 - 116	15 - 15	108 - 132	-10 - 20
Cycle 28 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	118.0 (NE)	17.0 (NE)	109.8 (15.1)	-18.0 (14.7)
Median	118.0	17.0	109.0	-20.5
Min - Max	118 - 118	17 - 17	95 - 126	-33 - 2
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	110.0 (NE)	9.0 (NE)	113.3 (17.3)	-14.5 (15.5)
Median	110.0	9.0	115.0	-19.5
Min - Max	110 - 110	9 - 9	91 - 132	-27 - 8
Cycle 28 Day 15				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	115.0 (NE)	14.0 (NE)	118.2 (14.6)	-8.0 (14.6)
Median	115.0	14.0	118.0	-10.5
Min - Max	115 - 115	14 - 14	97 - 141	-21 - 10

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	114.0 (NE)	13.0 (NE)	124.0 (21.0)	-2.2 (15.2)
Median	114.0	13.0	115.0	-2.5
Min - Max	114 - 114	13 - 13	106 - 160	-21 - 24
Cycle 29 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	120.0 (NE)	19.0 (NE)	117.5 (11.3)	-8.7 (7.6)
Median	120.0	19.0	120.5	-9.5
Min - Max	120 - 120	19 - 19	100 - 132	-17 - 4
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	128.0 (NE)	27.0 (NE)	123.0 (16.8)	-2.8 (9.9)
Median	128.0	27.0	123.5	0.0
Min - Max	128 - 128	27 - 27	107 - 138	-17 - 6
Cycle 29 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	129.0 (NE)	28.0 (NE)	121.8 (9.1)	-4.0 (18.2)
Median	129.0	28.0	124.0	-6.5
Min - Max	129 - 129	28 - 28	109 - 130	-23 - 20
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	122.0 (NE)	21.0 (NE)	124.8 (5.7)	-1.0 (14.0)
Median	122.0	21.0	126.0	-7.5
Min - Max	122 - 122	21 - 21	117 - 130	-9 - 20
Cycle 29 Day 15				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	118.0 (NE)	17.0 (NE)	122.5 (6.9)	-5.3 (9.8)
Median	118.0	17.0	123.5	-3.0
Min - Max	118 - 118	17 - 17	114 - 129	-18 - 3
AFTER PAC INFUSION				
n	1	1	3	3
Mean (SD)	115.0 (NE)	14.0 (NE)	127.7 (18.0)	-3.3 (16.4)
Median	115.0	14.0	127.0	3.0
Min - Max	115 - 115	14 - 14	110 - 146	-22 - 9
Cycle 30 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	120.0 (NE)	19.0 (NE)	115.2 (12.7)	-11.0 (9.9)
Median	120.0	19.0	114.5	-8.5
Min - Max	120 - 120	19 - 19	96 - 134	-24 - 0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	110.0 (NE)	9.0 (NE)	135.5 (10.6)	9.8 (3.8)
Median	110.0	9.0	139.0	8.5
Min - Max	110 - 110	9 - 9	120 - 144	7 - 15
Cycle 30 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	126.0 (NE)	25.0 (NE)	115.3 (7.9)	-10.5 (8.6)
Median	126.0	25.0	112.0	-10.5
Min - Max	126 - 126	25 - 25	110 - 127	-21 - 0
AFTER PAC INFUSION				
n	1	1	3	3
Mean (SD)	112.0 (NE)	11.0 (NE)	131.7 (12.0)	8.0 (1.7)
Median	112.0	11.0	131.0	7.0
Min - Max	112 - 112	11 - 11	120 - 144	7 - 10
Cycle 30 Day 15				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	108.0 (NE)	7.0 (NE)	123.5 (3.3)	-2.3 (11.1)
Median	108.0	7.0	123.0	-2.5
Min - Max	108 - 108	7 - 7	120 - 128	-14 - 10
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	110.0 (NE)	9.0 (NE)	117.3 (11.3)	-8.5 (15.2)
Median	110.0	9.0	115.0	-8.5
Min - Max	110 - 110	9 - 9	107 - 132	-25 - 8
Cycle 31 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	116.0 (NE)	15.0 (NE)	118.0 (1.4)	-16.0 (1.4)
Median	116.0	15.0	118.0	-16.0
Min - Max	116 - 116	15 - 15	117 - 119	-17 - -15
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	112.0 (NE)	11.0 (NE)	111.0 (NE)	-21.0 (NE)
Median	112.0	11.0	111.0	-21.0
Min - Max	112 - 112	11 - 11	111 - 111	-21 - -21
Cycle 31 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	122.0 (NE)	21.0 (NE)	129.0 (NE)	-3.0 (NE)
Median	122.0	21.0	129.0	-3.0
Min - Max	122 - 122	21 - 21	129 - 129	-3 - -3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	110.0 (NE)	9.0 (NE)	129.0 (NE)	-3.0 (NE)
Median	110.0	9.0	129.0	-3.0
Min - Max	110 - 110	9 - 9	129 - 129	-3 - -3
Cycle 31 Day 15				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	120.5 (9.2)	-7.5 (3.5)
Median	NE	NE	120.5	-7.5
Min - Max	NE - NE	NE - NE	114 - 127	-10 - -5
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	113.5 (7.8)	-14.5 (13.4)
Median	NE	NE	113.5	-14.5
Min - Max	NE - NE	NE - NE	108 - 119	-24 - -5
Cycle 32 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	126.0 (NE)	-10.0 (NE)
Median	NE	NE	126.0	-10.0
Min - Max	NE - NE	NE - NE	126 - 126	-10 - -10
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	134.5 (3.5)	6.5 (2.1)
Median	NE	NE	134.5	6.5
Min - Max	NE - NE	NE - NE	132 - 137	5 - 8
Cycle 32 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	118.0 (NE)	17.0 (NE)	NE (NE)	NE (NE)
Median	118.0	17.0	NE	NE
Min - Max	118 - 118	17 - 17	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	108.0 (NE)	7.0 (NE)	109.0 (7.1)	-19.0 (12.7)
Median	108.0	7.0	109.0	-19.0
Min - Max	108 - 108	7 - 7	104 - 114	-28 - -10
Cycle 32 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	114.0 (NE)	13.0 (NE)	NE (NE)	NE (NE)
Median	114.0	13.0	NE	NE
Min - Max	114 - 114	13 - 13	NE - NE	NE - NE

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	112.0 (NE)	11.0 (NE)	111.5 (9.2)	-16.5 (14.8)
Median	112.0	11.0	111.5	-16.5
Min - Max	112 - 112	11 - 11	105 - 118	-27 - -6
Cycle 33 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	110.0 (NE)	9.0 (NE)	122.0 (NE)	-14.0 (NE)
Median	110.0	9.0	122.0	-14.0
Min - Max	110 - 110	9 - 9	122 - 122	-14 - -14
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	114.0 (NE)	13.0 (NE)	123.0 (8.5)	-5.0 (2.8)
Median	114.0	13.0	123.0	-5.0
Min - Max	114 - 114	13 - 13	117 - 129	-7 - -3
Cycle 33 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	110.0 (NE)	9.0 (NE)	NE (NE)	NE (NE)
Median	110.0	9.0	NE	NE
Min - Max	110 - 110	9 - 9	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	108.0 (NE)	7.0 (NE)	120.5 (17.7)	-7.5 (23.3)
Median	108.0	7.0	120.5	-7.5
Min - Max	108 - 108	7 - 7	108 - 133	-24 - 9
Cycle 33 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	112.0 (NE)	11.0 (NE)	NE (NE)	NE (NE)
Median	112.0	11.0	NE	NE
Min - Max	112 - 112	11 - 11	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	110.0 (NE)	9.0 (NE)	124.5 (9.2)	-3.5 (14.8)
Median	110.0	9.0	124.5	-3.5
Min - Max	110 - 110	9 - 9	118 - 131	-14 - 7
Cycle 34 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	108.0 (NE)	7.0 (NE)	122.0 (NE)	-14.0 (NE)
Median	108.0	7.0	122.0	-14.0
Min - Max	108 - 108	7 - 7	122 - 122	-14 - -14

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	110.0 (NE)	9.0 (NE)	123.0 (NE)	-9.0 (NE)
Median	110.0	9.0	123.0	-9.0
Min - Max	110 - 110	9 - 9	123 - 123	-9 - -9
Cycle 34 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	112.0 (NE)	11.0 (NE)	NE (NE)	NE (NE)
Median	112.0	11.0	NE	NE
Min - Max	112 - 112	11 - 11	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	115.0 (NE)	14.0 (NE)	107.0 (NE)	-25.0 (NE)
Median	115.0	14.0	107.0	-25.0
Min - Max	115 - 115	14 - 14	107 - 107	-25 - -25
Cycle 34 Day 15				
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	116.0 (NE)	15.0 (NE)	107.0 (NE)	-25.0 (NE)
Median	116.0	15.0	107.0	-25.0
Min - Max	116 - 116	15 - 15	107 - 107	-25 - -25
Cycle 35 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	116.0 (NE)	15.0 (NE)	108.0 (NE)	-28.0 (NE)
Median	116.0	15.0	108.0	-28.0
Min - Max	116 - 116	15 - 15	108 - 108	-28 - -28
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	110.0 (NE)	9.0 (NE)	111.0 (NE)	-21.0 (NE)
Median	110.0	9.0	111.0	-21.0
Min - Max	110 - 110	9 - 9	111 - 111	-21 - -21
Cycle 35 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	116.0 (NE)	15.0 (NE)	NE (NE)	NE (NE)
Median	116.0	15.0	NE	NE
Min - Max	116 - 116	15 - 15	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	104.0 (NE)	3.0 (NE)	111.0 (NE)	-21.0 (NE)
Median	104.0	3.0	111.0	-21.0
Min - Max	104 - 104	3 - 3	111 - 111	-21 - -21

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 35 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	115.0 (NE)	14.0 (NE)	NE (NE)	NE (NE)
Median	115.0	14.0	NE	NE
Min - Max	115 - 115	14 - 14	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	108.0 (NE)	7.0 (NE)	102.0 (NE)	-30.0 (NE)
Median	108.0	7.0	102.0	-30.0
Min - Max	108 - 108	7 - 7	102 - 102	-30 - -30
Cycle 36 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	115.0 (NE)	14.0 (NE)	114.0 (NE)	-22.0 (NE)
Median	115.0	14.0	114.0	-22.0
Min - Max	115 - 115	14 - 14	114 - 114	-22 - -22
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	108.0 (NE)	7.0 (NE)	109.0 (NE)	-23.0 (NE)
Median	108.0	7.0	109.0	-23.0
Min - Max	108 - 108	7 - 7	109 - 109	-23 - -23
Cycle 36 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	116.0 (NE)	15.0 (NE)	NE (NE)	NE (NE)
Median	116.0	15.0	NE	NE
Min - Max	116 - 116	15 - 15	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	110.0 (NE)	9.0 (NE)	106.0 (NE)	-26.0 (NE)
Median	110.0	9.0	106.0	-26.0
Min - Max	110 - 110	9 - 9	106 - 106	-26 - -26
Cycle 36 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	119.0 (NE)	18.0 (NE)	NE (NE)	NE (NE)
Median	119.0	18.0	NE	NE
Min - Max	119 - 119	18 - 18	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	110.0 (NE)	9.0 (NE)	119.0 (NE)	-13.0 (NE)
Median	110.0	9.0	119.0	-13.0
Min - Max	110 - 110	9 - 9	119 - 119	-13 - -13

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
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Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 37 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	114.0 (NE)	13.0 (NE)	116.0 (NE)	-20.0 (NE)
Median	114.0	13.0	116.0	-20.0
Min - Max	114 - 114	13 - 13	116 - 116	-20 - -20
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	110.0 (NE)	9.0 (NE)	124.0 (NE)	-8.0 (NE)
Median	110.0	9.0	124.0	-8.0
Min - Max	110 - 110	9 - 9	124 - 124	-8 - -8
Cycle 37 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	116.0 (NE)	15.0 (NE)	NE (NE)	NE (NE)
Median	116.0	15.0	NE	NE
Min - Max	116 - 116	15 - 15	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	110.0 (NE)	9.0 (NE)	105.0 (NE)	-27.0 (NE)
Median	110.0	9.0	105.0	-27.0
Min - Max	110 - 110	9 - 9	105 - 105	-27 - -27
Cycle 37 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	118.0 (NE)	17.0 (NE)	NE (NE)	NE (NE)
Median	118.0	17.0	NE	NE
Min - Max	118 - 118	17 - 17	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	112.0 (NE)	11.0 (NE)	100.0 (NE)	-32.0 (NE)
Median	112.0	11.0	100.0	-32.0
Min - Max	112 - 112	11 - 11	100 - 100	-32 - -32
Cycle 38 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	121.0 (NE)	20.0 (NE)	112.0 (NE)	-24.0 (NE)
Median	121.0	20.0	112.0	-24.0
Min - Max	121 - 121	20 - 20	112 - 112	-24 - -24
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	117.0 (NE)	16.0 (NE)	115.0 (NE)	-17.0 (NE)
Median	117.0	16.0	115.0	-17.0
Min - Max	117 - 117	16 - 16	115 - 115	-17 - -17

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
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Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 38 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	118.0 (NE)	17.0 (NE)	NE (NE)	NE (NE)
Median	118.0	17.0	NE	NE
Min - Max	118 - 118	17 - 17	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	120.0 (NE)	19.0 (NE)	102.0 (NE)	-30.0 (NE)
Median	120.0	19.0	102.0	-30.0
Min - Max	120 - 120	19 - 19	102 - 102	-30 - -30
Cycle 38 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	122.0 (NE)	21.0 (NE)	NE (NE)	NE (NE)
Median	122.0	21.0	NE	NE
Min - Max	122 - 122	21 - 21	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	120.0 (NE)	19.0 (NE)	102.0 (NE)	-30.0 (NE)
Median	120.0	19.0	102.0	-30.0
Min - Max	120 - 120	19 - 19	102 - 102	-30 - -30
Cycle 39 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	121.0 (NE)	20.0 (NE)	127.0 (NE)	-9.0 (NE)
Median	121.0	20.0	127.0	-9.0
Min - Max	121 - 121	20 - 20	127 - 127	-9 - -9
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	118.0 (NE)	17.0 (NE)	NE (NE)	NE (NE)
Median	118.0	17.0	NE	NE
Min - Max	118 - 118	17 - 17	NE - NE	NE - NE
Cycle 39 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	124.0 (NE)	23.0 (NE)	108.0 (NE)	-24.0 (NE)
Median	124.0	23.0	108.0	-24.0
Min - Max	124 - 124	23 - 23	108 - 108	-24 - -24
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	116.0 (NE)	15.0 (NE)	NE (NE)	NE (NE)
Median	116.0	15.0	NE	NE
Min - Max	116 - 116	15 - 15	NE - NE	NE - NE

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
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Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 39 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	128.0 (NE)	27.0 (NE)	101.0 (NE)	-31.0 (NE)
Median	128.0	27.0	101.0	-31.0
Min - Max	128 - 128	27 - 27	101 - 101	-31 - -31
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	119.0 (NE)	18.0 (NE)	NE (NE)	NE (NE)
Median	119.0	18.0	NE	NE
Min - Max	119 - 119	18 - 18	NE - NE	NE - NE
Cycle 40 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	122.0 (NE)	21.0 (NE)	120.0 (7.1)	-14.0 (4.2)
Median	122.0	21.0	120.0	-14.0
Min - Max	122 - 122	21 - 21	115 - 125	-17 - -11
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	120.0 (NE)	19.0 (NE)	NE (NE)	NE (NE)
Median	120.0	19.0	NE	NE
Min - Max	120 - 120	19 - 19	NE - NE	NE - NE
Cycle 40 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	124.0 (NE)	23.0 (NE)	101.0 (NE)	-31.0 (NE)
Median	124.0	23.0	101.0	-31.0
Min - Max	124 - 124	23 - 23	101 - 101	-31 - -31
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	124.0 (NE)	23.0 (NE)	NE (NE)	NE (NE)
Median	124.0	23.0	NE	NE
Min - Max	124 - 124	23 - 23	NE - NE	NE - NE
Cycle 40 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	122.0 (NE)	21.0 (NE)	103.0 (NE)	-29.0 (NE)
Median	122.0	21.0	103.0	-29.0
Min - Max	122 - 122	21 - 21	103 - 103	-29 - -29
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	118.0 (NE)	17.0 (NE)	NE (NE)	NE (NE)
Median	118.0	17.0	NE	NE
Min - Max	118 - 118	17 - 17	NE - NE	NE - NE

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
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Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 41 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	122.0 (NE)	21.0 (NE)	113.5 (4.9)	-20.5 (7.8)
Median	122.0	21.0	113.5	-20.5
Min - Max	122 - 122	21 - 21	110 - 117	-26 - -15
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	116.0 (NE)	15.0 (NE)	NE (NE)	NE (NE)
Median	116.0	15.0	NE	NE
Min - Max	116 - 116	15 - 15	NE - NE	NE - NE
Cycle 41 Day 8				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	106.0 (NE)	-26.0 (NE)
Median	NE	NE	106.0	-26.0
Min - Max	NE - NE	NE - NE	106 - 106	-26 - -26
Cycle 41 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	119.0 (NE)	18.0 (NE)	102.0 (NE)	-30.0 (NE)
Median	119.0	18.0	102.0	-30.0
Min - Max	119 - 119	18 - 18	102 - 102	-30 - -30
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	122.0 (NE)	21.0 (NE)	NE (NE)	NE (NE)
Median	122.0	21.0	NE	NE
Min - Max	122 - 122	21 - 21	NE - NE	NE - NE
Cycle 42 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	132.0 (NE)	31.0 (NE)	115.0 (NE)	-21.0 (NE)
Median	132.0	31.0	115.0	-21.0
Min - Max	132 - 132	31 - 31	115 - 115	-21 - -21
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	127.0 (NE)	26.0 (NE)	NE (NE)	NE (NE)
Median	127.0	26.0	NE	NE
Min - Max	127 - 127	26 - 26	NE - NE	NE - NE
Cycle 42 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	128.0 (NE)	27.0 (NE)	NE (NE)	NE (NE)
Median	128.0	27.0	NE	NE
Min - Max	128 - 128	27 - 27	NE - NE	NE - NE

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	125.0 (NE)	24.0 (NE)	NE (NE)	NE (NE)
Median	125.0	24.0	NE	NE
Min - Max	125 - 125	24 - 24	NE - NE	NE - NE
Cycle 42 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	126.0 (NE)	25.0 (NE)	NE (NE)	NE (NE)
Median	126.0	25.0	NE	NE
Min - Max	126 - 126	25 - 25	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	122.0 (NE)	21.0 (NE)	NE (NE)	NE (NE)
Median	122.0	21.0	NE	NE
Min - Max	122 - 122	21 - 21	NE - NE	NE - NE
Cycle 43 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	119.0 (NE)	18.0 (NE)	127.0 (NE)	-9.0 (NE)
Median	119.0	18.0	127.0	-9.0
Min - Max	119 - 119	18 - 18	127 - 127	-9 - -9
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	110.0 (NE)	9.0 (NE)	NE (NE)	NE (NE)
Median	110.0	9.0	NE	NE
Min - Max	110 - 110	9 - 9	NE - NE	NE - NE
Cycle 43 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	112.0 (NE)	11.0 (NE)	NE (NE)	NE (NE)
Median	112.0	11.0	NE	NE
Min - Max	112 - 112	11 - 11	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	110.0 (NE)	9.0 (NE)	NE (NE)	NE (NE)
Median	110.0	9.0	NE	NE
Min - Max	110 - 110	9 - 9	NE - NE	NE - NE
Cycle 43 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	116.0 (NE)	15.0 (NE)	NE (NE)	NE (NE)
Median	116.0	15.0	NE	NE
Min - Max	116 - 116	15 - 15	NE - NE	NE - NE

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
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Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	116.0 (NE)	15.0 (NE)	NE (NE)	NE (NE)
Median	116.0	15.0	NE	NE
Min - Max	116 - 116	15 - 15	NE - NE	NE - NE
Cycle 44 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	127.0 (NE)	-9.0 (NE)
Median	NE	NE	127.0	-9.0
Min - Max	NE - NE	NE - NE	127 - 127	-9 - -9
Cycle 45 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	110.0 (NE)	-26.0 (NE)
Median	NE	NE	110.0	-26.0
Min - Max	NE - NE	NE - NE	110 - 110	-26 - -26
Cycle 46 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	106.0 (NE)	-30.0 (NE)
Median	NE	NE	106.0	-30.0
Min - Max	NE - NE	NE - NE	106 - 106	-30 - -30
Study Drug Discontinuation				
n	75	74	140	139
Mean (SD)	121.6 (13.5)	-4.7 (13.1)	122.1 (15.5)	-2.8 (16.7)
Median	121.0	-3.5	122.0	0.0
Min - Max	94 - 175	-44 - 25	80 - 185	-82 - 36
Post-Baseline Last				
n	79	79	138	138
Mean (SD)	121.6 (13.5)	-4.3 (13.3)	122.1 (15.6)	-2.8 (16.6)
Median	121.0	-3.0	122.0	0.0
Min - Max	94 - 175	-44 - 25	80 - 185	-82 - 36
PRE PAC INFUSION				
n	1	1	5	5
Mean (SD)	74.0 (NE)	-45.0 (NE)	123.2 (10.5)	-3.4 (15.5)
Median	74.0	-45.0	118.0	0.0
Min - Max	74 - 74	-45 - -45	115 - 140	-23 - 15
AFTER PAC INFUSION				
n	6	6	21	21
Mean (SD)	121.8 (7.9)	5.0 (9.1)	119.8 (15.6)	-6.8 (14.5)
Median	123.5	8.5	116.0	-8.0
Min - Max	110 - 130	-11 - 13	100 - 151	-30 - 20

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
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Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Post-Baseline Minimum				
n	1	1	9	9
Mean (SD)	98.0 (NE)	-27.0 (NE)	98.9 (19.6)	-23.0 (25.9)
Median	98.0	-27.0	104.0	-17.0
Min - Max	98 - 98	-27 - -27	63 - 121	-82 - 0
PRE PAC INFUSION				
n	57	57	112	112
Mean (SD)	101.1 (10.6)	-25.0 (17.1)	103.5 (12.3)	-21.9 (15.8)
Median	100.0	-22.0	100.0	-20.0
Min - Max	74 - 119	-82 - 10	79 - 137	-60 - 10
AFTER PAC INFUSION				
n	28	28	43	43
Mean (SD)	99.1 (7.5)	-24.5 (13.4)	102.5 (11.1)	-22.9 (13.2)
Median	99.5	-25.5	103.0	-24.0
Min - Max	85 - 114	-48 - 0	75 - 127	-66 - 0
Post-Baseline Maximum				
n	5	5	11	11
Mean (SD)	140.0 (9.4)	20.0 (11.0)	152.5 (25.8)	21.7 (19.3)
Median	135.0	20.0	143.0	15.0
Min - Max	130 - 150	4 - 35	125 - 210	0 - 70
PRE PAC INFUSION				
n	40	40	72	72
Mean (SD)	140.8 (16.2)	15.5 (14.8)	140.7 (15.3)	14.6 (15.9)
Median	138.0	15.5	139.0	12.0
Min - Max	120 - 201	-16 - 64	110 - 182	-18 - 60
AFTER PAC INFUSION				
n	41	41	81	81
Mean (SD)	136.2 (14.4)	10.4 (11.9)	142.8 (17.5)	19.2 (16.3)
Median	135.0	9.0	140.0	18.0
Min - Max	94 - 168	-25 - 36	110 - 196	-15 - 90

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Baseline				
n	86		164	
Mean (SD)	81.7 (12.3)		79.7 (11.9)	
Median	82.0		78.0	
Min - Max	52 - 125		54 - 126	
Cycle 1 Day 1				
PRE PAC INFUSION				
n	84	83	145	144
Mean (SD)	82.1 (11.7)	0.5 (10.1)	79.7 (12.5)	-0.1 (11.3)
Median	80.0	0.0	78.0	0.0
Min - Max	60 - 127	-28 - 37	55 - 129	-40 - 33
AFTER PAC INFUSION				
n	84	83	158	157
Mean (SD)	80.9 (11.6)	-0.6 (10.4)	77.4 (11.6)	-1.7 (10.9)
Median	79.5	-2.0	78.0	-1.0
Min - Max	56 - 130	-26 - 33	46 - 124	-40 - 29
Cycle 1 Day 8				
PRE PAC INFUSION				
n	86	85	160	158
Mean (SD)	82.6 (13.0)	1.3 (12.0)	80.0 (13.4)	0.3 (11.5)
Median	81.0	-1.0	78.0	0.0
Min - Max	50 - 119	-28 - 34	54 - 124	-34 - 32
AFTER PAC INFUSION				
n	78	77	148	146
Mean (SD)	81.4 (10.4)	-0.9 (10.7)	78.0 (10.5)	-1.2 (10.7)
Median	80.0	-1.0	78.0	-1.0
Min - Max	45 - 107	-33 - 24	53 - 125	-41 - 36
Cycle 1 Day 15				
PRE PAC INFUSION				
n	81	80	148	146
Mean (SD)	80.8 (11.9)	-0.3 (9.9)	79.0 (13.1)	-0.8 (12.9)
Median	80.0	-1.5	78.0	0.0
Min - Max	55 - 115	-20 - 26	51 - 131	-57 - 30
AFTER PAC INFUSION				
n	74	73	133	132
Mean (SD)	79.8 (10.6)	-1.5 (9.1)	78.1 (11.7)	-1.6 (11.9)
Median	80.0	-2.0	77.0	0.0
Min - Max	51 - 115	-27 - 18	56 - 115	-62 - 24
Cycle 2 Day 1				
PRE PAC INFUSION				
n	78	77	161	159
Mean (SD)	81.9 (11.7)	0.5 (11.8)	79.1 (11.4)	-0.6 (11.9)
Median	80.0	-1.0	77.0	-1.0
Min - Max	54 - 115	-24 - 36	60 - 122	-44 - 32

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	74	73	153	152
Mean (SD)	80.5 (9.5)	-1.6 (10.3)	76.6 (10.6)	-2.7 (11.5)
Median	80.0	-2.0	75.0	-2.0
Min - Max	62 - 106	-27 - 20	56 - 118	-54 - 28
Cycle 2 Day 8				
PRE PAC INFUSION				
n	79	78	153	151
Mean (SD)	84.6 (11.1)	2.8 (9.8)	79.9 (11.0)	0.1 (11.8)
Median	83.0	3.0	78.0	1.0
Min - Max	60 - 112	-19 - 30	54 - 107	-59 - 30
AFTER PAC INFUSION				
n	72	71	149	147
Mean (SD)	81.7 (10.9)	-0.1 (10.8)	78.4 (9.7)	-1.0 (11.6)
Median	82.0	0.0	78.0	-1.0
Min - Max	52 - 110	-31 - 23	58 - 113	-43 - 28
Cycle 2 Day 15				
PRE PAC INFUSION				
n	77	76	148	146
Mean (SD)	82.6 (12.4)	0.8 (11.0)	80.7 (11.9)	1.6 (11.6)
Median	80.0	1.0	80.0	2.0
Min - Max	60 - 120	-23 - 26	50 - 116	-36 - 34
AFTER PAC INFUSION				
n	71	70	146	144
Mean (SD)	81.3 (10.9)	-0.6 (10.4)	78.4 (10.1)	-0.9 (11.3)
Median	79.0	-1.5	79.0	-1.0
Min - Max	60 - 110	-27 - 22	53 - 111	-36 - 24
Cycle 3 Day 1				
PRE PAC INFUSION				
n	75	74	143	141
Mean (SD)	81.3 (11.5)	-0.4 (13.1)	80.9 (12.6)	2.1 (13.3)
Median	79.0	0.0	79.0	2.0
Min - Max	56 - 117	-61 - 30	50 - 122	-32 - 48
AFTER PAC INFUSION				
n	70	69	134	132
Mean (SD)	81.4 (10.6)	-0.5 (11.8)	79.3 (10.5)	0.4 (12.8)
Median	80.0	-1.0	79.0	1.0
Min - Max	62 - 119	-31 - 35	59 - 109	-50 - 39
Cycle 3 Day 8				
PRE PAC INFUSION				
n	73	72	140	138
Mean (SD)	84.2 (12.2)	2.3 (11.1)	81.2 (12.7)	2.6 (13.0)
Median	83.0	2.0	79.5	3.0
Min - Max	62 - 115	-24 - 31	50 - 115	-37 - 41

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	69	68	138	136
Mean (SD)	81.4 (10.4)	-0.5 (11.7)	79.8 (10.8)	1.1 (11.6)
Median	80.0	-0.5	79.0	2.0
Min - Max	62 - 110	-31 - 26	54 - 112	-41 - 30
Cycle 3 Day 15				
PRE PAC INFUSION				
n	67	66	136	135
Mean (SD)	83.1 (11.6)	0.9 (10.5)	81.7 (13.3)	3.2 (14.7)
Median	81.0	0.0	80.0	2.0
Min - Max	56 - 115	-25 - 26	56 - 128	-39 - 53
AFTER PAC INFUSION				
n	67	66	129	128
Mean (SD)	84.1 (11.9)	1.9 (12.5)	80.1 (11.0)	1.5 (12.7)
Median	80.0	1.0	79.0	2.0
Min - Max	56 - 111	-24 - 45	60 - 116	-34 - 34
Cycle 4 Day 1				
PRE PAC INFUSION				
n	69	68	132	130
Mean (SD)	81.9 (11.1)	0.1 (10.4)	80.8 (11.0)	2.0 (10.9)
Median	80.0	1.0	78.5	1.0
Min - Max	55 - 112	-24 - 24	57 - 105	-27 - 27
AFTER PAC INFUSION				
n	65	64	122	120
Mean (SD)	80.2 (10.0)	-2.0 (10.0)	78.8 (11.5)	0.4 (13.1)
Median	79.0	-1.0	78.0	0.0
Min - Max	56 - 105	-27 - 30	52 - 113	-44 - 39
Cycle 4 Day 8				
PRE PAC INFUSION				
n	68	67	127	126
Mean (SD)	84.0 (11.6)	1.8 (10.4)	81.4 (11.6)	2.5 (11.5)
Median	82.0	2.0	80.0	2.0
Min - Max	55 - 110	-22 - 29	48 - 112	-31 - 31
AFTER PAC INFUSION				
n	65	64	120	119
Mean (SD)	81.8 (10.0)	-0.5 (10.3)	79.9 (12.1)	1.2 (11.8)
Median	81.0	-1.0	78.5	1.0
Min - Max	62 - 106	-28 - 25	48 - 117	-38 - 31
Cycle 4 Day 15				
PRE PAC INFUSION				
n	67	66	126	124
Mean (SD)	83.9 (12.1)	2.3 (10.6)	81.7 (12.7)	2.7 (12.4)
Median	81.0	2.0	80.0	1.0
Min - Max	60 - 117	-19 - 36	57 - 124	-25 - 42

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	66	65	115	113
Mean (SD)	82.2 (11.0)	0.3 (9.7)	78.7 (11.3)	0.6 (12.1)
Median	80.0	0.0	78.0	1.0
Min - Max	60 - 109	-21 - 28	56 - 116	-38 - 27
Cycle 5 Day 1				
PRE PAC INFUSION				
n	61	60	103	101
Mean (SD)	81.7 (11.0)	-0.7 (11.0)	80.1 (11.5)	1.7 (11.3)
Median	80.0	2.0	78.0	1.0
Min - Max	62 - 112	-27 - 20	60 - 115	-29 - 32
AFTER PAC INFUSION				
n	57	56	96	94
Mean (SD)	80.6 (11.1)	-1.2 (10.0)	78.2 (11.1)	0.6 (12.3)
Median	78.0	0.0	78.0	1.0
Min - Max	61 - 111	-24 - 17	49 - 107	-46 - 29
Cycle 5 Day 8				
PRE PAC INFUSION				
n	53	52	96	95
Mean (SD)	84.4 (12.2)	1.5 (10.6)	80.7 (12.1)	2.4 (11.6)
Median	83.0	0.5	80.0	2.0
Min - Max	63 - 112	-18 - 29	53 - 118	-30 - 36
AFTER PAC INFUSION				
n	52	51	89	88
Mean (SD)	81.6 (10.0)	-1.1 (10.9)	77.9 (11.3)	0.2 (13.0)
Median	81.0	-2.0	77.0	1.0
Min - Max	63 - 109	-23 - 28	53 - 104	-37 - 32
Cycle 5 Day 15				
PRE PAC INFUSION				
n	56	55	91	90
Mean (SD)	83.2 (11.4)	0.4 (11.4)	79.1 (10.7)	1.9 (11.2)
Median	84.0	1.0	78.0	1.0
Min - Max	61 - 110	-25 - 31	57 - 112	-36 - 36
AFTER PAC INFUSION				
n	52	51	78	77
Mean (SD)	80.3 (10.6)	-2.8 (10.3)	77.9 (9.5)	0.8 (11.2)
Median	79.5	0.0	78.0	1.0
Min - Max	57 - 101	-27 - 16	54 - 100	-42 - 20
Cycle 6 Day 1				
PRE PAC INFUSION				
n	56	55	91	90
Mean (SD)	81.8 (10.6)	0.0 (11.8)	78.9 (11.6)	1.1 (12.6)
Median	79.5	0.0	77.0	-1.0
Min - Max	63 - 113	-27 - 48	51 - 115	-34 - 41

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	49	48	85	84
Mean (SD)	79.6 (9.1)	-2.8 (10.1)	79.0 (10.5)	1.5 (12.0)
Median	79.0	-0.5	78.0	1.5
Min - Max	62 - 110	-29 - 16	53 - 105	-36 - 37
Cycle 6 Day 8				
PRE PAC INFUSION				
n	49	48	87	86
Mean (SD)	84.4 (13.0)	1.9 (12.2)	80.1 (11.6)	2.1 (11.7)
Median	83.0	2.0	79.0	1.0
Min - Max	58 - 121	-35 - 32	52 - 130	-36 - 34
AFTER PAC INFUSION				
n	48	47	83	82
Mean (SD)	81.0 (9.0)	-1.2 (11.4)	78.2 (10.9)	0.8 (12.0)
Median	79.5	-1.0	78.0	0.0
Min - Max	61 - 102	-33 - 22	55 - 116	-41 - 25
Cycle 6 Day 15				
PRE PAC INFUSION				
n	49	48	84	83
Mean (SD)	83.6 (12.7)	1.6 (12.0)	80.6 (11.8)	3.4 (12.1)
Median	81.0	1.5	80.0	2.0
Min - Max	65 - 110	-19 - 33	49 - 109	-31 - 36
AFTER PAC INFUSION				
n	47	46	80	79
Mean (SD)	81.0 (10.5)	-0.8 (11.2)	79.0 (10.2)	2.4 (11.0)
Median	80.0	1.5	78.0	2.0
Min - Max	57 - 109	-25 - 23	58 - 102	-38 - 37
Cycle 7 Day 1				
PRE PAC INFUSION				
n	42	41	76	75
Mean (SD)	81.1 (10.4)	-1.2 (10.9)	79.4 (10.3)	1.6 (11.4)
Median	80.0	-1.0	78.5	2.0
Min - Max	60 - 110	-25 - 23	56 - 109	-35 - 32
AFTER PAC INFUSION				
n	37	36	67	66
Mean (SD)	78.8 (9.0)	-3.0 (10.6)	77.8 (10.2)	0.4 (10.8)
Median	78.0	-3.5	78.0	0.0
Min - Max	59 - 112	-26 - 17	50 - 108	-46 - 25
Cycle 7 Day 8				
PRE PAC INFUSION				
n	35	34	67	66
Mean (SD)	84.0 (11.6)	1.9 (11.3)	80.8 (11.1)	3.0 (11.1)
Median	82.0	2.0	78.0	2.0
Min - Max	67 - 111	-24 - 37	62 - 129	-16 - 39

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	34	33	63	62
Mean (SD)	80.9 (10.5)	-1.0 (11.1)	80.4 (10.1)	2.7 (10.6)
Median	80.0	0.0	79.0	0.0
Min - Max	60 - 109	-25 - 38	57 - 108	-17 - 29
Cycle 7 Day 15				
PRE PAC INFUSION				
n	34	33	69	68
Mean (SD)	83.5 (11.2)	0.4 (12.1)	78.3 (9.7)	0.5 (11.9)
Median	80.5	0.0	76.0	1.5
Min - Max	68 - 112	-22 - 29	53 - 112	-43 - 38
AFTER PAC INFUSION				
n	34	33	66	65
Mean (SD)	80.7 (10.5)	-2.5 (12.9)	77.1 (9.8)	0.1 (10.8)
Median	77.0	-4.0	75.5	2.0
Min - Max	64 - 112	-25 - 33	59 - 106	-31 - 21
Cycle 8 Day 1				
PRE PAC INFUSION				
n	33	32	70	69
Mean (SD)	79.8 (11.5)	-2.4 (12.6)	79.5 (11.3)	2.5 (11.9)
Median	78.0	-2.5	78.0	2.0
Min - Max	65 - 119	-27 - 30	59 - 112	-26 - 33
AFTER PAC INFUSION				
n	27	26	63	62
Mean (SD)	78.0 (11.2)	-5.4 (11.6)	78.3 (11.4)	1.3 (12.0)
Median	75.0	-6.0	78.0	0.0
Min - Max	65 - 116	-27 - 28	60 - 112	-35 - 33
Cycle 8 Day 8				
PRE PAC INFUSION				
n	29	28	64	63
Mean (SD)	81.0 (13.9)	-0.4 (8.1)	80.4 (13.0)	2.9 (13.1)
Median	79.0	-1.5	80.0	4.0
Min - Max	60 - 120	-13 - 18	56 - 138	-36 - 48
AFTER PAC INFUSION				
n	27	26	60	59
Mean (SD)	80.0 (12.0)	-1.7 (9.2)	79.9 (11.6)	3.0 (11.9)
Median	81.0	-2.0	80.0	4.0
Min - Max	62 - 116	-18 - 17	62 - 114	-31 - 28
Cycle 8 Day 15				
PRE PAC INFUSION				
n	29	28	61	60
Mean (SD)	81.7 (12.2)	-0.8 (10.6)	79.6 (9.5)	2.1 (11.1)
Median	77.0	-0.5	78.0	2.5
Min - Max	65 - 110	-23 - 20	63 - 106	-33 - 25

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	27	26	58	57
Mean (SD)	79.1 (10.9)	-2.3 (10.8)	78.9 (10.2)	1.0 (13.5)
Median	76.0	-1.0	79.5	1.0
Min - Max	67 - 107	-21 - 20	44 - 107	-52 - 27
Cycle 9 Day 1				
PRE PAC INFUSION				
n	27	26	57	56
Mean (SD)	80.0 (11.8)	-3.0 (12.8)	78.3 (11.9)	0.8 (11.3)
Median	78.0	-1.5	76.0	0.0
Min - Max	59 - 113	-26 - 27	60 - 113	-28 - 32
AFTER PAC INFUSION				
n	22	21	52	51
Mean (SD)	78.5 (11.6)	-3.9 (16.5)	77.5 (10.9)	0.4 (12.7)
Median	76.5	-7.0	76.0	-1.0
Min - Max	57 - 112	-27 - 46	50 - 104	-46 - 28
Cycle 9 Day 8				
PRE PAC INFUSION				
n	24	23	51	50
Mean (SD)	80.8 (13.3)	-2.2 (9.3)	83.0 (12.6)	5.6 (12.7)
Median	81.5	-1.0	80.0	5.5
Min - Max	54 - 110	-23 - 12	63 - 133	-25 - 43
AFTER PAC INFUSION				
n	21	20	50	49
Mean (SD)	79.0 (9.2)	-5.4 (11.1)	80.3 (11.3)	3.1 (12.4)
Median	80.0	-2.5	78.5	5.0
Min - Max	60 - 102	-25 - 14	62 - 102	-26 - 36
Cycle 9 Day 15				
PRE PAC INFUSION				
n	22	21	51	50
Mean (SD)	80.6 (11.2)	-4.0 (9.9)	82.5 (12.3)	5.5 (13.2)
Median	79.0	-7.0	80.0	6.0
Min - Max	60 - 109	-24 - 14	63 - 114	-29 - 32
AFTER PAC INFUSION				
n	20	19	48	47
Mean (SD)	79.8 (10.3)	-4.9 (10.6)	79.0 (12.0)	1.9 (13.8)
Median	80.5	-4.0	77.0	2.0
Min - Max	59 - 108	-20 - 14	51 - 111	-45 - 32
Cycle 10 Day 1				
PRE PAC INFUSION				
n	22	22	55	54
Mean (SD)	82.3 (11.1)	-2.5 (10.4)	78.6 (11.9)	2.5 (11.1)
Median	78.0	-3.0	78.0	2.5
Min - Max	67 - 109	-21 - 23	60 - 114	-27 - 34

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	19	19	44	43
Mean (SD)	82.1 (11.1)	-2.9 (9.8)	77.8 (11.7)	1.2 (12.8)
Median	82.0	-3.0	75.5	2.0
Min - Max	65 - 107	-19 - 15	58 - 105	-38 - 32
Cycle 10 Day 8				
PRE PAC INFUSION				
n	19	18	43	42
Mean (SD)	80.2 (12.7)	-2.2 (11.0)	81.1 (12.8)	3.9 (12.5)
Median	80.0	-1.5	79.0	4.5
Min - Max	59 - 109	-25 - 13	59 - 114	-24 - 33
AFTER PAC INFUSION				
n	18	17	40	39
Mean (SD)	80.4 (11.9)	-2.2 (11.0)	78.8 (11.0)	1.3 (11.1)
Median	81.5	-4.0	78.5	2.0
Min - Max	61 - 105	-20 - 14	54 - 102	-19 - 27
Cycle 10 Day 15				
PRE PAC INFUSION				
n	18	17	46	45
Mean (SD)	81.1 (11.8)	-0.9 (8.9)	81.4 (11.6)	3.5 (13.1)
Median	82.0	0.0	78.0	4.0
Min - Max	56 - 104	-17 - 13	61 - 108	-25 - 29
AFTER PAC INFUSION				
n	16	15	41	40
Mean (SD)	81.9 (8.7)	-1.2 (8.7)	77.1 (11.4)	-1.4 (13.6)
Median	83.0	-2.0	76.0	1.5
Min - Max	67 - 102	-16 - 9	53 - 102	-43 - 23
Cycle 11 Day 1				
PRE PAC INFUSION				
n	17	16	48	47
Mean (SD)	84.3 (10.8)	1.5 (12.9)	78.1 (9.9)	1.1 (12.7)
Median	85.0	0.5	76.0	-1.0
Min - Max	67 - 104	-16 - 39	61 - 100	-27 - 32
AFTER PAC INFUSION				
n	14	13	40	39
Mean (SD)	77.9 (8.4)	-6.5 (11.2)	75.2 (10.3)	-2.9 (12.3)
Median	78.5	-4.0	74.5	-2.0
Min - Max	64 - 90	-24 - 10	53 - 97	-43 - 23
Cycle 11 Day 8				
PRE PAC INFUSION				
n	15	14	35	34
Mean (SD)	82.6 (11.4)	-1.0 (10.0)	79.8 (11.9)	2.3 (11.8)
Median	82.0	0.0	80.0	2.0
Min - Max	64 - 103	-21 - 19	61 - 100	-27 - 29

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	14	13	33	32
Mean (SD)	77.1 (7.8)	-7.2 (9.4)	78.7 (10.7)	0.1 (12.3)
Median	78.5	-9.0	79.0	2.0
Min - Max	62 - 90	-22 - 7	58 - 104	-26 - 28
Cycle 11 Day 15				
PRE PAC INFUSION				
n	17	16	39	38
Mean (SD)	79.8 (11.2)	-5.1 (13.9)	80.6 (12.7)	3.8 (15.3)
Median	76.0	-3.5	82.0	2.0
Min - Max	64 - 103	-37 - 16	62 - 119	-32 - 48
AFTER PAC INFUSION				
n	14	13	36	35
Mean (SD)	82.2 (10.4)	-3.0 (13.3)	78.4 (11.6)	0.7 (13.6)
Median	81.5	-3.0	77.0	1.0
Min - Max	67 - 101	-21 - 18	60 - 107	-32 - 36
Cycle 12 Day 1				
PRE PAC INFUSION				
n	17	17	43	43
Mean (SD)	84.5 (10.1)	-0.3 (11.4)	77.9 (11.6)	0.6 (12.6)
Median	85.0	0.0	76.0	0.0
Min - Max	63 - 100	-27 - 26	60 - 108	-36 - 29
AFTER PAC INFUSION				
n	14	14	35	35
Mean (SD)	79.7 (7.8)	-4.9 (8.8)	78.2 (11.1)	0.0 (11.9)
Median	79.5	-1.5	78.0	0.0
Min - Max	69 - 90	-24 - 5	60 - 104	-29 - 29
Cycle 12 Day 8				
PRE PAC INFUSION				
n	16	15	33	33
Mean (SD)	83.6 (11.8)	-1.3 (12.7)	80.5 (11.0)	2.2 (11.8)
Median	79.5	-2.0	80.0	0.0
Min - Max	70 - 108	-30 - 18	59 - 111	-20 - 31
AFTER PAC INFUSION				
n	14	13	32	32
Mean (SD)	82.2 (9.1)	-2.9 (11.7)	81.4 (10.9)	2.9 (11.8)
Median	82.5	-3.0	80.0	4.0
Min - Max	68 - 98	-19 - 19	62 - 110	-18 - 29
Cycle 12 Day 15				
PRE PAC INFUSION				
n	16	15	33	33
Mean (SD)	80.6 (11.6)	-3.9 (14.1)	81.7 (12.5)	3.2 (14.9)
Median	81.0	-6.0	80.0	1.0
Min - Max	60 - 100	-27 - 34	64 - 112	-29 - 34

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	14	13	30	30
Mean (SD)	79.1 (7.7)	-5.9 (10.8)	80.9 (11.4)	2.4 (13.5)
Median	80.0	-5.0	81.0	4.0
Min - Max	65 - 92	-22 - 15	52 - 108	-44 - 25
Cycle 13 Day 1				
PRE PAC INFUSION				
n	14	13	33	33
Mean (SD)	82.2 (9.9)	-2.5 (15.1)	81.7 (10.9)	2.8 (11.8)
Median	82.5	-4.0	82.0	5.0
Min - Max	60 - 98	-29 - 25	58 - 104	-30 - 30
AFTER PAC INFUSION				
n	12	11	27	27
Mean (SD)	77.9 (7.6)	-7.2 (8.2)	78.9 (13.0)	-1.5 (13.8)
Median	79.0	-6.0	79.0	0.0
Min - Max	64 - 90	-21 - 4	57 - 110	-39 - 21
Cycle 13 Day 8				
PRE PAC INFUSION				
n	12	11	27	27
Mean (SD)	84.5 (10.5)	0.2 (11.2)	82.4 (11.3)	2.7 (10.4)
Median	86.5	-4.0	81.0	3.0
Min - Max	66 - 101	-13 - 25	60 - 111	-24 - 24
AFTER PAC INFUSION				
n	11	10	24	24
Mean (SD)	81.6 (11.6)	-4.3 (12.5)	81.3 (12.7)	1.0 (12.3)
Median	80.0	-4.0	81.0	-0.5
Min - Max	60 - 105	-22 - 18	59 - 114	-29 - 21
Cycle 13 Day 15				
PRE PAC INFUSION				
n	12	11	27	27
Mean (SD)	84.6 (9.6)	-0.1 (10.5)	83.0 (10.1)	3.2 (10.9)
Median	83.5	-2.0	81.0	7.0
Min - Max	70 - 100	-13 - 23	65 - 107	-18 - 29
AFTER PAC INFUSION				
n	11	10	23	23
Mean (SD)	80.2 (8.1)	-5.9 (9.8)	83.5 (12.8)	3.5 (14.5)
Median	83.0	-6.0	85.0	6.0
Min - Max	60 - 88	-19 - 12	54 - 105	-42 - 28
Cycle 14 Day 1				
PRE PAC INFUSION				
n	13	12	32	32
Mean (SD)	84.0 (11.6)	-1.3 (13.8)	80.0 (9.6)	0.8 (9.8)
Median	84.0	-0.5	79.0	1.0
Min - Max	59 - 100	-35 - 23	64 - 101	-22 - 17

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	11	10	26	26
Mean (SD)	78.4 (8.3)	-6.2 (9.0)	78.0 (11.4)	-2.3 (9.5)
Median	81.0	-4.0	79.0	-2.0
Min - Max	65 - 91	-20 - 8	61 - 100	-33 - 11
Cycle 14 Day 8				
PRE PAC INFUSION				
n	11	10	26	26
Mean (SD)	82.3 (11.0)	-1.9 (12.4)	82.9 (12.4)	2.8 (13.0)
Median	83.0	-1.0	81.5	0.5
Min - Max	64 - 101	-21 - 17	60 - 106	-23 - 29
AFTER PAC INFUSION				
n	10	9	24	24
Mean (SD)	80.1 (10.5)	-5.6 (11.6)	81.0 (11.9)	1.5 (9.7)
Median	81.0	-12.0	81.0	1.5
Min - Max	60 - 95	-17 - 11	58 - 104	-20 - 18
Cycle 14 Day 15				
PRE PAC INFUSION				
n	11	10	26	26
Mean (SD)	88.1 (12.4)	5.7 (13.9)	81.2 (11.2)	1.0 (11.8)
Median	88.0	5.0	81.5	0.5
Min - Max	65 - 109	-23 - 24	61 - 109	-22 - 23
AFTER PAC INFUSION				
n	10	9	24	24
Mean (SD)	86.9 (10.8)	2.2 (10.8)	79.2 (10.8)	-1.0 (13.0)
Median	88.5	3.0	82.0	0.5
Min - Max	67 - 103	-14 - 19	55 - 98	-41 - 16
Cycle 15 Day 1				
PRE PAC INFUSION				
n	11	11	28	28
Mean (SD)	85.5 (9.8)	-0.8 (12.2)	79.5 (8.8)	1.3 (11.4)
Median	84.0	-3.0	79.0	2.5
Min - Max	70 - 103	-20 - 21	64 - 101	-29 - 19
AFTER PAC INFUSION				
n	10	10	22	22
Mean (SD)	78.3 (6.5)	-6.4 (10.8)	77.4 (10.6)	-2.7 (11.2)
Median	78.0	-6.5	75.5	-1.5
Min - Max	67 - 89	-28 - 13	60 - 104	-33 - 18
Cycle 15 Day 8				
PRE PAC INFUSION				
n	11	10	21	21
Mean (SD)	84.6 (12.4)	2.1 (12.9)	81.7 (10.2)	2.9 (12.6)
Median	84.0	1.0	82.0	1.0
Min - Max	63 - 112	-18 - 22	65 - 106	-23 - 35

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	10	9	18	18
Mean (SD)	79.0 (11.1)	-6.2 (12.4)	79.2 (9.9)	-0.2 (9.0)
Median	76.0	-10.0	76.0	-1.5
Min - Max	64 - 100	-22 - 10	64 - 98	-17 - 20
Cycle 15 Day 15				
PRE PAC INFUSION				
n	10	9	22	22
Mean (SD)	79.2 (10.4)	-3.0 (12.5)	80.6 (12.5)	2.1 (12.1)
Median	82.0	-9.0	80.5	3.0
Min - Max	62 - 93	-16 - 17	60 - 108	-30 - 26
AFTER PAC INFUSION				
n	9	8	20	20
Mean (SD)	76.4 (9.0)	-8.1 (10.8)	76.5 (12.2)	-2.0 (13.6)
Median	78.0	-13.0	75.5	-0.5
Min - Max	61 - 87	-17 - 15	50 - 98	-46 - 21
Cycle 16 Day 1				
PRE PAC INFUSION				
n	11	10	24	24
Mean (SD)	85.6 (10.2)	0.6 (11.7)	77.5 (11.7)	-0.3 (11.1)
Median	83.0	1.0	76.0	1.5
Min - Max	70 - 100	-22 - 17	62 - 103	-32 - 16
AFTER PAC INFUSION				
n	10	9	20	20
Mean (SD)	79.3 (11.5)	-3.9 (12.5)	77.6 (13.2)	-0.9 (14.5)
Median	81.5	0.0	75.5	1.0
Min - Max	65 - 97	-24 - 16	51 - 106	-45 - 16
Cycle 16 Day 8				
PRE PAC INFUSION				
n	11	10	19	19
Mean (SD)	86.5 (9.7)	3.6 (10.4)	81.5 (13.9)	3.9 (11.2)
Median	87.0	3.0	78.0	5.0
Min - Max	69 - 103	-15 - 20	62 - 120	-25 - 27
AFTER PAC INFUSION				
n	10	9	19	19
Mean (SD)	93.3 (34.0)	8.7 (34.8)	79.8 (10.2)	2.3 (9.3)
Median	81.5	-3.0	80.0	3.0
Min - Max	73 - 188	-22 - 98	63 - 101	-16 - 18
Cycle 16 Day 15				
PRE PAC INFUSION				
n	10	9	21	21
Mean (SD)	80.3 (11.3)	-1.1 (9.1)	80.3 (12.6)	2.3 (11.6)
Median	82.5	1.0	80.0	4.0
Min - Max	56 - 95	-13 - 15	60 - 107	-28 - 19

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	9	8	19	19
Mean (SD)	79.7 (9.3)	-4.6 (9.5)	78.6 (12.9)	0.3 (12.9)
Median	81.0	-6.5	84.0	2.0
Min - Max	62 - 92	-15 - 13	58 - 98	-38 - 16
Cycle 17 Day 1				
PRE PAC INFUSION				
n	8	7	23	23
Mean (SD)	83.1 (12.5)	-3.9 (7.2)	82.2 (11.2)	4.2 (11.6)
Median	82.5	-6.0	82.0	3.0
Min - Max	66 - 97	-13 - 7	66 - 108	-26 - 29
AFTER PAC INFUSION				
n	7	6	20	20
Mean (SD)	75.1 (8.4)	-10.0 (6.9)	78.6 (11.5)	0.4 (14.2)
Median	75.0	-10.5	81.5	1.5
Min - Max	63 - 90	-19 - 0	55 - 106	-41 - 20
Cycle 17 Day 8				
PRE PAC INFUSION				
n	6	5	18	18
Mean (SD)	85.2 (11.8)	-1.0 (9.6)	84.1 (12.2)	6.3 (8.1)
Median	80.5	-7.0	84.0	7.5
Min - Max	75 - 104	-9 - 10	64 - 108	-10 - 18
AFTER PAC INFUSION				
n	6	5	18	18
Mean (SD)	79.5 (6.0)	-6.4 (4.2)	81.4 (11.8)	3.7 (7.5)
Median	78.5	-4.0	82.5	3.0
Min - Max	73 - 90	-13 - -3	62 - 104	-7 - 21
Cycle 17 Day 15				
PRE PAC INFUSION				
n	7	6	19	19
Mean (SD)	81.4 (9.0)	-3.7 (6.0)	82.1 (10.4)	4.1 (7.2)
Median	84.0	-2.5	82.0	5.0
Min - Max	69 - 90	-12 - 4	63 - 104	-12 - 15
AFTER PAC INFUSION				
n	7	6	19	19
Mean (SD)	77.1 (8.3)	-8.3 (7.7)	79.1 (11.0)	1.1 (11.8)
Median	75.0	-10.0	80.0	3.0
Min - Max	67 - 92	-19 - 2	56 - 99	-40 - 14
Cycle 18 Day 1				
PRE PAC INFUSION				
n	7	7	21	21
Mean (SD)	83.3 (8.6)	-6.1 (11.4)	80.8 (11.7)	3.0 (11.2)
Median	80.0	-6.0	81.0	-3.0
Min - Max	74 - 97	-29 - 7	64 - 106	-13 - 24

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	6	6	17	17
Mean (SD)	81.7 (9.0)	-5.5 (6.8)	77.0 (13.3)	-1.6 (12.3)
Median	80.5	-3.5	73.0	1.0
Min - Max	67 - 93	-19 - -1	58 - 101	-38 - 15
Cycle 18 Day 8				
PRE PAC INFUSION				
n	6	6	15	15
Mean (SD)	85.0 (5.4)	-2.2 (2.1)	80.1 (9.4)	2.1 (8.0)
Median	84.5	-1.5	80.0	0.0
Min - Max	78 - 94	-6 - 0	68 - 97	-9 - 15
AFTER PAC INFUSION				
n	6	6	14	14
Mean (SD)	83.7 (7.2)	-3.5 (5.7)	78.2 (16.3)	-0.6 (9.6)
Median	86.0	-2.0	71.0	-1.5
Min - Max	73 - 91	-13 - 3	60 - 107	-11 - 21
Cycle 18 Day 15				
PRE PAC INFUSION				
n	7	6	17	17
Mean (SD)	80.0 (7.6)	-4.8 (3.4)	80.3 (11.4)	1.7 (13.7)
Median	83.0	-5.5	81.0	2.0
Min - Max	66 - 88	-10 - -1	65 - 104	-31 - 33
AFTER PAC INFUSION				
n	7	6	16	16
Mean (SD)	79.9 (10.5)	-4.3 (7.3)	80.4 (14.2)	0.3 (15.3)
Median	81.0	-4.5	82.0	2.5
Min - Max	62 - 91	-15 - 5	51 - 106	-45 - 20
Cycle 19 Day 1				
PRE PAC INFUSION				
n	7	6	18	18
Mean (SD)	81.4 (13.4)	-5.0 (17.2)	82.8 (10.7)	6.3 (9.1)
Median	82.0	-4.0	80.0	6.0
Min - Max	68 - 108	-31 - 22	64 - 101	-7 - 24
AFTER PAC INFUSION				
n	6	5	14	14
Mean (SD)	75.0 (11.3)	-7.8 (9.7)	78.0 (10.4)	-0.1 (9.1)
Median	74.5	-9.0	76.0	-0.5
Min - Max	60 - 89	-18 - 4	62 - 98	-16 - 14
Cycle 19 Day 8				
PRE PAC INFUSION				
n	6	5	13	13
Mean (SD)	79.5 (12.7)	-2.6 (8.6)	81.3 (9.6)	2.5 (8.2)
Median	81.0	0.0	80.0	1.0
Min - Max	61 - 93	-13 - 7	67 - 99	-9 - 16

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	Placebo + Paclitaxel (N=87) Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	Ipatasertib + Paclitaxel (N=166) Change from Baseline
AFTER PAC INFUSION				
n	5	4	12	12
Mean (SD)	73.8 (10.2)	-9.3 (11.2)	79.8 (8.8)	0.5 (8.3)
Median	70.0	-9.5	77.5	0.5
Min - Max	64 - 89	-22 - 4	69 - 98	-9 - 16
Cycle 19 Day 15				
PRE PAC INFUSION				
n	6	5	13	13
Mean (SD)	73.0 (6.9)	-10.2 (4.3)	81.2 (12.8)	2.8 (10.6)
Median	75.0	-8.0	80.0	0.0
Min - Max	60 - 78	-17 - -7	57 - 108	-13 - 22
AFTER PAC INFUSION				
n	6	5	13	13
Mean (SD)	72.2 (3.6)	-12.4 (2.9)	78.9 (10.6)	0.5 (7.0)
Median	73.5	-11.0	76.0	2.0
Min - Max	66 - 76	-16 - -10	62 - 98	-9 - 18
Cycle 20 Day 1				
PRE PAC INFUSION				
n	6	5	16	16
Mean (SD)	77.3 (9.2)	-8.8 (10.3)	78.6 (11.9)	1.8 (11.5)
Median	78.5	-10.0	75.5	3.0
Min - Max	62 - 90	-22 - 6	64 - 107	-22 - 21
AFTER PAC INFUSION				
n	5	4	13	13
Mean (SD)	79.2 (5.0)	-5.8 (4.9)	77.2 (9.7)	-1.3 (8.8)
Median	82.0	-5.0	78.0	-2.0
Min - Max	72 - 83	-12 - -1	64 - 96	-18 - 16
Cycle 20 Day 8				
PRE PAC INFUSION				
n	6	5	12	12
Mean (SD)	78.0 (12.1)	-4.2 (7.7)	84.2 (11.8)	4.9 (11.2)
Median	76.0	-6.0	82.5	3.5
Min - Max	60 - 93	-11 - 7	67 - 110	-15 - 24
AFTER PAC INFUSION				
n	6	5	12	12
Mean (SD)	73.5 (6.8)	-10.4 (3.8)	78.4 (11.2)	-0.8 (9.1)
Median	73.5	-9.0	79.5	-1.5
Min - Max	64 - 83	-15 - -7	56 - 94	-14 - 16
Cycle 20 Day 15				
PRE PAC INFUSION				
n	6	5	12	12
Mean (SD)	78.7 (7.7)	-4.8 (5.3)	82.8 (15.3)	5.9 (10.6)
Median	79.0	-4.0	79.5	4.5
Min - Max	67 - 87	-11 - 3	63 - 117	-9 - 22

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	4	11	11
Mean (SD)	74.6 (6.5)	-9.3 (3.1)	79.9 (10.2)	2.4 (7.9)
Median	75.0	-10.0	78.0	1.0
Min - Max	65 - 81	-12 - -5	68 - 100	-9 - 18
Cycle 21 Day 1				
PRE PAC INFUSION				
n	5	5	13	13
Mean (SD)	79.8 (5.5)	-9.4 (12.9)	81.9 (14.4)	3.1 (12.3)
Median	82.0	-6.0	79.0	6.0
Min - Max	71 - 84	-32 - 0	56 - 108	-15 - 28
AFTER PAC INFUSION				
n	3	3	11	11
Mean (SD)	79.3 (1.2)	-7.0 (2.6)	81.2 (10.9)	2.1 (7.3)
Median	80.0	-6.0	80.0	2.0
Min - Max	78 - 80	-10 - -5	71 - 105	-11 - 13
Cycle 21 Day 8				
PRE PAC INFUSION				
n	3	3	11	11
Mean (SD)	77.0 (6.6)	-9.3 (9.5)	81.0 (13.7)	1.9 (11.4)
Median	78.0	-6.0	82.0	1.0
Min - Max	70 - 83	-20 - -2	60 - 104	-15 - 15
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	79.0 (12.7)	-5.5 (12.0)	85.0 (8.8)	4.9 (7.8)
Median	79.0	-5.5	82.0	4.5
Min - Max	70 - 88	-14 - 3	76 - 99	-6 - 17
Cycle 21 Day 15				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	73.0 (1.4)	-11.5 (2.1)	82.7 (10.4)	2.6 (8.1)
Median	73.0	-11.5	79.0	0.5
Min - Max	72 - 74	-13 - -10	71 - 97	-6 - 18
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	76.5 (3.5)	-8.0 (2.8)	82.6 (12.5)	2.5 (8.8)
Median	76.5	-8.0	79.0	4.0
Min - Max	74 - 79	-10 - -6	71 - 102	-11 - 14
Cycle 22 Day 1				
PRE PAC INFUSION				
n	4	4	13	13
Mean (SD)	81.3 (13.0)	-9.3 (14.3)	82.2 (9.0)	3.4 (5.7)
Median	77.5	-11.5	81.0	2.0
Min - Max	70 - 100	-24 - 10	71 - 98	-5 - 16

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	11	11
Mean (SD)	80.3 (8.5)	-6.0 (5.6)	79.2 (11.1)	0.1 (6.7)
Median	80.0	-5.0	78.0	-1.0
Min - Max	72 - 89	-12 - -1	63 - 99	-10 - 14
Cycle 22 Day 8				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	78.0 (8.5)	-6.5 (7.8)	84.3 (11.9)	4.2 (10.4)
Median	78.0	-6.5	81.0	4.0
Min - Max	72 - 84	-12 - -1	63 - 104	-15 - 18
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	77.0 (4.2)	-7.5 (3.5)	83.8 (11.6)	3.7 (7.4)
Median	77.0	-7.5	80.0	3.0
Min - Max	74 - 80	-10 - -5	70 - 102	-5 - 15
Cycle 22 Day 15				
PRE PAC INFUSION				
n	2	2	9	9
Mean (SD)	75.0 (7.1)	-9.5 (6.4)	83.1 (18.7)	3.1 (13.4)
Median	75.0	-9.5	74.0	1.0
Min - Max	70 - 80	-14 - -5	64 - 119	-10 - 33
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	71.0 (1.4)	-13.5 (2.1)	83.2 (16.0)	3.2 (11.5)
Median	71.0	-13.5	78.0	7.0
Min - Max	70 - 72	-15 - -12	59 - 107	-19 - 18
Cycle 23 Day 1				
PRE PAC INFUSION				
n	3	3	12	12
Mean (SD)	70.0 (4.0)	-20.7 (14.4)	81.3 (10.4)	2.7 (8.2)
Median	70.0	-15.0	77.5	3.0
Min - Max	66 - 74	-37 - -10	70 - 102	-10 - 16
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	71.0 (1.4)	-13.5 (0.7)	80.8 (12.9)	1.9 (9.6)
Median	71.0	-13.5	78.0	-0.5
Min - Max	70 - 72	-14 - -13	67 - 106	-11 - 20
Cycle 23 Day 8				
PRE PAC INFUSION				
n	2	2	9	9
Mean (SD)	81.0 (12.7)	-3.5 (12.0)	88.6 (16.2)	8.6 (11.4)
Median	81.0	-3.5	82.0	10.0
Min - Max	72 - 90	-12 - 5	59 - 111	-12 - 24

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	73.0 (7.1)	-11.5 (6.4)	85.2 (15.6)	5.2 (12.3)
Median	73.0	-11.5	80.0	0.0
Min - Max	68 - 78	-16 - -7	70 - 120	-5 - 34
Cycle 23 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	76.0 (8.5)	-8.5 (7.8)	85.9 (14.4)	4.4 (8.6)
Median	76.0	-8.5	81.0	2.5
Min - Max	70 - 82	-14 - -3	66 - 107	-5 - 21
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	74.0 (8.5)	-10.5 (7.8)	87.1 (18.2)	5.6 (12.7)
Median	74.0	-10.5	82.0	2.5
Min - Max	68 - 80	-16 - -5	68 - 120	-6 - 34
Cycle 24 Day 1				
PRE PAC INFUSION				
n	3	3	11	11
Mean (SD)	82.0 (5.3)	-8.7 (13.6)	83.9 (12.7)	4.3 (12.7)
Median	80.0	-7.0	83.0	7.0
Min - Max	78 - 88	-23 - 4	65 - 114	-17 - 28
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	77.5 (2.1)	-7.0 (2.8)	82.1 (13.1)	2.0 (9.7)
Median	77.5	-7.0	78.0	2.0
Min - Max	76 - 79	-9 - -5	68 - 107	-14 - 21
Cycle 24 Day 8				
PRE PAC INFUSION				
n	2	2	7	7
Mean (SD)	82.5 (0.7)	-2.0 (0.0)	84.6 (17.8)	1.6 (16.0)
Median	82.5	-2.0	87.0	-2.0
Min - Max	82 - 83	-2 - -2	66 - 116	-16 - 30
AFTER PAC INFUSION				
n	2	2	7	7
Mean (SD)	87.5 (3.5)	3.0 (4.2)	83.6 (14.4)	0.6 (10.8)
Median	87.5	3.0	78.0	-2.0
Min - Max	85 - 90	0 - 6	68 - 107	-11 - 21
Cycle 24 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	74.5 (4.9)	-10.0 (5.7)	82.1 (12.1)	0.6 (9.4)
Median	74.5	-10.0	79.0	1.5
Min - Max	71 - 78	-14 - -6	69 - 100	-12 - 13

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	7	7
Mean (SD)	73.5 (7.8)	-11.0 (8.5)	82.9 (13.9)	-0.1 (9.9)
Median	73.5	-11.0	79.0	3.0
Min - Max	68 - 79	-17 - -5	62 - 100	-16 - 13
Cycle 25 Day 1				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	81.0 (4.2)	-3.5 (3.5)	84.4 (11.3)	3.9 (11.3)
Median	81.0	-3.5	82.5	10.0
Min - Max	78 - 84	-6 - -1	65 - 101	-13 - 15
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	77.0 (1.4)	-7.5 (0.7)	82.0 (11.2)	0.8 (8.2)
Median	77.0	-7.5	81.5	-1.5
Min - Max	76 - 78	-8 - -7	67 - 96	-7 - 18
Cycle 25 Day 8				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	74.0 (5.7)	-10.5 (6.4)	84.6 (13.6)	3.1 (11.5)
Median	74.0	-10.5	80.5	0.5
Min - Max	70 - 78	-15 - -6	68 - 111	-14 - 25
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	74.0 (0.0)	-10.5 (0.7)	80.5 (14.0)	-1.0 (8.1)
Median	74.0	-10.5	78.0	-2.0
Min - Max	74 - 74	-11 - -10	66 - 102	-12 - 16
Cycle 25 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	78.0 (5.7)	-6.5 (4.9)	85.0 (13.0)	3.5 (8.9)
Median	78.0	-6.5	82.0	5.0
Min - Max	74 - 82	-10 - -3	71 - 111	-7 - 15
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	77.0 (1.4)	-7.5 (0.7)	83.5 (12.4)	2.0 (6.2)
Median	77.0	-7.5	78.0	1.5
Min - Max	76 - 78	-8 - -7	72 - 102	-6 - 11
Cycle 26 Day 1				
PRE PAC INFUSION				
n	2	2	11	11
Mean (SD)	73.0 (7.1)	-11.5 (6.4)	84.7 (12.6)	5.3 (10.6)
Median	73.0	-11.5	80.0	7.0
Min - Max	68 - 78	-16 - -7	67 - 111	-4 - 30

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	72.0 (2.8)	-12.5 (3.5)	81.0 (12.1)	0.8 (7.5)
Median	72.0	-12.5	81.5	1.5
Min - Max	70 - 74	-15 - -10	64 - 98	-13 - 10
Cycle 26 Day 8				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	75.0 (7.1)	-9.5 (6.4)	86.1 (10.4)	6.8 (9.5)
Median	75.0	-9.5	86.0	4.5
Min - Max	70 - 80	-14 - -5	69 - 98	-2 - 24
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	76.5 (0.7)	-8.0 (1.4)	81.8 (12.0)	2.4 (7.1)
Median	76.5	-8.0	81.0	0.0
Min - Max	76 - 77	-9 - -7	65 - 99	-6 - 17
Cycle 26 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	75.0 (4.2)	-9.5 (3.5)	80.9 (11.7)	-0.6 (8.9)
Median	75.0	-9.5	81.5	1.0
Min - Max	72 - 78	-12 - -7	61 - 96	-15 - 9
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	71.0 (1.4)	-13.5 (2.1)	81.9 (11.2)	0.4 (7.5)
Median	71.0	-13.5	83.5	-1.0
Min - Max	70 - 72	-15 - -12	66 - 97	-11 - 11
Cycle 27 Day 1				
PRE PAC INFUSION				
n	1	1	8	8
Mean (SD)	78.0 (NE)	-6.0 (NE)	85.9 (10.2)	4.4 (12.9)
Median	78.0	-6.0	87.0	3.0
Min - Max	78 - 78	-6 - -6	72 - 100	-9 - 25
AFTER PAC INFUSION				
n	1	1	7	7
Mean (SD)	76.0 (NE)	-8.0 (NE)	80.7 (10.9)	-2.1 (4.6)
Median	76.0	-8.0	78.0	-4.0
Min - Max	76 - 76	-8 - -8	65 - 96	-6 - 7
Cycle 27 Day 8				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	80.0 (NE)	-4.0 (NE)	87.5 (9.3)	2.3 (11.6)
Median	80.0	-4.0	89.0	1.0
Min - Max	80 - 80	-4 - -4	76 - 100	-12 - 22

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	76.0 (NE)	-8.0 (NE)	87.2 (16.0)	2.0 (11.8)
Median	76.0	-8.0	84.5	-1.5
Min - Max	76 - 76	-8 - -8	72 - 117	-10 - 21
Cycle 27 Day 15				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	76.0 (NE)	-8.0 (NE)	86.7 (7.5)	5.7 (8.7)
Median	76.0	-8.0	85.0	7.5
Min - Max	76 - 76	-8 - -8	77 - 97	-5 - 15
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	72.0 (NE)	-12.0 (NE)	82.0 (2.8)	1.0 (9.6)
Median	72.0	-12.0	82.0	-1.0
Min - Max	72 - 72	-12 - -12	78 - 86	-12 - 13
Cycle 28 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	80.0 (NE)	-4.0 (NE)	82.7 (10.9)	3.8 (7.5)
Median	80.0	-4.0	82.0	4.0
Min - Max	80 - 80	-4 - -4	71 - 97	-6 - 16
AFTER PAC INFUSION				
n	1	1	5	5
Mean (SD)	76.0 (NE)	-8.0 (NE)	79.8 (10.6)	-1.0 (6.8)
Median	76.0	-8.0	79.0	-3.0
Min - Max	76 - 76	-8 - -8	65 - 90	-8 - 8
Cycle 28 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	76.0 (NE)	-8.0 (NE)	90.5 (14.2)	7.3 (20.3)
Median	76.0	-8.0	88.0	13.5
Min - Max	76 - 76	-8 - -8	76 - 110	-22 - 24
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	78.0 (NE)	-6.0 (NE)	86.8 (6.4)	3.5 (7.9)
Median	78.0	-6.0	86.5	6.5
Min - Max	78 - 78	-6 - -6	80 - 94	-8 - 9
Cycle 28 Day 15				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	82.0 (NE)	-2.0 (NE)	90.2 (8.5)	11.3 (8.6)
Median	82.0	-2.0	94.0	10.0
Min - Max	82 - 82	-2 - -2	78 - 97	-1 - 23

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	82.0 (NE)	-2.0 (NE)	85.0 (10.1)	6.2 (4.5)
Median	82.0	-2.0	84.0	8.0
Min - Max	82 - 82	-2 - -2	70 - 98	0 - 11
Cycle 29 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	76.0 (NE)	-8.0 (NE)	85.8 (16.2)	7.0 (12.3)
Median	76.0	-8.0	85.0	3.0
Min - Max	76 - 76	-8 - -8	65 - 107	-6 - 23
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	80.0 (NE)	-4.0 (NE)	85.0 (14.0)	3.5 (7.0)
Median	80.0	-4.0	86.0	2.5
Min - Max	80 - 80	-4 - -4	67 - 101	-4 - 13
Cycle 29 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	81.0 (NE)	-3.0 (NE)	91.0 (7.5)	9.5 (6.6)
Median	81.0	-3.0	91.5	10.0
Min - Max	81 - 81	-3 - -3	82 - 99	1 - 17
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	74.0 (NE)	-10.0 (NE)	83.0 (15.0)	1.5 (8.2)
Median	74.0	-10.0	84.0	-0.5
Min - Max	74 - 74	-10 - -10	66 - 98	-5 - 12
Cycle 29 Day 15				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	82.0 (NE)	-2.0 (NE)	84.0 (12.9)	0.8 (10.0)
Median	82.0	-2.0	87.5	2.0
Min - Max	82 - 82	-2 - -2	67 - 94	-11 - 10
AFTER PAC INFUSION				
n	1	1	3	3
Mean (SD)	79.0 (NE)	-5.0 (NE)	89.7 (8.7)	4.7 (5.1)
Median	79.0	-5.0	92.0	6.0
Min - Max	79 - 79	-5 - -5	80 - 97	-1 - 9
Cycle 30 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	78.0 (NE)	-6.0 (NE)	80.8 (12.6)	2.0 (10.3)
Median	78.0	-6.0	81.0	5.0
Min - Max	78 - 78	-6 - -6	60 - 99	-12 - 13

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	78.0 (NE)	-6.0 (NE)	80.5 (11.0)	-1.0 (8.8)
Median	78.0	-6.0	78.5	0.5
Min - Max	78 - 78	-6 - -6	71 - 94	-13 - 8
Cycle 30 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	76.0 (NE)	-8.0 (NE)	105.3 (36.4)	23.8 (35.6)
Median	76.0	-8.0	99.5	17.0
Min - Max	76 - 76	-8 - -8	68 - 154	-7 - 68
AFTER PAC INFUSION				
n	1	1	3	3
Mean (SD)	78.0 (NE)	-6.0 (NE)	85.0 (9.6)	5.0 (15.1)
Median	78.0	-6.0	89.0	3.0
Min - Max	78 - 78	-6 - -6	74 - 92	-9 - 21
Cycle 30 Day 15				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	74.0 (NE)	-10.0 (NE)	82.0 (16.0)	0.5 (7.3)
Median	74.0	-10.0	84.0	-0.5
Min - Max	74 - 74	-10 - -10	64 - 96	-7 - 10
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	72.0 (NE)	-12.0 (NE)	80.5 (15.2)	-1.0 (5.1)
Median	72.0	-12.0	81.0	-2.0
Min - Max	72 - 72	-12 - -12	65 - 95	-6 - 6
Cycle 31 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	70.0 (NE)	-14.0 (NE)	90.5 (16.3)	13.0 (4.2)
Median	70.0	-14.0	90.5	13.0
Min - Max	70 - 70	-14 - -14	79 - 102	10 - 16
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	74.0 (NE)	-10.0 (NE)	97.0 (NE)	11.0 (NE)
Median	74.0	-10.0	97.0	11.0
Min - Max	74 - 74	-10 - -10	97 - 97	11 - 11
Cycle 31 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	72.0 (NE)	-12.0 (NE)	105.0 (NE)	19.0 (NE)
Median	72.0	-12.0	105.0	19.0
Min - Max	72 - 72	-12 - -12	105 - 105	19 - 19

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	70.0 (NE)	-14.0 (NE)	107.0 (NE)	21.0 (NE)
Median	70.0	-14.0	107.0	21.0
Min - Max	70 - 70	-14 - -14	107 - 107	21 - 21
Cycle 31 Day 15				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	101.5 (7.8)	9.5 (16.3)
Median	NE	NE	101.5	9.5
Min - Max	NE - NE	NE - NE	96 - 107	-2 - 21
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	99.0 (0.0)	7.0 (8.5)
Median	NE	NE	99.0	7.0
Min - Max	NE - NE	NE - NE	99 - 99	1 - 13
Cycle 32 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	65.0 (NE)	-4.0 (NE)
Median	NE	NE	65.0	-4.0
Min - Max	NE - NE	NE - NE	65 - 65	-4 - -4
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	89.0 (2.8)	-3.0 (11.3)
Median	NE	NE	89.0	-3.0
Min - Max	NE - NE	NE - NE	87 - 91	-11 - 5
Cycle 32 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	-10.0 (NE)	NE (NE)	NE (NE)
Median	74.0	-10.0	NE	NE
Min - Max	74 - 74	-10 - -10	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	72.0 (NE)	-12.0 (NE)	95.0 (17.0)	3.0 (25.5)
Median	72.0	-12.0	95.0	3.0
Min - Max	72 - 72	-12 - -12	83 - 107	-15 - 21
Cycle 32 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	-10.0 (NE)	NE (NE)	NE (NE)
Median	74.0	-10.0	NE	NE
Min - Max	74 - 74	-10 - -10	NE - NE	NE - NE

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	76.0 (NE)	-8.0 (NE)	88.0 (4.2)	-4.0 (12.7)
Median	76.0	-8.0	88.0	-4.0
Min - Max	76 - 76	-8 - -8	85 - 91	-13 - 5
Cycle 33 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	78.0 (NE)	-6.0 (NE)	59.0 (NE)	-10.0 (NE)
Median	78.0	-6.0	59.0	-10.0
Min - Max	78 - 78	-6 - -6	59 - 59	-10 - -10
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	76.0 (NE)	-8.0 (NE)	91.5 (6.4)	-0.5 (14.8)
Median	76.0	-8.0	91.5	-0.5
Min - Max	76 - 76	-8 - -8	87 - 96	-11 - 10
Cycle 33 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	82.0 (NE)	-2.0 (NE)	NE (NE)	NE (NE)
Median	82.0	-2.0	NE	NE
Min - Max	82 - 82	-2 - -2	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	74.0 (NE)	-10.0 (NE)	97.5 (9.2)	5.5 (0.7)
Median	74.0	-10.0	97.5	5.5
Min - Max	74 - 74	-10 - -10	91 - 104	5 - 6
Cycle 33 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	78.0 (NE)	-6.0 (NE)	NE (NE)	NE (NE)
Median	78.0	-6.0	NE	NE
Min - Max	78 - 78	-6 - -6	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	76.0 (NE)	-8.0 (NE)	97.5 (2.1)	5.5 (10.6)
Median	76.0	-8.0	97.5	5.5
Min - Max	76 - 76	-8 - -8	96 - 99	-2 - 13
Cycle 34 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	72.0 (NE)	-12.0 (NE)	62.0 (NE)	-7.0 (NE)
Median	72.0	-12.0	62.0	-7.0
Min - Max	72 - 72	-12 - -12	62 - 62	-7 - -7

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	79.0 (NE)	-5.0 (NE)	88.0 (NE)	2.0 (NE)
Median	79.0	-5.0	88.0	2.0
Min - Max	79 - 79	-5 - -5	88 - 88	2 - 2
Cycle 34 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	-10.0 (NE)	NE (NE)	NE (NE)
Median	74.0	-10.0	NE	NE
Min - Max	74 - 74	-10 - -10	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	78.0 (NE)	-6.0 (NE)	92.0 (NE)	6.0 (NE)
Median	78.0	-6.0	92.0	6.0
Min - Max	78 - 78	-6 - -6	92 - 92	6 - 6
Cycle 34 Day 15				
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	86.0 (NE)	2.0 (NE)	95.0 (NE)	9.0 (NE)
Median	86.0	2.0	95.0	9.0
Min - Max	86 - 86	2 - 2	95 - 95	9 - 9
Cycle 35 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	76.0 (NE)	-8.0 (NE)	60.0 (NE)	-9.0 (NE)
Median	76.0	-8.0	60.0	-9.0
Min - Max	76 - 76	-8 - -8	60 - 60	-9 - -9
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	76.0 (NE)	-8.0 (NE)	94.0 (NE)	8.0 (NE)
Median	76.0	-8.0	94.0	8.0
Min - Max	76 - 76	-8 - -8	94 - 94	8 - 8
Cycle 35 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	78.0 (NE)	-6.0 (NE)	NE (NE)	NE (NE)
Median	78.0	-6.0	NE	NE
Min - Max	78 - 78	-6 - -6	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	76.0 (NE)	-8.0 (NE)	105.0 (NE)	19.0 (NE)
Median	76.0	-8.0	105.0	19.0
Min - Max	76 - 76	-8 - -8	105 - 105	19 - 19

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 35 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	84.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	84.0	0.0	NE	NE
Min - Max	84 - 84	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	78.0 (NE)	-6.0 (NE)	107.0 (NE)	21.0 (NE)
Median	78.0	-6.0	107.0	21.0
Min - Max	78 - 78	-6 - -6	107 - 107	21 - 21
Cycle 36 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	84.0 (NE)	0.0 (NE)	60.0 (NE)	-9.0 (NE)
Median	84.0	0.0	60.0	-9.0
Min - Max	84 - 84	0 - 0	60 - 60	-9 - -9
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	78.0 (NE)	-6.0 (NE)	101.0 (NE)	15.0 (NE)
Median	78.0	-6.0	101.0	15.0
Min - Max	78 - 78	-6 - -6	101 - 101	15 - 15
Cycle 36 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	78.0 (NE)	-6.0 (NE)	NE (NE)	NE (NE)
Median	78.0	-6.0	NE	NE
Min - Max	78 - 78	-6 - -6	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	70.0 (NE)	-14.0 (NE)	104.0 (NE)	18.0 (NE)
Median	70.0	-14.0	104.0	18.0
Min - Max	70 - 70	-14 - -14	104 - 104	18 - 18
Cycle 36 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	-10.0 (NE)	NE (NE)	NE (NE)
Median	74.0	-10.0	NE	NE
Min - Max	74 - 74	-10 - -10	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	78.0 (NE)	-6.0 (NE)	108.0 (NE)	22.0 (NE)
Median	78.0	-6.0	108.0	22.0
Min - Max	78 - 78	-6 - -6	108 - 108	22 - 22

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 37 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	74.0 (NE)	-10.0 (NE)	57.0 (NE)	-12.0 (NE)
Median	74.0	-10.0	57.0	-12.0
Min - Max	74 - 74	-10 - -10	57 - 57	-12 - -12
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	78.0 (NE)	-6.0 (NE)	103.0 (NE)	17.0 (NE)
Median	78.0	-6.0	103.0	17.0
Min - Max	78 - 78	-6 - -6	103 - 103	17 - 17
Cycle 37 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	78.0 (NE)	-6.0 (NE)	NE (NE)	NE (NE)
Median	78.0	-6.0	NE	NE
Min - Max	78 - 78	-6 - -6	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	72.0 (NE)	-12.0 (NE)	102.0 (NE)	16.0 (NE)
Median	72.0	-12.0	102.0	16.0
Min - Max	72 - 72	-12 - -12	102 - 102	16 - 16
Cycle 37 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	78.0 (NE)	-6.0 (NE)	NE (NE)	NE (NE)
Median	78.0	-6.0	NE	NE
Min - Max	78 - 78	-6 - -6	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	74.0 (NE)	-10.0 (NE)	95.0 (NE)	9.0 (NE)
Median	74.0	-10.0	95.0	9.0
Min - Max	74 - 74	-10 - -10	95 - 95	9 - 9
Cycle 38 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	77.0 (NE)	-7.0 (NE)	57.0 (NE)	-12.0 (NE)
Median	77.0	-7.0	57.0	-12.0
Min - Max	77 - 77	-7 - -7	57 - 57	-12 - -12
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	79.0 (NE)	-5.0 (NE)	100.0 (NE)	14.0 (NE)
Median	79.0	-5.0	100.0	14.0
Min - Max	79 - 79	-5 - -5	100 - 100	14 - 14

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 38 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	78.0 (NE)	-6.0 (NE)	NE (NE)	NE (NE)
Median	78.0	-6.0	NE	NE
Min - Max	78 - 78	-6 - -6	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	80.0 (NE)	-4.0 (NE)	100.0 (NE)	14.0 (NE)
Median	80.0	-4.0	100.0	14.0
Min - Max	80 - 80	-4 - -4	100 - 100	14 - 14
Cycle 38 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	76.0 (NE)	-8.0 (NE)	NE (NE)	NE (NE)
Median	76.0	-8.0	NE	NE
Min - Max	76 - 76	-8 - -8	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	78.0 (NE)	-6.0 (NE)	100.0 (NE)	14.0 (NE)
Median	78.0	-6.0	100.0	14.0
Min - Max	78 - 78	-6 - -6	100 - 100	14 - 14
Cycle 39 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	69.0 (NE)	-15.0 (NE)	60.0 (NE)	-9.0 (NE)
Median	69.0	-15.0	60.0	-9.0
Min - Max	69 - 69	-15 - -15	60 - 60	-9 - -9
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	77.0 (NE)	-7.0 (NE)	NE (NE)	NE (NE)
Median	77.0	-7.0	NE	NE
Min - Max	77 - 77	-7 - -7	NE - NE	NE - NE
Cycle 39 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	68.0 (NE)	-16.0 (NE)	107.0 (NE)	21.0 (NE)
Median	68.0	-16.0	107.0	21.0
Min - Max	68 - 68	-16 - -16	107 - 107	21 - 21
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	76.0 (NE)	-8.0 (NE)	NE (NE)	NE (NE)
Median	76.0	-8.0	NE	NE
Min - Max	76 - 76	-8 - -8	NE - NE	NE - NE

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 39 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	76.0 (NE)	-8.0 (NE)	100.0 (NE)	14.0 (NE)
Median	76.0	-8.0	100.0	14.0
Min - Max	76 - 76	-8 - -8	100 - 100	14 - 14
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	-10.0 (NE)	NE (NE)	NE (NE)
Median	74.0	-10.0	NE	NE
Min - Max	74 - 74	-10 - -10	NE - NE	NE - NE
Cycle 40 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	84.0 (NE)	0.0 (NE)	79.0 (22.6)	1.5 (10.6)
Median	84.0	0.0	79.0	1.5
Min - Max	84 - 84	0 - 0	63 - 95	-6 - 9
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	78.0 (NE)	-6.0 (NE)	NE (NE)	NE (NE)
Median	78.0	-6.0	NE	NE
Min - Max	78 - 78	-6 - -6	NE - NE	NE - NE
Cycle 40 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	80.0 (NE)	-4.0 (NE)	99.0 (NE)	13.0 (NE)
Median	80.0	-4.0	99.0	13.0
Min - Max	80 - 80	-4 - -4	99 - 99	13 - 13
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	76.0 (NE)	-8.0 (NE)	NE (NE)	NE (NE)
Median	76.0	-8.0	NE	NE
Min - Max	76 - 76	-8 - -8	NE - NE	NE - NE
Cycle 40 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	78.0 (NE)	-6.0 (NE)	101.0 (NE)	15.0 (NE)
Median	78.0	-6.0	101.0	15.0
Min - Max	78 - 78	-6 - -6	101 - 101	15 - 15
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	78.0 (NE)	-6.0 (NE)	NE (NE)	NE (NE)
Median	78.0	-6.0	NE	NE
Min - Max	78 - 78	-6 - -6	NE - NE	NE - NE

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 41 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	78.0 (NE)	-6.0 (NE)	79.5 (27.6)	2.0 (15.6)
Median	78.0	-6.0	79.5	2.0
Min - Max	78 - 78	-6 - -6	60 - 99	-9 - 13
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	78.0 (NE)	-6.0 (NE)	NE (NE)	NE (NE)
Median	78.0	-6.0	NE	NE
Min - Max	78 - 78	-6 - -6	NE - NE	NE - NE
Cycle 41 Day 8				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	112.0 (NE)	26.0 (NE)
Median	NE	NE	112.0	26.0
Min - Max	NE - NE	NE - NE	112 - 112	26 - 26
Cycle 41 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	78.0 (NE)	-6.0 (NE)	104.0 (NE)	18.0 (NE)
Median	78.0	-6.0	104.0	18.0
Min - Max	78 - 78	-6 - -6	104 - 104	18 - 18
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	-10.0 (NE)	NE (NE)	NE (NE)
Median	74.0	-10.0	NE	NE
Min - Max	74 - 74	-10 - -10	NE - NE	NE - NE
Cycle 42 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	84.0 (NE)	0.0 (NE)	65.0 (NE)	-4.0 (NE)
Median	84.0	0.0	65.0	-4.0
Min - Max	84 - 84	0 - 0	65 - 65	-4 - -4
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	84.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	84.0	0.0	NE	NE
Min - Max	84 - 84	0 - 0	NE - NE	NE - NE
Cycle 42 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	78.0 (NE)	-6.0 (NE)	NE (NE)	NE (NE)
Median	78.0	-6.0	NE	NE
Min - Max	78 - 78	-6 - -6	NE - NE	NE - NE

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	-10.0 (NE)	NE (NE)	NE (NE)
Median	74.0	-10.0	NE	NE
Min - Max	74 - 74	-10 - -10	NE - NE	NE - NE
Cycle 42 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	76.0 (NE)	-8.0 (NE)	NE (NE)	NE (NE)
Median	76.0	-8.0	NE	NE
Min - Max	76 - 76	-8 - -8	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	76.0 (NE)	-8.0 (NE)	NE (NE)	NE (NE)
Median	76.0	-8.0	NE	NE
Min - Max	76 - 76	-8 - -8	NE - NE	NE - NE
Cycle 43 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	78.0 (NE)	-6.0 (NE)	62.0 (NE)	-7.0 (NE)
Median	78.0	-6.0	62.0	-7.0
Min - Max	78 - 78	-6 - -6	62 - 62	-7 - -7
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	76.0 (NE)	-8.0 (NE)	NE (NE)	NE (NE)
Median	76.0	-8.0	NE	NE
Min - Max	76 - 76	-8 - -8	NE - NE	NE - NE
Cycle 43 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	70.0 (NE)	-14.0 (NE)	NE (NE)	NE (NE)
Median	70.0	-14.0	NE	NE
Min - Max	70 - 70	-14 - -14	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	71.0 (NE)	-13.0 (NE)	NE (NE)	NE (NE)
Median	71.0	-13.0	NE	NE
Min - Max	71 - 71	-13 - -13	NE - NE	NE - NE
Cycle 43 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	-10.0 (NE)	NE (NE)	NE (NE)
Median	74.0	-10.0	NE	NE
Min - Max	74 - 74	-10 - -10	NE - NE	NE - NE

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	74.0 (NE)	-10.0 (NE)	NE (NE)	NE (NE)
Median	74.0	-10.0	NE	NE
Min - Max	74 - 74	-10 - -10	NE - NE	NE - NE
Cycle 44 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	61.0 (NE)	-8.0 (NE)
Median	NE	NE	61.0	-8.0
Min - Max	NE - NE	NE - NE	61 - 61	-8 - -8
Cycle 45 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	59.0 (NE)	-10.0 (NE)
Median	NE	NE	59.0	-10.0
Min - Max	NE - NE	NE - NE	59 - 59	-10 - -10
Cycle 46 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	56.0 (NE)	-13.0 (NE)
Median	NE	NE	56.0	-13.0
Min - Max	NE - NE	NE - NE	56 - 56	-13 - -13
Study Drug Discontinuation				
n	75	74	140	139
Mean (SD)	81.8 (12.3)	0.7 (10.8)	82.2 (12.9)	3.1 (12.5)
Median	79.0	1.5	81.0	2.0
Min - Max	60 - 124	-31 - 22	53 - 131	-27 - 47
Post-Baseline Last				
n	79	79	138	138
Mean (SD)	81.9 (12.3)	0.5 (10.7)	81.9 (13.2)	3.1 (12.6)
Median	80.0	2.0	81.0	2.5
Min - Max	60 - 124	-31 - 22	52 - 131	-27 - 47
PRE PAC INFUSION				
n	1	1	5	5
Mean (SD)	84.0 (NE)	-10.0 (NE)	96.0 (8.5)	8.8 (16.6)
Median	84.0	-10.0	96.0	10.0
Min - Max	84 - 84	-10 - -10	88 - 108	-10 - 32
AFTER PAC INFUSION				
n	6	6	21	21
Mean (SD)	81.3 (9.6)	-1.7 (11.4)	82.3 (10.0)	-1.6 (12.1)
Median	79.5	-3.5	82.0	2.0
Min - Max	70 - 95	-19 - 12	64 - 104	-36 - 16

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Post-Baseline Minimum				
n	5	5	6	6
Mean (SD)	71.0 (3.2)	-7.4 (14.2)	62.8 (11.1)	-14.3 (3.1)
Median	72.0	-4.0	60.5	-15.0
Min - Max	66 - 74	-31 - 4	52 - 81	-18 - -9
PRE PAC INFUSION				
n	48	48	85	85
Mean (SD)	66.6 (7.5)	-14.8 (11.6)	65.9 (8.7)	-12.8 (10.1)
Median	66.0	-13.0	66.0	-12.0
Min - Max	51 - 90	-61 - 5	48 - 96	-44 - 4
AFTER PAC INFUSION				
n	33	33	73	73
Mean (SD)	69.7 (9.4)	-12.8 (9.6)	64.4 (8.3)	-16.7 (12.3)
Median	69.0	-10.0	64.0	-14.0
Min - Max	45 - 99	-33 - 2	44 - 85	-62 - 5
Post-Baseline Maximum				
n	8	8	18	18
Mean (SD)	98.1 (11.8)	16.6 (9.0)	97.6 (15.8)	19.1 (14.1)
Median	96.5	18.0	96.5	17.0
Min - Max	84 - 116	4 - 32	75 - 131	-2 - 47
PRE PAC INFUSION				
n	53	53	106	106
Mean (SD)	99.2 (11.7)	16.3 (12.1)	99.4 (14.2)	17.9 (14.8)
Median	99.0	16.0	98.0	16.0
Min - Max	74 - 127	-10 - 50	68 - 154	-15 - 68
AFTER PAC INFUSION				
n	25	25	40	40
Mean (SD)	97.2 (21.9)	18.1 (20.3)	90.5 (11.4)	14.8 (11.6)
Median	90.0	14.0	88.0	15.0
Min - Max	80 - 188	-4 - 98	72 - 116	-5 - 39

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Baseline				
n	86		164	
Mean (SD)	17.4 (2.6)		17.2 (2.3)	
Median	17.0		17.0	
Min - Max	12 - 24		12 - 24	
Cycle 1 Day 1				
PRE PAC INFUSION				
n	84	83	145	144
Mean (SD)	17.5 (2.6)	0.2 (2.2)	17.6 (2.4)	0.3 (2.0)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 26	-8 - 8	12 - 23	-5 - 7
AFTER PAC INFUSION				
n	84	83	156	155
Mean (SD)	17.5 (2.5)	0.1 (2.3)	17.6 (2.3)	0.4 (2.2)
Median	18.0	0.0	18.0	0.0
Min - Max	9 - 22	-11 - 5	11 - 24	-9 - 7
Cycle 1 Day 8				
PRE PAC INFUSION				
n	86	85	160	158
Mean (SD)	17.6 (3.2)	0.2 (3.3)	17.4 (2.4)	0.2 (2.0)
Median	17.0	0.0	18.0	0.0
Min - Max	8 - 37	-12 - 19	12 - 28	-5 - 7
AFTER PAC INFUSION				
n	78	77	146	145
Mean (SD)	17.7 (3.3)	0.2 (3.3)	17.5 (2.2)	0.3 (1.7)
Median	18.0	0.0	18.0	0.0
Min - Max	9 - 37	-6 - 19	12 - 24	-4 - 4
Cycle 1 Day 15				
PRE PAC INFUSION				
n	81	80	148	146
Mean (SD)	17.3 (2.3)	0.0 (2.3)	17.4 (2.3)	0.2 (2.0)
Median	18.0	0.0	17.0	0.0
Min - Max	11 - 22	-9 - 6	12 - 28	-8 - 7
AFTER PAC INFUSION				
n	74	73	132	131
Mean (SD)	17.4 (2.7)	0.0 (2.4)	17.5 (2.5)	0.4 (2.2)
Median	17.5	0.0	18.0	0.0
Min - Max	11 - 30	-6 - 9	12 - 28	-6 - 9
Cycle 2 Day 1				
PRE PAC INFUSION				
n	77	76	159	158
Mean (SD)	17.6 (2.1)	0.2 (2.1)	17.4 (2.4)	0.2 (2.2)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 22	-5 - 5	12 - 24	-6 - 9

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	73	72	152	151
Mean (SD)	17.8 (2.4)	0.4 (2.8)	17.5 (2.4)	0.3 (2.5)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 22	-6 - 10	12 - 26	-6 - 14
Cycle 2 Day 8				
PRE PAC INFUSION				
n	79	78	153	151
Mean (SD)	17.8 (2.4)	0.4 (2.4)	17.4 (2.4)	0.2 (2.1)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 24	-6 - 8	12 - 23	-6 - 9
AFTER PAC INFUSION				
n	72	71	148	147
Mean (SD)	17.5 (2.3)	0.1 (2.3)	17.3 (2.3)	0.1 (2.2)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 24	-6 - 5	12 - 24	-7 - 10
Cycle 2 Day 15				
PRE PAC INFUSION				
n	77	76	147	145
Mean (SD)	17.4 (2.4)	0.0 (2.3)	17.6 (2.4)	0.2 (2.5)
Median	18.0	0.0	18.0	0.0
Min - Max	11 - 22	-6 - 9	12 - 28	-8 - 14
AFTER PAC INFUSION				
n	71	70	145	143
Mean (SD)	17.5 (2.4)	0.2 (2.2)	17.6 (2.1)	0.4 (2.1)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 24	-6 - 6	12 - 24	-4 - 10
Cycle 3 Day 1				
PRE PAC INFUSION				
n	74	73	143	141
Mean (SD)	17.3 (2.3)	-0.1 (2.2)	17.6 (2.4)	0.3 (2.3)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 22	-7 - 6	12 - 24	-6 - 9
AFTER PAC INFUSION				
n	70	69	134	132
Mean (SD)	17.6 (2.2)	0.3 (2.3)	17.6 (2.3)	0.4 (2.4)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 24	-6 - 7	12 - 24	-6 - 10
Cycle 3 Day 8				
PRE PAC INFUSION				
n	73	72	140	138
Mean (SD)	17.4 (2.3)	0.1 (2.8)	17.5 (2.5)	0.3 (2.2)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 24	-8 - 10	12 - 24	-7 - 7

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	69	68	136	134
Mean (SD)	17.6 (2.3)	0.3 (2.5)	17.3 (2.2)	0.2 (2.2)
Median	18.0	0.0	17.5	0.0
Min - Max	12 - 24	-8 - 8	10 - 23	-7 - 9
Cycle 3 Day 15				
PRE PAC INFUSION				
n	66	65	136	135
Mean (SD)	17.5 (2.5)	0.4 (2.3)	17.4 (2.3)	0.2 (2.2)
Median	18.0	0.0	17.0	0.0
Min - Max	12 - 24	-7 - 7	12 - 24	-5 - 9
AFTER PAC INFUSION				
n	67	66	129	128
Mean (SD)	17.5 (2.5)	0.2 (2.5)	17.6 (2.4)	0.4 (2.2)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 24	-6 - 8	10 - 24	-6 - 8
Cycle 4 Day 1				
PRE PAC INFUSION				
n	69	68	131	129
Mean (SD)	17.4 (2.0)	0.2 (2.1)	17.5 (2.2)	0.3 (2.4)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 20	-4 - 6	12 - 24	-6 - 10
AFTER PAC INFUSION				
n	65	64	121	119
Mean (SD)	17.7 (2.7)	0.5 (2.6)	17.5 (2.1)	0.2 (2.3)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 27	-3 - 11	12 - 23	-6 - 9
Cycle 4 Day 8				
PRE PAC INFUSION				
n	67	66	127	126
Mean (SD)	17.3 (2.4)	0.0 (2.7)	17.6 (2.3)	0.4 (2.3)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 24	-8 - 8	12 - 24	-6 - 10
AFTER PAC INFUSION				
n	64	63	120	119
Mean (SD)	17.4 (2.5)	0.0 (2.5)	17.6 (2.3)	0.4 (2.5)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 24	-8 - 6	12 - 26	-6 - 9
Cycle 4 Day 15				
PRE PAC INFUSION				
n	67	66	126	124
Mean (SD)	17.3 (2.5)	0.1 (2.4)	17.6 (2.3)	0.4 (2.4)
Median	17.0	0.0	18.0	0.0
Min - Max	12 - 24	-8 - 7	12 - 24	-5 - 9

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	66	65	115	113
Mean (SD)	17.6 (2.2)	0.4 (2.3)	17.6 (2.0)	0.5 (2.1)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 22	-6 - 8	13 - 22	-4 - 7
Cycle 5 Day 1				
PRE PAC INFUSION				
n	61	60	103	101
Mean (SD)	17.2 (2.3)	-0.2 (2.0)	17.5 (2.4)	0.4 (2.3)
Median	17.0	0.0	17.0	0.0
Min - Max	12 - 22	-6 - 5	12 - 24	-4 - 10
AFTER PAC INFUSION				
n	57	56	95	93
Mean (SD)	17.5 (2.0)	0.1 (2.0)	17.4 (2.3)	0.4 (2.4)
Median	18.0	0.0	17.0	0.0
Min - Max	14 - 22	-4 - 5	12 - 24	-6 - 8
Cycle 5 Day 8				
PRE PAC INFUSION				
n	52	51	95	94
Mean (SD)	18.1 (3.6)	0.7 (3.8)	17.6 (2.1)	0.3 (2.3)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 36	-9 - 20	12 - 22	-6 - 7
AFTER PAC INFUSION				
n	51	50	87	86
Mean (SD)	17.6 (2.5)	0.1 (2.7)	17.6 (2.6)	0.5 (2.5)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 26	-8 - 10	10 - 24	-7 - 8
Cycle 5 Day 15				
PRE PAC INFUSION				
n	54	53	90	89
Mean (SD)	17.3 (2.4)	0.1 (2.4)	17.5 (2.1)	0.3 (2.2)
Median	18.0	0.0	17.5	0.0
Min - Max	12 - 22	-8 - 8	12 - 22	-5 - 6
AFTER PAC INFUSION				
n	51	50	78	77
Mean (SD)	17.5 (2.4)	0.4 (2.2)	17.5 (1.9)	0.1 (1.9)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 24	-8 - 6	14 - 22	-4 - 6
Cycle 6 Day 1				
PRE PAC INFUSION				
n	56	55	91	90
Mean (SD)	17.1 (2.4)	-0.1 (2.3)	17.4 (2.1)	0.2 (2.3)
Median	17.0	0.0	18.0	0.0
Min - Max	12 - 24	-8 - 8	12 - 25	-6 - 11

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	49	48	85	84
Mean (SD)	17.3 (2.6)	-0.1 (2.9)	17.6 (1.9)	0.3 (1.9)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 24	-8 - 8	12 - 22	-4 - 6
Cycle 6 Day 8				
PRE PAC INFUSION				
n	49	48	87	86
Mean (SD)	17.8 (2.4)	0.3 (2.4)	17.4 (2.1)	0.1 (1.9)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 23	-8 - 8	12 - 23	-5 - 6
AFTER PAC INFUSION				
n	48	47	83	82
Mean (SD)	17.6 (2.5)	0.2 (2.4)	17.6 (2.1)	0.3 (2.2)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 24	-8 - 8	12 - 22	-6 - 6
Cycle 6 Day 15				
PRE PAC INFUSION				
n	49	48	83	82
Mean (SD)	17.4 (2.3)	0.0 (2.0)	17.3 (2.1)	0.0 (2.2)
Median	18.0	0.0	17.0	0.0
Min - Max	12 - 22	-8 - 4	12 - 23	-5 - 8
AFTER PAC INFUSION				
n	47	46	79	78
Mean (SD)	17.6 (2.2)	0.3 (2.0)	17.2 (2.1)	-0.1 (2.3)
Median	18.0	0.0	17.0	0.0
Min - Max	12 - 22	-8 - 4	12 - 21	-6 - 7
Cycle 7 Day 1				
PRE PAC INFUSION				
n	42	41	76	75
Mean (SD)	17.7 (2.8)	0.1 (2.3)	17.7 (2.0)	0.5 (2.1)
Median	18.0	0.0	18.0	0.0
Min - Max	11 - 24	-8 - 5	14 - 23	-4 - 9
AFTER PAC INFUSION				
n	37	36	66	65
Mean (SD)	17.6 (2.5)	0.2 (2.8)	17.5 (1.9)	0.2 (1.9)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 22	-8 - 8	12 - 21	-5 - 5
Cycle 7 Day 8				
PRE PAC INFUSION				
n	35	34	67	66
Mean (SD)	17.6 (2.7)	0.2 (2.4)	17.4 (2.2)	0.2 (2.2)
Median	18.0	0.0	17.0	0.0
Min - Max	12 - 22	-8 - 5	12 - 25	-4 - 7

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	34	33	63	62
Mean (SD)	17.9 (2.5)	0.4 (3.0)	17.4 (2.2)	0.2 (2.3)
Median	18.0	0.0	17.0	0.0
Min - Max	12 - 22	-8 - 7	12 - 23	-7 - 6
Cycle 7 Day 15				
PRE PAC INFUSION				
n	34	33	69	68
Mean (SD)	17.4 (2.6)	-0.2 (2.4)	17.6 (2.2)	0.4 (2.3)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 22	-8 - 5	12 - 26	-4 - 6
AFTER PAC INFUSION				
n	34	33	66	65
Mean (SD)	17.9 (2.5)	0.4 (2.6)	17.5 (2.0)	0.3 (2.2)
Median	18.0	0.0	17.5	0.0
Min - Max	12 - 24	-8 - 6	12 - 24	-5 - 4
Cycle 8 Day 1				
PRE PAC INFUSION				
n	33	32	70	69
Mean (SD)	17.8 (2.4)	0.3 (1.9)	17.5 (2.3)	0.6 (2.5)
Median	18.0	0.0	17.5	0.0
Min - Max	12 - 22	-3 - 6	12 - 22	-7 - 6
AFTER PAC INFUSION				
n	27	26	63	62
Mean (SD)	17.9 (3.1)	0.7 (2.9)	17.4 (2.0)	0.4 (2.1)
Median	18.0	0.0	18.0	0.0
Min - Max	10 - 24	-4 - 12	12 - 22	-7 - 4
Cycle 8 Day 8				
PRE PAC INFUSION				
n	29	28	64	63
Mean (SD)	17.8 (2.7)	0.6 (2.4)	17.6 (2.2)	0.6 (2.3)
Median	19.0	0.0	17.5	0.0
Min - Max	12 - 22	-3 - 7	12 - 24	-4 - 7
AFTER PAC INFUSION				
n	27	26	60	59
Mean (SD)	17.9 (2.8)	0.8 (2.7)	17.5 (2.1)	0.4 (2.2)
Median	19.0	0.0	18.0	0.0
Min - Max	12 - 24	-2 - 10	12 - 22	-5 - 8
Cycle 8 Day 15				
PRE PAC INFUSION				
n	28	27	60	59
Mean (SD)	17.2 (2.7)	0.1 (2.4)	17.3 (1.9)	0.3 (2.1)
Median	18.0	0.0	17.5	0.0
Min - Max	12 - 22	-3 - 8	13 - 22	-5 - 6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	27	26	58	57
Mean (SD)	17.5 (2.7)	0.3 (2.0)	17.4 (2.4)	0.3 (2.5)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 24	-2 - 7	12 - 26	-6 - 9
Cycle 9 Day 1				
PRE PAC INFUSION				
n	27	26	57	56
Mean (SD)	17.5 (2.5)	0.0 (1.4)	17.4 (1.9)	0.3 (2.1)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 20	-2 - 3	13 - 22	-4 - 7
AFTER PAC INFUSION				
n	22	21	52	51
Mean (SD)	17.9 (2.1)	0.3 (1.7)	17.4 (2.0)	0.1 (1.8)
Median	18.0	0.0	17.0	0.0
Min - Max	12 - 20	-2 - 4	13 - 23	-4 - 5
Cycle 9 Day 8				
PRE PAC INFUSION				
n	24	23	51	50
Mean (SD)	17.3 (2.6)	0.1 (1.6)	17.6 (2.1)	0.4 (2.2)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 20	-2 - 4	12 - 22	-4 - 7
AFTER PAC INFUSION				
n	21	20	50	49
Mean (SD)	17.1 (2.4)	-0.2 (1.4)	17.4 (2.0)	0.2 (2.0)
Median	18.0	0.0	17.0	0.0
Min - Max	12 - 20	-2 - 2	12 - 20	-7 - 4
Cycle 9 Day 15				
PRE PAC INFUSION				
n	22	21	51	50
Mean (SD)	17.1 (2.4)	0.0 (1.4)	17.7 (2.1)	0.4 (1.8)
Median	17.0	0.0	18.0	0.0
Min - Max	12 - 20	-2 - 4	12 - 22	-2 - 7
AFTER PAC INFUSION				
n	20	19	48	47
Mean (SD)	17.2 (2.4)	0.1 (1.6)	17.3 (2.0)	0.0 (1.9)
Median	18.0	0.0	17.0	0.0
Min - Max	12 - 20	-2 - 4	12 - 21	-8 - 4
Cycle 10 Day 1				
PRE PAC INFUSION				
n	22	22	54	53
Mean (SD)	17.5 (2.4)	-0.1 (1.7)	17.3 (2.2)	0.1 (2.6)
Median	18.0	0.0	16.5	0.0
Min - Max	12 - 20	-4 - 4	12 - 24	-6 - 10

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	19	19	44	43
Mean (SD)	17.3 (2.1)	-0.3 (1.8)	17.5 (1.9)	-0.1 (1.9)
Median	18.0	0.0	17.5	0.0
Min - Max	12 - 20	-4 - 4	14 - 21	-6 - 4
Cycle 10 Day 8				
PRE PAC INFUSION				
n	19	18	43	42
Mean (SD)	17.3 (3.1)	-0.1 (1.3)	17.4 (2.1)	0.0 (2.3)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 24	-2 - 2	13 - 23	-6 - 9
AFTER PAC INFUSION				
n	18	17	40	39
Mean (SD)	17.8 (3.3)	0.4 (1.9)	17.4 (2.4)	0.0 (1.9)
Median	18.0	0.0	17.0	0.0
Min - Max	12 - 24	-2 - 6	13 - 24	-5 - 4
Cycle 10 Day 15				
PRE PAC INFUSION				
n	18	17	46	45
Mean (SD)	17.9 (2.2)	0.9 (1.8)	17.4 (2.1)	-0.1 (2.1)
Median	18.0	0.0	17.0	0.0
Min - Max	14 - 22	-1 - 5	12 - 22	-5 - 7
AFTER PAC INFUSION				
n	16	15	41	40
Mean (SD)	16.9 (2.8)	-0.1 (1.6)	17.6 (2.1)	0.0 (1.9)
Median	16.5	0.0	18.0	0.0
Min - Max	12 - 22	-2 - 3	12 - 23	-4 - 4
Cycle 11 Day 1				
PRE PAC INFUSION				
n	17	16	48	47
Mean (SD)	17.8 (3.5)	0.3 (2.7)	17.4 (2.1)	0.2 (2.2)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 24	-4 - 8	12 - 23	-5 - 9
AFTER PAC INFUSION				
n	14	13	40	39
Mean (SD)	17.1 (2.5)	-0.2 (1.7)	17.7 (2.1)	0.2 (2.0)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 20	-4 - 2	12 - 22	-5 - 6
Cycle 11 Day 8				
PRE PAC INFUSION				
n	15	14	34	33
Mean (SD)	16.9 (2.9)	-0.4 (1.5)	17.7 (2.1)	0.3 (2.3)
Median	18.0	-1.0	18.0	0.0
Min - Max	12 - 20	-2 - 2	12 - 21	-7 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	14	13	33	32
Mean (SD)	17.7 (2.4)	0.5 (2.2)	17.6 (2.2)	0.1 (2.2)
Median	18.0	0.0	18.0	0.0
Min - Max	14 - 22	-2 - 6	12 - 22	-6 - 4
Cycle 11 Day 15				
PRE PAC INFUSION				
n	17	16	39	38
Mean (SD)	17.4 (2.9)	-0.3 (2.2)	17.8 (1.9)	0.4 (1.9)
Median	18.0	-0.5	18.0	0.0
Min - Max	12 - 22	-4 - 4	14 - 23	-6 - 4
AFTER PAC INFUSION				
n	14	13	36	35
Mean (SD)	18.4 (2.0)	0.5 (2.1)	18.0 (1.8)	0.5 (2.0)
Median	18.5	0.0	18.0	0.0
Min - Max	15 - 22	-2 - 5	14 - 22	-5 - 4
Cycle 12 Day 1				
PRE PAC INFUSION				
n	17	17	43	43
Mean (SD)	17.9 (4.0)	0.0 (2.8)	17.0 (2.1)	-0.1 (1.9)
Median	18.0	0.0	17.0	0.0
Min - Max	12 - 28	-2 - 10	12 - 22	-5 - 4
AFTER PAC INFUSION				
n	14	14	35	35
Mean (SD)	17.7 (2.4)	-0.1 (1.2)	17.5 (2.6)	0.1 (2.6)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 20	-2 - 2	12 - 25	-6 - 9
Cycle 12 Day 8				
PRE PAC INFUSION				
n	16	15	32	32
Mean (SD)	17.6 (2.6)	-0.2 (2.0)	17.8 (2.0)	0.4 (2.1)
Median	18.5	0.0	18.0	0.0
Min - Max	12 - 20	-2 - 4	14 - 22	-4 - 6
AFTER PAC INFUSION				
n	14	13	32	32
Mean (SD)	17.9 (2.4)	0.0 (2.4)	17.6 (2.0)	0.1 (2.0)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 20	-2 - 6	14 - 22	-6 - 6
Cycle 12 Day 15				
PRE PAC INFUSION				
n	16	15	32	32
Mean (SD)	18.2 (2.7)	0.5 (2.4)	17.3 (2.0)	-0.2 (2.0)
Median	19.0	0.0	17.0	0.0
Min - Max	12 - 22	-2 - 6	14 - 22	-6 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	14	13	30	30
Mean (SD)	18.4 (2.3)	0.6 (2.6)	17.6 (2.0)	-0.1 (2.0)
Median	18.5	0.0	18.0	0.0
Min - Max	14 - 23	-2 - 7	13 - 22	-5 - 4
Cycle 13 Day 1				
PRE PAC INFUSION				
n	14	13	32	32
Mean (SD)	18.2 (3.3)	0.5 (2.9)	17.1 (2.0)	0.0 (1.9)
Median	19.0	0.0	16.5	0.0
Min - Max	12 - 25	-2 - 9	14 - 21	-6 - 4
AFTER PAC INFUSION				
n	12	11	27	27
Mean (SD)	18.6 (2.6)	0.5 (2.3)	17.8 (2.6)	-0.1 (2.7)
Median	20.0	0.0	18.0	0.0
Min - Max	14 - 22	-2 - 6	13 - 24	-7 - 6
Cycle 13 Day 8				
PRE PAC INFUSION				
n	12	11	27	27
Mean (SD)	17.9 (1.7)	0.2 (2.1)	17.7 (2.1)	-0.2 (1.7)
Median	18.0	0.0	18.0	0.0
Min - Max	14 - 20	-4 - 4	14 - 23	-5 - 4
AFTER PAC INFUSION				
n	11	10	24	24
Mean (SD)	18.1 (1.9)	0.6 (2.6)	17.9 (2.0)	0.0 (1.7)
Median	18.0	0.5	18.0	0.0
Min - Max	14 - 20	-3 - 6	14 - 22	-6 - 4
Cycle 13 Day 15				
PRE PAC INFUSION				
n	12	11	26	26
Mean (SD)	18.1 (2.2)	0.4 (2.0)	17.6 (1.9)	-0.3 (1.8)
Median	18.5	0.0	18.0	0.0
Min - Max	14 - 20	-3 - 3	15 - 22	-5 - 4
AFTER PAC INFUSION				
n	11	10	23	23
Mean (SD)	18.0 (2.5)	0.5 (2.4)	18.1 (1.7)	0.0 (1.9)
Median	19.0	1.0	18.0	0.0
Min - Max	13 - 21	-3 - 5	15 - 23	-6 - 4
Cycle 14 Day 1				
PRE PAC INFUSION				
n	13	12	32	32
Mean (SD)	18.3 (2.5)	0.9 (3.0)	17.1 (2.1)	-0.4 (2.0)
Median	18.0	0.0	16.5	0.0
Min - Max	14 - 24	-4 - 8	12 - 22	-6 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	11	10	26	26
Mean (SD)	18.1 (2.0)	0.2 (1.7)	18.1 (2.1)	0.2 (2.6)
Median	19.0	0.0	18.0	0.0
Min - Max	14 - 20	-3 - 2	14 - 24	-5 - 8
Cycle 14 Day 8				
PRE PAC INFUSION				
n	11	10	25	25
Mean (SD)	18.2 (2.9)	0.7 (2.9)	17.6 (1.8)	-0.1 (1.8)
Median	18.0	0.0	18.0	0.0
Min - Max	14 - 24	-2 - 8	14 - 20	-5 - 4
AFTER PAC INFUSION				
n	10	9	24	24
Mean (SD)	18.3 (2.8)	0.9 (2.7)	17.9 (1.8)	0.0 (2.1)
Median	18.5	0.0	18.0	0.0
Min - Max	12 - 22	-2 - 6	15 - 22	-6 - 4
Cycle 14 Day 15				
PRE PAC INFUSION				
n	11	10	26	26
Mean (SD)	18.5 (2.6)	0.3 (2.2)	17.6 (2.4)	-0.2 (2.3)
Median	19.0	0.0	18.0	0.0
Min - Max	12 - 22	-3 - 5	12 - 24	-6 - 4
AFTER PAC INFUSION				
n	10	9	24	24
Mean (SD)	18.2 (3.3)	0.2 (2.5)	17.8 (2.2)	-0.2 (2.5)
Median	19.0	0.0	18.0	0.0
Min - Max	10 - 22	-4 - 4	14 - 25	-7 - 4
Cycle 15 Day 1				
PRE PAC INFUSION				
n	11	11	28	28
Mean (SD)	18.2 (1.7)	0.5 (1.8)	17.5 (1.6)	-0.1 (2.1)
Median	18.0	1.0	17.0	0.0
Min - Max	16 - 20	-3 - 2	15 - 20	-6 - 4
AFTER PAC INFUSION				
n	10	10	22	22
Mean (SD)	18.3 (2.6)	0.2 (2.3)	18.3 (2.3)	0.1 (2.6)
Median	19.0	0.0	18.0	0.0
Min - Max	12 - 21	-3 - 5	15 - 24	-5 - 6
Cycle 15 Day 8				
PRE PAC INFUSION				
n	11	10	21	21
Mean (SD)	18.7 (1.3)	0.6 (2.5)	18.5 (1.9)	0.3 (2.2)
Median	19.0	0.5	18.0	0.0
Min - Max	16 - 20	-4 - 4	15 - 22	-7 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	10	9	18	18
Mean (SD)	18.3 (1.5)	0.3 (2.4)	18.0 (2.0)	-0.2 (2.4)
Median	18.0	0.0	18.0	0.0
Min - Max	16 - 20	-4 - 4	15 - 21	-6 - 5
Cycle 15 Day 15				
PRE PAC INFUSION				
n	10	9	22	22
Mean (SD)	18.3 (1.1)	0.1 (2.4)	18.3 (1.8)	0.1 (1.9)
Median	18.0	0.0	18.0	0.5
Min - Max	16 - 20	-4 - 4	15 - 23	-4 - 4
AFTER PAC INFUSION				
n	8	7	20	20
Mean (SD)	18.8 (2.6)	0.4 (3.8)	18.1 (2.1)	-0.2 (2.3)
Median	18.0	0.0	18.0	0.0
Min - Max	16 - 24	-4 - 8	15 - 23	-6 - 6
Cycle 16 Day 1				
PRE PAC INFUSION				
n	11	10	24	24
Mean (SD)	17.5 (2.2)	0.0 (1.6)	17.3 (2.3)	-0.5 (1.8)
Median	18.0	0.0	18.0	0.0
Min - Max	14 - 20	-3 - 2	12 - 22	-4 - 2
AFTER PAC INFUSION				
n	10	9	20	20
Mean (SD)	18.3 (1.8)	0.4 (1.9)	18.3 (2.3)	0.2 (2.7)
Median	18.5	0.0	18.0	0.0
Min - Max	16 - 20	-2 - 4	15 - 24	-6 - 8
Cycle 16 Day 8				
PRE PAC INFUSION				
n	11	10	19	19
Mean (SD)	18.4 (2.6)	0.1 (1.4)	17.7 (2.0)	-0.5 (1.7)
Median	19.0	0.0	18.0	0.0
Min - Max	12 - 22	-2 - 2	15 - 24	-4 - 3
AFTER PAC INFUSION				
n	10	9	19	19
Mean (SD)	19.0 (1.6)	1.0 (2.0)	17.8 (2.1)	-0.5 (1.7)
Median	19.0	0.0	18.0	0.0
Min - Max	16 - 22	-2 - 4	14 - 23	-5 - 2
Cycle 16 Day 15				
PRE PAC INFUSION				
n	10	9	21	21
Mean (SD)	18.1 (1.4)	0.0 (2.0)	17.6 (1.7)	-0.6 (1.7)
Median	18.0	0.0	18.0	0.0
Min - Max	16 - 20	-4 - 2	14 - 22	-5 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	9	8	19	19
Mean (SD)	18.1 (1.7)	0.1 (2.2)	17.8 (2.6)	-0.7 (2.3)
Median	18.0	0.5	18.0	0.0
Min - Max	15 - 20	-4 - 2	12 - 24	-6 - 3
Cycle 17 Day 1				
PRE PAC INFUSION				
n	8	7	23	23
Mean (SD)	17.5 (2.6)	-0.6 (2.3)	17.7 (2.2)	-0.1 (2.4)
Median	18.0	-1.0	18.0	0.0
Min - Max	12 - 20	-4 - 2	14 - 23	-5 - 6
AFTER PAC INFUSION				
n	7	6	20	20
Mean (SD)	18.4 (1.3)	-0.2 (2.7)	18.4 (1.9)	0.2 (2.3)
Median	19.0	0.0	18.0	0.0
Min - Max	16 - 20	-4 - 4	16 - 23	-6 - 4
Cycle 17 Day 8				
PRE PAC INFUSION				
n	6	5	18	18
Mean (SD)	18.7 (2.2)	-0.2 (2.3)	17.9 (2.1)	-0.3 (2.4)
Median	18.5	0.0	18.0	0.0
Min - Max	16 - 22	-4 - 2	14 - 22	-7 - 4
AFTER PAC INFUSION				
n	6	5	18	18
Mean (SD)	17.8 (2.4)	-1.2 (1.3)	17.7 (2.7)	-0.5 (2.6)
Median	18.5	-1.0	18.0	-0.5
Min - Max	14 - 20	-3 - 0	12 - 23	-6 - 6
Cycle 17 Day 15				
PRE PAC INFUSION				
n	7	6	19	19
Mean (SD)	18.0 (3.0)	-0.8 (1.7)	18.0 (2.4)	-0.3 (2.4)
Median	19.0	-1.0	18.0	0.0
Min - Max	12 - 20	-3 - 1	15 - 22	-7 - 4
AFTER PAC INFUSION				
n	7	6	19	19
Mean (SD)	18.9 (1.5)	0.2 (3.2)	18.4 (2.2)	0.1 (2.7)
Median	19.0	-0.5	18.0	0.0
Min - Max	16 - 20	-3 - 6	15 - 23	-7 - 6
Cycle 18 Day 1				
PRE PAC INFUSION				
n	7	7	21	21
Mean (SD)	17.6 (2.3)	-0.3 (1.9)	17.1 (2.2)	-0.6 (2.3)
Median	18.0	0.0	17.0	0.0
Min - Max	14 - 20	-3 - 2	12 - 22	-6 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	6	6	17	17
Mean (SD)	17.5 (2.2)	-1.0 (1.3)	17.8 (2.2)	-0.5 (2.7)
Median	18.0	-0.5	18.0	0.0
Min - Max	14 - 20	-3 - 0	14 - 23	-7 - 4
Cycle 18 Day 8				
PRE PAC INFUSION				
n	6	6	15	15
Mean (SD)	17.7 (3.4)	-0.8 (1.5)	17.9 (1.9)	-0.5 (2.7)
Median	18.5	-0.5	18.0	0.0
Min - Max	12 - 22	-3 - 1	16 - 22	-6 - 4
AFTER PAC INFUSION				
n	6	6	14	14
Mean (SD)	18.3 (1.5)	-0.2 (2.2)	17.6 (2.1)	-0.6 (2.8)
Median	18.0	-0.5	18.0	0.0
Min - Max	16 - 20	-2 - 4	14 - 22	-8 - 4
Cycle 18 Day 15				
PRE PAC INFUSION				
n	7	6	17	17
Mean (SD)	17.7 (2.9)	-1.2 (1.8)	17.4 (2.3)	-0.9 (2.4)
Median	19.0	-1.0	18.0	0.0
Min - Max	12 - 20	-4 - 1	12 - 23	-6 - 4
AFTER PAC INFUSION				
n	7	6	16	16
Mean (SD)	18.3 (1.7)	-0.5 (1.8)	17.9 (2.2)	-0.6 (2.7)
Median	19.0	0.0	18.0	0.0
Min - Max	16 - 20	-3 - 2	14 - 24	-8 - 4
Cycle 19 Day 1				
PRE PAC INFUSION				
n	7	6	18	18
Mean (SD)	17.4 (1.4)	0.0 (1.9)	18.1 (2.3)	0.2 (2.7)
Median	18.0	0.0	18.0	0.0
Min - Max	16 - 19	-3 - 2	14 - 24	-5 - 8
AFTER PAC INFUSION				
n	6	5	14	14
Mean (SD)	17.2 (2.8)	-1.0 (1.6)	17.9 (2.3)	-0.6 (2.8)
Median	18.5	-1.0	18.0	0.0
Min - Max	12 - 19	-3 - 1	15 - 23	-7 - 5
Cycle 19 Day 8				
PRE PAC INFUSION				
n	6	5	13	13
Mean (SD)	17.5 (3.0)	-0.6 (1.9)	17.7 (1.8)	-0.8 (2.2)
Median	19.0	0.0	18.0	-1.0
Min - Max	12 - 20	-3 - 2	15 - 20	-4 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	4	12	12
Mean (SD)	17.8 (1.6)	-0.3 (2.1)	18.1 (1.8)	-0.5 (2.4)
Median	19.0	0.0	18.0	0.0
Min - Max	16 - 19	-3 - 2	16 - 21	-6 - 4
Cycle 19 Day 15				
PRE PAC INFUSION				
n	6	5	13	13
Mean (SD)	17.0 (2.7)	-1.0 (1.6)	18.2 (1.9)	-0.4 (2.8)
Median	18.0	-1.0	18.0	0.0
Min - Max	12 - 19	-3 - 1	15 - 22	-7 - 4
AFTER PAC INFUSION				
n	6	5	13	13
Mean (SD)	17.5 (2.6)	-0.6 (1.5)	18.2 (2.5)	-0.3 (3.0)
Median	18.5	0.0	18.0	0.0
Min - Max	13 - 20	-3 - 1	15 - 24	-7 - 5
Cycle 20 Day 1				
PRE PAC INFUSION				
n	6	5	16	16
Mean (SD)	18.0 (2.4)	-0.2 (1.8)	17.6 (2.5)	-0.4 (2.5)
Median	19.0	0.0	17.5	0.0
Min - Max	14 - 20	-3 - 2	12 - 23	-5 - 4
AFTER PAC INFUSION				
n	5	4	13	13
Mean (SD)	18.8 (1.6)	-0.3 (1.9)	18.0 (2.3)	-0.5 (2.9)
Median	19.0	0.5	18.0	0.0
Min - Max	16 - 20	-3 - 1	15 - 23	-7 - 4
Cycle 20 Day 8				
PRE PAC INFUSION				
n	6	5	12	12
Mean (SD)	17.3 (2.9)	-0.8 (1.9)	18.7 (2.1)	0.1 (2.6)
Median	18.5	-1.0	18.5	0.0
Min - Max	12 - 20	-3 - 2	16 - 23	-6 - 4
AFTER PAC INFUSION				
n	6	5	12	12
Mean (SD)	17.8 (1.5)	-0.2 (2.3)	18.1 (2.5)	-0.5 (3.1)
Median	18.5	0.0	18.0	0.0
Min - Max	16 - 19	-4 - 2	14 - 23	-8 - 4
Cycle 20 Day 15				
PRE PAC INFUSION				
n	6	5	12	12
Mean (SD)	17.5 (1.2)	-0.4 (2.3)	17.3 (2.2)	-1.0 (3.0)
Median	18.0	0.0	16.5	-1.0
Min - Max	16 - 19	-4 - 2	15 - 23	-7 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	4	11	11
Mean (SD)	16.6 (2.8)	-0.5 (1.0)	17.6 (2.0)	-0.7 (3.0)
Median	18.0	0.0	17.0	0.0
Min - Max	12 - 19	-2 - 0	15 - 22	-7 - 4
Cycle 21 Day 1				
PRE PAC INFUSION				
n	5	5	13	13
Mean (SD)	17.4 (2.4)	-0.4 (1.8)	17.5 (2.6)	-0.6 (2.5)
Median	18.0	0.0	17.0	0.0
Min - Max	14 - 20	-3 - 2	14 - 23	-7 - 2
AFTER PAC INFUSION				
n	3	3	11	11
Mean (SD)	18.3 (2.1)	0.7 (0.6)	17.7 (2.2)	-0.9 (2.1)
Median	19.0	1.0	18.0	0.0
Min - Max	16 - 20	0 - 1	16 - 23	-6 - 2
Cycle 21 Day 8				
PRE PAC INFUSION				
n	3	3	11	11
Mean (SD)	17.7 (2.1)	0.0 (2.0)	17.5 (1.6)	-1.2 (1.8)
Median	17.0	0.0	18.0	-1.0
Min - Max	16 - 20	-2 - 2	15 - 20	-5 - 2
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	18.1 (2.3)	-0.6 (2.7)
Median	17.0	-0.5	18.0	0.0
Min - Max	16 - 18	-1 - 0	15 - 23	-7 - 2
Cycle 21 Day 15				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	18.2 (2.1)	-0.5 (2.0)
Median	17.0	-0.5	18.0	-0.5
Min - Max	16 - 18	-1 - 0	16 - 23	-4 - 2
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	17.5 (2.1)	0.0 (0.0)	18.1 (2.4)	-0.6 (2.3)
Median	17.5	0.0	17.5	-0.5
Min - Max	16 - 19	0 - 0	15 - 23	-6 - 2
Cycle 22 Day 1				
PRE PAC INFUSION				
n	4	4	13	13
Mean (SD)	17.3 (2.8)	0.5 (1.0)	17.5 (2.4)	-0.6 (2.3)
Median	17.5	0.0	17.0	0.0
Min - Max	14 - 20	0 - 2	14 - 23	-6 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	11	11
Mean (SD)	17.7 (1.5)	0.0 (0.0)	17.5 (1.8)	-1.1 (2.1)
Median	18.0	0.0	17.0	-1.0
Min - Max	16 - 19	0 - 0	15 - 20	-5 - 2
Cycle 22 Day 8				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	18.0 (2.8)	0.5 (0.7)	17.6 (2.1)	-1.1 (2.3)
Median	18.0	0.5	17.5	-0.5
Min - Max	16 - 20	0 - 1	15 - 22	-5 - 2
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	17.5 (2.1)	0.0 (0.0)	17.8 (2.4)	-0.9 (3.0)
Median	17.5	0.0	17.5	-0.5
Min - Max	16 - 19	0 - 0	15 - 23	-7 - 2
Cycle 22 Day 15				
PRE PAC INFUSION				
n	2	2	9	9
Mean (SD)	16.5 (0.7)	-1.0 (1.4)	18.0 (2.4)	-1.0 (2.5)
Median	16.5	-1.0	18.0	-1.0
Min - Max	16 - 17	-2 - 0	15 - 23	-6 - 2
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	18.0 (2.1)	-1.0 (2.5)
Median	17.0	-0.5	18.0	-1.0
Min - Max	16 - 18	-1 - 0	15 - 22	-6 - 2
Cycle 23 Day 1				
PRE PAC INFUSION				
n	3	3	12	12
Mean (SD)	16.0 (1.0)	-0.3 (1.5)	17.4 (2.7)	-0.9 (2.4)
Median	16.0	0.0	18.0	-0.5
Min - Max	15 - 17	-2 - 1	12 - 23	-7 - 2
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	16.0 (0.0)	-1.5 (2.1)	18.2 (2.0)	-0.7 (2.5)
Median	16.0	-1.5	18.0	-0.5
Min - Max	16 - 16	-3 - 0	16 - 22	-6 - 3
Cycle 23 Day 8				
PRE PAC INFUSION				
n	2	2	9	9
Mean (SD)	18.0 (2.8)	0.5 (0.7)	18.1 (1.8)	-0.9 (2.3)
Median	18.0	0.5	18.0	-1.0
Min - Max	16 - 20	0 - 1	16 - 22	-5 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	17.9 (1.9)	-1.1 (2.6)
Median	17.0	-0.5	18.0	-1.0
Min - Max	16 - 18	-1 - 0	15 - 20	-7 - 2
Cycle 23 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	18.1 (2.4)	-0.8 (2.7)
Median	17.0	-0.5	18.0	-0.5
Min - Max	16 - 18	-1 - 0	16 - 23	-6 - 2
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	17.5 (2.6)	-1.4 (2.9)
Median	17.0	-0.5	17.5	-1.5
Min - Max	16 - 18	-1 - 0	14 - 22	-7 - 2
Cycle 24 Day 1				
PRE PAC INFUSION				
n	3	3	11	11
Mean (SD)	15.7 (1.5)	-0.7 (1.2)	17.4 (2.2)	-0.8 (2.2)
Median	16.0	0.0	17.0	0.0
Min - Max	14 - 17	-2 - 0	14 - 23	-6 - 2
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	18.0 (2.3)	-0.8 (2.1)
Median	17.0	-0.5	18.0	-1.0
Min - Max	16 - 18	-1 - 0	15 - 23	-5 - 2
Cycle 24 Day 8				
PRE PAC INFUSION				
n	2	2	7	7
Mean (SD)	17.0 (0.0)	-0.5 (2.1)	17.9 (2.5)	-1.1 (3.1)
Median	17.0	-0.5	18.0	0.0
Min - Max	17 - 17	-2 - 1	15 - 23	-7 - 2
AFTER PAC INFUSION				
n	2	2	7	7
Mean (SD)	17.5 (0.7)	0.0 (1.4)	17.9 (2.9)	-1.1 (2.9)
Median	17.5	0.0	18.0	-1.0
Min - Max	17 - 18	-1 - 1	15 - 23	-7 - 2
Cycle 24 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	16.5 (0.7)	-1.0 (1.4)	18.1 (2.4)	-0.8 (2.4)
Median	16.5	-1.0	18.0	0.0
Min - Max	16 - 17	-2 - 0	16 - 23	-6 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	7	7
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	18.1 (3.1)	-0.9 (3.1)
Median	17.0	-0.5	18.0	0.0
Min - Max	16 - 18	-1 - 0	15 - 24	-7 - 3
Cycle 25 Day 1				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	16.5 (0.7)	-1.0 (1.4)	17.2 (3.1)	-1.1 (2.6)
Median	16.5	-1.0	16.5	0.0
Min - Max	16 - 17	-2 - 0	12 - 23	-7 - 2
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	17.5 (2.6)	-1.5 (2.9)
Median	17.0	-0.5	17.5	-1.0
Min - Max	16 - 18	-1 - 0	14 - 22	-8 - 1
Cycle 25 Day 8				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	17.5 (2.0)	-1.4 (2.4)
Median	17.0	-0.5	18.0	-1.0
Min - Max	16 - 18	-1 - 0	15 - 20	-6 - 2
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	16.5 (0.7)	-1.0 (1.4)	17.8 (1.7)	-1.1 (2.4)
Median	16.5	-1.0	18.0	-1.0
Min - Max	16 - 17	-2 - 0	16 - 20	-6 - 2
Cycle 25 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	18.1 (2.0)	-0.8 (2.5)
Median	17.0	-0.5	18.0	-0.5
Min - Max	16 - 18	-1 - 0	15 - 22	-5 - 2
AFTER PAC INFUSION				
n	2	2	7	7
Mean (SD)	16.5 (0.7)	-1.0 (1.4)	17.9 (2.0)	-1.4 (2.9)
Median	16.5	-1.0	18.0	-1.0
Min - Max	16 - 17	-2 - 0	15 - 20	-7 - 2
Cycle 26 Day 1				
PRE PAC INFUSION				
n	2	2	11	11
Mean (SD)	16.5 (0.7)	-1.0 (1.4)	17.2 (2.2)	-0.9 (2.1)
Median	16.5	-1.0	16.0	0.0
Min - Max	16 - 17	-2 - 0	14 - 22	-6 - 1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	17.4 (2.5)	-1.1 (2.8)
Median	17.0	-0.5	16.5	-0.5
Min - Max	16 - 18	-1 - 0	14 - 23	-8 - 2
Cycle 26 Day 8				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	17.1 (2.2)	-1.1 (3.1)
Median	17.0	-0.5	17.0	-0.5
Min - Max	16 - 18	-1 - 0	15 - 21	-7 - 2
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	16.5 (0.7)	-1.0 (1.4)	17.3 (1.9)	-1.0 (2.8)
Median	16.5	-1.0	17.0	0.0
Min - Max	16 - 17	-2 - 0	15 - 21	-7 - 2
Cycle 26 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	17.5 (1.9)	-1.4 (2.2)
Median	17.0	-0.5	17.5	-1.0
Min - Max	16 - 18	-1 - 0	15 - 20	-6 - 1
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	16.5 (0.7)	-1.0 (1.4)	17.5 (2.0)	-1.4 (2.9)
Median	16.5	-1.0	17.5	-1.0
Min - Max	16 - 17	-2 - 0	14 - 20	-8 - 1
Cycle 27 Day 1				
PRE PAC INFUSION				
n	1	1	8	8
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (2.4)	-0.8 (2.4)
Median	16.0	0.0	18.0	0.0
Min - Max	16 - 16	0 - 0	14 - 22	-6 - 2
AFTER PAC INFUSION				
n	1	1	7	7
Mean (SD)	16.0 (NE)	0.0 (NE)	17.7 (2.6)	-1.7 (3.1)
Median	16.0	0.0	17.0	-1.0
Min - Max	16 - 16	0 - 0	14 - 22	-8 - 1
Cycle 27 Day 8				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	16.0 (NE)	0.0 (NE)	18.3 (2.4)	-1.3 (3.1)
Median	16.0	0.0	18.0	-1.0
Min - Max	16 - 16	0 - 0	15 - 22	-7 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	16.0 (NE)	0.0 (NE)	18.7 (2.1)	-1.0 (2.8)
Median	16.0	0.0	18.0	-0.5
Min - Max	16 - 16	0 - 0	16 - 22	-6 - 2
Cycle 27 Day 15				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (2.3)	-0.8 (1.5)
Median	16.0	0.0	18.0	-0.5
Min - Max	16 - 16	0 - 0	15 - 21	-3 - 1
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (2.1)	-0.8 (1.5)
Median	16.0	0.0	17.5	-0.5
Min - Max	16 - 16	0 - 0	16 - 21	-3 - 1
Cycle 28 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (1.1)	-0.3 (1.8)
Median	16.0	0.0	18.0	-0.5
Min - Max	16 - 16	0 - 0	17 - 20	-3 - 2
AFTER PAC INFUSION				
n	1	1	5	5
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (1.9)	-0.4 (2.3)
Median	16.0	0.0	18.0	-1.0
Min - Max	16 - 16	0 - 0	15 - 20	-3 - 2
Cycle 28 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	16.0 (NE)	0.0 (NE)	17.8 (2.1)	-1.0 (2.2)
Median	16.0	0.0	18.0	-1.5
Min - Max	16 - 16	0 - 0	15 - 20	-3 - 2
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (1.6)	-0.8 (1.9)
Median	16.0	0.0	18.0	-1.5
Min - Max	16 - 16	0 - 0	16 - 20	-2 - 2
Cycle 28 Day 15				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	16.0 (NE)	0.0 (NE)	18.2 (1.9)	-0.2 (2.1)
Median	16.0	0.0	18.5	0.0
Min - Max	16 - 16	0 - 0	15 - 20	-3 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	16.0 (NE)	0.0 (NE)	18.2 (1.6)	-0.2 (1.7)
Median	16.0	0.0	18.0	0.0
Min - Max	16 - 16	0 - 0	16 - 20	-2 - 2
Cycle 29 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	17.0 (NE)	1.0 (NE)	17.8 (1.6)	-0.5 (1.9)
Median	17.0	1.0	18.0	-0.5
Min - Max	17 - 17	1 - 1	15 - 20	-3 - 2
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	16.0 (NE)	0.0 (NE)	18.3 (2.5)	0.3 (2.4)
Median	16.0	0.0	18.5	1.0
Min - Max	16 - 16	0 - 0	15 - 21	-3 - 2
Cycle 29 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	16.0 (NE)	0.0 (NE)	17.5 (2.1)	-0.5 (1.9)
Median	16.0	0.0	17.5	0.0
Min - Max	16 - 16	0 - 0	15 - 20	-3 - 1
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	17.0 (NE)	1.0 (NE)	18.0 (1.6)	0.0 (1.8)
Median	17.0	1.0	18.0	0.0
Min - Max	17 - 17	1 - 1	16 - 20	-2 - 2
Cycle 29 Day 15				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (1.6)	-0.8 (1.9)
Median	16.0	0.0	18.0	-1.5
Min - Max	16 - 16	0 - 0	16 - 20	-2 - 2
AFTER PAC INFUSION				
n	1	1	3	3
Mean (SD)	16.0 (NE)	0.0 (NE)	17.3 (2.5)	-1.0 (2.0)
Median	16.0	0.0	17.0	-1.0
Min - Max	16 - 16	0 - 0	15 - 20	-3 - 1
Cycle 30 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (1.1)	-0.3 (1.2)
Median	16.0	0.0	18.0	-0.5
Min - Max	16 - 16	0 - 0	17 - 20	-2 - 1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (2.2)	0.0 (1.4)
Median	16.0	0.0	17.5	0.5
Min - Max	16 - 16	0 - 0	16 - 21	-2 - 1
Cycle 30 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	16.0 (NE)	0.0 (NE)	18.5 (2.1)	0.5 (1.9)
Median	16.0	0.0	18.5	1.0
Min - Max	16 - 16	0 - 0	16 - 21	-2 - 2
AFTER PAC INFUSION				
n	1	1	3	3
Mean (SD)	16.0 (NE)	0.0 (NE)	17.7 (2.5)	-1.0 (2.0)
Median	16.0	0.0	18.0	-1.0
Min - Max	16 - 16	0 - 0	15 - 20	-3 - 1
Cycle 30 Day 15				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	16.0 (NE)	0.0 (NE)	17.5 (2.1)	-0.5 (1.0)
Median	16.0	0.0	17.5	-1.0
Min - Max	16 - 16	0 - 0	15 - 20	-1 - 1
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	16.0 (NE)	0.0 (NE)	17.5 (2.4)	-0.5 (2.1)
Median	16.0	0.0	17.5	-0.5
Min - Max	16 - 16	0 - 0	15 - 20	-3 - 2
Cycle 31 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (2.8)	1.0 (1.4)
Median	16.0	0.0	18.0	1.0
Min - Max	16 - 16	0 - 0	16 - 20	0 - 2
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	16.0 (NE)	0.0 (NE)
Median	16.0	0.0	16.0	0.0
Min - Max	16 - 16	0 - 0	16 - 16	0 - 0
Cycle 31 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2
Cycle 31 Day 15				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	18.0 (0.0)	-0.5 (3.5)
Median	NE	NE	18.0	-0.5
Min - Max	NE - NE	NE - NE	18 - 18	-3 - 2
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	18.5 (2.1)	0.0 (1.4)
Median	NE	NE	18.5	0.0
Min - Max	NE - NE	NE - NE	17 - 20	-1 - 1
Cycle 32 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	18.0 (NE)	0.0 (NE)
Median	NE	NE	18.0	0.0
Min - Max	NE - NE	NE - NE	18 - 18	0 - 0
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	18.0 (2.8)	-0.5 (0.7)
Median	NE	NE	18.0	-0.5
Min - Max	NE - NE	NE - NE	16 - 20	-1 - 0
Cycle 32 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (2.8)	-0.5 (0.7)
Median	16.0	0.0	18.0	-0.5
Min - Max	16 - 16	0 - 0	16 - 20	-1 - 0
Cycle 32 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	16.0 (NE)	0.0 (NE)	19.0 (1.4)	0.5 (2.1)
Median	16.0	0.0	19.0	0.5
Min - Max	16 - 16	0 - 0	18 - 20	-1 - 2
Cycle 33 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	20.0 (NE)	2.0 (NE)
Median	16.0	0.0	20.0	2.0
Min - Max	16 - 16	0 - 0	20 - 20	2 - 2
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (2.8)	-0.5 (0.7)
Median	16.0	0.0	18.0	-0.5
Min - Max	16 - 16	0 - 0	16 - 20	-1 - 0
Cycle 33 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	16.0 (NE)	0.0 (NE)	17.5 (2.1)	-1.0 (1.4)
Median	16.0	0.0	17.5	-1.0
Min - Max	16 - 16	0 - 0	16 - 19	-2 - 0
Cycle 33 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (2.8)	-0.5 (0.7)
Median	16.0	0.0	18.0	-0.5
Min - Max	16 - 16	0 - 0	16 - 20	-1 - 0
Cycle 34 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	20.0 (NE)	2.0 (NE)
Median	16.0	0.0	20.0	2.0
Min - Max	16 - 16	0 - 0	20 - 20	2 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2
Cycle 34 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	17.0 (NE)	1.0 (NE)
Median	16.0	0.0	17.0	1.0
Min - Max	16 - 16	0 - 0	17 - 17	1 - 1
Cycle 34 Day 15				
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2
Cycle 35 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	17.0 (NE)	1.0 (NE)	18.0 (NE)	0.0 (NE)
Median	17.0	1.0	18.0	0.0
Min - Max	17 - 17	1 - 1	18 - 18	0 - 0
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	16.0 (NE)	0.0 (NE)
Median	16.0	0.0	16.0	0.0
Min - Max	16 - 16	0 - 0	16 - 16	0 - 0
Cycle 35 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	17.0 (NE)	1.0 (NE)
Median	16.0	0.0	17.0	1.0
Min - Max	16 - 16	0 - 0	17 - 17	1 - 1

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 35 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2
Cycle 36 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	0.0 (NE)
Median	16.0	0.0	18.0	0.0
Min - Max	16 - 16	0 - 0	18 - 18	0 - 0
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	16.0 (NE)	0.0 (NE)
Median	16.0	0.0	16.0	0.0
Min - Max	16 - 16	0 - 0	16 - 16	0 - 0
Cycle 36 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2
Cycle 36 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 37 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	0.0 (NE)
Median	16.0	0.0	18.0	0.0
Min - Max	16 - 16	0 - 0	18 - 18	0 - 0
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2
Cycle 37 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2
Cycle 37 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2
Cycle 38 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	20.0 (NE)	2.0 (NE)
Median	16.0	0.0	20.0	2.0
Min - Max	16 - 16	0 - 0	20 - 20	2 - 2
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	17.0 (NE)	1.0 (NE)	18.0 (NE)	2.0 (NE)
Median	17.0	1.0	18.0	2.0
Min - Max	17 - 17	1 - 1	18 - 18	2 - 2

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 38 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	19.0 (NE)	3.0 (NE)
Median	16.0	0.0	19.0	3.0
Min - Max	16 - 16	0 - 0	19 - 19	3 - 3
Cycle 38 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2
Cycle 39 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	20.0 (NE)	2.0 (NE)
Median	16.0	0.0	20.0	2.0
Min - Max	16 - 16	0 - 0	20 - 20	2 - 2
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	17.0 (NE)	1.0 (NE)	NE (NE)	NE (NE)
Median	17.0	1.0	NE	NE
Min - Max	17 - 17	1 - 1	NE - NE	NE - NE
Cycle 39 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 39 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	17.0 (NE)	1.0 (NE)	18.0 (NE)	2.0 (NE)
Median	17.0	1.0	18.0	2.0
Min - Max	17 - 17	1 - 1	18 - 18	2 - 2
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
Cycle 40 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	17.0 (NE)	1.0 (NE)	19.0 (1.4)	2.0 (0.0)
Median	17.0	1.0	19.0	2.0
Min - Max	17 - 17	1 - 1	18 - 20	2 - 2
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
Cycle 40 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
Cycle 40 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 41 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	17.0 (NE)	1.0 (NE)	19.0 (1.4)	2.0 (0.0)
Median	17.0	1.0	19.0	2.0
Min - Max	17 - 17	1 - 1	18 - 20	2 - 2
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
Cycle 41 Day 8				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	16.0 (NE)	0.0 (NE)
Median	NE	NE	16.0	0.0
Min - Max	NE - NE	NE - NE	16 - 16	0 - 0
Cycle 41 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	2.0 (NE)
Median	16.0	0.0	18.0	2.0
Min - Max	16 - 16	0 - 0	18 - 18	2 - 2
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
Cycle 42 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	0.0 (NE)
Median	16.0	0.0	18.0	0.0
Min - Max	16 - 16	0 - 0	18 - 18	0 - 0
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
Cycle 42 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
Cycle 42 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
Cycle 43 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	16.0 (NE)	0.0 (NE)	18.0 (NE)	0.0 (NE)
Median	16.0	0.0	18.0	0.0
Min - Max	16 - 16	0 - 0	18 - 18	0 - 0
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
Cycle 43 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
Cycle 43 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	17.0 (NE)	1.0 (NE)	NE (NE)	NE (NE)
Median	17.0	1.0	NE	NE
Min - Max	17 - 17	1 - 1	NE - NE	NE - NE

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	0.0 (NE)	NE (NE)	NE (NE)
Median	16.0	0.0	NE	NE
Min - Max	16 - 16	0 - 0	NE - NE	NE - NE
Cycle 44 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	18.0 (NE)	0.0 (NE)
Median	NE	NE	18.0	0.0
Min - Max	NE - NE	NE - NE	18 - 18	0 - 0
Cycle 45 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	16.0 (NE)	-2.0 (NE)
Median	NE	NE	16.0	-2.0
Min - Max	NE - NE	NE - NE	16 - 16	-2 - -2
Cycle 46 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	18.0 (NE)	0.0 (NE)
Median	NE	NE	18.0	0.0
Min - Max	NE - NE	NE - NE	18 - 18	0 - 0
Study Drug Discontinuation				
n	73	72	140	139
Mean (SD)	17.3 (2.3)	-0.2 (2.9)	17.4 (2.2)	0.2 (1.9)
Median	18.0	0.0	17.0	0.0
Min - Max	12 - 22	-8 - 10	12 - 24	-6 - 6
Post-Baseline Last				
n	77	77	138	138
Mean (SD)	17.3 (2.3)	-0.2 (2.8)	17.5 (2.6)	0.3 (2.3)
Median	18.0	0.0	17.0	0.0
Min - Max	12 - 22	-8 - 10	12 - 34	-6 - 16
PRE PAC INFUSION				
n	1	1	5	5
Mean (SD)	18.0 (NE)	0.0 (NE)	17.0 (1.9)	0.4 (2.1)
Median	18.0	0.0	17.0	0.0
Min - Max	18 - 18	0 - 0	15 - 20	-2 - 3
AFTER PAC INFUSION				
n	8	8	21	21
Mean (SD)	17.3 (2.1)	0.9 (2.0)	17.3 (2.3)	-0.3 (1.6)
Median	17.0	1.0	17.0	0.0
Min - Max	14 - 20	-3 - 4	12 - 20	-4 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Post-Baseline Minimum				
n	7	7	8	8
Mean (SD)	16.1 (2.5)	-1.9 (3.1)	15.8 (2.1)	-0.8 (1.6)
Median	18.0	-1.0	16.0	-0.5
Min - Max	12 - 18	-6 - 2	13 - 19	-3 - 2
PRE PAC INFUSION				
n	50	50	93	93
Mean (SD)	15.1 (2.7)	-2.3 (2.7)	15.5 (2.1)	-1.8 (1.8)
Median	15.0	-2.0	16.0	-2.0
Min - Max	8 - 20	-12 - 0	12 - 20	-7 - 4
AFTER PAC INFUSION				
n	29	29	63	63
Mean (SD)	15.2 (2.6)	-2.0 (2.2)	14.9 (2.3)	-2.4 (2.6)
Median	16.0	-2.0	15.0	-2.0
Min - Max	9 - 19	-6 - 2	10 - 20	-9 - 4
Post-Baseline Maximum				
n	3	3	8	8
Mean (SD)	18.7 (1.2)	5.7 (2.5)	22.4 (5.0)	4.8 (4.9)
Median	18.0	6.0	21.5	4.0
Min - Max	18 - 20	3 - 8	17 - 34	-1 - 16
PRE PAC INFUSION				
n	53	53	90	90
Mean (SD)	19.9 (4.3)	1.9 (4.4)	20.0 (2.8)	2.4 (2.6)
Median	20.0	1.0	20.0	2.0
Min - Max	12 - 37	-8 - 20	14 - 28	-2 - 14
AFTER PAC INFUSION				
n	30	30	66	66
Mean (SD)	20.6 (3.3)	3.8 (3.7)	19.7 (2.8)	3.0 (2.9)
Median	20.0	2.0	20.0	2.0
Min - Max	16 - 30	-2 - 12	15 - 26	-2 - 14

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Baseline				
n	85		164	
Mean (SD)	36.45 (0.47)		36.46 (0.43)	
Median	36.50		36.50	
Min - Max	35.0 - 37.4		33.9 - 37.3	
Cycle 1 Day 1				
PRE PAC INFUSION				
n	83	82	145	144
Mean (SD)	36.51 (0.37)	0.04 (0.38)	36.49 (0.44)	0.02 (0.35)
Median	36.50	0.00	36.50	0.00
Min - Max	35.7 - 37.3	-0.9 - 1.1	34.0 - 37.4	-1.1 - 1.0
AFTER PAC INFUSION				
n	83	82	158	157
Mean (SD)	36.50 (0.40)	0.05 (0.43)	36.49 (0.47)	0.03 (0.36)
Median	36.50	0.00	36.50	0.00
Min - Max	35.5 - 37.3	-1.0 - 1.1	34.0 - 37.7	-1.0 - 1.0
Cycle 1 Day 8				
PRE PAC INFUSION				
n	85	84	160	158
Mean (SD)	36.46 (0.46)	0.00 (0.45)	36.50 (0.44)	0.05 (0.37)
Median	36.50	0.00	36.50	0.00
Min - Max	35.0 - 37.5	-1.8 - 1.9	33.9 - 37.8	-1.0 - 1.3
AFTER PAC INFUSION				
n	77	76	147	145
Mean (SD)	36.58 (0.37)	0.11 (0.42)	36.46 (0.48)	0.02 (0.40)
Median	36.60	0.00	36.50	0.00
Min - Max	35.5 - 37.4	-0.8 - 1.7	33.9 - 37.7	-1.1 - 1.2
Cycle 1 Day 15				
PRE PAC INFUSION				
n	80	79	147	145
Mean (SD)	36.48 (0.40)	0.04 (0.43)	36.47 (0.49)	0.04 (0.39)
Median	36.50	0.10	36.50	0.00
Min - Max	35.4 - 37.3	-1.3 - 1.2	33.9 - 37.7	-1.2 - 1.2
AFTER PAC INFUSION				
n	73	72	132	131
Mean (SD)	36.52 (0.37)	0.07 (0.39)	36.45 (0.47)	0.01 (0.41)
Median	36.60	0.10	36.50	0.00
Min - Max	35.6 - 37.3	-0.8 - 1.2	33.9 - 37.4	-1.6 - 1.3
Cycle 2 Day 1				
PRE PAC INFUSION				
n	77	76	161	159
Mean (SD)	36.40 (0.44)	-0.04 (0.47)	36.46 (0.51)	0.00 (0.44)
Median	36.50	-0.10	36.50	0.00
Min - Max	35.2 - 37.4	-1.3 - 1.4	34.0 - 37.8	-1.4 - 1.2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	72	71	153	152
Mean (SD)	36.46 (0.43)	0.01 (0.47)	36.49 (0.54)	0.04 (0.48)
Median	36.50	0.00	36.50	0.00
Min - Max	35.5 - 37.6	-1.2 - 1.3	34.0 - 37.8	-1.4 - 1.7
Cycle 2 Day 8				
PRE PAC INFUSION				
n	78	77	153	151
Mean (SD)	36.51 (0.46)	0.06 (0.48)	36.41 (0.49)	-0.03 (0.41)
Median	36.50	0.10	36.50	0.00
Min - Max	35.4 - 38.5	-1.5 - 1.4	33.6 - 37.6	-1.3 - 1.1
AFTER PAC INFUSION				
n	71	70	149	147
Mean (SD)	36.49 (0.42)	0.02 (0.49)	36.42 (0.50)	-0.01 (0.43)
Median	36.50	0.00	36.50	0.00
Min - Max	35.2 - 37.8	-1.0 - 1.3	33.8 - 38.0	-1.4 - 1.5
Cycle 2 Day 15				
PRE PAC INFUSION				
n	76	75	148	146
Mean (SD)	36.46 (0.41)	-0.01 (0.44)	36.46 (0.52)	0.02 (0.38)
Median	36.45	0.00	36.50	0.00
Min - Max	35.5 - 37.3	-1.0 - 1.5	33.8 - 37.8	-1.2 - 1.4
AFTER PAC INFUSION				
n	71	69	146	144
Mean (SD)	36.48 (0.43)	0.01 (0.45)	36.49 (0.51)	0.06 (0.43)
Median	36.50	0.00	36.50	0.00
Min - Max	35.0 - 37.6	-1.2 - 1.5	34.0 - 38.3	-1.1 - 1.8
Cycle 3 Day 1				
PRE PAC INFUSION				
n	74	73	143	141
Mean (SD)	36.46 (0.40)	0.02 (0.45)	36.43 (0.55)	-0.03 (0.43)
Median	36.50	0.00	36.50	0.00
Min - Max	35.2 - 37.3	-0.8 - 1.5	33.8 - 38.9	-1.7 - 1.7
AFTER PAC INFUSION				
n	69	68	134	132
Mean (SD)	36.51 (0.51)	0.07 (0.45)	36.46 (0.49)	0.01 (0.43)
Median	36.50	0.05	36.50	0.00
Min - Max	35.0 - 38.1	-0.8 - 1.4	33.8 - 37.5	-1.7 - 1.1
Cycle 3 Day 8				
PRE PAC INFUSION				
n	72	71	140	138
Mean (SD)	36.42 (0.38)	-0.02 (0.40)	36.42 (0.48)	-0.02 (0.38)
Median	36.50	-0.10	36.50	0.00
Min - Max	35.4 - 37.2	-1.0 - 1.0	33.8 - 37.6	-1.1 - 1.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	68	67	138	136
Mean (SD)	36.53 (0.44)	0.10 (0.47)	36.52 (0.50)	0.08 (0.44)
Median	36.55	0.00	36.50	0.00
Min - Max	35.6 - 37.9	-0.8 - 1.7	33.9 - 38.0	-1.4 - 1.5
Cycle 3 Day 15				
PRE PAC INFUSION				
n	66	65	136	135
Mean (SD)	36.50 (0.39)	0.06 (0.45)	36.40 (0.55)	-0.05 (0.49)
Median	36.60	0.00	36.45	0.00
Min - Max	35.4 - 37.5	-1.7 - 1.1	33.7 - 37.5	-2.4 - 0.9
AFTER PAC INFUSION				
n	66	65	129	128
Mean (SD)	36.55 (0.35)	0.10 (0.49)	36.46 (0.56)	0.01 (0.49)
Median	36.60	0.10	36.50	0.00
Min - Max	35.4 - 37.3	-0.8 - 1.5	33.9 - 38.0	-2.4 - 1.5
Cycle 4 Day 1				
PRE PAC INFUSION				
n	68	67	132	130
Mean (SD)	36.44 (0.37)	0.01 (0.42)	36.47 (0.50)	0.02 (0.44)
Median	36.45	0.00	36.50	0.00
Min - Max	35.4 - 37.0	-1.0 - 1.4	33.7 - 37.8	-1.5 - 1.1
AFTER PAC INFUSION				
n	64	63	122	120
Mean (SD)	36.50 (0.37)	0.07 (0.42)	36.49 (0.50)	0.03 (0.38)
Median	36.50	0.00	36.60	0.00
Min - Max	35.3 - 38.0	-1.0 - 1.3	33.8 - 37.4	-1.0 - 1.2
Cycle 4 Day 8				
PRE PAC INFUSION				
n	67	66	127	126
Mean (SD)	36.50 (0.42)	0.07 (0.39)	36.43 (0.50)	-0.03 (0.43)
Median	36.50	0.00	36.50	0.00
Min - Max	35.1 - 37.8	-1.0 - 1.4	33.8 - 37.7	-1.4 - 1.3
AFTER PAC INFUSION				
n	64	63	120	119
Mean (SD)	36.56 (0.39)	0.12 (0.42)	36.49 (0.50)	0.02 (0.43)
Median	36.50	0.10	36.50	0.00
Min - Max	35.5 - 37.5	-0.7 - 1.3	33.9 - 37.6	-1.3 - 1.2
Cycle 4 Day 15				
PRE PAC INFUSION				
n	66	65	126	124
Mean (SD)	36.51 (0.42)	0.08 (0.49)	36.42 (0.43)	-0.04 (0.37)
Median	36.60	0.00	36.50	0.00
Min - Max	35.0 - 37.3	-1.5 - 2.3	33.9 - 37.2	-1.0 - 0.9

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	65	64	115	113
Mean (SD)	36.46 (0.48)	0.03 (0.53)	36.47 (0.50)	0.01 (0.43)
Median	36.50	0.00	36.50	0.00
Min - Max	35.0 - 37.6	-1.1 - 1.7	34.0 - 37.9	-1.0 - 1.4
Cycle 5 Day 1				
PRE PAC INFUSION				
n	60	59	103	101
Mean (SD)	36.45 (0.39)	0.05 (0.40)	36.44 (0.50)	-0.05 (0.43)
Median	36.50	0.00	36.50	0.00
Min - Max	35.4 - 37.2	-1.0 - 1.0	33.8 - 37.7	-1.3 - 0.9
AFTER PAC INFUSION				
n	56	55	95	93
Mean (SD)	36.53 (0.37)	0.13 (0.40)	36.50 (0.53)	0.02 (0.44)
Median	36.50	0.13	36.60	0.00
Min - Max	35.4 - 37.2	-0.9 - 1.3	33.9 - 37.7	-1.3 - 1.2
Cycle 5 Day 8				
PRE PAC INFUSION				
n	52	51	96	95
Mean (SD)	36.42 (0.43)	0.01 (0.59)	36.44 (0.51)	-0.05 (0.44)
Median	36.45	0.00	36.50	0.00
Min - Max	35.6 - 37.9	-1.4 - 1.7	33.8 - 37.7	-1.3 - 1.0
AFTER PAC INFUSION				
n	51	50	89	88
Mean (SD)	36.45 (0.44)	0.03 (0.49)	36.44 (0.50)	-0.05 (0.45)
Median	36.50	0.10	36.50	0.00
Min - Max	35.1 - 37.2	-1.3 - 1.0	33.9 - 37.9	-1.3 - 1.4
Cycle 5 Day 15				
PRE PAC INFUSION				
n	55	54	90	89
Mean (SD)	36.39 (0.44)	0.01 (0.47)	36.45 (0.52)	-0.03 (0.39)
Median	36.40	0.10	36.60	-0.10
Min - Max	35.2 - 37.4	-1.1 - 1.3	33.8 - 37.4	-1.5 - 0.7
AFTER PAC INFUSION				
n	51	50	78	77
Mean (SD)	36.46 (0.37)	0.06 (0.46)	36.44 (0.45)	-0.01 (0.40)
Median	36.50	0.05	36.50	0.00
Min - Max	35.5 - 37.1	-1.2 - 1.1	33.9 - 37.2	-1.0 - 1.0
Cycle 6 Day 1				
PRE PAC INFUSION				
n	55	54	91	90
Mean (SD)	36.41 (0.37)	0.00 (0.47)	36.46 (0.39)	-0.05 (0.37)
Median	36.50	0.00	36.50	0.00
Min - Max	35.5 - 37.1	-1.5 - 1.3	35.1 - 37.4	-1.0 - 0.8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	48	47	85	84
Mean (SD)	36.45 (0.34)	0.02 (0.48)	36.53 (0.36)	0.02 (0.38)
Median	36.50	0.00	36.50	0.00
Min - Max	35.6 - 37.1	-1.0 - 1.2	35.6 - 37.4	-0.9 - 0.9
Cycle 6 Day 8				
PRE PAC INFUSION				
n	48	47	87	86
Mean (SD)	36.45 (0.36)	-0.02 (0.45)	36.46 (0.39)	-0.05 (0.38)
Median	36.50	0.00	36.50	-0.10
Min - Max	35.7 - 37.3	-1.1 - 0.9	35.5 - 37.3	-1.0 - 0.9
AFTER PAC INFUSION				
n	47	46	83	82
Mean (SD)	36.51 (0.41)	0.05 (0.42)	36.48 (0.41)	-0.03 (0.45)
Median	36.60	0.10	36.50	0.00
Min - Max	35.3 - 37.3	-0.8 - 0.8	35.4 - 38.0	-1.3 - 1.5
Cycle 6 Day 15				
PRE PAC INFUSION				
n	48	47	84	83
Mean (SD)	36.49 (0.52)	0.04 (0.55)	36.45 (0.43)	-0.06 (0.42)
Median	36.50	0.10	36.50	0.00
Min - Max	34.9 - 37.9	-1.6 - 1.1	35.3 - 37.7	-1.2 - 1.3
AFTER PAC INFUSION				
n	46	45	80	79
Mean (SD)	36.49 (0.43)	0.02 (0.45)	36.46 (0.40)	-0.03 (0.37)
Median	36.50	0.00	36.50	0.00
Min - Max	35.4 - 37.4	-1.1 - 0.9	35.2 - 37.5	-0.7 - 1.0
Cycle 7 Day 1				
PRE PAC INFUSION				
n	41	40	76	75
Mean (SD)	36.43 (0.50)	-0.01 (0.53)	36.47 (0.37)	-0.03 (0.41)
Median	36.50	0.00	36.50	0.00
Min - Max	34.6 - 37.0	-1.9 - 1.0	35.3 - 37.5	-1.4 - 1.3
AFTER PAC INFUSION				
n	36	35	67	66
Mean (SD)	36.45 (0.42)	-0.02 (0.47)	36.52 (0.37)	0.02 (0.40)
Median	36.50	0.00	36.60	0.00
Min - Max	35.2 - 37.2	-1.2 - 1.0	35.4 - 37.3	-1.0 - 1.0
Cycle 7 Day 8				
PRE PAC INFUSION				
n	34	33	66	65
Mean (SD)	36.48 (0.36)	-0.03 (0.39)	36.37 (0.38)	-0.13 (0.39)
Median	36.60	0.00	36.40	-0.10
Min - Max	35.6 - 37.1	-0.9 - 0.7	35.4 - 37.2	-1.0 - 0.9

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	33	32	63	62
Mean (SD)	36.48 (0.31)	-0.02 (0.36)	36.44 (0.38)	-0.04 (0.44)
Median	36.50	0.00	36.40	0.00
Min - Max	36.0 - 37.0	-0.7 - 0.5	35.3 - 37.1	-1.1 - 1.2
Cycle 7 Day 15				
PRE PAC INFUSION				
n	33	32	69	68
Mean (SD)	36.40 (0.47)	-0.07 (0.49)	36.43 (0.33)	-0.05 (0.36)
Median	36.50	0.05	36.40	0.00
Min - Max	35.2 - 37.0	-1.2 - 0.7	35.5 - 37.2	-0.9 - 0.7
AFTER PAC INFUSION				
n	33	32	66	65
Mean (SD)	36.45 (0.39)	-0.01 (0.49)	36.49 (0.38)	0.02 (0.40)
Median	36.50	0.05	36.50	0.00
Min - Max	35.5 - 37.1	-1.3 - 1.0	35.7 - 38.0	-1.0 - 1.5
Cycle 8 Day 1				
PRE PAC INFUSION				
n	32	31	70	69
Mean (SD)	36.43 (0.46)	0.01 (0.49)	36.41 (0.40)	-0.08 (0.47)
Median	36.55	0.10	36.40	0.00
Min - Max	35.0 - 37.2	-1.5 - 0.8	35.0 - 37.1	-1.7 - 0.9
AFTER PAC INFUSION				
n	26	25	63	62
Mean (SD)	36.50 (0.49)	0.09 (0.44)	36.47 (0.39)	-0.02 (0.38)
Median	36.55	0.20	36.50	0.00
Min - Max	35.2 - 37.2	-1.0 - 0.7	35.5 - 37.6	-1.0 - 1.1
Cycle 8 Day 8				
PRE PAC INFUSION				
n	28	27	64	63
Mean (SD)	36.41 (0.41)	-0.08 (0.47)	36.43 (0.44)	-0.05 (0.48)
Median	36.50	0.00	36.50	0.00
Min - Max	35.1 - 37.0	-1.4 - 0.8	35.0 - 37.5	-2.0 - 1.0
AFTER PAC INFUSION				
n	26	25	60	59
Mean (SD)	36.43 (0.41)	-0.07 (0.46)	36.44 (0.38)	-0.05 (0.47)
Median	36.60	0.03	36.50	0.00
Min - Max	35.6 - 37.1	-1.0 - 0.7	35.5 - 38.1	-1.1 - 1.6
Cycle 8 Day 15				
PRE PAC INFUSION				
n	28	27	61	60
Mean (SD)	36.39 (0.45)	-0.07 (0.55)	36.45 (0.40)	-0.05 (0.50)
Median	36.40	0.00	36.40	0.00
Min - Max	35.3 - 37.1	-1.4 - 0.9	35.2 - 37.3	-1.8 - 0.9

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	26	25	58	57
Mean (SD)	36.53 (0.35)	0.09 (0.49)	36.47 (0.39)	-0.02 (0.45)
Median	36.55	0.10	36.50	0.00
Min - Max	35.6 - 37.1	-1.5 - 1.3	35.5 - 37.8	-1.0 - 1.3
Cycle 9 Day 1				
PRE PAC INFUSION				
n	26	25	57	56
Mean (SD)	36.47 (0.37)	0.05 (0.49)	36.45 (0.35)	-0.05 (0.38)
Median	36.50	0.10	36.50	0.00
Min - Max	35.6 - 37.3	-1.3 - 1.0	35.8 - 37.1	-1.0 - 0.9
AFTER PAC INFUSION				
n	21	20	52	51
Mean (SD)	36.54 (0.41)	0.11 (0.56)	36.45 (0.37)	-0.03 (0.39)
Median	36.50	0.22	36.50	0.00
Min - Max	35.8 - 37.5	-1.3 - 1.0	35.7 - 37.0	-1.5 - 0.8
Cycle 9 Day 8				
PRE PAC INFUSION				
n	24	22	51	50
Mean (SD)	36.25 (0.73)	-0.27 (0.67)	36.51 (0.40)	0.03 (0.41)
Median	36.50	0.00	36.50	0.00
Min - Max	34.0 - 37.0	-2.5 - 0.5	35.6 - 37.7	-0.9 - 0.9
AFTER PAC INFUSION				
n	21	19	50	49
Mean (SD)	36.37 (0.40)	-0.20 (0.53)	36.54 (0.40)	0.07 (0.45)
Median	36.50	0.00	36.50	0.10
Min - Max	35.5 - 37.0	-1.4 - 0.5	35.6 - 37.6	-1.3 - 1.1
Cycle 9 Day 15				
PRE PAC INFUSION				
n	22	20	51	50
Mean (SD)	36.35 (0.40)	-0.10 (0.53)	36.46 (0.41)	-0.03 (0.40)
Median	36.35	0.00	36.50	0.00
Min - Max	35.6 - 37.1	-1.6 - 0.7	35.2 - 37.3	-0.8 - 0.9
AFTER PAC INFUSION				
n	20	18	48	47
Mean (SD)	36.43 (0.51)	0.00 (0.55)	36.45 (0.34)	-0.03 (0.43)
Median	36.35	0.10	36.45	0.00
Min - Max	35.6 - 37.8	-1.2 - 1.0	35.7 - 37.8	-0.9 - 1.3
Cycle 10 Day 1				
PRE PAC INFUSION				
n	22	21	55	54
Mean (SD)	36.32 (0.46)	-0.08 (0.48)	36.48 (0.35)	-0.02 (0.43)
Median	36.40	0.00	36.50	0.00
Min - Max	35.1 - 37.0	-1.3 - 0.7	35.6 - 37.3	-1.3 - 0.9

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	19	18	44	43
Mean (SD)	36.44 (0.44)	0.01 (0.51)	36.42 (0.31)	-0.07 (0.39)
Median	36.40	0.17	36.40	-0.20
Min - Max	35.6 - 37.1	-1.3 - 0.7	35.5 - 37.1	-0.9 - 0.9
Cycle 10 Day 8				
PRE PAC INFUSION				
n	19	17	43	42
Mean (SD)	36.32 (0.39)	-0.12 (0.46)	36.48 (0.38)	-0.03 (0.37)
Median	36.30	-0.10	36.50	0.00
Min - Max	35.5 - 36.9	-1.1 - 0.7	35.4 - 37.4	-0.7 - 0.6
AFTER PAC INFUSION				
n	18	16	40	39
Mean (SD)	36.39 (0.42)	-0.07 (0.51)	36.43 (0.35)	-0.06 (0.35)
Median	36.55	0.10	36.50	0.00
Min - Max	35.5 - 37.0	-1.1 - 0.6	35.2 - 36.8	-0.9 - 0.6
Cycle 10 Day 15				
PRE PAC INFUSION				
n	18	16	46	45
Mean (SD)	36.36 (0.36)	-0.02 (0.30)	36.40 (0.38)	-0.12 (0.33)
Median	36.50	0.05	36.45	-0.10
Min - Max	35.6 - 36.9	-0.6 - 0.6	35.5 - 37.0	-1.0 - 0.5
AFTER PAC INFUSION				
n	15	13	41	40
Mean (SD)	36.42 (0.37)	0.03 (0.32)	36.42 (0.27)	-0.09 (0.30)
Median	36.40	0.00	36.50	-0.05
Min - Max	35.8 - 37.0	-0.5 - 0.6	35.7 - 36.9	-0.7 - 0.5
Cycle 11 Day 1				
PRE PAC INFUSION				
n	17	15	48	47
Mean (SD)	36.44 (0.36)	0.03 (0.39)	36.48 (0.39)	-0.05 (0.54)
Median	36.50	0.10	36.50	-0.20
Min - Max	35.7 - 37.0	-0.6 - 0.6	35.2 - 37.5	-1.2 - 2.1
AFTER PAC INFUSION				
n	14	12	40	39
Mean (SD)	36.39 (0.47)	0.00 (0.53)	36.52 (0.37)	0.02 (0.42)
Median	36.45	0.10	36.50	0.00
Min - Max	35.1 - 37.0	-1.4 - 0.7	35.6 - 37.7	-0.9 - 1.2
Cycle 11 Day 8				
PRE PAC INFUSION				
n	15	13	35	34
Mean (SD)	36.42 (0.26)	0.04 (0.28)	36.40 (0.42)	-0.13 (0.48)
Median	36.30	0.00	36.40	-0.15
Min - Max	36.1 - 37.0	-0.4 - 0.5	35.5 - 37.4	-0.9 - 0.9

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	14	12	33	32
Mean (SD)	36.27 (0.48)	-0.11 (0.49)	36.38 (0.30)	-0.14 (0.39)
Median	36.40	0.10	36.40	-0.15
Min - Max	35.2 - 36.8	-1.3 - 0.4	35.6 - 37.0	-0.8 - 0.9
Cycle 11 Day 15				
PRE PAC INFUSION				
n	17	15	39	38
Mean (SD)	36.44 (0.26)	-0.01 (0.35)	36.42 (0.43)	-0.09 (0.45)
Median	36.40	0.10	36.50	-0.10
Min - Max	35.9 - 36.9	-0.8 - 0.5	35.5 - 37.4	-1.2 - 0.9
AFTER PAC INFUSION				
n	14	12	36	35
Mean (SD)	36.44 (0.40)	-0.01 (0.41)	36.52 (0.43)	0.02 (0.43)
Median	36.40	0.05	36.55	0.00
Min - Max	35.6 - 37.1	-0.8 - 0.5	35.2 - 37.5	-0.7 - 1.0
Cycle 12 Day 1				
PRE PAC INFUSION				
n	17	16	43	43
Mean (SD)	36.48 (0.33)	0.06 (0.41)	36.45 (0.34)	-0.12 (0.40)
Median	36.50	0.00	36.40	-0.10
Min - Max	36.0 - 37.1	-0.7 - 0.7	35.7 - 37.1	-0.9 - 0.9
AFTER PAC INFUSION				
n	14	13	35	35
Mean (SD)	36.54 (0.24)	0.11 (0.29)	36.52 (0.42)	-0.03 (0.45)
Median	36.55	0.20	36.50	-0.20
Min - Max	36.2 - 36.9	-0.5 - 0.5	35.5 - 37.8	-0.7 - 1.3
Cycle 12 Day 8				
PRE PAC INFUSION				
n	16	14	33	33
Mean (SD)	36.38 (0.36)	-0.08 (0.45)	36.46 (0.43)	-0.14 (0.40)
Median	36.40	0.00	36.60	-0.10
Min - Max	35.3 - 36.9	-1.2 - 0.6	35.0 - 37.0	-1.0 - 0.9
AFTER PAC INFUSION				
n	14	12	32	32
Mean (SD)	36.42 (0.25)	0.04 (0.41)	36.48 (0.36)	-0.11 (0.35)
Median	36.45	0.20	36.50	-0.15
Min - Max	35.9 - 36.9	-0.8 - 0.7	35.2 - 37.0	-0.8 - 0.9
Cycle 12 Day 15				
PRE PAC INFUSION				
n	16	14	33	33
Mean (SD)	36.52 (0.41)	0.02 (0.47)	36.46 (0.34)	-0.13 (0.38)
Median	36.60	0.15	36.50	-0.10
Min - Max	35.4 - 37.1	-1.1 - 0.5	35.7 - 37.1	-1.1 - 0.6

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	14	12	30	30
Mean (SD)	36.55 (0.38)	0.11 (0.45)	36.51 (0.38)	-0.05 (0.38)
Median	36.50	0.12	36.50	-0.05
Min - Max	35.9 - 37.5	-0.7 - 0.9	35.6 - 37.6	-0.7 - 1.1
Cycle 13 Day 1				
PRE PAC INFUSION				
n	14	13	33	33
Mean (SD)	36.46 (0.29)	0.00 (0.33)	36.42 (0.43)	-0.14 (0.41)
Median	36.45	0.00	36.40	-0.20
Min - Max	36.0 - 37.1	-0.5 - 0.6	35.0 - 37.2	-1.0 - 0.9
AFTER PAC INFUSION				
n	12	11	27	27
Mean (SD)	36.54 (0.45)	0.07 (0.34)	36.49 (0.50)	-0.04 (0.57)
Median	36.35	0.10	36.50	0.00
Min - Max	36.0 - 37.7	-0.5 - 0.5	35.1 - 37.4	-1.2 - 1.1
Cycle 13 Day 8				
PRE PAC INFUSION				
n	12	11	27	27
Mean (SD)	36.42 (0.51)	-0.03 (0.58)	36.49 (0.48)	-0.04 (0.45)
Median	36.50	0.10	36.50	0.00
Min - Max	35.5 - 37.3	-1.0 - 0.8	35.0 - 37.6	-1.0 - 0.9
AFTER PAC INFUSION				
n	11	10	24	24
Mean (SD)	36.53 (0.41)	0.11 (0.42)	36.54 (0.41)	-0.01 (0.44)
Median	36.50	0.27	36.60	0.00
Min - Max	36.0 - 37.1	-0.7 - 0.6	35.5 - 37.1	-0.7 - 0.9
Cycle 13 Day 15				
PRE PAC INFUSION				
n	12	11	27	27
Mean (SD)	36.39 (0.61)	-0.10 (0.64)	36.46 (0.38)	-0.08 (0.40)
Median	36.50	0.10	36.50	-0.10
Min - Max	34.7 - 37.1	-1.8 - 0.5	35.0 - 37.0	-1.0 - 0.9
AFTER PAC INFUSION				
n	11	10	23	23
Mean (SD)	36.56 (0.29)	0.11 (0.45)	36.58 (0.47)	0.07 (0.50)
Median	36.50	0.17	36.60	0.00
Min - Max	36.1 - 37.1	-0.5 - 0.7	35.5 - 37.5	-0.8 - 1.0
Cycle 14 Day 1				
PRE PAC INFUSION				
n	13	12	32	32
Mean (SD)	36.58 (0.60)	0.11 (0.68)	36.45 (0.30)	-0.15 (0.30)
Median	36.60	0.17	36.45	-0.20
Min - Max	35.5 - 38.0	-1.0 - 1.4	35.6 - 37.0	-0.8 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	11	10	26	26
Mean (SD)	36.45 (0.40)	-0.02 (0.48)	36.53 (0.44)	-0.05 (0.38)
Median	36.50	0.12	36.60	0.00
Min - Max	35.7 - 37.0	-0.8 - 0.5	35.0 - 37.2	-0.8 - 0.7
Cycle 14 Day 8				
PRE PAC INFUSION				
n	11	10	26	26
Mean (SD)	36.33 (0.49)	-0.13 (0.58)	36.46 (0.31)	-0.11 (0.41)
Median	36.40	0.10	36.50	-0.05
Min - Max	35.2 - 37.0	-1.3 - 0.4	35.6 - 37.0	-1.0 - 0.9
AFTER PAC INFUSION				
n	10	9	24	24
Mean (SD)	36.40 (0.58)	-0.04 (0.74)	36.53 (0.36)	0.00 (0.43)
Median	36.45	0.10	36.55	0.00
Min - Max	35.0 - 37.2	-1.5 - 0.6	36.0 - 37.6	-0.7 - 0.8
Cycle 14 Day 15				
PRE PAC INFUSION				
n	11	10	26	26
Mean (SD)	36.55 (0.66)	-0.04 (0.84)	36.49 (0.26)	-0.08 (0.46)
Median	36.70	0.30	36.50	-0.15
Min - Max	35.0 - 37.5	-1.5 - 0.8	35.7 - 37.0	-0.9 - 1.2
AFTER PAC INFUSION				
n	10	9	24	24
Mean (SD)	36.65 (0.35)	0.09 (0.64)	36.45 (0.34)	-0.13 (0.41)
Median	36.65	0.30	36.40	-0.15
Min - Max	36.2 - 37.2	-1.1 - 0.8	35.6 - 37.0	-1.1 - 0.9
Cycle 15 Day 1				
PRE PAC INFUSION				
n	11	11	28	28
Mean (SD)	36.47 (0.48)	-0.08 (0.42)	36.45 (0.41)	-0.11 (0.44)
Median	36.60	-0.10	36.50	-0.20
Min - Max	35.3 - 37.1	-0.9 - 0.6	35.4 - 37.1	-1.1 - 0.8
AFTER PAC INFUSION				
n	10	10	22	22
Mean (SD)	36.52 (0.48)	-0.04 (0.45)	36.44 (0.33)	-0.10 (0.32)
Median	36.40	0.00	36.45	-0.15
Min - Max	35.6 - 37.2	-0.9 - 0.5	35.7 - 37.0	-0.7 - 0.5
Cycle 15 Day 8				
PRE PAC INFUSION				
n	11	10	21	21
Mean (SD)	36.47 (0.53)	-0.11 (0.54)	36.39 (0.39)	-0.14 (0.39)
Median	36.70	0.05	36.40	-0.20
Min - Max	35.3 - 37.2	-1.2 - 0.6	35.4 - 37.0	-0.7 - 0.5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	10	9	18	18
Mean (SD)	36.68 (0.31)	0.13 (0.47)	36.46 (0.36)	-0.09 (0.38)
Median	36.65	0.33	36.45	-0.15
Min - Max	36.2 - 37.2	-0.7 - 0.6	35.6 - 37.0	-0.7 - 0.9
Cycle 15 Day 15				
PRE PAC INFUSION				
n	10	9	22	22
Mean (SD)	36.37 (0.43)	-0.17 (0.57)	36.53 (0.35)	-0.01 (0.47)
Median	36.50	0.00	36.60	-0.05
Min - Max	35.3 - 36.7	-1.2 - 0.4	35.7 - 37.1	-0.8 - 0.9
AFTER PAC INFUSION				
n	9	8	20	20
Mean (SD)	36.50 (0.24)	0.00 (0.52)	36.56 (0.35)	0.01 (0.36)
Median	36.50	0.20	36.60	0.00
Min - Max	36.1 - 36.8	-0.8 - 0.5	35.6 - 37.0	-0.8 - 0.9
Cycle 16 Day 1				
PRE PAC INFUSION				
n	11	10	24	24
Mean (SD)	36.57 (0.34)	0.09 (0.37)	36.48 (0.43)	-0.02 (0.44)
Median	36.60	0.10	36.50	0.00
Min - Max	36.0 - 37.1	-0.5 - 0.6	35.5 - 37.2	-0.8 - 1.1
AFTER PAC INFUSION				
n	10	9	20	20
Mean (SD)	36.55 (0.41)	0.06 (0.44)	36.56 (0.35)	0.08 (0.39)
Median	36.65	0.10	36.50	0.10
Min - Max	35.9 - 37.0	-0.6 - 0.6	36.0 - 37.1	-0.5 - 0.9
Cycle 16 Day 8				
PRE PAC INFUSION				
n	11	10	19	19
Mean (SD)	36.55 (0.28)	0.00 (0.43)	36.41 (0.44)	-0.06 (0.44)
Median	36.60	-0.04	36.40	-0.10
Min - Max	36.1 - 37.0	-0.7 - 0.6	35.5 - 37.0	-1.0 - 0.5
AFTER PAC INFUSION				
n	10	9	19	19
Mean (SD)	36.51 (0.28)	-0.03 (0.49)	36.54 (0.31)	0.06 (0.42)
Median	36.55	0.00	36.50	0.00
Min - Max	35.9 - 37.0	-0.7 - 0.6	36.1 - 37.1	-0.6 - 0.8
Cycle 16 Day 15				
PRE PAC INFUSION				
n	10	9	21	21
Mean (SD)	36.40 (0.59)	-0.14 (0.69)	36.37 (0.46)	-0.11 (0.44)
Median	36.50	0.10	36.50	-0.20
Min - Max	35.1 - 37.1	-1.4 - 0.6	35.5 - 37.0	-0.9 - 0.9

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	9	8	19	19
Mean (SD)	36.46 (0.56)	-0.08 (0.71)	36.57 (0.34)	0.07 (0.34)
Median	36.60	0.15	36.60	0.10
Min - Max	35.2 - 37.1	-1.3 - 0.6	35.5 - 37.0	-0.4 - 0.9
Cycle 17 Day 1				
PRE PAC INFUSION				
n	8	7	23	23
Mean (SD)	36.41 (0.27)	-0.18 (0.55)	36.34 (0.45)	-0.17 (0.36)
Median	36.45	0.00	36.50	-0.10
Min - Max	36.0 - 36.8	-1.3 - 0.4	35.0 - 37.0	-0.9 - 0.5
AFTER PAC INFUSION				
n	7	6	20	20
Mean (SD)	36.44 (0.40)	-0.20 (0.50)	36.50 (0.33)	0.00 (0.37)
Median	36.50	-0.24	36.55	0.00
Min - Max	35.6 - 36.8	-0.9 - 0.5	35.9 - 37.0	-0.7 - 0.7
Cycle 17 Day 8				
PRE PAC INFUSION				
n	6	5	18	18
Mean (SD)	36.37 (0.35)	-0.28 (0.57)	36.43 (0.53)	-0.06 (0.48)
Median	36.50	-0.60	36.60	-0.10
Min - Max	35.8 - 36.7	-0.7 - 0.6	35.3 - 37.1	-0.8 - 0.9
AFTER PAC INFUSION				
n	6	5	18	18
Mean (SD)	36.33 (0.47)	-0.34 (0.91)	36.47 (0.49)	-0.02 (0.48)
Median	36.35	-0.50	36.40	-0.15
Min - Max	35.7 - 36.9	-1.6 - 0.6	35.6 - 37.4	-0.7 - 0.9
Cycle 17 Day 15				
PRE PAC INFUSION				
n	7	6	19	19
Mean (SD)	36.36 (0.45)	-0.28 (0.57)	36.46 (0.35)	-0.06 (0.55)
Median	36.40	-0.30	36.60	0.00
Min - Max	35.5 - 37.0	-1.0 - 0.4	35.7 - 37.0	-0.8 - 1.3
AFTER PAC INFUSION				
n	7	6	19	19
Mean (SD)	36.36 (0.47)	-0.30 (0.72)	36.49 (0.32)	-0.03 (0.44)
Median	36.50	-0.34	36.50	0.00
Min - Max	35.4 - 36.8	-1.1 - 0.6	36.0 - 37.0	-0.8 - 0.9
Cycle 18 Day 1				
PRE PAC INFUSION				
n	7	7	21	21
Mean (SD)	36.43 (0.59)	-0.18 (0.64)	36.40 (0.49)	-0.14 (0.43)
Median	36.50	-0.10	36.50	-0.10
Min - Max	35.3 - 37.1	-1.2 - 0.5	35.3 - 37.0	-1.0 - 0.5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	6	6	17	17
Mean (SD)	36.43 (0.34)	-0.20 (0.66)	36.64 (0.43)	0.09 (0.55)
Median	36.40	-0.19	36.50	-0.10
Min - Max	36.1 - 36.8	-1.1 - 0.6	36.0 - 37.9	-0.8 - 1.4
Cycle 18 Day 8				
PRE PAC INFUSION				
n	6	6	15	15
Mean (SD)	36.38 (0.54)	-0.25 (0.75)	36.42 (0.41)	-0.13 (0.44)
Median	36.40	-0.19	36.50	-0.20
Min - Max	35.5 - 37.0	-1.1 - 0.6	35.7 - 37.1	-0.8 - 0.6
AFTER PAC INFUSION				
n	6	6	14	14
Mean (SD)	36.25 (0.58)	-0.38 (0.78)	36.44 (0.33)	-0.11 (0.32)
Median	36.35	-0.34	36.45	-0.10
Min - Max	35.2 - 36.8	-1.3 - 0.5	35.7 - 37.0	-0.7 - 0.5
Cycle 18 Day 15				
PRE PAC INFUSION				
n	7	6	17	17
Mean (SD)	36.43 (0.53)	-0.21 (0.71)	36.36 (0.40)	-0.18 (0.50)
Median	36.50	-0.19	36.50	-0.10
Min - Max	35.4 - 37.0	-1.1 - 0.5	35.5 - 36.9	-1.0 - 0.8
AFTER PAC INFUSION				
n	7	6	16	16
Mean (SD)	36.50 (0.29)	-0.13 (0.70)	36.51 (0.31)	-0.04 (0.42)
Median	36.50	-0.04	36.50	-0.05
Min - Max	36.0 - 36.9	-1.3 - 0.6	36.0 - 37.1	-0.7 - 0.8
Cycle 19 Day 1				
PRE PAC INFUSION				
n	7	6	18	18
Mean (SD)	36.46 (0.62)	-0.20 (0.74)	36.41 (0.51)	-0.12 (0.40)
Median	36.40	0.12	36.50	-0.20
Min - Max	35.2 - 37.1	-1.3 - 0.4	35.0 - 37.2	-0.7 - 0.7
AFTER PAC INFUSION				
n	6	5	14	14
Mean (SD)	36.57 (0.32)	-0.07 (0.64)	36.57 (0.32)	0.04 (0.33)
Median	36.65	0.03	36.65	0.00
Min - Max	36.1 - 36.9	-1.0 - 0.5	35.8 - 37.0	-0.6 - 0.7
Cycle 19 Day 8				
PRE PAC INFUSION				
n	6	5	13	13
Mean (SD)	36.57 (0.52)	-0.01 (0.79)	36.45 (0.32)	-0.08 (0.45)
Median	36.55	0.40	36.50	-0.10
Min - Max	35.9 - 37.4	-1.1 - 0.6	36.0 - 37.0	-0.7 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	4	12	12
Mean (SD)	36.34 (0.61)	-0.25 (0.93)	36.54 (0.27)	0.03 (0.46)
Median	36.50	-0.20	36.50	0.00
Min - Max	35.3 - 36.9	-1.2 - 0.6	36.1 - 37.0	-0.7 - 0.9
Cycle 19 Day 15				
PRE PAC INFUSION				
n	6	5	13	13
Mean (SD)	36.43 (0.54)	-0.13 (0.59)	36.41 (0.50)	-0.10 (0.43)
Median	36.45	0.00	36.40	-0.10
Min - Max	35.5 - 37.0	-1.0 - 0.5	35.1 - 37.1	-0.7 - 0.6
AFTER PAC INFUSION				
n	6	5	13	13
Mean (SD)	36.40 (0.38)	-0.19 (0.56)	36.48 (0.26)	-0.02 (0.38)
Median	36.40	-0.37	36.50	-0.10
Min - Max	35.7 - 36.8	-0.8 - 0.4	36.0 - 37.0	-0.4 - 0.8
Cycle 20 Day 1				
PRE PAC INFUSION				
n	6	5	16	16
Mean (SD)	36.57 (0.27)	-0.01 (0.48)	36.41 (0.47)	-0.11 (0.50)
Median	36.50	0.00	36.45	-0.15
Min - Max	36.4 - 37.1	-0.8 - 0.4	35.6 - 37.2	-0.8 - 0.7
AFTER PAC INFUSION				
n	5	4	13	13
Mean (SD)	36.60 (0.31)	0.01 (0.78)	36.50 (0.36)	-0.01 (0.47)
Median	36.50	0.27	36.40	0.00
Min - Max	36.2 - 37.0	-1.1 - 0.6	35.9 - 37.1	-0.7 - 0.6
Cycle 20 Day 8				
PRE PAC INFUSION				
n	6	5	12	12
Mean (SD)	36.50 (0.33)	-0.11 (0.62)	36.43 (0.29)	-0.09 (0.31)
Median	36.45	0.10	36.50	-0.05
Min - Max	36.2 - 37.1	-1.1 - 0.4	35.7 - 36.7	-0.6 - 0.3
AFTER PAC INFUSION				
n	6	5	12	12
Mean (SD)	36.50 (0.35)	-0.09 (0.72)	36.40 (0.43)	-0.12 (0.40)
Median	36.55	0.23	36.45	-0.15
Min - Max	36.1 - 37.0	-1.2 - 0.6	35.5 - 37.2	-0.7 - 0.7
Cycle 20 Day 15				
PRE PAC INFUSION				
n	6	5	12	12
Mean (SD)	36.30 (0.63)	-0.31 (0.91)	36.46 (0.53)	-0.03 (0.42)
Median	36.45	0.23	36.55	-0.05
Min - Max	35.2 - 37.0	-1.3 - 0.5	35.0 - 36.9	-0.9 - 0.5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	4	11	11
Mean (SD)	36.42 (0.45)	0.01 (0.59)	36.48 (0.35)	-0.02 (0.29)
Median	36.40	0.17	36.50	-0.10
Min - Max	35.7 - 36.9	-0.8 - 0.5	35.7 - 37.0	-0.5 - 0.5
Cycle 21 Day 1				
PRE PAC INFUSION				
n	5	5	13	13
Mean (SD)	36.60 (0.54)	0.01 (0.87)	36.45 (0.47)	-0.03 (0.40)
Median	36.60	0.40	36.40	-0.10
Min - Max	35.8 - 37.3	-1.5 - 0.6	35.3 - 37.0	-0.8 - 0.6
AFTER PAC INFUSION				
n	3	3	11	11
Mean (SD)	36.70 (0.30)	0.31 (0.09)	36.39 (0.50)	-0.07 (0.31)
Median	36.70	0.30	36.50	-0.10
Min - Max	36.4 - 37.0	0.2 - 0.4	35.1 - 36.8	-0.5 - 0.4
Cycle 21 Day 8				
PRE PAC INFUSION				
n	3	3	11	11
Mean (SD)	36.77 (0.35)	0.38 (0.04)	36.50 (0.46)	0.04 (0.41)
Median	36.80	0.40	36.40	0.00
Min - Max	36.4 - 37.1	0.3 - 0.4	35.5 - 37.1	-0.6 - 0.7
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	36.65 (0.21)	0.45 (0.07)	36.44 (0.41)	-0.03 (0.56)
Median	36.65	0.45	36.50	-0.05
Min - Max	36.5 - 36.8	0.4 - 0.5	35.6 - 37.0	-0.8 - 1.0
Cycle 21 Day 15				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	36.65 (0.21)	0.45 (0.07)	36.46 (0.33)	-0.01 (0.44)
Median	36.65	0.45	36.40	-0.10
Min - Max	36.5 - 36.8	0.4 - 0.5	36.1 - 36.9	-0.6 - 0.7
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	36.75 (0.21)	0.55 (0.07)	36.44 (0.41)	-0.03 (0.37)
Median	36.75	0.55	36.45	-0.15
Min - Max	36.6 - 36.9	0.5 - 0.6	35.8 - 37.1	-0.6 - 0.6
Cycle 22 Day 1				
PRE PAC INFUSION				
n	4	4	13	13
Mean (SD)	36.80 (0.42)	0.38 (0.32)	36.47 (0.41)	-0.01 (0.36)
Median	36.75	0.52	36.40	-0.10
Min - Max	36.4 - 37.3	-0.1 - 0.6	35.8 - 37.0	-0.5 - 0.5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	11	11
Mean (SD)	36.70 (0.10)	0.31 (0.34)	36.49 (0.43)	0.03 (0.37)
Median	36.70	0.40	36.50	0.00
Min - Max	36.6 - 36.8	-0.1 - 0.6	35.6 - 37.1	-0.5 - 0.6
Cycle 22 Day 8				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	36.60 (0.00)	0.40 (0.28)	36.36 (0.40)	-0.11 (0.32)
Median	36.60	0.40	36.50	0.00
Min - Max	36.6 - 36.6	0.2 - 0.6	35.6 - 36.9	-0.7 - 0.3
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	36.65 (0.07)	0.45 (0.21)	36.23 (0.29)	-0.24 (0.34)
Median	36.65	0.45	36.35	-0.30
Min - Max	36.6 - 36.7	0.3 - 0.6	35.8 - 36.6	-0.6 - 0.4
Cycle 22 Day 15				
PRE PAC INFUSION				
n	2	2	9	9
Mean (SD)	36.55 (0.21)	0.35 (0.07)	36.48 (0.37)	0.04 (0.25)
Median	36.55	0.35	36.50	0.00
Min - Max	36.4 - 36.7	0.3 - 0.4	35.7 - 36.9	-0.3 - 0.3
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	36.65 (0.35)	0.45 (0.07)	36.46 (0.42)	0.02 (0.43)
Median	36.65	0.45	36.30	-0.10
Min - Max	36.4 - 36.9	0.4 - 0.5	36.0 - 37.0	-0.5 - 0.6
Cycle 23 Day 1				
PRE PAC INFUSION				
n	3	3	12	12
Mean (SD)	36.47 (0.12)	0.17 (0.25)	36.43 (0.40)	-0.02 (0.34)
Median	36.40	0.20	36.55	-0.05
Min - Max	36.4 - 36.6	-0.1 - 0.4	35.6 - 37.1	-0.6 - 0.6
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	36.45 (0.07)	0.25 (0.35)	36.47 (0.38)	0.04 (0.34)
Median	36.45	0.25	36.50	0.05
Min - Max	36.4 - 36.5	0.0 - 0.5	35.8 - 37.0	-0.6 - 0.4
Cycle 23 Day 8				
PRE PAC INFUSION				
n	2	2	9	9
Mean (SD)	36.55 (0.07)	0.35 (0.21)	36.50 (0.24)	0.07 (0.37)
Median	36.55	0.35	36.50	0.00
Min - Max	36.5 - 36.6	0.2 - 0.5	36.1 - 36.8	-0.6 - 0.8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	36.45 (0.07)	0.25 (0.35)	36.57 (0.21)	0.13 (0.51)
Median	36.45	0.25	36.60	0.00
Min - Max	36.4 - 36.5	0.0 - 0.5	36.1 - 36.8	-0.6 - 1.3
Cycle 23 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	36.45 (0.21)	0.25 (0.49)	36.55 (0.39)	0.13 (0.38)
Median	36.45	0.25	36.45	0.00
Min - Max	36.3 - 36.6	-0.1 - 0.6	36.0 - 37.2	-0.3 - 0.7
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	36.50 (0.14)	0.30 (0.42)	36.56 (0.39)	0.14 (0.40)
Median	36.50	0.30	36.55	0.10
Min - Max	36.4 - 36.6	0.0 - 0.6	36.0 - 37.0	-0.6 - 0.6
Cycle 24 Day 1				
PRE PAC INFUSION				
n	3	3	11	11
Mean (SD)	36.37 (0.15)	0.07 (0.38)	36.64 (0.28)	0.19 (0.28)
Median	36.40	-0.10	36.70	0.20
Min - Max	36.2 - 36.5	-0.2 - 0.5	36.1 - 37.0	-0.3 - 0.7
AFTER PAC INFUSION				
n	2	2	9	9
Mean (SD)	36.45 (0.07)	0.25 (0.35)	36.71 (0.40)	0.29 (0.29)
Median	36.45	0.25	36.70	0.20
Min - Max	36.4 - 36.5	0.0 - 0.5	36.0 - 37.2	-0.2 - 0.7
Cycle 24 Day 8				
PRE PAC INFUSION				
n	2	2	7	7
Mean (SD)	36.35 (0.07)	0.15 (0.21)	36.44 (0.48)	0.03 (0.32)
Median	36.35	0.15	36.70	0.10
Min - Max	36.3 - 36.4	0.0 - 0.3	35.5 - 36.8	-0.6 - 0.4
AFTER PAC INFUSION				
n	2	2	7	7
Mean (SD)	36.50 (0.00)	0.30 (0.28)	36.56 (0.32)	0.14 (0.33)
Median	36.50	0.30	36.60	0.10
Min - Max	36.5 - 36.5	0.1 - 0.5	36.0 - 36.9	-0.3 - 0.6
Cycle 24 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	36.35 (0.35)	0.15 (0.64)	36.48 (0.41)	0.05 (0.35)
Median	36.35	0.15	36.65	0.20
Min - Max	36.1 - 36.6	-0.3 - 0.6	35.7 - 36.8	-0.7 - 0.3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	7	7
Mean (SD)	36.40 (0.00)	0.20 (0.28)	36.39 (0.58)	-0.03 (0.35)
Median	36.40	0.20	36.50	0.00
Min - Max	36.4 - 36.4	0.0 - 0.4	35.5 - 37.1	-0.6 - 0.5
Cycle 25 Day 1				
PRE PAC INFUSION				
n	2	2	10	10
Mean (SD)	36.30 (0.14)	0.10 (0.42)	36.64 (0.34)	0.09 (0.34)
Median	36.30	0.10	36.70	0.10
Min - Max	36.2 - 36.4	-0.2 - 0.4	36.2 - 37.2	-0.5 - 0.7
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	36.35 (0.07)	0.15 (0.21)	36.55 (0.33)	0.00 (0.33)
Median	36.35	0.15	36.50	-0.10
Min - Max	36.3 - 36.4	0.0 - 0.3	36.1 - 37.0	-0.3 - 0.5
Cycle 25 Day 8				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	36.20 (0.14)	0.00 (0.42)	36.50 (0.58)	0.08 (0.43)
Median	36.20	0.00	36.60	0.15
Min - Max	36.1 - 36.3	-0.3 - 0.3	35.3 - 37.1	-0.6 - 0.6
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	36.40 (0.00)	0.20 (0.28)	36.63 (0.57)	0.20 (0.19)
Median	36.40	0.20	36.70	0.20
Min - Max	36.4 - 36.4	0.0 - 0.4	35.3 - 37.2	-0.1 - 0.5
Cycle 25 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	36.40 (0.14)	0.20 (0.42)	36.28 (0.54)	-0.15 (0.30)
Median	36.40	0.20	36.40	-0.20
Min - Max	36.3 - 36.5	-0.1 - 0.5	35.1 - 36.8	-0.7 - 0.3
AFTER PAC INFUSION				
n	2	2	7	7
Mean (SD)	36.40 (0.14)	0.20 (0.42)	36.57 (0.26)	0.14 (0.43)
Median	36.40	0.20	36.50	0.00
Min - Max	36.3 - 36.5	-0.1 - 0.5	36.3 - 37.0	-0.4 - 0.9
Cycle 26 Day 1				
PRE PAC INFUSION				
n	2	2	11	11
Mean (SD)	36.40 (0.00)	0.20 (0.28)	36.43 (0.25)	-0.01 (0.26)
Median	36.40	0.20	36.40	-0.10
Min - Max	36.4 - 36.4	0.0 - 0.4	35.9 - 36.8	-0.4 - 0.5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	10	10
Mean (SD)	36.30 (0.00)	0.10 (0.28)	36.51 (0.53)	0.05 (0.37)
Median	36.30	0.10	36.50	0.00
Min - Max	36.3 - 36.3	-0.1 - 0.3	35.3 - 37.1	-0.6 - 0.5
Cycle 26 Day 8				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	36.40 (0.28)	0.20 (0.57)	36.59 (0.34)	0.15 (0.35)
Median	36.40	0.20	36.70	0.20
Min - Max	36.2 - 36.6	-0.2 - 0.6	35.9 - 37.1	-0.4 - 0.7
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	36.40 (0.28)	0.20 (0.57)	36.38 (0.45)	-0.06 (0.13)
Median	36.40	0.20	36.50	-0.05
Min - Max	36.2 - 36.6	-0.2 - 0.6	35.4 - 36.9	-0.2 - 0.1
Cycle 26 Day 15				
PRE PAC INFUSION				
n	2	2	8	8
Mean (SD)	36.45 (0.07)	0.25 (0.35)	36.64 (0.52)	0.21 (0.39)
Median	36.45	0.25	36.75	0.20
Min - Max	36.4 - 36.5	0.0 - 0.5	35.6 - 37.3	-0.5 - 0.8
AFTER PAC INFUSION				
n	2	2	8	8
Mean (SD)	36.55 (0.07)	0.35 (0.21)	36.56 (0.40)	0.14 (0.32)
Median	36.55	0.35	36.65	0.15
Min - Max	36.5 - 36.6	0.2 - 0.5	35.9 - 37.0	-0.4 - 0.5
Cycle 27 Day 1				
PRE PAC INFUSION				
n	1	1	8	8
Mean (SD)	36.50 (NE)	0.50 (NE)	36.35 (0.32)	-0.16 (0.37)
Median	36.50	0.50	36.30	-0.15
Min - Max	36.5 - 36.5	0.5 - 0.5	35.8 - 36.8	-0.9 - 0.3
AFTER PAC INFUSION				
n	1	1	7	7
Mean (SD)	36.50 (NE)	0.50 (NE)	36.36 (0.29)	-0.20 (0.23)
Median	36.50	0.50	36.40	-0.10
Min - Max	36.5 - 36.5	0.5 - 0.5	35.9 - 36.8	-0.5 - 0.0
Cycle 27 Day 8				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	36.60 (NE)	0.60 (NE)	36.45 (0.33)	-0.13 (0.42)
Median	36.60	0.60	36.60	0.00
Min - Max	36.6 - 36.6	0.6 - 0.6	35.8 - 36.7	-0.9 - 0.2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	36.50 (NE)	0.50 (NE)	36.45 (0.34)	-0.13 (0.29)
Median	36.50	0.50	36.45	-0.10
Min - Max	36.5 - 36.5	0.5 - 0.5	35.9 - 36.8	-0.5 - 0.3
Cycle 27 Day 15				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	36.50 (NE)	0.50 (NE)	36.45 (0.24)	0.05 (0.55)
Median	36.50	0.50	36.50	0.05
Min - Max	36.5 - 36.5	0.5 - 0.5	36.0 - 36.7	-0.7 - 1.0
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	36.60 (NE)	0.60 (NE)	36.37 (0.27)	-0.03 (0.56)
Median	36.60	0.60	36.35	-0.15
Min - Max	36.6 - 36.6	0.6 - 0.6	36.0 - 36.8	-0.7 - 1.0
Cycle 28 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	36.50 (NE)	0.50 (NE)	36.33 (0.48)	-0.05 (0.34)
Median	36.50	0.50	36.40	0.05
Min - Max	36.5 - 36.5	0.5 - 0.5	35.6 - 36.9	-0.7 - 0.2
AFTER PAC INFUSION				
n	1	1	5	5
Mean (SD)	36.50 (NE)	0.50 (NE)	36.50 (0.75)	0.12 (0.45)
Median	36.50	0.50	36.70	0.30
Min - Max	36.5 - 36.5	0.5 - 0.5	35.4 - 37.2	-0.6 - 0.6
Cycle 28 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	36.60 (NE)	0.60 (NE)	36.43 (0.36)	-0.20 (0.43)
Median	36.60	0.60	36.55	-0.10
Min - Max	36.6 - 36.6	0.6 - 0.6	35.9 - 36.7	-0.8 - 0.2
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	36.60 (NE)	0.60 (NE)	36.48 (0.52)	-0.15 (0.41)
Median	36.60	0.60	36.40	-0.10
Min - Max	36.6 - 36.6	0.6 - 0.6	36.0 - 37.1	-0.6 - 0.2
Cycle 28 Day 15				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	36.60 (NE)	0.60 (NE)	36.30 (0.64)	-0.08 (0.39)
Median	36.60	0.60	36.30	-0.05
Min - Max	36.6 - 36.6	0.6 - 0.6	35.3 - 37.0	-0.6 - 0.5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	6	6
Mean (SD)	36.40 (NE)	0.40 (NE)	36.25 (0.62)	-0.13 (0.28)
Median	36.40	0.40	36.40	-0.05
Min - Max	36.4 - 36.4	0.4 - 0.4	35.1 - 36.8	-0.6 - 0.2
Cycle 29 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	36.60 (NE)	0.60 (NE)	36.55 (0.36)	0.17 (0.48)
Median	36.60	0.60	36.60	0.15
Min - Max	36.6 - 36.6	0.6 - 0.6	36.1 - 36.9	-0.6 - 0.8
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	36.60 (NE)	0.60 (NE)	36.55 (0.25)	0.30 (0.37)
Median	36.60	0.60	36.60	0.25
Min - Max	36.6 - 36.6	0.6 - 0.6	36.2 - 36.8	-0.1 - 0.8
Cycle 29 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	36.40 (NE)	0.40 (NE)	36.33 (0.59)	0.08 (0.42)
Median	36.40	0.40	36.35	0.15
Min - Max	36.4 - 36.4	0.4 - 0.4	35.6 - 37.0	-0.5 - 0.5
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	36.50 (NE)	0.50 (NE)	36.23 (0.56)	-0.03 (0.39)
Median	36.50	0.50	36.30	0.10
Min - Max	36.5 - 36.5	0.5 - 0.5	35.5 - 36.8	-0.6 - 0.3
Cycle 29 Day 15				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	36.60 (NE)	0.60 (NE)	36.53 (0.38)	-0.10 (0.41)
Median	36.60	0.60	36.60	0.05
Min - Max	36.6 - 36.6	0.6 - 0.6	36.0 - 36.9	-0.7 - 0.2
AFTER PAC INFUSION				
n	1	1	3	3
Mean (SD)	36.60 (NE)	0.60 (NE)	36.27 (0.23)	-0.27 (0.38)
Median	36.60	0.60	36.40	-0.10
Min - Max	36.6 - 36.6	0.6 - 0.6	36.0 - 36.4	-0.7 - 0.0
Cycle 30 Day 1				
PRE PAC INFUSION				
n	1	1	6	6
Mean (SD)	36.40 (NE)	0.40 (NE)	36.30 (0.46)	-0.08 (0.45)
Median	36.40	0.40	36.25	0.00
Min - Max	36.4 - 36.4	0.4 - 0.4	35.8 - 36.8	-0.8 - 0.4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	4	4
Mean (SD)	36.50 (NE)	0.50 (NE)	36.40 (0.50)	0.15 (0.55)
Median	36.50	0.50	36.35	0.20
Min - Max	36.5 - 36.5	0.5 - 0.5	35.9 - 37.0	-0.5 - 0.7
Cycle 30 Day 8				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	36.50 (NE)	0.50 (NE)	36.53 (0.93)	0.28 (1.01)
Median	36.50	0.50	36.40	0.45
Min - Max	36.5 - 36.5	0.5 - 0.5	35.6 - 37.7	-1.1 - 1.3
AFTER PAC INFUSION				
n	1	1	3	3
Mean (SD)	36.60 (NE)	0.60 (NE)	35.77 (0.71)	-0.43 (0.35)
Median	36.60	0.60	35.90	-0.40
Min - Max	36.6 - 36.6	0.6 - 0.6	35.0 - 36.4	-0.8 - -0.1
Cycle 30 Day 15				
PRE PAC INFUSION				
n	1	1	4	4
Mean (SD)	36.30 (NE)	0.30 (NE)	36.45 (0.26)	0.20 (0.50)
Median	36.30	0.30	36.40	0.20
Min - Max	36.3 - 36.3	0.3 - 0.3	36.2 - 36.8	-0.4 - 0.8
AFTER PAC INFUSION				
n	1	1	3	3
Mean (SD)	36.50 (NE)	0.50 (NE)	36.37 (0.40)	0.17 (1.00)
Median	36.50	0.50	36.60	0.10
Min - Max	36.5 - 36.5	0.5 - 0.5	35.9 - 36.6	-0.8 - 1.2
Cycle 31 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.50 (NE)	0.50 (NE)	36.25 (0.64)	-0.15 (0.64)
Median	36.50	0.50	36.25	-0.15
Min - Max	36.5 - 36.5	0.5 - 0.5	35.8 - 36.7	-0.6 - 0.3
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.50 (NE)	0.50 (NE)	35.90 (NE)	-0.50 (NE)
Median	36.50	0.50	35.90	-0.50
Min - Max	36.5 - 36.5	0.5 - 0.5	35.9 - 35.9	-0.5 - -0.5
Cycle 31 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.60 (NE)	0.60 (NE)	36.40 (NE)	0.00 (NE)
Median	36.60	0.60	36.40	0.00
Min - Max	36.6 - 36.6	0.6 - 0.6	36.4 - 36.4	0.0 - 0.0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.40 (NE)	0.40 (NE)	35.90 (NE)	-0.50 (NE)
Median	36.40	0.40	35.90	-0.50
Min - Max	36.4 - 36.4	0.4 - 0.4	35.9 - 35.9	-0.5 - -0.5
Cycle 31 Day 15				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	36.50 (0.28)	-0.05 (0.49)
Median	NE	NE	36.50	-0.05
Min - Max	NE - NE	NE - NE	36.3 - 36.7	-0.4 - 0.3
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	36.40 (0.14)	-0.15 (0.35)
Median	NE	NE	36.40	-0.15
Min - Max	NE - NE	NE - NE	36.3 - 36.5	-0.4 - 0.1
Cycle 32 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	35.60 (NE)	-0.80 (NE)
Median	NE	NE	35.60	-0.80
Min - Max	NE - NE	NE - NE	35.6 - 35.6	-0.8 - -0.8
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	36.15 (0.35)	-0.40 (0.14)
Median	NE	NE	36.15	-0.40
Min - Max	NE - NE	NE - NE	35.9 - 36.4	-0.5 - -0.3
Cycle 32 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.50 (NE)	0.50 (NE)	NE (NE)	NE (NE)
Median	36.50	0.50	NE	NE
Min - Max	36.5 - 36.5	0.5 - 0.5	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.40 (NE)	0.40 (NE)	36.60 (0.71)	0.05 (0.92)
Median	36.40	0.40	36.60	0.05
Min - Max	36.4 - 36.4	0.4 - 0.4	36.1 - 37.1	-0.6 - 0.7
Cycle 32 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.50 (NE)	0.50 (NE)	NE (NE)	NE (NE)
Median	36.50	0.50	NE	NE
Min - Max	36.5 - 36.5	0.5 - 0.5	NE - NE	NE - NE

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.60 (NE)	0.60 (NE)	35.95 (0.21)	-0.60 (0.00)
Median	36.60	0.60	35.95	-0.60
Min - Max	36.6 - 36.6	0.6 - 0.6	35.8 - 36.1	-0.6 - -0.6
Cycle 33 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.40 (NE)	0.40 (NE)	36.10 (NE)	-0.30 (NE)
Median	36.40	0.40	36.10	-0.30
Min - Max	36.4 - 36.4	0.4 - 0.4	36.1 - 36.1	-0.3 - -0.3
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.50 (NE)	0.50 (NE)	36.25 (0.35)	-0.30 (0.57)
Median	36.50	0.50	36.25	-0.30
Min - Max	36.5 - 36.5	0.5 - 0.5	36.0 - 36.5	-0.7 - 0.1
Cycle 33 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.60 (NE)	0.60 (NE)	NE (NE)	NE (NE)
Median	36.60	0.60	NE	NE
Min - Max	36.6 - 36.6	0.6 - 0.6	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.50 (NE)	0.50 (NE)	36.30 (0.14)	-0.25 (0.35)
Median	36.50	0.50	36.30	-0.25
Min - Max	36.5 - 36.5	0.5 - 0.5	36.2 - 36.4	-0.5 - 0.0
Cycle 33 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.50 (NE)	0.50 (NE)	NE (NE)	NE (NE)
Median	36.50	0.50	NE	NE
Min - Max	36.5 - 36.5	0.5 - 0.5	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.60 (NE)	0.60 (NE)	35.90 (0.00)	-0.65 (0.21)
Median	36.60	0.60	35.90	-0.65
Min - Max	36.6 - 36.6	0.6 - 0.6	35.9 - 35.9	-0.8 - -0.5
Cycle 34 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.40 (NE)	0.40 (NE)	36.00 (NE)	-0.40 (NE)
Median	36.40	0.40	36.00	-0.40
Min - Max	36.4 - 36.4	0.4 - 0.4	36.0 - 36.0	-0.4 - -0.4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.50 (NE)	0.50 (NE)	35.60 (NE)	-0.80 (NE)
Median	36.50	0.50	35.60	-0.80
Min - Max	36.5 - 36.5	0.5 - 0.5	35.6 - 35.6	-0.8 - -0.8
Cycle 34 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.60 (NE)	0.60 (NE)	NE (NE)	NE (NE)
Median	36.60	0.60	NE	NE
Min - Max	36.6 - 36.6	0.6 - 0.6	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.60 (NE)	0.60 (NE)	36.00 (NE)	-0.40 (NE)
Median	36.60	0.60	36.00	-0.40
Min - Max	36.6 - 36.6	0.6 - 0.6	36.0 - 36.0	-0.4 - -0.4
Cycle 34 Day 15				
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.50 (NE)	0.50 (NE)	35.70 (NE)	-0.70 (NE)
Median	36.50	0.50	35.70	-0.70
Min - Max	36.5 - 36.5	0.5 - 0.5	35.7 - 35.7	-0.7 - -0.7
Cycle 35 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.50 (NE)	0.50 (NE)	36.10 (NE)	-0.30 (NE)
Median	36.50	0.50	36.10	-0.30
Min - Max	36.5 - 36.5	0.5 - 0.5	36.1 - 36.1	-0.3 - -0.3
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.40 (NE)	0.40 (NE)	36.30 (NE)	-0.10 (NE)
Median	36.40	0.40	36.30	-0.10
Min - Max	36.4 - 36.4	0.4 - 0.4	36.3 - 36.3	-0.1 - -0.1
Cycle 35 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.60 (NE)	0.60 (NE)	NE (NE)	NE (NE)
Median	36.60	0.60	NE	NE
Min - Max	36.6 - 36.6	0.6 - 0.6	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.40 (NE)	0.40 (NE)	36.00 (NE)	-0.40 (NE)
Median	36.40	0.40	36.00	-0.40
Min - Max	36.4 - 36.4	0.4 - 0.4	36.0 - 36.0	-0.4 - -0.4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 35 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.50 (NE)	0.50 (NE)	NE (NE)	NE (NE)
Median	36.50	0.50	NE	NE
Min - Max	36.5 - 36.5	0.5 - 0.5	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.60 (NE)	0.60 (NE)	36.10 (NE)	-0.30 (NE)
Median	36.60	0.60	36.10	-0.30
Min - Max	36.6 - 36.6	0.6 - 0.6	36.1 - 36.1	-0.3 - -0.3
Cycle 36 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.50 (NE)	0.50 (NE)	36.20 (NE)	-0.20 (NE)
Median	36.50	0.50	36.20	-0.20
Min - Max	36.5 - 36.5	0.5 - 0.5	36.2 - 36.2	-0.2 - -0.2
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.60 (NE)	0.60 (NE)	36.30 (NE)	-0.10 (NE)
Median	36.60	0.60	36.30	-0.10
Min - Max	36.6 - 36.6	0.6 - 0.6	36.3 - 36.3	-0.1 - -0.1
Cycle 36 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.40 (NE)	0.40 (NE)	NE (NE)	NE (NE)
Median	36.40	0.40	NE	NE
Min - Max	36.4 - 36.4	0.4 - 0.4	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.50 (NE)	0.50 (NE)	36.20 (NE)	-0.20 (NE)
Median	36.50	0.50	36.20	-0.20
Min - Max	36.5 - 36.5	0.5 - 0.5	36.2 - 36.2	-0.2 - -0.2
Cycle 36 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.50 (NE)	0.50 (NE)	NE (NE)	NE (NE)
Median	36.50	0.50	NE	NE
Min - Max	36.5 - 36.5	0.5 - 0.5	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.40 (NE)	0.40 (NE)	35.80 (NE)	-0.60 (NE)
Median	36.40	0.40	35.80	-0.60
Min - Max	36.4 - 36.4	0.4 - 0.4	35.8 - 35.8	-0.6 - -0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 37 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.60 (NE)	0.60 (NE)	36.40 (NE)	0.00 (NE)
Median	36.60	0.60	36.40	0.00
Min - Max	36.6 - 36.6	0.6 - 0.6	36.4 - 36.4	0.0 - 0.0
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.40 (NE)	0.40 (NE)	35.00 (NE)	-1.40 (NE)
Median	36.40	0.40	35.00	-1.40
Min - Max	36.4 - 36.4	0.4 - 0.4	35.0 - 35.0	-1.4 - -1.4
Cycle 37 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.40 (NE)	0.40 (NE)	NE (NE)	NE (NE)
Median	36.40	0.40	NE	NE
Min - Max	36.4 - 36.4	0.4 - 0.4	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.60 (NE)	0.60 (NE)	36.10 (NE)	-0.30 (NE)
Median	36.60	0.60	36.10	-0.30
Min - Max	36.6 - 36.6	0.6 - 0.6	36.1 - 36.1	-0.3 - -0.3
Cycle 37 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.50 (NE)	0.50 (NE)	NE (NE)	NE (NE)
Median	36.50	0.50	NE	NE
Min - Max	36.5 - 36.5	0.5 - 0.5	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.40 (NE)	0.40 (NE)	36.00 (NE)	-0.40 (NE)
Median	36.40	0.40	36.00	-0.40
Min - Max	36.4 - 36.4	0.4 - 0.4	36.0 - 36.0	-0.4 - -0.4
Cycle 38 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.50 (NE)	0.50 (NE)	36.20 (NE)	-0.20 (NE)
Median	36.50	0.50	36.20	-0.20
Min - Max	36.5 - 36.5	0.5 - 0.5	36.2 - 36.2	-0.2 - -0.2
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.50 (NE)	0.50 (NE)	36.10 (NE)	-0.30 (NE)
Median	36.50	0.50	36.10	-0.30
Min - Max	36.5 - 36.5	0.5 - 0.5	36.1 - 36.1	-0.3 - -0.3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 38 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.40 (NE)	0.40 (NE)	NE (NE)	NE (NE)
Median	36.40	0.40	NE	NE
Min - Max	36.4 - 36.4	0.4 - 0.4	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.60 (NE)	0.60 (NE)	36.30 (NE)	-0.10 (NE)
Median	36.60	0.60	36.30	-0.10
Min - Max	36.6 - 36.6	0.6 - 0.6	36.3 - 36.3	-0.1 - -0.1
Cycle 38 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.60 (NE)	0.60 (NE)	NE (NE)	NE (NE)
Median	36.60	0.60	NE	NE
Min - Max	36.6 - 36.6	0.6 - 0.6	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.50 (NE)	0.50 (NE)	35.80 (NE)	-0.60 (NE)
Median	36.50	0.50	35.80	-0.60
Min - Max	36.5 - 36.5	0.5 - 0.5	35.8 - 35.8	-0.6 - -0.6
Cycle 39 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.80 (NE)	0.80 (NE)	36.10 (NE)	-0.30 (NE)
Median	36.80	0.80	36.10	-0.30
Min - Max	36.8 - 36.8	0.8 - 0.8	36.1 - 36.1	-0.3 - -0.3
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.50 (NE)	0.50 (NE)	NE (NE)	NE (NE)
Median	36.50	0.50	NE	NE
Min - Max	36.5 - 36.5	0.5 - 0.5	NE - NE	NE - NE
Cycle 39 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.60 (NE)	0.60 (NE)	36.40 (NE)	0.00 (NE)
Median	36.60	0.60	36.40	0.00
Min - Max	36.6 - 36.6	0.6 - 0.6	36.4 - 36.4	0.0 - 0.0
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.40 (NE)	0.40 (NE)	NE (NE)	NE (NE)
Median	36.40	0.40	NE	NE
Min - Max	36.4 - 36.4	0.4 - 0.4	NE - NE	NE - NE

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 39 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.60 (NE)	0.60 (NE)	36.00 (NE)	-0.40 (NE)
Median	36.60	0.60	36.00	-0.40
Min - Max	36.6 - 36.6	0.6 - 0.6	36.0 - 36.0	-0.4 - -0.4
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.50 (NE)	0.50 (NE)	NE (NE)	NE (NE)
Median	36.50	0.50	NE	NE
Min - Max	36.5 - 36.5	0.5 - 0.5	NE - NE	NE - NE
Cycle 40 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.50 (NE)	0.50 (NE)	36.15 (0.07)	-0.25 (0.07)
Median	36.50	0.50	36.15	-0.25
Min - Max	36.5 - 36.5	0.5 - 0.5	36.1 - 36.2	-0.3 - -0.2
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.60 (NE)	0.60 (NE)	NE (NE)	NE (NE)
Median	36.60	0.60	NE	NE
Min - Max	36.6 - 36.6	0.6 - 0.6	NE - NE	NE - NE
Cycle 40 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.40 (NE)	0.40 (NE)	35.90 (NE)	-0.50 (NE)
Median	36.40	0.40	35.90	-0.50
Min - Max	36.4 - 36.4	0.4 - 0.4	35.9 - 35.9	-0.5 - -0.5
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.40 (NE)	0.40 (NE)	NE (NE)	NE (NE)
Median	36.40	0.40	NE	NE
Min - Max	36.4 - 36.4	0.4 - 0.4	NE - NE	NE - NE
Cycle 40 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.60 (NE)	0.60 (NE)	35.80 (NE)	-0.60 (NE)
Median	36.60	0.60	35.80	-0.60
Min - Max	36.6 - 36.6	0.6 - 0.6	35.8 - 35.8	-0.6 - -0.6
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.50 (NE)	0.50 (NE)	NE (NE)	NE (NE)
Median	36.50	0.50	NE	NE
Min - Max	36.5 - 36.5	0.5 - 0.5	NE - NE	NE - NE

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Cycle 41 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.30 (NE)	0.30 (NE)	35.95 (0.21)	-0.45 (0.21)
Median	36.30	0.30	35.95	-0.45
Min - Max	36.3 - 36.3	0.3 - 0.3	35.8 - 36.1	-0.6 - -0.3
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.70 (NE)	0.70 (NE)	NE (NE)	NE (NE)
Median	36.70	0.70	NE	NE
Min - Max	36.7 - 36.7	0.7 - 0.7	NE - NE	NE - NE
Cycle 41 Day 8				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	36.30 (NE)	-0.10 (NE)
Median	NE	NE	36.30	-0.10
Min - Max	NE - NE	NE - NE	36.3 - 36.3	-0.1 - -0.1
Cycle 41 Day 15				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.60 (NE)	0.60 (NE)	36.00 (NE)	-0.40 (NE)
Median	36.60	0.60	36.00	-0.40
Min - Max	36.6 - 36.6	0.6 - 0.6	36.0 - 36.0	-0.4 - -0.4
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.50 (NE)	0.50 (NE)	NE (NE)	NE (NE)
Median	36.50	0.50	NE	NE
Min - Max	36.5 - 36.5	0.5 - 0.5	NE - NE	NE - NE
Cycle 42 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.50 (NE)	0.50 (NE)	36.00 (NE)	-0.40 (NE)
Median	36.50	0.50	36.00	-0.40
Min - Max	36.5 - 36.5	0.5 - 0.5	36.0 - 36.0	-0.4 - -0.4
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.70 (NE)	0.70 (NE)	NE (NE)	NE (NE)
Median	36.70	0.70	NE	NE
Min - Max	36.7 - 36.7	0.7 - 0.7	NE - NE	NE - NE
Cycle 42 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.60 (NE)	0.60 (NE)	NE (NE)	NE (NE)
Median	36.60	0.60	NE	NE
Min - Max	36.6 - 36.6	0.6 - 0.6	NE - NE	NE - NE

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.60 (NE)	0.60 (NE)	NE (NE)	NE (NE)
Median	36.60	0.60	NE	NE
Min - Max	36.6 - 36.6	0.6 - 0.6	NE - NE	NE - NE
Cycle 42 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.50 (NE)	0.50 (NE)	NE (NE)	NE (NE)
Median	36.50	0.50	NE	NE
Min - Max	36.5 - 36.5	0.5 - 0.5	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.40 (NE)	0.40 (NE)	NE (NE)	NE (NE)
Median	36.40	0.40	NE	NE
Min - Max	36.4 - 36.4	0.4 - 0.4	NE - NE	NE - NE
Cycle 43 Day 1				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.50 (NE)	0.50 (NE)	35.80 (NE)	-0.60 (NE)
Median	36.50	0.50	35.80	-0.60
Min - Max	36.5 - 36.5	0.5 - 0.5	35.8 - 35.8	-0.6 - -0.6
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.40 (NE)	0.40 (NE)	NE (NE)	NE (NE)
Median	36.40	0.40	NE	NE
Min - Max	36.4 - 36.4	0.4 - 0.4	NE - NE	NE - NE
Cycle 43 Day 8				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.60 (NE)	0.60 (NE)	NE (NE)	NE (NE)
Median	36.60	0.60	NE	NE
Min - Max	36.6 - 36.6	0.6 - 0.6	NE - NE	NE - NE
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.50 (NE)	0.50 (NE)	NE (NE)	NE (NE)
Median	36.50	0.50	NE	NE
Min - Max	36.5 - 36.5	0.5 - 0.5	NE - NE	NE - NE
Cycle 43 Day 15				
PRE PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.80 (NE)	0.80 (NE)	NE (NE)	NE (NE)
Median	36.80	0.80	NE	NE
Min - Max	36.8 - 36.8	0.8 - 0.8	NE - NE	NE - NE

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.60 (NE)	0.60 (NE)	NE (NE)	NE (NE)
Median	36.60	0.60	NE	NE
Min - Max	36.6 - 36.6	0.6 - 0.6	NE - NE	NE - NE
Cycle 44 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	35.90 (NE)	-0.50 (NE)
Median	NE	NE	35.90	-0.50
Min - Max	NE - NE	NE - NE	35.9 - 35.9	-0.5 - -0.5
Cycle 45 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	35.80 (NE)	-0.60 (NE)
Median	NE	NE	35.80	-0.60
Min - Max	NE - NE	NE - NE	35.8 - 35.8	-0.6 - -0.6
Cycle 46 Day 1				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	35.80 (NE)	-0.60 (NE)
Median	NE	NE	35.80	-0.60
Min - Max	NE - NE	NE - NE	35.8 - 35.8	-0.6 - -0.6
Study Drug Discontinuation				
n	74	72	140	139
Mean (SD)	36.45 (0.46)	0.00 (0.40)	36.44 (0.38)	-0.02 (0.39)
Median	36.50	0.00	36.50	0.00
Min - Max	35.0 - 37.5	-1.6 - 1.0	35.4 - 37.2	-1.1 - 1.1
Post-Baseline Last				
n	77	77	138	138
Mean (SD)	36.46 (0.46)	0.02 (0.41)	36.42 (0.44)	-0.02 (0.39)
Median	36.50	0.00	36.50	0.00
Min - Max	35.0 - 37.5	-1.6 - 1.0	33.6 - 37.2	-1.1 - 1.1
PRE PAC INFUSION				
n	1	1	5	5
Mean (SD)	35.00 (NE)	-1.80 (NE)	36.92 (0.22)	0.16 (0.29)
Median	35.00	-1.80	36.90	0.10
Min - Max	35.0 - 35.0	-1.8 - -1.8	36.6 - 37.2	-0.2 - 0.5
AFTER PAC INFUSION				
n	7	7	21	21
Mean (SD)	36.76 (0.22)	0.24 (0.21)	36.50 (0.48)	-0.02 (0.46)
Median	36.80	0.20	36.50	0.00
Min - Max	36.4 - 37.1	0.0 - 0.7	35.6 - 37.3	-1.4 - 0.9

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort A: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=87) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=166) Value at Visit	 Change from Baseline
Post-Baseline Minimum				
n	6	6	12	12
Mean (SD)	35.70 (0.52)	-0.58 (0.63)	36.10 (0.31)	-0.39 (0.38)
Median	35.75	-0.65	36.00	-0.35
Min - Max	35.0 - 36.4	-1.6 - 0.3	35.5 - 36.6	-1.0 - 0.2
PRE PAC INFUSION				
n	42	42	100	100
Mean (SD)	35.81 (0.52)	-0.59 (0.57)	35.83 (0.56)	-0.62 (0.48)
Median	36.00	-0.50	36.00	-0.50
Min - Max	34.0 - 36.6	-2.5 - 0.4	33.6 - 36.9	-2.4 - 0.0
AFTER PAC INFUSION				
n	37	37	52	52
Mean (SD)	35.93 (0.47)	-0.61 (0.40)	35.89 (0.50)	-0.58 (0.47)
Median	36.00	-0.50	36.00	-0.50
Min - Max	35.0 - 36.9	-1.4 - 0.0	35.0 - 36.9	-1.6 - 0.5
Post-Baseline Maximum				
n	6	6	8	8
Mean (SD)	37.43 (0.94)	0.68 (1.24)	36.96 (0.55)	0.65 (0.50)
Median	37.10	0.10	36.95	0.60
Min - Max	36.8 - 39.3	-0.1 - 3.1	35.9 - 37.8	0.0 - 1.4
PRE PAC INFUSION				
n	36	36	97	97
Mean (SD)	37.04 (0.43)	0.68 (0.53)	36.96 (0.51)	0.51 (0.43)
Median	36.95	0.60	36.90	0.50
Min - Max	36.5 - 38.5	0.0 - 2.3	34.0 - 38.9	-0.3 - 2.1
AFTER PAC INFUSION				
n	43	43	59	59
Mean (SD)	37.09 (0.46)	0.59 (0.49)	37.07 (0.38)	0.60 (0.42)
Median	37.00	0.60	37.00	0.50
Min - Max	35.9 - 38.1	-0.9 - 1.7	36.3 - 38.3	0.0 - 1.8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_A_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
Baseline				
n	72		144	
Mean (SD)	75.7 (7.8)		76.5 (10.0)	
Median	74.5		78.0	
Min - Max	57 - 92		41 - 95	
Cycle 1 Day 1				
PRE PAC INFUSION				
n	69	67	140	139
Mean (SD)	74.6 (8.1)	-1.3 (8.4)	75.7 (10.0)	-0.7 (9.9)
Median	74.0	0.0	78.0	0.0
Min - Max	46 - 92	-24 - 16	49 - 100	-27 - 28
AFTER PAC INFUSION				
n	71	69	140	139
Mean (SD)	75.8 (8.3)	-0.1 (9.6)	78.3 (10.3)	2.0 (11.3)
Median	76.0	0.0	78.0	2.0
Min - Max	51 - 102	-20 - 37	50 - 107	-27 - 43
Cycle 1 Day 8				
PRE PAC INFUSION				
n	72	69	135	135
Mean (SD)	73.3 (11.6)	-2.6 (11.0)	74.0 (9.7)	-2.3 (10.3)
Median	73.0	-2.0	76.0	0.0
Min - Max	18 - 99	-47 - 22	48 - 96	-31 - 26
AFTER PAC INFUSION				
n	62	61	126	126
Mean (SD)	74.1 (9.5)	-1.4 (9.8)	75.8 (10.6)	-0.5 (11.2)
Median	75.5	-1.0	77.5	-0.5
Min - Max	47 - 98	-35 - 18	46 - 109	-30 - 29
Cycle 1 Day 15				
PRE PAC INFUSION				
n	70	67	130	130
Mean (SD)	74.0 (8.0)	-2.2 (9.0)	73.7 (10.1)	-3.1 (10.6)
Median	75.0	-1.0	75.0	-2.0
Min - Max	54 - 90	-30 - 18	53 - 97	-27 - 25
AFTER PAC INFUSION				
n	57	55	116	116
Mean (SD)	74.2 (8.9)	-1.6 (9.5)	73.8 (8.8)	-2.8 (10.5)
Median	75.0	0.0	73.5	-2.5
Min - Max	56 - 98	-30 - 33	51 - 105	-31 - 28
Cycle 2 Day 1				
PRE PAC INFUSION				
n	73	71	130	129
Mean (SD)	74.8 (8.2)	-1.1 (7.9)	74.8 (10.7)	-1.7 (10.7)
Median	74.0	0.0	75.0	-1.0
Min - Max	50 - 93	-22 - 20	51 - 111	-28 - 31

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	67	66	123	122
Mean (SD)	75.3 (8.4)	-0.5 (8.4)	77.2 (9.7)	0.2 (11.0)
Median	75.0	0.0	78.0	0.0
Min - Max	57 - 100	-17 - 30	56 - 113	-25 - 33
Cycle 2 Day 8				
PRE PAC INFUSION				
n	72	70	127	126
Mean (SD)	74.6 (7.2)	-1.5 (7.8)	74.1 (10.4)	-2.9 (9.2)
Median	75.0	-1.0	75.0	-3.0
Min - Max	57 - 92	-16 - 20	50 - 97	-30 - 21
AFTER PAC INFUSION				
n	68	66	122	121
Mean (SD)	74.7 (8.1)	-1.6 (8.4)	75.8 (9.9)	-1.3 (10.9)
Median	75.0	-2.0	78.0	-1.0
Min - Max	57 - 95	-20 - 20	55 - 100	-28 - 34
Cycle 2 Day 15				
PRE PAC INFUSION				
n	69	67	123	122
Mean (SD)	73.3 (8.2)	-2.5 (8.7)	74.2 (9.0)	-3.1 (9.3)
Median	74.0	-2.0	75.0	-3.5
Min - Max	53 - 95	-24 - 20	54 - 98	-23 - 24
AFTER PAC INFUSION				
n	66	64	110	109
Mean (SD)	74.4 (9.9)	-1.2 (10.4)	74.2 (10.4)	-3.2 (11.2)
Median	73.0	-1.0	75.0	-3.0
Min - Max	53 - 100	-20 - 35	47 - 107	-32 - 27
Cycle 3 Day 1				
PRE PAC INFUSION				
n	70	68	121	121
Mean (SD)	75.7 (8.3)	-0.5 (8.9)	74.6 (9.3)	-3.0 (10.1)
Median	76.0	-0.5	76.0	-3.0
Min - Max	54 - 91	-20 - 23	48 - 97	-31 - 31
AFTER PAC INFUSION				
n	65	63	111	111
Mean (SD)	76.6 (9.8)	0.4 (9.4)	76.7 (11.1)	-0.9 (11.4)
Median	78.0	0.0	78.0	0.0
Min - Max	47 - 100	-24 - 30	43 - 120	-25 - 40
Cycle 3 Day 8				
PRE PAC INFUSION				
n	65	63	116	115
Mean (SD)	74.3 (8.7)	-2.1 (9.0)	73.8 (10.2)	-3.4 (10.2)
Median	75.0	-1.0	76.5	-2.0
Min - Max	54 - 93	-20 - 20	46 - 95	-30 - 24

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	59	57	105	104
Mean (SD)	73.6 (9.2)	-2.3 (10.1)	75.4 (10.0)	-1.9 (11.1)
Median	76.0	-1.0	76.0	-2.0
Min - Max	44 - 90	-27 - 20	54 - 117	-30 - 37
Cycle 3 Day 15				
PRE PAC INFUSION				
n	64	62	116	115
Mean (SD)	73.8 (8.2)	-2.1 (8.9)	73.4 (9.7)	-3.7 (9.5)
Median	75.0	-2.5	75.0	-4.0
Min - Max	49 - 90	-30 - 20	52 - 95	-32 - 26
AFTER PAC INFUSION				
n	60	58	107	107
Mean (SD)	74.6 (8.6)	-1.5 (8.9)	75.3 (9.6)	-1.8 (11.0)
Median	75.0	-2.5	76.0	-4.0
Min - Max	57 - 100	-20 - 30	50 - 116	-27 - 36
Cycle 4 Day 1				
PRE PAC INFUSION				
n	62	60	114	113
Mean (SD)	74.6 (9.0)	-2.2 (8.7)	73.5 (10.7)	-3.7 (11.4)
Median	74.5	-1.5	75.0	-4.0
Min - Max	60 - 95	-30 - 20	42 - 99	-31 - 22
AFTER PAC INFUSION				
n	60	58	105	105
Mean (SD)	75.7 (9.4)	-1.0 (9.2)	75.1 (9.8)	-2.2 (10.5)
Median	75.5	-0.5	75.0	-2.0
Min - Max	50 - 103	-21 - 30	54 - 110	-29 - 30
Cycle 4 Day 8				
PRE PAC INFUSION				
n	62	60	114	114
Mean (SD)	74.0 (9.7)	-2.8 (10.6)	74.0 (9.8)	-3.3 (10.8)
Median	74.5	-1.0	75.0	-2.5
Min - Max	34 - 95	-48 - 20	53 - 98	-29 - 28
AFTER PAC INFUSION				
n	60	58	107	107
Mean (SD)	75.7 (9.8)	-1.2 (10.3)	74.6 (11.1)	-2.9 (11.8)
Median	75.0	0.5	75.0	-4.0
Min - Max	52 - 103	-30 - 30	56 - 128	-27 - 48
Cycle 4 Day 15				
PRE PAC INFUSION				
n	57	55	105	105
Mean (SD)	73.7 (8.6)	-2.7 (10.0)	73.3 (9.4)	-4.0 (10.3)
Median	72.0	-3.0	74.0	-4.0
Min - Max	58 - 110	-22 - 40	47 - 99	-33 - 25

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	53	51	98	98
Mean (SD)	75.5 (7.8)	-1.0 (8.7)	73.9 (9.8)	-3.4 (11.1)
Median	76.0	-1.0	75.0	-1.5
Min - Max	58 - 95	-20 - 20	50 - 95	-26 - 24
Cycle 5 Day 1				
PRE PAC INFUSION				
n	56	55	108	108
Mean (SD)	74.2 (8.4)	-2.1 (9.4)	73.9 (9.7)	-3.0 (9.5)
Median	73.0	-1.0	75.0	-2.0
Min - Max	58 - 100	-23 - 30	51 - 94	-24 - 20
AFTER PAC INFUSION				
n	50	49	102	102
Mean (SD)	76.1 (8.0)	-0.3 (9.0)	75.9 (9.5)	-0.9 (10.0)
Median	76.0	0.0	76.0	0.0
Min - Max	60 - 100	-30 - 30	57 - 108	-25 - 27
Cycle 5 Day 8				
PRE PAC INFUSION				
n	55	54	105	105
Mean (SD)	74.6 (8.6)	-1.3 (8.9)	73.5 (9.9)	-3.4 (10.7)
Median	72.0	-0.5	74.0	-3.0
Min - Max	57 - 100	-20 - 30	46 - 94	-25 - 27
AFTER PAC INFUSION				
n	52	51	101	101
Mean (SD)	73.8 (8.6)	-2.0 (8.2)	75.0 (11.0)	-2.1 (11.8)
Median	75.0	-1.0	73.0	-2.0
Min - Max	53 - 100	-20 - 30	54 - 111	-30 - 31
Cycle 5 Day 15				
PRE PAC INFUSION				
n	51	50	100	100
Mean (SD)	73.0 (9.5)	-2.7 (9.9)	73.5 (10.3)	-3.3 (11.6)
Median	73.0	-2.5	73.5	-3.0
Min - Max	51 - 100	-30 - 30	51 - 105	-29 - 27
AFTER PAC INFUSION				
n	49	48	96	96
Mean (SD)	73.8 (9.5)	-2.0 (10.8)	75.3 (9.0)	-1.7 (11.0)
Median	74.0	-3.0	76.0	-2.0
Min - Max	51 - 100	-28 - 30	55 - 109	-26 - 29
Cycle 6 Day 1				
PRE PAC INFUSION				
n	52	51	101	101
Mean (SD)	73.2 (8.2)	-2.2 (9.2)	73.7 (11.6)	-3.3 (12.3)
Median	74.0	-2.0	76.0	-4.0
Min - Max	52 - 100	-24 - 30	39 - 97	-33 - 32

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	50	49	96	96
Mean (SD)	75.2 (8.3)	-0.3 (9.5)	77.5 (9.8)	0.8 (11.4)
Median	75.5	0.0	78.0	0.5
Min - Max	59 - 100	-30 - 30	52 - 109	-23 - 33
Cycle 6 Day 8				
PRE PAC INFUSION				
n	52	51	102	102
Mean (SD)	73.0 (8.1)	-2.6 (8.8)	74.5 (10.5)	-2.5 (11.2)
Median	75.5	-1.0	76.0	-1.0
Min - Max	56 - 90	-31 - 13	45 - 98	-34 - 24
AFTER PAC INFUSION				
n	48	47	97	97
Mean (SD)	74.0 (8.6)	-1.8 (7.7)	75.4 (10.3)	-1.7 (11.6)
Median	74.5	0.0	76.0	-3.0
Min - Max	55 - 95	-20 - 12	55 - 115	-30 - 35
Cycle 6 Day 15				
PRE PAC INFUSION				
n	51	50	98	98
Mean (SD)	74.1 (9.7)	-1.5 (11.4)	73.8 (10.6)	-3.2 (11.4)
Median	75.0	0.0	75.0	-2.0
Min - Max	47 - 110	-25 - 40	48 - 100	-33 - 30
AFTER PAC INFUSION				
n	48	47	91	91
Mean (SD)	74.4 (10.3)	-1.7 (12.6)	74.3 (10.6)	-2.9 (12.5)
Median	74.0	0.0	75.0	-3.0
Min - Max	53 - 110	-30 - 40	53 - 113	-28 - 33
Cycle 7 Day 1				
PRE PAC INFUSION				
n	49	49	93	93
Mean (SD)	72.1 (12.0)	-3.1 (12.2)	74.8 (12.3)	-2.3 (12.6)
Median	71.0	-3.0	75.0	-2.0
Min - Max	45 - 120	-25 - 50	43 - 122	-35 - 42
AFTER PAC INFUSION				
n	46	46	83	83
Mean (SD)	73.0 (7.8)	-2.1 (9.8)	75.3 (10.5)	-1.7 (13.6)
Median	72.0	-3.5	75.0	-1.0
Min - Max	56 - 100	-21 - 30	50 - 100	-38 - 30
Cycle 7 Day 8				
PRE PAC INFUSION				
n	49	49	85	85
Mean (SD)	71.9 (8.9)	-3.3 (9.5)	74.2 (11.5)	-2.5 (11.7)
Median	74.0	-4.0	75.0	-1.0
Min - Max	49 - 90	-23 - 20	45 - 101	-49 - 21

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	47	47	79	79
Mean (SD)	74.1 (6.9)	-1.3 (9.0)	73.8 (10.1)	-2.9 (11.7)
Median	75.0	0.0	74.0	-4.0
Min - Max	56 - 90	-20 - 20	56 - 107	-26 - 30
Cycle 7 Day 15				
PRE PAC INFUSION				
n	47	47	83	83
Mean (SD)	72.4 (8.5)	-2.6 (10.3)	72.5 (10.3)	-4.3 (12.0)
Median	74.0	-3.0	72.0	-4.0
Min - Max	53 - 88	-23 - 26	46 - 100	-44 - 25
AFTER PAC INFUSION				
n	42	42	80	80
Mean (SD)	72.6 (7.5)	-2.6 (9.3)	73.5 (10.1)	-3.7 (12.4)
Median	74.5	-2.0	73.0	-4.5
Min - Max	53 - 82	-30 - 20	53 - 117	-29 - 37
Cycle 8 Day 1				
PRE PAC INFUSION				
n	47	47	90	90
Mean (SD)	73.1 (8.2)	-2.0 (9.5)	75.0 (9.9)	-1.8 (9.7)
Median	75.0	-2.0	78.0	-1.5
Min - Max	49 - 90	-21 - 20	49 - 90	-30 - 23
AFTER PAC INFUSION				
n	45	45	78	78
Mean (SD)	73.8 (8.9)	-1.7 (9.9)	75.3 (11.8)	-1.8 (13.2)
Median	76.0	-2.0	76.0	0.0
Min - Max	53 - 90	-20 - 20	7 - 110	-71 - 30
Cycle 8 Day 8				
PRE PAC INFUSION				
n	45	45	81	81
Mean (SD)	73.5 (10.3)	-1.8 (12.0)	73.6 (10.2)	-3.1 (11.1)
Median	75.0	-2.0	74.0	-3.0
Min - Max	42 - 100	-33 - 30	42 - 100	-34 - 22
AFTER PAC INFUSION				
n	39	39	76	76
Mean (SD)	73.5 (8.6)	-2.0 (10.1)	74.6 (9.4)	-2.2 (11.4)
Median	75.0	-1.0	76.0	-1.5
Min - Max	48 - 88	-30 - 26	54 - 100	-30 - 27
Cycle 8 Day 15				
PRE PAC INFUSION				
n	45	45	77	77
Mean (SD)	74.2 (11.2)	-1.1 (12.7)	74.6 (9.7)	-2.7 (10.6)
Median	75.0	-2.0	75.0	-2.0
Min - Max	46 - 110	-30 - 45	48 - 104	-32 - 25

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	43	43	69	69
Mean (SD)	71.8 (8.9)	-3.7 (10.4)	74.8 (10.0)	-2.9 (11.8)
Median	72.0	-3.0	73.0	-3.0
Min - Max	51 - 90	-30 - 20	55 - 121	-25 - 41
Cycle 9 Day 1				
PRE PAC INFUSION				
n	37	37	77	77
Mean (SD)	74.3 (8.1)	-1.0 (10.3)	72.9 (9.4)	-3.5 (10.8)
Median	75.0	0.0	73.0	-4.0
Min - Max	59 - 100	-20 - 30	54 - 92	-30 - 19
AFTER PAC INFUSION				
n	35	35	65	65
Mean (SD)	73.3 (7.0)	-2.4 (8.9)	74.2 (9.9)	-2.3 (11.5)
Median	75.0	-1.0	75.0	-1.0
Min - Max	56 - 88	-30 - 14	48 - 105	-25 - 25
Cycle 9 Day 8				
PRE PAC INFUSION				
n	39	39	66	66
Mean (SD)	71.9 (10.1)	-3.7 (12.4)	71.5 (10.7)	-4.9 (10.8)
Median	75.0	-3.0	71.0	-6.0
Min - Max	49 - 95	-30 - 30	50 - 97	-33 - 25
AFTER PAC INFUSION				
n	39	39	61	61
Mean (SD)	73.5 (8.1)	-2.0 (10.1)	73.8 (11.1)	-2.5 (12.2)
Median	75.0	-1.0	73.0	-1.0
Min - Max	55 - 90	-30 - 20	52 - 103	-25 - 28
Cycle 9 Day 15				
PRE PAC INFUSION				
n	39	39	62	62
Mean (SD)	72.5 (9.8)	-3.0 (11.3)	72.3 (10.1)	-3.5 (10.7)
Median	74.0	-4.0	71.5	-0.5
Min - Max	47 - 95	-29 - 30	52 - 100	-29 - 22
AFTER PAC INFUSION				
n	37	37	55	55
Mean (SD)	74.2 (8.8)	-1.3 (10.3)	73.9 (10.4)	-2.2 (12.4)
Median	75.0	-1.0	74.0	0.0
Min - Max	49 - 100	-22 - 30	56 - 100	-28 - 29
Cycle 10 Day 1				
PRE PAC INFUSION				
n	39	39	70	70
Mean (SD)	72.9 (9.6)	-2.6 (10.7)	72.1 (10.9)	-4.7 (12.3)
Median	75.0	-3.0	72.5	-3.0
Min - Max	46 - 90	-26 - 20	37 - 94	-53 - 24

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	37	37	58	58
Mean (SD)	75.0 (9.5)	-0.5 (11.4)	75.8 (9.2)	-1.1 (11.5)
Median	75.0	-1.0	73.5	0.0
Min - Max	52 - 100	-20 - 30	57 - 100	-24 - 28
Cycle 10 Day 8				
PRE PAC INFUSION				
n	38	38	61	61
Mean (SD)	71.7 (10.6)	-4.2 (11.1)	71.3 (10.7)	-5.7 (11.8)
Median	72.5	-4.0	72.0	-2.0
Min - Max	48 - 100	-27 - 30	41 - 91	-40 - 22
AFTER PAC INFUSION				
n	37	37	57	57
Mean (SD)	74.9 (10.0)	-1.2 (11.0)	71.7 (9.9)	-4.8 (12.6)
Median	74.0	0.0	73.0	-2.0
Min - Max	60 - 100	-20 - 30	47 - 92	-38 - 22
Cycle 10 Day 15				
PRE PAC INFUSION				
n	36	36	59	59
Mean (SD)	72.4 (9.1)	-3.0 (10.6)	71.0 (9.3)	-5.9 (11.7)
Median	73.0	-2.0	71.0	-4.0
Min - Max	55 - 100	-21 - 30	55 - 93	-34 - 21
AFTER PAC INFUSION				
n	34	34	52	52
Mean (SD)	73.3 (8.5)	-2.1 (9.9)	72.6 (9.3)	-4.1 (12.1)
Median	75.0	-0.5	71.5	-4.5
Min - Max	57 - 85	-20 - 20	50 - 96	-35 - 20
Cycle 11 Day 1				
PRE PAC INFUSION				
n	35	35	64	64
Mean (SD)	73.8 (10.8)	-2.0 (12.2)	72.6 (10.7)	-4.3 (11.3)
Median	74.0	-2.0	73.0	-2.5
Min - Max	48 - 100	-28 - 30	43 - 90	-40 - 17
AFTER PAC INFUSION				
n	34	34	49	49
Mean (SD)	75.1 (8.8)	-1.2 (10.4)	73.4 (10.0)	-3.1 (12.0)
Median	75.5	-3.0	75.0	-2.0
Min - Max	56 - 100	-18 - 30	44 - 101	-39 - 26
Cycle 11 Day 8				
PRE PAC INFUSION				
n	33	33	48	48
Mean (SD)	73.4 (11.3)	-2.9 (13.8)	74.1 (11.3)	-2.2 (11.9)
Median	73.0	-2.0	75.0	-1.5
Min - Max	55 - 110	-30 - 40	51 - 100	-29 - 30

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	31	31	46	46
Mean (SD)	76.4 (10.1)	-0.1 (12.6)	73.7 (10.7)	-2.9 (12.8)
Median	76.0	-1.0	73.5	-1.0
Min - Max	59 - 110	-22 - 40	48 - 100	-27 - 30
Cycle 11 Day 15				
PRE PAC INFUSION				
n	34	34	44	44
Mean (SD)	72.6 (7.9)	-3.7 (9.6)	71.8 (10.2)	-4.4 (11.7)
Median	73.5	-2.5	70.5	-5.5
Min - Max	53 - 90	-23 - 15	52 - 88	-35 - 23
AFTER PAC INFUSION				
n	31	31	44	44
Mean (SD)	73.5 (8.9)	-3.1 (11.1)	73.0 (9.2)	-3.3 (11.6)
Median	73.0	-5.0	72.5	-2.0
Min - Max	55 - 100	-20 - 30	47 - 91	-25 - 24
Cycle 12 Day 1				
PRE PAC INFUSION				
n	33	33	57	57
Mean (SD)	73.7 (8.9)	-3.0 (11.1)	73.3 (10.2)	-3.5 (11.5)
Median	74.0	-4.0	73.0	-2.0
Min - Max	58 - 90	-22 - 20	48 - 100	-30 - 30
AFTER PAC INFUSION				
n	30	30	43	43
Mean (SD)	75.0 (9.4)	-2.4 (12.0)	76.1 (9.9)	-0.3 (11.8)
Median	75.0	-2.0	78.0	0.0
Min - Max	50 - 100	-29 - 30	55 - 98	-26 - 26
Cycle 12 Day 8				
PRE PAC INFUSION				
n	30	30	42	42
Mean (SD)	73.3 (7.8)	-3.9 (10.4)	70.5 (11.7)	-5.4 (11.4)
Median	74.0	-2.5	70.5	-4.0
Min - Max	60 - 90	-25 - 23	48 - 100	-34 - 16
AFTER PAC INFUSION				
n	24	24	40	40
Mean (SD)	73.9 (7.1)	-4.3 (7.8)	74.0 (11.2)	-1.4 (10.5)
Median	75.5	-4.5	73.5	0.0
Min - Max	59 - 88	-19 - 11	56 - 108	-28 - 19
Cycle 12 Day 15				
PRE PAC INFUSION				
n	30	30	43	43
Mean (SD)	72.0 (8.7)	-5.4 (10.4)	73.4 (9.6)	-3.3 (10.9)
Median	70.0	-7.5	73.0	-2.0
Min - Max	55 - 85	-24 - 14	52 - 94	-31 - 16

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	26	26	40	40
Mean (SD)	75.3 (6.9)	-2.3 (9.1)	73.3 (9.5)	-3.3 (11.5)
Median	76.5	-3.0	72.0	-0.5
Min - Max	60 - 87	-19 - 13	52 - 94	-30 - 22
Cycle 13 Day 1				
PRE PAC INFUSION				
n	28	28	49	49
Mean (SD)	73.9 (8.7)	-2.9 (11.7)	72.2 (10.4)	-4.3 (11.1)
Median	74.5	-4.0	72.0	-1.0
Min - Max	57 - 90	-22 - 25	37 - 88	-33 - 17
AFTER PAC INFUSION				
n	25	25	36	36
Mean (SD)	73.2 (6.8)	-4.3 (8.0)	73.7 (9.5)	-3.3 (10.5)
Median	74.0	-5.0	72.5	0.0
Min - Max	60 - 88	-20 - 13	56 - 95	-25 - 16
Cycle 13 Day 8				
PRE PAC INFUSION				
n	26	26	36	36
Mean (SD)	69.9 (9.1)	-7.5 (8.7)	73.3 (10.7)	-3.2 (12.7)
Median	72.5	-8.0	72.5	-3.5
Min - Max	55 - 83	-23 - 9	52 - 104	-34 - 20
AFTER PAC INFUSION				
n	25	25	36	36
Mean (SD)	73.4 (7.3)	-4.5 (7.1)	74.0 (11.2)	-2.5 (11.8)
Median	74.0	-2.0	75.0	-1.0
Min - Max	59 - 88	-19 - 8	51 - 96	-30 - 22
Cycle 13 Day 15				
PRE PAC INFUSION				
n	25	25	35	35
Mean (SD)	72.3 (8.1)	-5.2 (9.5)	72.3 (10.0)	-5.0 (13.0)
Median	72.0	-5.0	76.0	-3.0
Min - Max	50 - 89	-20 - 13	51 - 89	-32 - 23
AFTER PAC INFUSION				
n	23	23	35	35
Mean (SD)	73.3 (8.9)	-4.7 (8.1)	74.4 (8.1)	-2.9 (11.6)
Median	75.0	-5.0	74.0	-4.0
Min - Max	52 - 94	-18 - 9	58 - 95	-27 - 24
Cycle 14 Day 1				
PRE PAC INFUSION				
n	26	26	42	42
Mean (SD)	71.3 (9.1)	-5.8 (10.8)	74.0 (9.5)	-2.3 (12.2)
Median	73.0	-5.0	75.5	-2.0
Min - Max	50 - 85	-22 - 11	53 - 93	-27 - 22

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	24	24	33	33
Mean (SD)	72.6 (8.0)	-4.7 (8.8)	76.7 (11.2)	0.1 (12.6)
Median	74.0	-6.5	78.0	0.0
Min - Max	50 - 84	-21 - 11	49 - 98	-18 - 30
Cycle 14 Day 8				
PRE PAC INFUSION				
n	25	25	32	32
Mean (SD)	72.0 (7.4)	-5.4 (9.6)	73.5 (10.7)	-4.0 (12.2)
Median	72.0	-6.0	74.5	-1.0
Min - Max	57 - 83	-25 - 7	42 - 100	-38 - 22
AFTER PAC INFUSION				
n	24	24	31	31
Mean (SD)	71.1 (9.0)	-6.7 (9.9)	74.1 (8.9)	-3.8 (10.2)
Median	71.0	-5.5	75.0	-4.0
Min - Max	49 - 83	-30 - 10	54 - 90	-22 - 24
Cycle 14 Day 15				
PRE PAC INFUSION				
n	25	25	29	29
Mean (SD)	70.8 (7.4)	-6.6 (9.7)	73.8 (9.4)	-2.7 (12.7)
Median	71.0	-9.0	75.0	-1.0
Min - Max	50 - 82	-25 - 6	54 - 92	-28 - 26
AFTER PAC INFUSION				
n	24	24	28	28
Mean (SD)	70.9 (8.5)	-7.0 (10.4)	75.4 (8.8)	-1.6 (12.7)
Median	70.0	-9.0	78.0	-1.5
Min - Max	50 - 83	-30 - 10	53 - 90	-30 - 24
Cycle 15 Day 1				
PRE PAC INFUSION				
n	20	20	35	35
Mean (SD)	74.0 (8.9)	-3.2 (9.5)	74.0 (11.4)	-2.9 (12.2)
Median	74.0	-1.5	72.0	0.0
Min - Max	50 - 85	-26 - 10	46 - 103	-31 - 23
AFTER PAC INFUSION				
n	19	19	25	25
Mean (SD)	75.2 (8.4)	-2.3 (8.3)	74.0 (10.2)	-3.4 (13.0)
Median	78.0	-1.0	74.0	-1.0
Min - Max	50 - 88	-20 - 9	52 - 100	-31 - 24
Cycle 15 Day 8				
PRE PAC INFUSION				
n	18	18	27	27
Mean (SD)	74.2 (6.4)	-3.2 (8.0)	72.6 (9.4)	-4.7 (11.3)
Median	75.0	-6.5	70.0	-4.0
Min - Max	60 - 82	-14 - 12	48 - 88	-32 - 23

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	18	18	27	27
Mean (SD)	75.6 (7.3)	-1.8 (8.0)	74.6 (8.6)	-2.7 (12.4)
Median	76.0	-1.5	76.0	0.0
Min - Max	60 - 87	-12 - 13	57 - 90	-19 - 27
Cycle 15 Day 15				
PRE PAC INFUSION				
n	19	19	25	25
Mean (SD)	70.3 (7.2)	-7.3 (8.9)	73.0 (10.8)	-5.2 (11.6)
Median	70.0	-6.0	73.0	-5.0
Min - Max	56 - 83	-27 - 6	47 - 94	-33 - 19
AFTER PAC INFUSION				
n	19	19	25	25
Mean (SD)	74.4 (8.6)	-3.3 (10.8)	73.1 (9.4)	-5.1 (12.2)
Median	75.0	-3.0	71.0	-2.0
Min - Max	61 - 101	-19 - 27	60 - 94	-28 - 23
Cycle 16 Day 1				
PRE PAC INFUSION				
n	21	21	32	32
Mean (SD)	75.8 (7.4)	-1.5 (10.6)	74.6 (10.0)	-3.1 (13.1)
Median	75.0	-3.0	74.0	-3.0
Min - Max	62 - 98	-20 - 24	54 - 100	-26 - 30
AFTER PAC INFUSION				
n	20	20	24	24
Mean (SD)	74.8 (7.1)	-2.9 (7.3)	78.5 (9.3)	1.8 (12.8)
Median	76.5	-1.5	79.5	1.5
Min - Max	60 - 87	-19 - 13	60 - 100	-20 - 30
Cycle 16 Day 8				
PRE PAC INFUSION				
n	20	20	23	23
Mean (SD)	72.8 (5.9)	-4.9 (7.5)	70.9 (10.6)	-5.4 (13.0)
Median	73.0	-5.5	71.0	-3.0
Min - Max	61 - 84	-21 - 10	46 - 88	-34 - 23
AFTER PAC INFUSION				
n	19	19	23	23
Mean (SD)	74.1 (7.3)	-3.2 (6.5)	76.0 (11.7)	-0.4 (13.7)
Median	74.0	-5.0	79.0	0.0
Min - Max	58 - 88	-13 - 14	42 - 94	-34 - 24
Cycle 16 Day 15				
PRE PAC INFUSION				
n	18	18	25	25
Mean (SD)	71.8 (8.1)	-6.2 (8.5)	73.1 (9.6)	-3.2 (13.4)
Median	72.0	-5.5	72.0	-1.0
Min - Max	60 - 84	-24 - 7	53 - 97	-27 - 22

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	17	17	24	24
Mean (SD)	75.2 (8.4)	-2.4 (7.4)	74.7 (8.5)	-1.5 (11.1)
Median	76.0	-6.0	75.5	-1.0
Min - Max	54 - 86	-11 - 10	54 - 90	-22 - 24
Cycle 17 Day 1				
PRE PAC INFUSION				
n	18	18	31	31
Mean (SD)	71.2 (5.8)	-5.1 (7.7)	73.2 (10.9)	-4.2 (14.6)
Median	70.5	-4.0	74.0	-5.0
Min - Max	61 - 80	-17 - 6	51 - 95	-30 - 22
AFTER PAC INFUSION				
n	17	17	23	23
Mean (SD)	74.4 (7.5)	-2.3 (8.8)	75.5 (9.1)	-0.8 (11.8)
Median	75.0	-4.0	76.0	0.0
Min - Max	58 - 85	-16 - 11	55 - 99	-25 - 20
Cycle 17 Day 8				
PRE PAC INFUSION				
n	16	16	20	20
Mean (SD)	71.4 (7.7)	-5.4 (10.3)	72.5 (10.4)	-3.4 (14.2)
Median	71.5	-7.0	71.0	-2.0
Min - Max	60 - 84	-23 - 13	49 - 90	-31 - 28
AFTER PAC INFUSION				
n	16	16	20	20
Mean (SD)	71.4 (7.4)	-5.4 (7.2)	73.9 (9.7)	-1.9 (14.1)
Median	72.0	-7.0	73.5	-2.0
Min - Max	60 - 82	-15 - 12	52 - 92	-24 - 26
Cycle 17 Day 15				
PRE PAC INFUSION				
n	17	17	21	21
Mean (SD)	71.8 (8.2)	-5.2 (10.2)	74.6 (12.7)	-0.5 (15.4)
Median	70.0	-5.0	74.0	-1.0
Min - Max	58 - 92	-27 - 18	47 - 100	-33 - 30
AFTER PAC INFUSION				
n	17	17	22	22
Mean (SD)	72.1 (7.9)	-4.9 (7.6)	75.1 (12.1)	0.0 (14.0)
Median	74.0	-6.0	72.5	-1.0
Min - Max	58 - 86	-22 - 12	53 - 100	-23 - 30
Cycle 18 Day 1				
PRE PAC INFUSION				
n	16	16	24	24
Mean (SD)	72.6 (7.7)	-4.3 (10.3)	71.9 (11.6)	-3.7 (16.9)
Median	73.0	-3.5	71.0	-5.5
Min - Max	60 - 86	-25 - 12	48 - 100	-32 - 30

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	14	14	21	21
Mean (SD)	73.1 (8.0)	-4.6 (8.9)	75.0 (10.0)	-0.4 (14.0)
Median	73.0	-7.0	73.0	0.0
Min - Max	60 - 88	-16 - 14	50 - 94	-26 - 22
Cycle 18 Day 8				
PRE PAC INFUSION				
n	14	14	21	21
Mean (SD)	71.9 (9.2)	-4.8 (10.0)	72.8 (9.4)	-2.1 (12.0)
Median	73.5	-5.0	71.0	-2.0
Min - Max	56 - 83	-22 - 11	57 - 100	-23 - 30
AFTER PAC INFUSION				
n	14	14	20	20
Mean (SD)	73.6 (8.1)	-3.1 (7.3)	76.0 (9.6)	1.4 (13.9)
Median	74.0	-3.0	73.0	0.0
Min - Max	59 - 86	-13 - 12	60 - 100	-19 - 30
Cycle 18 Day 15				
PRE PAC INFUSION				
n	15	15	20	20
Mean (SD)	73.2 (6.8)	-4.1 (7.9)	71.6 (10.7)	-3.3 (15.6)
Median	72.0	-8.0	72.5	-4.0
Min - Max	60 - 85	-13 - 10	44 - 84	-36 - 25
AFTER PAC INFUSION				
n	15	15	19	19
Mean (SD)	76.2 (8.2)	-1.1 (9.1)	73.2 (10.8)	-1.3 (13.2)
Median	76.0	-4.0	72.0	1.0
Min - Max	60 - 96	-11 - 22	56 - 97	-26 - 24
Cycle 19 Day 1				
PRE PAC INFUSION				
n	11	11	26	26
Mean (SD)	72.2 (6.1)	-5.5 (8.5)	73.2 (9.1)	-2.9 (12.2)
Median	72.0	-3.0	72.0	-1.5
Min - Max	63 - 80	-22 - 5	54 - 90	-22 - 23
AFTER PAC INFUSION				
n	10	10	19	19
Mean (SD)	69.9 (7.4)	-8.0 (8.6)	76.5 (10.1)	2.8 (14.4)
Median	70.0	-10.0	77.0	5.0
Min - Max	56 - 84	-17 - 10	59 - 97	-31 - 31
Cycle 19 Day 8				
PRE PAC INFUSION				
n	9	9	20	20
Mean (SD)	70.9 (7.3)	-6.1 (10.0)	74.4 (8.6)	-0.3 (12.0)
Median	70.0	-7.0	73.5	-1.5
Min - Max	63 - 85	-19 - 11	62 - 90	-16 - 24

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	9	9	19	19
Mean (SD)	72.3 (8.7)	-4.7 (8.0)	75.9 (9.9)	2.0 (13.0)
Median	71.0	0.0	77.0	3.0
Min - Max	57 - 86	-17 - 6	53 - 100	-23 - 30
Cycle 19 Day 15				
PRE PAC INFUSION				
n	10	10	20	20
Mean (SD)	71.9 (7.4)	-6.0 (10.5)	73.5 (11.8)	-0.8 (14.9)
Median	71.5	-4.5	70.0	0.0
Min - Max	59 - 82	-23 - 12	59 - 100	-27 - 30
AFTER PAC INFUSION				
n	9	9	19	19
Mean (SD)	77.1 (4.6)	-1.7 (4.4)	73.6 (11.0)	0.2 (16.2)
Median	78.0	0.0	75.0	2.0
Min - Max	70 - 85	-7 - 4	50 - 92	-34 - 24
Cycle 20 Day 1				
PRE PAC INFUSION				
n	11	11	23	23
Mean (SD)	73.8 (8.1)	-3.8 (7.4)	73.6 (12.8)	-3.4 (14.2)
Median	74.0	-7.0	72.0	-4.0
Min - Max	60 - 87	-11 - 13	50 - 100	-28 - 30
AFTER PAC INFUSION				
n	10	10	17	17
Mean (SD)	75.4 (8.7)	-2.5 (11.2)	77.7 (13.5)	2.1 (17.0)
Median	74.0	-4.5	79.0	2.0
Min - Max	63 - 90	-19 - 20	48 - 112	-28 - 32
Cycle 20 Day 8				
PRE PAC INFUSION				
n	9	9	16	16
Mean (SD)	72.2 (7.8)	-4.9 (9.2)	74.9 (10.9)	-1.2 (12.9)
Median	70.0	-5.0	70.5	-1.0
Min - Max	61 - 86	-21 - 12	62 - 100	-20 - 30
AFTER PAC INFUSION				
n	9	9	16	16
Mean (SD)	74.4 (8.6)	-2.7 (10.4)	76.9 (10.1)	0.8 (11.8)
Median	72.0	-6.0	75.5	2.5
Min - Max	68 - 96	-12 - 22	60 - 91	-22 - 20
Cycle 20 Day 15				
PRE PAC INFUSION				
n	10	10	16	16
Mean (SD)	71.3 (6.8)	-6.6 (7.9)	72.6 (7.9)	-3.3 (10.4)
Median	71.5	-6.0	71.0	-2.0
Min - Max	58 - 80	-19 - 4	61 - 90	-19 - 20

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	10	10	16	16
Mean (SD)	75.0 (5.7)	-2.9 (7.7)	73.6 (10.5)	-2.3 (11.3)
Median	73.5	-4.0	75.5	1.0
Min - Max	68 - 84	-10 - 10	49 - 90	-27 - 20
Cycle 21 Day 1				
PRE PAC INFUSION				
n	9	9	21	21
Mean (SD)	72.1 (8.1)	-5.3 (12.2)	74.0 (8.9)	-3.5 (12.8)
Median	75.0	0.0	72.0	-4.0
Min - Max	58 - 81	-27 - 10	62 - 90	-32 - 23
AFTER PAC INFUSION				
n	6	6	15	15
Mean (SD)	69.3 (7.0)	-8.5 (8.3)	76.8 (6.3)	0.6 (12.1)
Median	70.0	-6.5	76.0	4.0
Min - Max	58 - 79	-24 - 0	62 - 90	-32 - 19
Cycle 21 Day 8				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	72.0 (9.2)	-5.6 (9.8)	72.1 (10.2)	-3.9 (12.4)
Median	73.0	-4.0	70.5	-0.5
Min - Max	57 - 84	-28 - 5	57 - 87	-22 - 15
AFTER PAC INFUSION				
n	9	9	14	14
Mean (SD)	74.2 (7.1)	-3.3 (7.2)	77.5 (9.0)	1.6 (11.4)
Median	74.0	-6.0	77.0	3.0
Min - Max	62 - 87	-10 - 13	62 - 94	-20 - 19
Cycle 21 Day 15				
PRE PAC INFUSION				
n	9	9	15	15
Mean (SD)	74.1 (8.5)	-4.7 (8.8)	70.9 (9.4)	-5.3 (10.4)
Median	76.0	-5.0	70.0	-3.0
Min - Max	60 - 88	-20 - 6	60 - 88	-20 - 10
AFTER PAC INFUSION				
n	8	8	15	15
Mean (SD)	71.3 (9.7)	-7.3 (4.6)	74.8 (10.4)	-1.4 (11.6)
Median	75.5	-6.5	74.0	2.0
Min - Max	55 - 80	-16 - 0	54 - 90	-22 - 13
Cycle 22 Day 1				
PRE PAC INFUSION				
n	10	10	21	21
Mean (SD)	72.3 (8.6)	-4.5 (10.1)	73.3 (6.8)	-4.2 (12.6)
Median	71.0	-5.5	72.0	-2.0
Min - Max	60 - 91	-16 - 17	59 - 83	-28 - 25

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	7	7	15	15
Mean (SD)	73.4 (10.1)	-3.9 (10.6)	77.4 (7.9)	1.2 (10.8)
Median	74.0	-5.0	79.0	5.0
Min - Max	60 - 87	-21 - 13	60 - 90	-16 - 23
Cycle 22 Day 8				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	73.3 (5.3)	-4.2 (5.7)	70.0 (9.1)	-5.9 (15.5)
Median	71.0	-3.0	71.0	-1.0
Min - Max	68 - 83	-12 - 6	54 - 86	-35 - 20
AFTER PAC INFUSION				
n	9	9	14	14
Mean (SD)	75.2 (12.9)	-2.3 (10.2)	74.6 (7.2)	-1.3 (11.4)
Median	70.0	-2.0	75.5	0.5
Min - Max	56 - 99	-15 - 14	60 - 86	-22 - 22
Cycle 22 Day 15				
PRE PAC INFUSION				
n	7	7	14	14
Mean (SD)	70.4 (7.7)	-7.0 (11.1)	72.5 (7.3)	-2.7 (9.9)
Median	70.0	-4.0	70.5	-1.5
Min - Max	61 - 81	-24 - 7	62 - 85	-19 - 11
AFTER PAC INFUSION				
n	7	7	14	14
Mean (SD)	71.3 (8.0)	-6.1 (7.9)	76.9 (13.5)	1.7 (15.8)
Median	72.0	-7.0	78.5	4.0
Min - Max	56 - 80	-15 - 5	43 - 96	-33 - 27
Cycle 23 Day 1				
PRE PAC INFUSION				
n	9	9	19	19
Mean (SD)	69.6 (8.5)	-7.4 (12.6)	73.9 (9.3)	-3.1 (11.5)
Median	70.0	-7.0	78.0	-2.0
Min - Max	57 - 85	-25 - 15	56 - 85	-20 - 17
AFTER PAC INFUSION				
n	7	7	13	13
Mean (SD)	71.3 (3.4)	-6.0 (7.4)	73.1 (10.6)	-2.2 (13.1)
Median	72.0	-8.0	75.0	2.0
Min - Max	65 - 75	-17 - 3	52 - 92	-27 - 16
Cycle 23 Day 8				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	68.0 (6.1)	-8.5 (7.4)	71.5 (8.3)	-3.9 (13.6)
Median	69.5	-9.0	70.0	-2.0
Min - Max	60 - 77	-24 - 0	57 - 85	-22 - 19

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	70.5 (11.4)	-6.0 (10.8)	73.6 (8.4)	-1.7 (11.6)
Median	73.0	-4.0	73.0	-2.0
Min - Max	55 - 84	-24 - 11	54 - 86	-22 - 17
Cycle 23 Day 15				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	68.8 (6.9)	-7.8 (7.3)	71.0 (7.5)	-3.8 (11.0)
Median	70.0	-7.0	72.0	-3.0
Min - Max	60 - 80	-23 - 0	60 - 85	-20 - 11
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	74.0 (8.9)	-2.5 (8.4)	76.2 (9.0)	1.4 (10.7)
Median	78.0	-2.0	79.0	5.0
Min - Max	55 - 81	-16 - 10	54 - 87	-22 - 16
Cycle 24 Day 1				
PRE PAC INFUSION				
n	9	9	17	17
Mean (SD)	75.2 (6.8)	-1.8 (10.2)	71.6 (10.2)	-7.3 (9.4)
Median	73.0	-2.0	70.0	-6.0
Min - Max	68 - 87	-14 - 17	58 - 90	-20 - 10
AFTER PAC INFUSION				
n	7	7	12	12
Mean (SD)	73.0 (6.4)	-4.3 (9.5)	73.8 (11.4)	-3.1 (11.9)
Median	70.0	-5.0	74.5	0.0
Min - Max	65 - 82	-17 - 12	54 - 90	-28 - 10
Cycle 24 Day 8				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	64.8 (8.3)	-11.8 (11.2)	70.8 (9.2)	-5.8 (9.9)
Median	64.0	-10.0	70.0	-2.0
Min - Max	51 - 78	-34 - 4	55 - 87	-21 - 9
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	69.8 (11.2)	-6.8 (9.1)	73.7 (8.0)	-2.9 (10.6)
Median	70.0	-8.5	73.0	1.0
Min - Max	50 - 84	-20 - 9	57 - 85	-19 - 12
Cycle 24 Day 15				
PRE PAC INFUSION				
n	8	8	12	12
Mean (SD)	72.4 (8.2)	-4.1 (10.7)	71.5 (9.6)	-5.4 (12.0)
Median	71.5	-1.5	72.5	-3.5
Min - Max	57 - 83	-28 - 9	48 - 86	-28 - 10

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	8	8	12	12
Mean (SD)	75.9 (11.2)	-0.6 (12.8)	71.9 (7.2)	-5.0 (10.4)
Median	72.5	-2.5	72.5	-3.5
Min - Max	59 - 89	-17 - 18	58 - 81	-24 - 10
Cycle 25 Day 1				
PRE PAC INFUSION				
n	8	8	14	14
Mean (SD)	69.6 (7.6)	-7.8 (11.7)	73.5 (11.0)	-5.6 (11.4)
Median	70.0	-5.0	73.0	-5.0
Min - Max	58 - 82	-24 - 4	53 - 90	-27 - 10
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	70.4 (6.3)	-6.4 (9.3)	70.4 (10.5)	-7.7 (11.2)
Median	70.0	-9.0	72.0	-8.0
Min - Max	62 - 81	-16 - 11	48 - 81	-28 - 6
Cycle 25 Day 8				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	70.6 (4.6)	-6.3 (7.7)	73.2 (6.8)	-4.1 (8.6)
Median	71.0	-5.0	75.0	-8.0
Min - Max	65 - 78	-17 - 4	62 - 84	-14 - 8
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	73.6 (7.7)	-3.3 (6.8)	72.8 (7.0)	-4.6 (8.9)
Median	74.0	-3.0	72.0	-6.0
Min - Max	60 - 82	-10 - 9	61 - 85	-15 - 9
Cycle 25 Day 15				
PRE PAC INFUSION				
n	7	7	10	10
Mean (SD)	69.6 (8.2)	-7.3 (9.1)	72.2 (8.0)	-5.4 (9.5)
Median	69.0	-2.0	74.0	-5.0
Min - Max	59 - 80	-23 - 0	54 - 81	-22 - 8
AFTER PAC INFUSION				
n	7	7	10	10
Mean (SD)	73.3 (10.9)	-3.6 (14.2)	73.0 (12.6)	-4.6 (12.6)
Median	76.0	0.0	74.0	-2.0
Min - Max	52 - 85	-30 - 14	50 - 91	-26 - 11
Cycle 26 Day 1				
PRE PAC INFUSION				
n	8	8	14	14
Mean (SD)	69.3 (9.0)	-8.1 (12.8)	71.0 (10.8)	-9.4 (11.4)
Median	67.5	-10.0	72.0	-9.0
Min - Max	60 - 85	-25 - 15	48 - 90	-32 - 6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	74.1 (8.6)	-2.7 (10.1)	71.9 (9.3)	-6.6 (10.0)
Median	70.0	-3.0	75.0	-9.0
Min - Max	65 - 85	-17 - 15	54 - 81	-22 - 5
Cycle 26 Day 8				
PRE PAC INFUSION				
n	7	7	7	7
Mean (SD)	70.9 (4.7)	-6.0 (9.3)	70.3 (13.7)	-8.3 (15.3)
Median	70.0	-4.0	75.0	-8.0
Min - Max	63 - 77	-22 - 7	50 - 93	-29 - 13
AFTER PAC INFUSION				
n	7	7	7	7
Mean (SD)	71.0 (7.8)	-5.9 (8.0)	72.6 (15.3)	-6.0 (18.1)
Median	70.0	-4.0	77.0	3.0
Min - Max	61 - 81	-20 - 3	42 - 90	-41 - 10
Cycle 26 Day 15				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	71.0 (8.8)	-5.9 (11.2)	70.9 (8.5)	-7.6 (8.7)
Median	73.0	0.0	75.0	-6.0
Min - Max	55 - 80	-30 - 2	54 - 79	-22 - 5
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	73.4 (5.6)	-3.4 (5.5)	77.7 (11.0)	-0.8 (11.0)
Median	73.0	-5.0	79.0	1.0
Min - Max	65 - 83	-10 - 5	52 - 88	-24 - 10
Cycle 27 Day 1				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	70.7 (7.8)	-7.7 (10.0)	75.3 (7.7)	-5.1 (9.0)
Median	70.0	-10.0	76.5	-3.0
Min - Max	62 - 83	-20 - 13	61 - 87	-20 - 8
AFTER PAC INFUSION				
n	8	8	8	8
Mean (SD)	72.5 (7.7)	-5.5 (5.3)	69.6 (13.7)	-7.4 (14.2)
Median	70.0	-5.0	71.0	-5.5
Min - Max	60 - 85	-13 - 0	50 - 95	-26 - 15
Cycle 27 Day 8				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	72.8 (6.4)	-2.7 (7.8)	73.0 (6.9)	-5.3 (7.1)
Median	72.0	0.0	72.0	-5.5
Min - Max	64 - 80	-18 - 4	60 - 84	-16 - 6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	6	6	8	8
Mean (SD)	70.8 (7.5)	-4.7 (8.4)	72.1 (8.8)	-6.1 (10.0)
Median	70.0	-5.0	75.5	-3.0
Min - Max	60 - 82	-15 - 6	52 - 80	-24 - 5
Cycle 27 Day 15				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	76.1 (6.1)	-0.9 (7.7)	74.1 (5.9)	-4.3 (10.1)
Median	80.0	0.0	74.0	-6.0
Min - Max	69 - 83	-13 - 13	68 - 86	-21 - 10
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	75.1 (9.8)	-1.9 (6.1)	75.6 (7.9)	-2.9 (9.9)
Median	77.0	-2.0	75.0	1.0
Min - Max	58 - 86	-13 - 6	61 - 90	-17 - 10
Cycle 28 Day 1				
PRE PAC INFUSION				
n	7	7	13	13
Mean (SD)	71.7 (8.9)	-4.6 (11.3)	71.8 (12.6)	-8.8 (14.9)
Median	72.0	0.0	69.0	-13.0
Min - Max	56 - 80	-26 - 9	60 - 98	-30 - 18
AFTER PAC INFUSION				
n	6	6	6	6
Mean (SD)	72.0 (9.7)	-3.5 (9.8)	74.0 (9.2)	-4.7 (12.7)
Median	73.0	-2.5	76.5	-3.5
Min - Max	60 - 82	-18 - 10	58 - 82	-20 - 12
Cycle 28 Day 8				
PRE PAC INFUSION				
n	6	6	7	7
Mean (SD)	72.2 (5.7)	-3.3 (9.0)	66.4 (8.9)	-11.6 (10.2)
Median	70.0	-4.0	68.0	-15.0
Min - Max	67 - 82	-14 - 12	51 - 79	-23 - 2
AFTER PAC INFUSION				
n	6	6	7	7
Mean (SD)	74.3 (8.5)	-1.2 (3.7)	72.1 (6.5)	-5.9 (9.3)
Median	75.0	0.0	75.0	-6.0
Min - Max	63 - 85	-8 - 3	59 - 77	-17 - 5
Cycle 28 Day 15				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	74.0 (4.8)	-1.5 (4.7)	71.9 (6.6)	-6.4 (9.0)
Median	72.0	0.0	71.0	-7.5
Min - Max	70 - 80	-11 - 2	62 - 81	-19 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	6	6	8	8
Mean (SD)	74.8 (9.2)	-0.7 (10.1)	69.6 (9.7)	-8.6 (11.2)
Median	75.0	0.0	70.0	-6.5
Min - Max	62 - 86	-13 - 16	50 - 84	-26 - 5
Cycle 29 Day 1				
PRE PAC INFUSION				
n	7	7	11	11
Mean (SD)	72.4 (10.0)	-6.1 (11.0)	73.3 (6.7)	-6.5 (10.1)
Median	78.0	-4.0	73.0	-6.0
Min - Max	59 - 82	-23 - 11	60 - 85	-20 - 7
AFTER PAC INFUSION				
n	6	6	6	6
Mean (SD)	76.7 (7.2)	-1.5 (10.7)	73.3 (9.4)	-3.0 (11.8)
Median	80.0	0.0	75.5	1.0
Min - Max	62 - 80	-20 - 10	61 - 83	-20 - 10
Cycle 29 Day 8				
PRE PAC INFUSION				
n	6	6	5	5
Mean (SD)	75.8 (8.8)	-2.3 (10.7)	67.0 (8.9)	-9.6 (11.2)
Median	76.5	0.0	68.0	-14.0
Min - Max	63 - 85	-19 - 11	55 - 78	-21 - 8
AFTER PAC INFUSION				
n	6	6	5	5
Mean (SD)	77.7 (5.4)	-0.5 (4.1)	65.2 (9.0)	-11.4 (11.4)
Median	78.5	-1.0	66.0	-15.0
Min - Max	68 - 84	-5 - 7	53 - 77	-23 - 7
Cycle 29 Day 15				
PRE PAC INFUSION				
n	6	6	7	7
Mean (SD)	73.2 (5.1)	-5.0 (8.1)	71.9 (9.0)	-4.7 (10.6)
Median	73.5	-5.0	76.0	-4.0
Min - Max	66 - 80	-16 - 5	60 - 84	-16 - 8
AFTER PAC INFUSION				
n	6	6	7	7
Mean (SD)	72.8 (11.5)	-5.3 (6.2)	70.0 (11.9)	-6.6 (13.0)
Median	79.0	-3.0	73.0	0.0
Min - Max	54 - 82	-17 - 0	54 - 87	-23 - 7
Cycle 30 Day 1				
PRE PAC INFUSION				
n	7	7	12	12
Mean (SD)	75.4 (6.0)	-3.1 (6.7)	74.6 (10.0)	-5.0 (11.5)
Median	78.0	-4.0	74.5	-7.0
Min - Max	67 - 82	-12 - 8	61 - 100	-20 - 20

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	7	7
Mean (SD)	77.2 (10.7)	-0.2 (10.3)	77.4 (10.6)	0.9 (12.3)
Median	83.0	-3.0	74.0	-4.0
Min - Max	62 - 86	-10 - 15	66 - 96	-11 - 23
Cycle 30 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	73.8 (4.5)	-3.6 (6.2)	71.6 (9.0)	-5.6 (10.3)
Median	76.0	-4.0	71.0	-5.0
Min - Max	68 - 78	-10 - 6	59 - 82	-17 - 5
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	74.8 (9.2)	-2.6 (8.0)	70.6 (9.1)	-6.6 (11.0)
Median	76.0	-6.0	68.0	-11.0
Min - Max	62 - 86	-10 - 6	61 - 84	-15 - 11
Cycle 30 Day 15				
PRE PAC INFUSION				
n	4	4	7	7
Mean (SD)	76.3 (5.7)	-0.5 (5.6)	69.7 (5.6)	-6.9 (6.8)
Median	78.5	-1.5	69.0	-7.0
Min - Max	68 - 80	-6 - 7	61 - 76	-16 - 3
AFTER PAC INFUSION				
n	4	4	7	7
Mean (SD)	70.3 (11.4)	-6.5 (5.3)	72.9 (14.8)	-3.7 (16.4)
Median	71.5	-6.5	75.0	3.0
Min - Max	58 - 80	-13 - 0	52 - 94	-24 - 21
Cycle 31 Day 1				
PRE PAC INFUSION				
n	6	6	12	12
Mean (SD)	76.0 (7.1)	-2.3 (8.0)	71.5 (11.4)	-8.1 (12.4)
Median	77.5	-6.0	74.0	-8.5
Min - Max	63 - 83	-8 - 13	46 - 88	-30 - 10
AFTER PAC INFUSION				
n	4	4	6	6
Mean (SD)	79.0 (11.3)	2.3 (11.7)	74.8 (13.9)	-2.8 (15.4)
Median	82.0	-1.0	71.5	-7.0
Min - Max	63 - 89	-8 - 19	57 - 94	-19 - 21
Cycle 31 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	74.4 (7.6)	-3.0 (6.2)	71.2 (8.7)	-6.0 (9.7)
Median	73.0	-6.0	70.0	-11.0
Min - Max	65 - 84	-10 - 4	61 - 81	-15 - 6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	73.2 (8.3)	-4.2 (4.4)	69.0 (10.3)	-8.2 (11.9)
Median	70.0	-4.0	65.0	-15.0
Min - Max	64 - 82	-10 - 2	59 - 81	-18 - 8
Cycle 31 Day 15				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	76.3 (9.2)	-0.5 (3.9)	68.2 (8.3)	-9.5 (7.6)
Median	77.5	-0.5	70.5	-9.5
Min - Max	66 - 84	-5 - 4	56 - 79	-20 - 1
AFTER PAC INFUSION				
n	4	4	6	6
Mean (SD)	76.3 (6.9)	-0.5 (3.5)	67.5 (12.4)	-10.2 (14.2)
Median	77.5	-0.5	65.0	-13.0
Min - Max	68 - 82	-4 - 3	55 - 83	-27 - 10
Cycle 32 Day 1				
PRE PAC INFUSION				
n	7	7	11	11
Mean (SD)	75.6 (6.9)	-3.0 (10.9)	72.3 (11.6)	-8.2 (13.0)
Median	76.0	-8.0	70.0	-15.0
Min - Max	65 - 85	-17 - 15	54 - 90	-22 - 10
AFTER PAC INFUSION				
n	5	5	6	6
Mean (SD)	74.2 (11.3)	-3.2 (5.7)	71.7 (10.7)	-6.0 (12.4)
Median	80.0	-3.0	70.5	-8.5
Min - Max	60 - 84	-11 - 4	60 - 90	-16 - 17
Cycle 32 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	79.6 (6.2)	2.2 (7.5)	68.0 (12.1)	-9.2 (11.6)
Median	82.0	0.0	76.0	-7.0
Min - Max	69 - 85	-4 - 15	50 - 77	-26 - 3
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	71.0 (11.7)	-6.4 (9.8)	69.0 (10.0)	-8.2 (10.4)
Median	74.0	-2.0	70.0	-13.0
Min - Max	58 - 85	-20 - 4	57 - 81	-19 - 3
Cycle 32 Day 15				
PRE PAC INFUSION				
n	4	4	5	5
Mean (SD)	68.0 (9.9)	-7.3 (11.0)	69.8 (12.2)	-8.8 (11.9)
Median	67.5	-7.0	64.0	-12.0
Min - Max	59 - 78	-20 - 5	56 - 85	-20 - 7

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	4	4	5	5
Mean (SD)	73.3 (8.8)	-2.0 (6.7)	69.4 (9.2)	-9.2 (8.1)
Median	70.5	-2.0	69.0	-11.0
Min - Max	66 - 86	-10 - 6	58 - 83	-18 - 3
Cycle 33 Day 1				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	75.9 (7.8)	-2.7 (9.8)	73.0 (10.0)	-8.2 (9.4)
Median	78.0	-3.0	75.0	-10.0
Min - Max	64 - 85	-18 - 15	60 - 90	-24 - 5
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	74.0 (9.3)	-3.4 (4.4)	74.6 (11.6)	-2.0 (11.6)
Median	80.0	-4.0	81.0	3.0
Min - Max	62 - 82	-9 - 2	62 - 85	-14 - 12
Cycle 33 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	79.5 (6.6)	2.8 (11.7)	71.8 (10.6)	-4.0 (10.6)
Median	81.5	3.0	71.0	-3.5
Min - Max	70 - 85	-10 - 15	61 - 84	-15 - 6
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	73.3 (5.9)	-3.5 (4.8)	74.5 (19.4)	-1.3 (20.5)
Median	70.5	-2.5	71.0	-6.0
Min - Max	70 - 82	-10 - 1	57 - 99	-19 - 26
Cycle 33 Day 15				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	77.8 (5.2)	0.4 (9.0)	65.8 (4.4)	-10.8 (4.8)
Median	80.0	0.0	64.0	-10.0
Min - Max	71 - 84	-9 - 14	62 - 73	-18 - -5
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	75.6 (8.4)	-1.8 (4.7)	73.6 (15.7)	-3.0 (16.0)
Median	72.0	0.0	78.0	-2.0
Min - Max	67 - 88	-9 - 2	57 - 89	-19 - 16
Cycle 34 Day 1				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	75.3 (8.0)	-3.3 (9.3)	70.1 (9.9)	-11.1 (8.0)
Median	75.0	-7.0	71.0	-11.0
Min - Max	64 - 87	-10 - 17	56 - 80	-21 - 1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	73.0 (11.2)	-4.4 (11.1)	67.5 (9.7)	-10.0 (9.5)
Median	73.0	-7.0	65.5	-12.5
Min - Max	56 - 84	-15 - 14	58 - 81	-18 - 3
Cycle 34 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	75.0 (11.3)	-1.8 (10.2)	75.0 (18.5)	-0.8 (19.0)
Median	76.5	-4.5	75.0	-2.0
Min - Max	61 - 86	-10 - 12	58 - 92	-18 - 19
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	71.8 (13.2)	-5.0 (9.6)	79.5 (19.1)	3.8 (19.9)
Median	75.0	-3.5	82.5	5.5
Min - Max	53 - 84	-18 - 5	54 - 99	-22 - 26
Cycle 34 Day 15				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	74.8 (6.3)	-2.6 (7.3)	72.4 (12.5)	-4.2 (11.0)
Median	78.0	-6.0	74.0	-6.0
Min - Max	65 - 80	-8 - 9	56 - 87	-17 - 9
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	73.8 (7.4)	-3.6 (7.5)	78.0 (11.4)	1.4 (11.6)
Median	78.0	-8.0	79.0	1.0
Min - Max	62 - 80	-9 - 8	64 - 90	-12 - 17
Cycle 35 Day 1				
PRE PAC INFUSION				
n	7	7	8	8
Mean (SD)	74.7 (9.0)	-3.9 (10.4)	74.4 (12.3)	-7.0 (10.3)
Median	73.0	-5.0	75.5	-5.5
Min - Max	60 - 88	-20 - 13	55 - 96	-21 - 6
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	71.2 (10.4)	-6.2 (10.0)	76.0 (14.8)	0.3 (15.9)
Median	74.0	-6.0	75.0	-2.0
Min - Max	60 - 84	-20 - 7	60 - 94	-16 - 21
Cycle 35 Day 8				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	77.2 (5.4)	-0.2 (5.1)	70.0 (11.9)	-5.8 (12.6)
Median	78.0	-1.0	72.0	-5.0
Min - Max	70 - 84	-6 - 8	55 - 81	-21 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	74.2 (7.7)	-3.2 (3.3)	72.3 (14.6)	-3.5 (15.9)
Median	72.0	-2.0	71.0	-6.0
Min - Max	65 - 84	-8 - 0	56 - 91	-20 - 18
Cycle 35 Day 15				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	72.0 (8.7)	-5.4 (5.5)	72.0 (11.7)	-3.8 (11.8)
Median	74.0	-6.0	73.0	-1.5
Min - Max	58 - 80	-13 - 0	58 - 84	-18 - 6
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	77.4 (4.6)	0.0 (7.6)	75.5 (13.0)	-0.3 (14.2)
Median	80.0	0.0	74.0	-3.0
Min - Max	72 - 82	-7 - 12	62 - 92	-14 - 19
Cycle 36 Day 1				
PRE PAC INFUSION				
n	7	7	8	8
Mean (SD)	74.1 (5.2)	-4.4 (7.0)	72.1 (11.6)	-9.3 (12.5)
Median	73.0	-5.0	78.5	-9.5
Min - Max	68 - 82	-10 - 10	57 - 84	-31 - 6
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	71.0 (12.5)	-6.4 (9.0)	71.5 (10.7)	-4.3 (12.0)
Median	73.0	-4.0	71.0	-6.0
Min - Max	51 - 85	-20 - 3	59 - 85	-17 - 12
Cycle 36 Day 8				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	71.8 (8.6)	-5.6 (3.4)	69.3 (2.8)	-6.5 (3.9)
Median	73.0	-6.0	69.5	-7.5
Min - Max	61 - 80	-9 - 0	66 - 72	-10 - -1
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	74.2 (6.0)	-3.2 (5.2)	76.8 (11.0)	1.0 (11.9)
Median	74.0	-5.0	77.0	0.0
Min - Max	66 - 80	-9 - 4	64 - 89	-12 - 16
Cycle 36 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	71.0 (6.4)	-5.8 (3.7)	78.0 (7.1)	2.3 (5.8)
Median	69.5	-6.0	76.0	1.5
Min - Max	65 - 80	-10 - -1	72 - 88	-4 - 10

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	68.5 (11.1)	-8.3 (6.0)	75.3 (13.4)	-0.5 (14.5)
Median	68.5	-7.0	74.0	-3.0
Min - Max	55 - 82	-16 - -3	61 - 92	-15 - 19
Cycle 37 Day 1				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	74.7 (6.5)	-5.3 (4.3)	74.6 (9.9)	-6.8 (9.5)
Median	74.0	-5.5	72.0	-5.0
Min - Max	67 - 84	-12 - 0	59 - 90	-20 - 7
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	74.5 (6.4)	-4.8 (4.3)	71.5 (16.3)	-4.3 (17.4)
Median	75.0	-4.5	68.5	-8.5
Min - Max	68 - 80	-10 - 0	57 - 92	-19 - 19
Cycle 37 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	74.8 (4.6)	-4.5 (7.2)	68.0 (8.5)	-7.8 (7.1)
Median	74.5	-7.0	67.0	-7.5
Min - Max	70 - 80	-10 - 6	60 - 78	-16 - 0
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	72.8 (6.1)	-6.5 (2.4)	72.5 (15.6)	-3.3 (17.0)
Median	72.5	-5.5	68.0	-9.0
Min - Max	66 - 80	-10 - -5	60 - 94	-16 - 21
Cycle 37 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	71.0 (6.3)	-8.3 (1.3)	68.8 (3.0)	-7.0 (3.4)
Median	71.5	-8.0	69.0	-7.0
Min - Max	63 - 78	-10 - -7	65 - 72	-11 - -3
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	71.5 (12.5)	-7.8 (7.6)	71.8 (18.6)	-4.0 (19.0)
Median	76.5	-6.5	74.0	-2.5
Min - Max	53 - 80	-18 - 0	51 - 88	-25 - 14
Cycle 38 Day 1				
PRE PAC INFUSION				
n	5	5	8	8
Mean (SD)	71.0 (8.8)	-7.8 (7.4)	74.6 (9.1)	-6.8 (8.1)
Median	70.0	-10.0	76.5	-5.0
Min - Max	61 - 80	-18 - 0	60 - 88	-18 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	66.7 (15.3)	-10.3 (10.5)	70.0 (9.1)	-5.8 (10.4)
Median	70.0	-10.0	67.5	-9.5
Min - Max	50 - 80	-21 - 0	63 - 82	-13 - 9
Cycle 38 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	73.8 (10.7)	-5.5 (5.3)	69.8 (9.0)	-6.0 (7.9)
Median	75.5	-5.5	69.0	-6.5
Min - Max	60 - 84	-11 - 0	62 - 79	-14 - 3
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	74.5 (9.5)	-4.8 (4.1)	69.0 (11.5)	-6.8 (12.8)
Median	77.5	-4.5	66.5	-10.5
Min - Max	61 - 82	-10 - 0	59 - 84	-17 - 11
Cycle 38 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	73.8 (7.0)	-5.5 (3.1)	71.0 (11.3)	-4.8 (11.4)
Median	72.5	-4.5	72.5	-2.5
Min - Max	67 - 83	-10 - -3	57 - 82	-19 - 5
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	70.5 (11.2)	-8.8 (5.6)	73.3 (10.7)	-2.5 (11.9)
Median	73.5	-8.0	73.5	-3.5
Min - Max	55 - 80	-16 - -3	60 - 86	-16 - 13
Cycle 39 Day 1				
PRE PAC INFUSION				
n	5	5	8	8
Mean (SD)	71.6 (6.7)	-8.0 (3.1)	78.0 (7.4)	-3.4 (11.3)
Median	70.0	-7.0	80.0	-4.0
Min - Max	64 - 82	-12 - -4	65 - 85	-23 - 9
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	75.5 (12.4)	-3.8 (7.1)	79.8 (9.1)	4.0 (10.4)
Median	73.5	-5.5	80.5	3.5
Min - Max	63 - 92	-10 - 6	68 - 90	-8 - 17
Cycle 39 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	74.0 (9.1)	-5.3 (4.1)	67.0 (4.8)	-8.8 (3.8)
Median	76.0	-6.0	67.0	-7.5
Min - Max	62 - 82	-9 - 0	62 - 72	-14 - -6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	70.8 (10.2)	-8.5 (4.2)	78.5 (9.3)	2.8 (10.5)
Median	71.0	-9.0	78.0	1.0
Min - Max	58 - 83	-13 - -3	68 - 90	-8 - 17
Cycle 39 Day 15				
PRE PAC INFUSION				
n	4	4	3	3
Mean (SD)	75.3 (5.9)	-4.0 (3.2)	65.7 (4.2)	-9.3 (2.5)
Median	76.5	-4.5	67.0	-9.0
Min - Max	68 - 80	-7 - 0	61 - 69	-12 - -7
AFTER PAC INFUSION				
n	4	4	3	3
Mean (SD)	72.3 (13.3)	-7.0 (7.7)	80.3 (15.3)	5.3 (16.5)
Median	75.5	-5.5	86.0	10.0
Min - Max	54 - 84	-17 - 0	63 - 92	-13 - 19
Cycle 40 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	69.8 (11.5)	-9.8 (7.4)	72.5 (8.4)	-8.9 (7.9)
Median	68.0	-9.0	70.5	-8.0
Min - Max	59 - 84	-19 - -2	62 - 87	-20 - 4
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	71.0 (4.0)	-8.0 (3.6)	68.7 (3.2)	-8.0 (2.6)
Median	71.0	-9.0	70.0	-7.0
Min - Max	67 - 75	-11 - -4	65 - 71	-11 - -6
Cycle 40 Day 8				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	76.0 (8.7)	-3.0 (2.6)	66.5 (6.0)	-9.3 (5.7)
Median	80.0	-4.0	66.0	-8.5
Min - Max	66 - 82	-5 - 0	60 - 74	-16 - -4
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	77.7 (11.8)	-1.3 (6.0)	69.5 (10.0)	-6.3 (11.4)
Median	84.0	-2.0	67.0	-10.0
Min - Max	64 - 85	-7 - 5	61 - 83	-15 - 10
Cycle 40 Day 15				
PRE PAC INFUSION				
n	2	2	4	4
Mean (SD)	74.5 (10.6)	-4.0 (0.0)	64.8 (12.3)	-11.0 (10.4)
Median	74.5	-4.0	63.0	-13.0
Min - Max	67 - 82	-4 - -4	52 - 81	-21 - 3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	4	4
Mean (SD)	74.0 (15.6)	-4.5 (4.9)	72.3 (13.9)	-3.5 (15.3)
Median	74.0	-4.5	69.5	-7.5
Min - Max	63 - 85	-8 - -1	59 - 91	-17 - 18
Cycle 41 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	74.8 (5.3)	-4.8 (4.6)	73.1 (7.4)	-8.3 (10.3)
Median	73.5	-5.0	72.5	-8.5
Min - Max	70 - 82	-10 - 1	62 - 83	-22 - 8
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	72.3 (10.7)	-6.7 (4.2)	72.0 (12.2)	-3.8 (13.6)
Median	70.0	-8.0	72.0	-5.0
Min - Max	63 - 84	-10 - -2	57 - 87	-19 - 14
Cycle 41 Day 8				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	72.3 (2.3)	-6.7 (5.9)	71.5 (9.9)	-4.3 (10.5)
Median	71.0	-9.0	71.5	-5.5
Min - Max	71 - 75	-11 - 0	62 - 81	-14 - 8
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	70.3 (15.3)	-8.7 (8.4)	77.0 (11.8)	1.3 (13.7)
Median	67.0	-13.0	73.0	-4.0
Min - Max	57 - 87	-14 - 1	68 - 94	-8 - 21
Cycle 41 Day 15				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	74.7 (6.4)	-4.3 (3.5)	70.3 (9.6)	-5.5 (8.3)
Median	72.0	-4.0	67.5	-7.0
Min - Max	70 - 82	-8 - -1	62 - 84	-14 - 6
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	70.7 (16.3)	-8.3 (8.7)	72.3 (11.2)	-3.5 (11.8)
Median	74.0	-6.0	76.0	0.5
Min - Max	53 - 85	-18 - -1	56 - 81	-20 - 5
Cycle 42 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	73.0 (5.0)	-6.5 (4.5)	76.5 (6.5)	-4.9 (11.4)
Median	71.5	-6.5	74.5	-4.5
Min - Max	69 - 80	-12 - -1	70 - 88	-20 - 11

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	66.7 (12.3)	-12.3 (4.9)	81.3 (10.8)	5.5 (12.0)
Median	70.0	-10.0	83.5	6.5
Min - Max	53 - 77	-18 - -9	67 - 91	-9 - 18
Cycle 42 Day 8				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	73.0 (1.4)	-2.5 (7.8)	68.5 (14.8)	-8.5 (13.4)
Median	73.0	-2.5	68.5	-8.5
Min - Max	72 - 74	-8 - 3	58 - 79	-18 - 1
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	72.5 (0.7)	-3.0 (5.7)	73.0 (15.6)	-4.0 (14.1)
Median	72.5	-3.0	73.0	-4.0
Min - Max	72 - 73	-7 - 1	62 - 84	-14 - 6
Cycle 42 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	71.0 (3.6)	-8.0 (4.4)	76.7 (10.6)	1.0 (9.5)
Median	70.0	-10.0	75.0	2.0
Min - Max	68 - 75	-11 - -3	67 - 88	-9 - 10
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	71.0 (9.5)	-8.0 (2.6)	80.0 (17.5)	4.3 (19.2)
Median	70.0	-9.0	79.0	1.0
Min - Max	62 - 81	-10 - -5	63 - 98	-13 - 25
Cycle 43 Day 1				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	76.0 (3.6)	-3.5 (7.0)	74.8 (6.3)	-6.0 (8.4)
Median	75.5	-6.5	77.0	-5.0
Min - Max	73 - 80	-8 - 7	63 - 80	-17 - 3
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	80.3 (9.5)	1.3 (15.4)	76.0 (14.2)	0.3 (15.2)
Median	80.0	-6.0	81.0	3.0
Min - Max	71 - 90	-9 - 19	60 - 87	-16 - 14
Cycle 43 Day 8				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	74.7 (8.1)	-4.3 (4.0)	73.0 (9.6)	-2.7 (7.5)
Median	71.0	-2.0	69.0	-7.0
Min - Max	69 - 84	-9 - -2	66 - 84	-7 - 6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	69.3 (9.8)	-9.7 (4.2)	71.7 (19.9)	-4.0 (21.1)
Median	75.0	-11.0	76.0	-2.0
Min - Max	58 - 75	-13 - -5	50 - 89	-26 - 16
Cycle 43 Day 15				
PRE PAC INFUSION				
n	3	3	1	1
Mean (SD)	76.3 (8.0)	-2.7 (0.6)	79.0 (NE)	1.0 (NE)
Median	77.0	-3.0	79.0	1.0
Min - Max	68 - 84	-3 - -2	79 - 79	1 - 1
AFTER PAC INFUSION				
n	3	3	1	1
Mean (SD)	69.3 (8.1)	-9.7 (2.3)	88.0 (NE)	10.0 (NE)
Median	73.0	-11.0	88.0	10.0
Min - Max	60 - 75	-11 - -7	88 - 88	10 - 10
Cycle 44 Day 1				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	72.5 (8.4)	-7.0 (6.1)	74.0 (5.7)	-6.8 (7.7)
Median	69.0	-6.5	74.5	-4.0
Min - Max	67 - 85	-14 - -1	67 - 80	-21 - 0
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	72.3 (17.0)	-6.7 (9.7)	82.0 (11.5)	6.3 (13.3)
Median	71.0	-9.0	81.0	3.0
Min - Max	56 - 90	-15 - 4	71 - 94	-5 - 21
Cycle 44 Day 8				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	74.3 (4.9)	-4.7 (5.1)	74.0 (12.2)	-1.7 (10.1)
Median	72.0	-6.0	68.0	-7.0
Min - Max	71 - 80	-9 - 1	66 - 88	-8 - 10
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	74.7 (9.1)	-4.3 (6.7)	81.3 (13.5)	5.7 (15.2)
Median	71.0	-1.0	81.0	3.0
Min - Max	68 - 85	-12 - 0	68 - 95	-8 - 22
Cycle 44 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	77.3 (6.4)	-1.7 (2.1)	71.0 (9.5)	-4.7 (8.6)
Median	80.0	-1.0	70.0	-3.0
Min - Max	70 - 82	-4 - 0	62 - 81	-14 - 3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	71.3 (11.7)	-7.7 (4.7)	72.7 (18.0)	-3.0 (19.5)
Median	76.0	-6.0	74.0	-4.0
Min - Max	58 - 80	-13 - -4	54 - 90	-22 - 17
Cycle 45 Day 1				
PRE PAC INFUSION				
n	4	4	5	5
Mean (SD)	75.0 (9.8)	-4.5 (7.0)	69.8 (13.6)	-11.6 (8.4)
Median	75.5	-7.5	77.0	-11.0
Min - Max	63 - 86	-9 - 6	54 - 82	-22 - 0
AFTER PAC INFUSION				
n	3	3	1	1
Mean (SD)	80.7 (6.8)	1.7 (1.5)	69.0 (NE)	-7.0 (NE)
Median	83.0	2.0	69.0	-7.0
Min - Max	73 - 86	0 - 3	69 - 69	-7 - -7
Cycle 45 Day 8				
PRE PAC INFUSION				
n	3	3	2	2
Mean (SD)	72.3 (2.5)	-6.7 (6.7)	68.0 (1.4)	-6.5 (3.5)
Median	72.0	-10.0	68.0	-6.5
Min - Max	70 - 75	-11 - 1	67 - 69	-9 - -4
AFTER PAC INFUSION				
n	3	3	2	2
Mean (SD)	74.0 (8.7)	-5.0 (4.4)	83.5 (19.1)	9.0 (21.2)
Median	70.0	-3.0	83.5	9.0
Min - Max	68 - 84	-10 - -2	70 - 97	-6 - 24
Cycle 45 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	75.3 (9.9)	-3.7 (4.9)	77.3 (6.4)	1.7 (6.8)
Median	80.0	-6.0	80.0	4.0
Min - Max	64 - 82	-7 - 2	70 - 82	-6 - 7
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	77.3 (11.0)	-1.7 (6.0)	77.0 (21.0)	1.3 (22.6)
Median	72.0	-1.0	77.0	-1.0
Min - Max	70 - 90	-8 - 4	56 - 98	-20 - 25
Cycle 46 Day 1				
PRE PAC INFUSION				
n	3	3	6	6
Mean (SD)	72.7 (11.6)	-6.7 (8.3)	74.7 (10.7)	-6.2 (12.8)
Median	67.0	-4.0	76.5	-2.0
Min - Max	65 - 86	-16 - 0	57 - 86	-31 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	76.0 (22.6)	-2.5 (12.0)	74.0 (14.1)	-0.5 (16.3)
Median	76.0	-2.5	74.0	-0.5
Min - Max	60 - 92	-11 - 6	64 - 84	-12 - 11
Cycle 46 Day 8				
PRE PAC INFUSION				
n	2	2	3	3
Mean (SD)	77.5 (7.8)	-1.0 (2.8)	76.7 (10.0)	1.0 (7.8)
Median	77.5	-1.0	73.0	-3.0
Min - Max	72 - 83	-3 - 1	69 - 88	-4 - 10
AFTER PAC INFUSION				
n	2	2	3	3
Mean (SD)	74.5 (29.0)	-4.0 (18.4)	86.3 (2.1)	10.7 (4.2)
Median	74.5	-4.0	87.0	12.0
Min - Max	54 - 95	-17 - 9	84 - 88	6 - 14
Cycle 46 Day 15				
PRE PAC INFUSION				
n	2	2	3	3
Mean (SD)	75.0 (7.1)	-3.5 (3.5)	76.0 (4.4)	0.3 (5.0)
Median	75.0	-3.5	78.0	1.0
Min - Max	70 - 80	-6 - -1	71 - 79	-5 - 5
AFTER PAC INFUSION				
n	2	2	3	3
Mean (SD)	75.0 (21.2)	-3.5 (10.6)	71.0 (11.5)	-4.7 (13.1)
Median	75.0	-3.5	72.0	-6.0
Min - Max	60 - 90	-11 - 4	59 - 82	-17 - 9
Cycle 47 Day 1				
PRE PAC INFUSION				
n	3	3	6	6
Mean (SD)	74.0 (7.0)	-5.3 (6.1)	75.5 (13.7)	-5.3 (11.1)
Median	71.0	-4.0	74.5	-4.0
Min - Max	69 - 82	-12 - 0	59 - 96	-19 - 6
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	66.5 (12.0)	-12.0 (1.4)	74.0 (4.2)	-3.0 (2.8)
Median	66.5	-12.0	74.0	-3.0
Min - Max	58 - 75	-13 - -11	71 - 77	-5 - -1
Cycle 47 Day 8				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	76.5 (12.0)	-2.0 (1.4)	69.5 (13.4)	-7.5 (12.0)
Median	76.5	-2.0	69.5	-7.5
Min - Max	68 - 85	-3 - -1	60 - 79	-16 - 1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	71.0 (15.6)	-7.5 (4.9)	65.0 (14.1)	-12.0 (12.7)
Median	71.0	-7.5	65.0	-12.0
Min - Max	60 - 82	-11 - -4	55 - 75	-21 - -3
Cycle 47 Day 15				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	75.0 (7.1)	-3.5 (3.5)	77.0 (4.2)	0.0 (2.8)
Median	75.0	-3.5	77.0	0.0
Min - Max	70 - 80	-6 - -1	74 - 80	-2 - 2
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	64.5 (19.1)	-14.0 (8.5)	60.0 (15.6)	-17.0 (14.1)
Median	64.5	-14.0	60.0	-17.0
Min - Max	51 - 78	-20 - -8	49 - 71	-27 - -7
Cycle 48 Day 1				
PRE PAC INFUSION				
n	1	1	5	5
Mean (SD)	76.0 (NE)	-10.0 (NE)	77.2 (11.2)	-5.2 (9.1)
Median	76.0	-10.0	80.0	0.0
Min - Max	76 - 76	-10 - -10	60 - 90	-16 - 4
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	85.0 (NE)	-1.0 (NE)	71.5 (3.5)	-5.5 (2.1)
Median	85.0	-1.0	71.5	-5.5
Min - Max	85 - 85	-1 - -1	69 - 74	-7 - -4
Cycle 48 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	80.0 (NE)	-6.0 (NE)	77.0 (8.5)	0.0 (7.1)
Median	80.0	-6.0	77.0	0.0
Min - Max	80 - 80	-6 - -6	71 - 83	-5 - 5
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	88.0 (NE)	2.0 (NE)	72.0 (14.1)	-5.0 (12.7)
Median	88.0	2.0	72.0	-5.0
Min - Max	88 - 88	2 - 2	62 - 82	-14 - 4
Cycle 48 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	75.0 (NE)	-11.0 (NE)	74.5 (3.5)	-2.5 (2.1)
Median	75.0	-11.0	74.5	-2.5
Min - Max	75 - 75	-11 - -11	72 - 77	-4 - -1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	94.0 (NE)	8.0 (NE)	64.0 (21.2)	-13.0 (19.8)
Median	94.0	8.0	64.0	-13.0
Min - Max	94 - 94	8 - 8	49 - 79	-27 - 1
Cycle 49 Day 1				
PRE PAC INFUSION				
n	1	1	3	3
Mean (SD)	78.0 (NE)	-8.0 (NE)	77.0 (13.0)	-4.3 (6.7)
Median	78.0	-8.0	77.0	-1.0
Min - Max	78 - 78	-8 - -8	64 - 90	-12 - 0
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	90.0 (NE)	4.0 (NE)	70.0 (4.2)	-7.0 (2.8)
Median	90.0	4.0	70.0	-7.0
Min - Max	90 - 90	4 - 4	67 - 73	-9 - -5
Cycle 49 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	80.0 (NE)	-6.0 (NE)	79.5 (2.1)	2.5 (0.7)
Median	80.0	-6.0	79.5	2.5
Min - Max	80 - 80	-6 - -6	78 - 81	2 - 3
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	86.0 (NE)	0.0 (NE)	76.0 (1.4)	-1.0 (0.0)
Median	86.0	0.0	76.0	-1.0
Min - Max	86 - 86	0 - 0	75 - 77	-1 - -1
Cycle 49 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	73.0 (NE)	-13.0 (NE)	73.5 (14.8)	-3.5 (13.4)
Median	73.0	-13.0	73.5	-3.5
Min - Max	73 - 73	-13 - -13	63 - 84	-13 - 6
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	80.0 (NE)	-6.0 (NE)	73.0 (9.9)	-4.0 (8.5)
Median	80.0	-6.0	73.0	-4.0
Min - Max	80 - 80	-6 - -6	66 - 80	-10 - 2
Cycle 50 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	80.0 (NE)	-6.0 (NE)	70.5 (0.7)	-6.5 (0.7)
Median	80.0	-6.0	70.5	-6.5
Min - Max	80 - 80	-6 - -6	70 - 71	-7 - -6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	76.0 (NE)	-10.0 (NE)	78.0 (NE)	2.0 (NE)
Median	76.0	-10.0	78.0	2.0
Min - Max	76 - 76	-10 - -10	78 - 78	2 - 2
Cycle 50 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	82.0 (NE)	-4.0 (NE)	74.0 (4.2)	-3.0 (2.8)
Median	82.0	-4.0	74.0	-3.0
Min - Max	82 - 82	-4 - -4	71 - 77	-5 - -1
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	80.0 (NE)	-6.0 (NE)	70.0 (7.1)	-7.0 (5.7)
Median	80.0	-6.0	70.0	-7.0
Min - Max	80 - 80	-6 - -6	65 - 75	-11 - -3
Cycle 50 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	74.0 (NE)	-12.0 (NE)	73.5 (10.6)	-3.5 (9.2)
Median	74.0	-12.0	73.5	-3.5
Min - Max	74 - 74	-12 - -12	66 - 81	-10 - 3
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	75.0 (NE)	-11.0 (NE)	70.5 (9.2)	-6.5 (7.8)
Median	75.0	-11.0	70.5	-6.5
Min - Max	75 - 75	-11 - -11	64 - 77	-12 - -1
Cycle 51 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	80.0 (NE)	-6.0 (NE)	74.0 (4.2)	-3.0 (2.8)
Median	80.0	-6.0	74.0	-3.0
Min - Max	80 - 80	-6 - -6	71 - 77	-5 - -1
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	80.0 (NE)	-6.0 (NE)	75.5 (4.9)	-1.5 (3.5)
Median	80.0	-6.0	75.5	-1.5
Min - Max	80 - 80	-6 - -6	72 - 79	-4 - 1
Cycle 51 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	84.0 (NE)	-2.0 (NE)	78.0 (NE)	0.0 (NE)
Median	84.0	-2.0	78.0	0.0
Min - Max	84 - 84	-2 - -2	78 - 78	0 - 0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	93.0 (NE)	7.0 (NE)	NE (NE)	NE (NE)
Median	93.0	7.0	NE	NE
Min - Max	93 - 93	7 - 7	NE - NE	NE - NE
Cycle 51 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	90.0 (NE)	4.0 (NE)	76.5 (3.5)	-0.5 (2.1)
Median	90.0	4.0	76.5	-0.5
Min - Max	90 - 90	4 - 4	74 - 79	-2 - 1
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	90.0 (NE)	4.0 (NE)	68.5 (7.8)	-8.5 (6.4)
Median	90.0	4.0	68.5	-8.5
Min - Max	90 - 90	4 - 4	63 - 74	-13 - -4
Cycle 52 Day 1				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	73.5 (6.4)	-3.5 (4.9)
Median	NE	NE	73.5	-3.5
Min - Max	NE - NE	NE - NE	69 - 78	-7 - 0
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	69.5 (3.5)	-7.5 (2.1)
Median	NE	NE	69.5	-7.5
Min - Max	NE - NE	NE - NE	67 - 72	-9 - -6
Cycle 52 Day 8				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	76.0 (0.0)	-1.0 (1.4)
Median	NE	NE	76.0	-1.0
Min - Max	NE - NE	NE - NE	76 - 76	-2 - 0
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	69.0 (12.7)	-8.0 (11.3)
Median	NE	NE	69.0	-8.0
Min - Max	NE - NE	NE - NE	60 - 78	-16 - 0
Cycle 52 Day 15				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	76.0 (5.7)	-1.0 (4.2)
Median	NE	NE	76.0	-1.0
Min - Max	NE - NE	NE - NE	72 - 80	-4 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	73.0 (4.2)	-4.0 (2.8)
Median	NE	NE	73.0	-4.0
Min - Max	NE - NE	NE - NE	70 - 76	-6 - -2
Cycle 53 Day 1				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	73.0 (8.5)	-4.0 (7.1)
Median	NE	NE	73.0	-4.0
Min - Max	NE - NE	NE - NE	67 - 79	-9 - 1
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	67.0 (7.1)	-10.0 (5.7)
Median	NE	NE	67.0	-10.0
Min - Max	NE - NE	NE - NE	62 - 72	-14 - -6
Cycle 53 Day 8				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	81.0 (NE)	3.0 (NE)
Median	NE	NE	81.0	3.0
Min - Max	NE - NE	NE - NE	81 - 81	3 - 3
AFTER PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	71.0 (NE)	-7.0 (NE)
Median	NE	NE	71.0	-7.0
Min - Max	NE - NE	NE - NE	71 - 71	-7 - -7
Cycle 53 Day 15				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	90.0 (NE)	12.0 (NE)
Median	NE	NE	90.0	12.0
Min - Max	NE - NE	NE - NE	90 - 90	12 - 12
Study Drug Discontinuation				
n	70	68	127	127
Mean (SD)	75.5 (9.2)	-0.9 (11.0)	74.6 (10.5)	-2.2 (11.5)
Median	75.0	0.0	76.0	-2.0
Min - Max	58 - 105	-28 - 23	50 - 99	-38 - 25
Post-Baseline Last				
n	69	69	128	128
Mean (SD)	75.2 (9.1)	-0.9 (11.0)	74.6 (10.4)	-2.2 (11.4)
Median	74.0	0.0	76.0	-2.0
Min - Max	58 - 105	-28 - 23	50 - 99	-38 - 25

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
PRE PAC INFUSION				
n	1	1	3	3
Mean (SD)	60.0 (NE)	0.0 (NE)	79.7 (8.4)	6.7 (20.8)
Median	60.0	0.0	84.0	15.0
Min - Max	60 - 60	0 - 0	70 - 85	-17 - 22
AFTER PAC INFUSION				
n	2	2	13	13
Mean (SD)	80.0 (7.1)	10.0 (7.1)	76.2 (7.2)	1.8 (6.0)
Median	80.0	10.0	80.0	0.0
Min - Max	75 - 85	5 - 15	67 - 90	-8 - 10
Post-Baseline Minimum				
n	2	2	6	6
Mean (SD)	66.0 (8.5)	-19.0 (8.5)	62.0 (10.6)	-8.0 (9.7)
Median	66.0	-19.0	58.5	-6.0
Min - Max	60 - 72	-25 - -13	50 - 79	-21 - 7
PRE PAC INFUSION				
n	49	49	81	81
Mean (SD)	59.2 (11.3)	-16.6 (12.0)	59.9 (9.7)	-15.3 (11.7)
Median	60.0	-17.0	60.0	-13.0
Min - Max	18 - 78	-48 - 10	37 - 91	-53 - 15
AFTER PAC INFUSION				
n	21	21	57	57
Mean (SD)	59.8 (9.2)	-14.8 (9.4)	60.7 (12.7)	-18.4 (12.6)
Median	59.0	-13.0	64.0	-18.0
Min - Max	44 - 78	-35 - 0	7 - 90	-71 - 10
Post-Baseline Maximum				
n	5	5	14	14
Mean (SD)	101.4 (20.3)	28.6 (20.6)	85.5 (7.3)	12.9 (9.7)
Median	94.0	22.0	85.5	11.5
Min - Max	84 - 135	14 - 65	73 - 99	-3 - 32
PRE PAC INFUSION				
n	27	27	56	56
Mean (SD)	89.7 (9.1)	13.3 (12.8)	90.4 (7.7)	12.8 (9.3)
Median	88.0	10.0	90.0	12.5
Min - Max	78 - 120	-10 - 50	75 - 105	-10 - 32
AFTER PAC INFUSION				
n	40	40	74	74
Mean (SD)	86.9 (7.8)	11.3 (7.6)	90.4 (10.1)	14.0 (11.1)
Median	87.5	10.5	90.0	13.0
Min - Max	71 - 103	-4 - 37	68 - 128	-5 - 48

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
Baseline				
n	72		144	
Mean (SD)	122.5 (13.1)		123.7 (13.3)	
Median	122.0		124.0	
Min - Max	98 - 159		90 - 170	
Cycle 1 Day 1				
PRE PAC INFUSION				
n	69	67	140	139
Mean (SD)	123.3 (14.6)	0.7 (12.6)	123.8 (13.8)	0.2 (11.9)
Median	124.0	0.0	125.0	0.0
Min - Max	97 - 159	-32 - 39	87 - 160	-29 - 42
AFTER PAC INFUSION				
n	71	69	140	139
Mean (SD)	125.3 (15.5)	2.1 (14.9)	127.7 (15.0)	4.2 (15.9)
Median	125.0	1.0	128.0	0.0
Min - Max	94 - 177	-26 - 64	92 - 190	-32 - 70
Cycle 1 Day 8				
PRE PAC INFUSION				
n	72	69	135	135
Mean (SD)	119.2 (15.6)	-3.7 (12.1)	120.2 (15.1)	-3.1 (15.0)
Median	119.0	-4.0	121.0	-3.0
Min - Max	90 - 161	-31 - 26	90 - 166	-40 - 42
AFTER PAC INFUSION				
n	62	61	126	126
Mean (SD)	122.9 (13.5)	-0.3 (12.8)	121.7 (15.1)	-1.8 (14.9)
Median	121.5	-1.0	120.0	-1.0
Min - Max	94 - 158	-37 - 45	94 - 175	-36 - 57
Cycle 1 Day 15				
PRE PAC INFUSION				
n	70	67	130	130
Mean (SD)	120.4 (13.5)	-2.3 (13.3)	119.8 (15.5)	-3.8 (14.6)
Median	120.0	0.0	120.0	-2.5
Min - Max	90 - 158	-30 - 38	83 - 159	-40 - 39
AFTER PAC INFUSION				
n	57	55	116	116
Mean (SD)	121.8 (17.1)	-1.5 (15.0)	120.8 (14.6)	-3.0 (15.1)
Median	121.0	-1.0	120.0	-2.5
Min - Max	88 - 174	-30 - 61	90 - 163	-37 - 43
Cycle 2 Day 1				
PRE PAC INFUSION				
n	73	71	130	129
Mean (SD)	120.5 (13.9)	-2.5 (12.0)	120.4 (15.4)	-3.1 (14.8)
Median	120.0	-1.0	120.0	-2.0
Min - Max	90 - 148	-30 - 26	82 - 167	-37 - 49

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	67	66	123	122
Mean (SD)	121.6 (14.3)	-2.3 (13.4)	123.6 (15.2)	-0.2 (15.9)
Median	120.0	-0.5	123.0	0.0
Min - Max	90 - 152	-39 - 30	91 - 198	-33 - 78
Cycle 2 Day 8				
PRE PAC INFUSION				
n	72	70	127	126
Mean (SD)	120.3 (12.4)	-3.2 (12.8)	118.4 (14.0)	-5.4 (13.8)
Median	120.0	-4.0	120.0	-5.5
Min - Max	90 - 154	-42 - 35	89 - 153	-39 - 40
AFTER PAC INFUSION				
n	68	66	122	121
Mean (SD)	123.9 (15.2)	-0.5 (13.1)	121.9 (15.6)	-2.2 (16.3)
Median	126.5	-1.0	120.0	-2.0
Min - Max	92 - 160	-22 - 35	90 - 180	-39 - 50
Cycle 2 Day 15				
PRE PAC INFUSION				
n	69	67	123	122
Mean (SD)	118.9 (15.1)	-4.3 (13.7)	118.9 (14.7)	-5.0 (14.8)
Median	119.0	-4.0	120.0	-4.0
Min - Max	90 - 160	-39 - 32	90 - 160	-49 - 40
AFTER PAC INFUSION				
n	66	64	110	109
Mean (SD)	122.1 (16.6)	-1.0 (14.3)	119.0 (15.1)	-4.6 (16.9)
Median	121.0	0.0	120.0	-5.0
Min - Max	90 - 180	-31 - 55	91 - 191	-39 - 71
Cycle 3 Day 1				
PRE PAC INFUSION				
n	70	68	121	121
Mean (SD)	121.7 (14.5)	-2.0 (12.1)	119.9 (14.9)	-4.5 (14.0)
Median	120.5	-2.0	120.0	-5.0
Min - Max	90 - 158	-26 - 36	90 - 160	-43 - 40
AFTER PAC INFUSION				
n	65	63	111	111
Mean (SD)	125.3 (16.3)	1.2 (15.2)	123.8 (17.0)	-0.3 (16.9)
Median	125.0	1.0	123.0	-1.0
Min - Max	90 - 184	-20 - 73	82 - 202	-31 - 82
Cycle 3 Day 8				
PRE PAC INFUSION				
n	65	63	116	115
Mean (SD)	119.2 (14.5)	-4.2 (13.2)	118.7 (15.5)	-5.1 (15.8)
Median	118.0	-3.0	120.0	-5.0
Min - Max	92 - 160	-49 - 22	84 - 164	-40 - 60

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	59	57	105	104
Mean (SD)	121.3 (14.6)	-2.5 (12.7)	123.2 (17.1)	-1.3 (16.7)
Median	121.0	-1.0	127.0	-2.0
Min - Max	87 - 155	-40 - 30	90 - 183	-37 - 65
Cycle 3 Day 15				
PRE PAC INFUSION				
n	64	62	116	115
Mean (SD)	121.5 (15.1)	-1.8 (15.9)	117.9 (16.4)	-5.7 (14.9)
Median	120.5	-0.5	119.5	-6.0
Min - Max	90 - 158	-30 - 45	85 - 185	-40 - 50
AFTER PAC INFUSION				
n	60	58	107	107
Mean (SD)	123.8 (14.5)	0.4 (13.1)	120.4 (15.2)	-3.1 (17.1)
Median	125.0	0.0	120.0	-3.0
Min - Max	90 - 160	-25 - 40	88 - 178	-44 - 58
Cycle 4 Day 1				
PRE PAC INFUSION				
n	62	60	114	113
Mean (SD)	119.6 (13.3)	-3.5 (11.9)	119.5 (14.7)	-4.1 (14.8)
Median	118.0	-3.0	120.0	-4.0
Min - Max	90 - 160	-33 - 18	90 - 155	-33 - 50
AFTER PAC INFUSION				
n	60	58	105	105
Mean (SD)	123.9 (15.1)	0.2 (13.2)	124.7 (14.7)	0.6 (16.5)
Median	122.0	0.0	125.0	-1.0
Min - Max	94 - 172	-33 - 46	82 - 168	-35 - 48
Cycle 4 Day 8				
PRE PAC INFUSION				
n	62	60	114	114
Mean (SD)	119.0 (12.7)	-4.4 (13.6)	119.1 (15.9)	-5.0 (15.8)
Median	120.0	-4.5	120.0	-5.0
Min - Max	84 - 140	-33 - 20	78 - 158	-45 - 40
AFTER PAC INFUSION				
n	60	58	107	107
Mean (SD)	123.2 (16.3)	-0.5 (15.7)	121.1 (16.1)	-3.4 (15.7)
Median	123.5	-0.5	120.0	-4.0
Min - Max	89 - 186	-33 - 60	89 - 177	-39 - 50
Cycle 4 Day 15				
PRE PAC INFUSION				
n	57	55	105	105
Mean (SD)	116.9 (12.5)	-5.7 (13.2)	118.7 (14.3)	-5.8 (15.3)
Median	118.0	-4.0	120.0	-6.0
Min - Max	85 - 150	-36 - 30	87 - 160	-39 - 50

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	53	51	98	98
Mean (SD)	121.9 (12.6)	-0.9 (11.5)	118.6 (16.1)	-5.7 (17.1)
Median	120.0	-1.0	120.0	-5.5
Min - Max	89 - 150	-27 - 29	90 - 166	-44 - 50
Cycle 5 Day 1				
PRE PAC INFUSION				
n	56	55	108	108
Mean (SD)	120.4 (11.6)	-2.2 (12.0)	119.5 (14.0)	-4.2 (14.1)
Median	120.0	-3.0	119.5	-3.0
Min - Max	100 - 150	-33 - 24	88 - 169	-33 - 40
AFTER PAC INFUSION				
n	50	49	102	102
Mean (SD)	123.3 (11.7)	1.4 (12.0)	124.6 (15.2)	0.7 (15.7)
Median	125.0	-1.0	125.0	0.0
Min - Max	100 - 153	-17 - 53	92 - 166	-29 - 50
Cycle 5 Day 8				
PRE PAC INFUSION				
n	55	54	105	105
Mean (SD)	119.4 (13.1)	-2.3 (10.9)	118.9 (13.6)	-5.5 (15.2)
Median	120.0	-3.0	120.0	-5.0
Min - Max	90 - 158	-26 - 20	91 - 154	-41 - 30
AFTER PAC INFUSION				
n	52	51	101	101
Mean (SD)	122.2 (11.9)	0.3 (10.5)	122.0 (17.2)	-2.5 (17.8)
Median	122.0	0.0	121.0	-2.0
Min - Max	90 - 154	-22 - 27	90 - 193	-34 - 73
Cycle 5 Day 15				
PRE PAC INFUSION				
n	51	50	100	100
Mean (SD)	116.5 (10.9)	-4.6 (11.3)	117.8 (14.9)	-6.1 (16.7)
Median	118.0	-4.5	119.0	-4.5
Min - Max	86 - 140	-33 - 20	84 - 159	-49 - 40
AFTER PAC INFUSION				
n	49	48	96	96
Mean (SD)	118.2 (14.7)	-3.6 (13.5)	119.9 (15.0)	-4.2 (16.8)
Median	119.0	-3.5	120.0	-5.0
Min - Max	80 - 150	-32 - 30	92 - 162	-41 - 50
Cycle 6 Day 1				
PRE PAC INFUSION				
n	52	51	101	101
Mean (SD)	119.5 (14.8)	-1.8 (14.6)	120.1 (13.3)	-4.0 (14.8)
Median	122.0	-3.0	120.0	-4.0
Min - Max	89 - 145	-47 - 25	93 - 158	-44 - 36

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	50	49	96	96
Mean (SD)	121.6 (12.1)	0.4 (11.9)	124.4 (14.1)	0.4 (15.4)
Median	121.5	0.0	126.5	-0.5
Min - Max	89 - 146	-23 - 30	94 - 172	-39 - 54
Cycle 6 Day 8				
PRE PAC INFUSION				
n	52	51	102	102
Mean (SD)	118.2 (12.5)	-2.8 (13.7)	119.6 (14.3)	-4.7 (16.3)
Median	118.5	-2.0	121.0	-3.5
Min - Max	90 - 142	-36 - 27	89 - 156	-50 - 40
AFTER PAC INFUSION				
n	48	47	97	97
Mean (SD)	119.8 (13.6)	-1.6 (14.3)	120.8 (15.6)	-3.2 (16.0)
Median	120.0	-2.0	122.0	-4.0
Min - Max	85 - 150	-40 - 28	84 - 161	-36 - 43
Cycle 6 Day 15				
PRE PAC INFUSION				
n	51	50	98	98
Mean (SD)	119.4 (13.2)	-2.2 (12.8)	118.9 (13.6)	-5.4 (15.3)
Median	120.0	-1.0	120.0	-5.0
Min - Max	96 - 153	-36 - 23	90 - 163	-40 - 41
AFTER PAC INFUSION				
n	48	47	91	91
Mean (SD)	119.5 (13.1)	-2.5 (14.6)	121.1 (14.1)	-3.4 (16.5)
Median	118.0	-4.0	120.0	-5.0
Min - Max	90 - 146	-46 - 30	91 - 167	-36 - 49
Cycle 7 Day 1				
PRE PAC INFUSION				
n	49	49	93	93
Mean (SD)	116.7 (12.2)	-3.6 (13.2)	120.3 (13.7)	-4.2 (16.0)
Median	116.0	-4.0	120.0	-3.0
Min - Max	78 - 141	-34 - 20	89 - 186	-46 - 68
AFTER PAC INFUSION				
n	46	46	83	83
Mean (SD)	120.2 (12.8)	-0.1 (14.1)	123.2 (14.1)	-0.9 (16.2)
Median	120.0	-2.0	120.0	0.0
Min - Max	88 - 150	-24 - 44	94 - 169	-39 - 49
Cycle 7 Day 8				
PRE PAC INFUSION				
n	49	49	85	85
Mean (SD)	114.2 (13.4)	-6.1 (12.8)	118.8 (14.7)	-4.6 (16.6)
Median	113.0	-6.0	119.0	-5.0
Min - Max	84 - 146	-44 - 20	88 - 165	-44 - 36

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
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Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	47	47	79	79
Mean (SD)	119.8 (14.1)	-0.8 (13.9)	119.9 (14.5)	-3.2 (17.3)
Median	118.0	-1.0	120.0	-3.0
Min - Max	87 - 155	-39 - 29	87 - 175	-39 - 55
Cycle 7 Day 15				
PRE PAC INFUSION				
n	47	47	83	83
Mean (SD)	114.4 (11.7)	-5.6 (13.7)	117.0 (15.2)	-6.4 (17.6)
Median	117.0	-5.0	116.0	-7.0
Min - Max	90 - 139	-46 - 26	89 - 157	-39 - 50
AFTER PAC INFUSION				
n	42	42	80	80
Mean (SD)	118.0 (14.4)	-2.5 (15.7)	118.5 (16.6)	-5.2 (18.4)
Median	118.5	-2.5	118.0	-7.0
Min - Max	85 - 156	-42 - 37	90 - 184	-35 - 64
Cycle 8 Day 1				
PRE PAC INFUSION				
n	47	47	90	90
Mean (SD)	118.1 (11.0)	-2.0 (11.7)	119.5 (12.7)	-4.7 (14.5)
Median	119.0	-1.0	120.0	-4.0
Min - Max	84 - 140	-28 - 23	91 - 155	-40 - 32
AFTER PAC INFUSION				
n	45	45	78	78
Mean (SD)	118.5 (12.3)	-1.8 (12.0)	122.5 (13.4)	-1.1 (15.0)
Median	120.0	0.0	124.0	0.0
Min - Max	88 - 143	-26 - 30	92 - 161	-40 - 40
Cycle 8 Day 8				
PRE PAC INFUSION				
n	45	45	81	81
Mean (SD)	116.1 (12.4)	-4.1 (12.1)	118.3 (14.9)	-5.2 (15.7)
Median	118.0	-2.0	118.0	-5.0
Min - Max	80 - 140	-41 - 13	88 - 154	-38 - 38
AFTER PAC INFUSION				
n	39	39	76	76
Mean (SD)	120.8 (11.3)	0.2 (11.3)	121.0 (13.5)	-2.6 (14.3)
Median	122.0	-1.0	120.0	0.0
Min - Max	95 - 156	-24 - 37	90 - 150	-35 - 40
Cycle 8 Day 15				
PRE PAC INFUSION				
n	45	45	77	77
Mean (SD)	117.4 (12.6)	-3.2 (12.9)	119.4 (14.0)	-4.4 (15.5)
Median	117.0	-3.0	120.0	-5.0
Min - Max	83 - 160	-41 - 35	90 - 150	-38 - 40

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	43	43	69	69
Mean (SD)	118.4 (13.1)	-2.0 (14.5)	121.4 (16.4)	-2.6 (18.1)
Median	120.0	-2.0	120.0	-2.0
Min - Max	82 - 153	-30 - 35	90 - 182	-32 - 64
Cycle 9 Day 1				
PRE PAC INFUSION				
n	37	37	77	77
Mean (SD)	119.2 (13.7)	-2.1 (14.1)	120.4 (14.8)	-3.5 (15.8)
Median	123.0	0.0	121.0	-2.0
Min - Max	80 - 150	-41 - 27	93 - 149	-40 - 40
AFTER PAC INFUSION				
n	35	35	65	65
Mean (SD)	120.3 (13.2)	-1.0 (12.7)	123.0 (15.0)	0.4 (17.6)
Median	124.0	0.0	123.0	1.0
Min - Max	90 - 141	-30 - 28	94 - 170	-30 - 50
Cycle 9 Day 8				
PRE PAC INFUSION				
n	39	39	66	66
Mean (SD)	116.3 (13.2)	-4.7 (14.5)	117.9 (14.6)	-4.4 (16.6)
Median	117.0	-3.0	118.0	-2.5
Min - Max	82 - 140	-44 - 20	90 - 154	-40 - 44
AFTER PAC INFUSION				
n	39	39	61	61
Mean (SD)	119.7 (13.5)	-1.3 (12.7)	120.4 (15.9)	-1.7 (17.1)
Median	120.0	0.0	119.0	-1.0
Min - Max	90 - 143	-27 - 29	84 - 162	-36 - 39
Cycle 9 Day 15				
PRE PAC INFUSION				
n	39	39	62	62
Mean (SD)	118.3 (12.7)	-2.7 (14.2)	117.2 (14.0)	-5.3 (15.7)
Median	120.0	-4.0	116.0	-4.0
Min - Max	88 - 140	-37 - 21	86 - 150	-36 - 28
AFTER PAC INFUSION				
n	37	37	55	55
Mean (SD)	120.5 (13.8)	-0.3 (13.7)	118.9 (14.7)	-4.5 (13.9)
Median	121.0	-2.0	120.0	-5.0
Min - Max	78 - 150	-34 - 30	89 - 151	-34 - 30
Cycle 10 Day 1				
PRE PAC INFUSION				
n	39	39	70	70
Mean (SD)	116.2 (12.7)	-4.8 (11.8)	118.8 (13.9)	-5.2 (15.6)
Median	119.0	-2.0	119.5	-5.0
Min - Max	88 - 140	-27 - 17	84 - 153	-39 - 30

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
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Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	37	37	58	58
Mean (SD)	120.1 (14.1)	-0.9 (13.8)	122.6 (14.6)	-0.2 (17.6)
Median	120.0	-1.0	120.5	0.0
Min - Max	87 - 161	-25 - 42	95 - 162	-32 - 42
Cycle 10 Day 8				
PRE PAC INFUSION				
n	38	38	61	61
Mean (SD)	115.8 (13.0)	-5.4 (14.4)	116.4 (14.3)	-7.0 (14.6)
Median	118.0	-4.5	117.0	-7.0
Min - Max	90 - 140	-40 - 20	80 - 145	-39 - 22
AFTER PAC INFUSION				
n	37	37	57	57
Mean (SD)	119.9 (15.7)	-1.5 (14.9)	118.6 (14.7)	-4.4 (15.8)
Median	121.0	1.0	118.0	-5.0
Min - Max	90 - 150	-32 - 31	88 - 166	-50 - 46
Cycle 10 Day 15				
PRE PAC INFUSION				
n	36	36	59	59
Mean (SD)	119.4 (13.5)	-1.6 (12.9)	115.9 (13.0)	-6.6 (14.8)
Median	120.0	-1.5	116.0	-5.0
Min - Max	90 - 165	-37 - 45	90 - 148	-38 - 30
AFTER PAC INFUSION				
n	35	35	52	52
Mean (SD)	120.3 (14.1)	-0.8 (12.0)	116.3 (14.2)	-5.7 (16.9)
Median	120.0	0.0	118.5	-5.0
Min - Max	90 - 160	-22 - 40	84 - 148	-51 - 30
Cycle 11 Day 1				
PRE PAC INFUSION				
n	35	35	64	64
Mean (SD)	118.5 (12.5)	-2.4 (13.5)	119.2 (14.7)	-5.3 (17.3)
Median	119.0	-2.0	119.5	-2.0
Min - Max	90 - 150	-30 - 30	82 - 150	-44 - 40
AFTER PAC INFUSION				
n	34	34	49	49
Mean (SD)	123.4 (13.2)	2.2 (14.6)	118.4 (13.6)	-3.7 (16.4)
Median	123.0	0.5	118.0	-2.0
Min - Max	94 - 150	-26 - 32	87 - 148	-34 - 40
Cycle 11 Day 8				
PRE PAC INFUSION				
n	33	33	48	48
Mean (SD)	119.1 (12.5)	-2.5 (14.4)	116.6 (13.3)	-5.9 (16.2)
Median	120.0	-3.0	111.0	-6.0
Min - Max	99 - 150	-38 - 30	99 - 147	-37 - 25

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
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Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	31	31	46	46
Mean (SD)	124.6 (14.0)	2.7 (15.3)	119.8 (13.5)	-2.5 (16.1)
Median	121.0	0.0	117.0	-1.5
Min - Max	100 - 160	-22 - 40	97 - 156	-29 - 35
Cycle 11 Day 15				
PRE PAC INFUSION				
n	34	34	44	44
Mean (SD)	118.9 (11.6)	-2.3 (14.3)	118.0 (15.9)	-4.1 (17.0)
Median	120.0	0.0	118.0	-3.5
Min - Max	89 - 150	-35 - 40	86 - 149	-39 - 30
AFTER PAC INFUSION				
n	31	31	44	44
Mean (SD)	118.4 (13.5)	-3.0 (14.9)	119.4 (14.0)	-2.8 (15.9)
Median	120.0	-1.0	120.0	-2.0
Min - Max	83 - 140	-33 - 30	90 - 152	-40 - 40
Cycle 12 Day 1				
PRE PAC INFUSION				
n	33	33	57	57
Mean (SD)	117.6 (13.3)	-3.7 (14.8)	120.1 (14.9)	-3.3 (15.2)
Median	120.0	-3.0	120.0	-1.0
Min - Max	93 - 150	-36 - 20	90 - 160	-38 - 30
AFTER PAC INFUSION				
n	30	30	43	43
Mean (SD)	121.1 (12.4)	-0.8 (13.6)	122.7 (16.1)	1.1 (17.0)
Median	120.0	-2.0	122.0	1.0
Min - Max	90 - 148	-37 - 35	92 - 176	-34 - 56
Cycle 12 Day 8				
PRE PAC INFUSION				
n	30	30	42	42
Mean (SD)	118.7 (11.3)	-3.6 (13.3)	118.6 (19.9)	-3.1 (23.1)
Median	120.5	-2.5	116.5	-2.0
Min - Max	87 - 132	-33 - 17	80 - 189	-41 - 79
AFTER PAC INFUSION				
n	24	24	40	40
Mean (SD)	121.3 (10.8)	-2.3 (12.2)	118.7 (16.2)	-2.5 (17.2)
Median	121.0	-1.0	116.5	-1.0
Min - Max	104 - 149	-23 - 36	89 - 164	-35 - 45
Cycle 12 Day 15				
PRE PAC INFUSION				
n	30	30	43	43
Mean (SD)	115.7 (12.8)	-6.2 (14.3)	119.1 (14.2)	-3.7 (17.6)
Median	117.0	-3.5	120.0	-5.0
Min - Max	90 - 150	-34 - 20	80 - 154	-40 - 50

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	26	26	40	40
Mean (SD)	119.2 (11.1)	-2.2 (11.9)	120.2 (13.4)	-2.6 (16.0)
Median	120.0	-3.0	119.5	-2.5
Min - Max	100 - 142	-21 - 29	91 - 154	-40 - 30
Cycle 13 Day 1				
PRE PAC INFUSION				
n	28	28	49	49
Mean (SD)	118.0 (12.5)	-3.2 (14.5)	118.8 (13.8)	-3.5 (16.0)
Median	120.0	-4.0	120.0	-2.0
Min - Max	93 - 143	-33 - 25	88 - 146	-37 - 40
AFTER PAC INFUSION				
n	25	25	36	36
Mean (SD)	118.6 (10.7)	-3.2 (13.7)	120.4 (15.1)	-2.0 (17.6)
Median	120.0	-6.0	117.0	0.5
Min - Max	100 - 142	-27 - 29	99 - 160	-32 - 30
Cycle 13 Day 8				
PRE PAC INFUSION				
n	26	26	36	36
Mean (SD)	114.0 (10.5)	-7.4 (11.5)	117.7 (13.6)	-3.7 (16.6)
Median	111.0	-6.0	117.0	-3.5
Min - Max	98 - 132	-36 - 10	85 - 149	-37 - 30
AFTER PAC INFUSION				
n	25	25	36	36
Mean (SD)	120.8 (11.2)	-1.2 (12.8)	119.9 (12.5)	-1.6 (13.8)
Median	120.0	0.0	120.0	0.0
Min - Max	103 - 147	-25 - 19	93 - 150	-22 - 30
Cycle 13 Day 15				
PRE PAC INFUSION				
n	25	25	35	35
Mean (SD)	119.3 (10.3)	-1.4 (13.1)	116.9 (14.7)	-4.9 (18.3)
Median	120.0	-4.0	120.0	-2.0
Min - Max	100 - 136	-24 - 25	80 - 141	-50 - 30
AFTER PAC INFUSION				
n	23	23	35	35
Mean (SD)	119.9 (11.3)	-1.1 (11.8)	119.1 (15.5)	-2.7 (18.1)
Median	124.0	0.0	113.0	-4.0
Min - Max	100 - 144	-21 - 17	88 - 156	-37 - 40
Cycle 14 Day 1				
PRE PAC INFUSION				
n	26	26	42	42
Mean (SD)	115.4 (10.5)	-5.3 (12.9)	119.6 (15.2)	-2.4 (15.8)
Median	116.0	-4.5	120.0	0.0
Min - Max	94 - 132	-31 - 17	85 - 160	-35 - 30

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	24	24	33	33
Mean (SD)	118.0 (11.1)	-2.7 (12.3)	120.0 (14.7)	-1.8 (15.0)
Median	120.0	-1.5	120.0	-6.0
Min - Max	97 - 140	-35 - 20	89 - 162	-25 - 35
Cycle 14 Day 8				
PRE PAC INFUSION				
n	25	25	32	32
Mean (SD)	117.0 (9.7)	-4.0 (11.0)	117.2 (15.6)	-4.9 (17.9)
Median	120.0	-4.0	120.0	-4.0
Min - Max	100 - 131	-24 - 15	92 - 154	-40 - 30
AFTER PAC INFUSION				
n	24	24	31	31
Mean (SD)	119.0 (11.3)	-2.5 (12.7)	117.0 (14.5)	-5.9 (16.6)
Median	120.5	-1.0	118.0	-8.0
Min - Max	99 - 140	-28 - 20	90 - 154	-36 - 40
Cycle 14 Day 15				
PRE PAC INFUSION				
n	25	25	29	29
Mean (SD)	116.3 (9.5)	-4.7 (10.7)	118.5 (14.2)	-1.4 (18.1)
Median	119.0	-4.0	117.0	-1.0
Min - Max	96 - 130	-29 - 10	91 - 146	-40 - 50
AFTER PAC INFUSION				
n	24	24	28	28
Mean (SD)	118.5 (11.4)	-3.0 (12.8)	120.0 (13.6)	-0.6 (16.8)
Median	119.5	-3.5	120.5	0.0
Min - Max	100 - 152	-31 - 19	93 - 146	-28 - 55
Cycle 15 Day 1				
PRE PAC INFUSION				
n	20	20	35	35
Mean (SD)	123.8 (13.8)	3.5 (13.8)	117.2 (12.7)	-5.0 (19.5)
Median	122.5	1.5	115.0	-7.0
Min - Max	100 - 162	-20 - 38	90 - 146	-48 - 40
AFTER PAC INFUSION				
n	19	19	25	25
Mean (SD)	123.3 (9.2)	3.3 (10.0)	120.3 (13.7)	-1.4 (19.6)
Median	126.0	4.0	119.0	2.0
Min - Max	100 - 142	-20 - 18	97 - 148	-34 - 45
Cycle 15 Day 8				
PRE PAC INFUSION				
n	18	18	27	27
Mean (SD)	116.8 (11.1)	-3.7 (11.6)	118.0 (12.4)	-3.5 (17.4)
Median	117.5	-3.0	117.0	2.0
Min - Max	100 - 145	-20 - 23	90 - 137	-35 - 40

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	18	18	27	27
Mean (SD)	122.2 (9.2)	1.7 (12.4)	118.5 (13.6)	-3.0 (17.7)
Median	123.5	1.0	118.0	-3.0
Min - Max	100 - 138	-20 - 31	89 - 145	-30 - 45
Cycle 15 Day 15				
PRE PAC INFUSION				
n	19	19	25	25
Mean (SD)	113.7 (8.1)	-6.4 (8.7)	119.5 (14.6)	-1.2 (17.8)
Median	113.0	-5.0	125.0	-1.0
Min - Max	101 - 130	-23 - 8	94 - 147	-40 - 40
AFTER PAC INFUSION				
n	19	19	25	25
Mean (SD)	118.4 (11.7)	-1.7 (9.5)	121.3 (13.9)	0.6 (19.0)
Median	115.0	-2.0	118.0	2.0
Min - Max	101 - 140	-17 - 19	98 - 149	-29 - 45
Cycle 16 Day 1				
PRE PAC INFUSION				
n	21	21	32	32
Mean (SD)	120.0 (10.5)	-0.6 (10.3)	118.6 (13.2)	-4.3 (16.5)
Median	120.0	3.0	115.0	-4.5
Min - Max	96 - 143	-18 - 16	94 - 144	-38 - 20
AFTER PAC INFUSION				
n	20	20	24	24
Mean (SD)	120.7 (10.1)	0.4 (8.9)	122.3 (14.0)	1.9 (16.4)
Median	121.5	1.0	119.0	0.0
Min - Max	107 - 148	-16 - 15	100 - 155	-24 - 35
Cycle 16 Day 8				
PRE PAC INFUSION				
n	20	20	23	23
Mean (SD)	118.4 (9.9)	-2.0 (7.7)	115.7 (12.8)	-3.7 (19.0)
Median	118.5	-3.0	115.0	-2.0
Min - Max	100 - 138	-15 - 11	90 - 136	-43 - 40
AFTER PAC INFUSION				
n	19	19	23	23
Mean (SD)	118.5 (9.3)	-2.4 (11.4)	121.6 (17.6)	2.1 (20.1)
Median	116.0	-4.0	120.0	2.0
Min - Max	104 - 138	-20 - 19	86 - 152	-30 - 62
Cycle 16 Day 15				
PRE PAC INFUSION				
n	18	18	25	25
Mean (SD)	113.7 (9.2)	-6.2 (10.1)	117.8 (15.0)	-2.2 (20.0)
Median	112.5	-7.0	117.0	-2.0
Min - Max	100 - 129	-21 - 15	90 - 159	-30 - 50

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	17	17	24	24
Mean (SD)	118.2 (7.8)	-2.2 (9.6)	118.5 (13.8)	-1.6 (16.1)
Median	120.0	-1.0	119.5	-4.0
Min - Max	100 - 129	-20 - 16	93 - 148	-26 - 50
Cycle 17 Day 1				
PRE PAC INFUSION				
n	18	18	31	31
Mean (SD)	115.6 (8.1)	-4.1 (9.0)	117.0 (14.1)	-5.3 (19.5)
Median	118.0	-3.0	121.0	-2.0
Min - Max	98 - 127	-18 - 10	90 - 144	-44 - 40
AFTER PAC INFUSION				
n	17	17	23	23
Mean (SD)	116.5 (9.6)	-2.8 (11.0)	121.2 (12.0)	2.4 (18.9)
Median	118.0	-3.0	122.0	2.0
Min - Max	98 - 132	-20 - 19	96 - 143	-29 - 40
Cycle 17 Day 8				
PRE PAC INFUSION				
n	16	16	20	20
Mean (SD)	117.4 (7.0)	-1.6 (9.4)	117.5 (16.6)	-3.2 (20.3)
Median	117.0	-1.5	117.5	-2.0
Min - Max	105 - 130	-21 - 20	99 - 160	-35 - 40
AFTER PAC INFUSION				
n	16	16	20	20
Mean (SD)	116.9 (9.5)	-2.1 (9.4)	125.0 (15.2)	4.3 (18.2)
Median	114.5	-1.5	122.5	1.0
Min - Max	103 - 136	-19 - 12	93 - 155	-26 - 50
Cycle 17 Day 15				
PRE PAC INFUSION				
n	17	17	21	21
Mean (SD)	117.9 (7.8)	-2.8 (9.7)	116.8 (15.1)	-3.2 (16.7)
Median	116.0	-3.0	116.0	0.0
Min - Max	107 - 130	-20 - 15	78 - 138	-36 - 20
AFTER PAC INFUSION				
n	17	17	22	22
Mean (SD)	120.7 (10.5)	0.0 (14.5)	119.2 (15.0)	-0.4 (15.4)
Median	120.0	-1.0	117.5	-2.0
Min - Max	107 - 148	-18 - 48	86 - 149	-24 - 25
Cycle 18 Day 1				
PRE PAC INFUSION				
n	16	16	24	24
Mean (SD)	119.3 (11.8)	-2.3 (11.7)	117.7 (14.2)	-3.9 (17.4)
Median	120.5	-2.5	119.0	-3.0
Min - Max	87 - 145	-27 - 29	84 - 143	-32 - 26

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	14	14	21	21
Mean (SD)	123.7 (10.3)	2.4 (9.5)	120.0 (14.3)	0.0 (14.7)
Median	125.0	1.5	119.0	-2.0
Min - Max	108 - 140	-10 - 25	88 - 141	-28 - 34
Cycle 18 Day 8				
PRE PAC INFUSION				
n	14	14	21	21
Mean (SD)	117.2 (9.9)	-3.2 (11.0)	114.9 (11.3)	-4.8 (15.5)
Median	118.5	-4.5	112.0	-9.0
Min - Max	103 - 132	-21 - 12	93 - 134	-33 - 24
AFTER PAC INFUSION				
n	14	14	20	20
Mean (SD)	118.6 (9.9)	-1.8 (9.1)	118.2 (11.8)	-1.5 (12.7)
Median	120.5	-1.0	119.5	-1.5
Min - Max	100 - 137	-20 - 14	95 - 143	-21 - 20
Cycle 18 Day 15				
PRE PAC INFUSION				
n	15	15	20	20
Mean (SD)	116.3 (11.0)	-5.1 (12.7)	116.5 (14.8)	-1.5 (16.5)
Median	120.0	-3.0	118.5	-1.0
Min - Max	100 - 132	-27 - 10	91 - 141	-33 - 28
AFTER PAC INFUSION				
n	15	15	19	19
Mean (SD)	121.1 (8.9)	-0.3 (9.1)	117.6 (14.8)	-0.2 (15.7)
Median	120.0	1.0	116.0	-2.0
Min - Max	100 - 134	-20 - 15	87 - 144	-23 - 25
Cycle 19 Day 1				
PRE PAC INFUSION				
n	11	11	26	26
Mean (SD)	116.8 (8.0)	-5.3 (10.0)	117.7 (14.1)	-3.8 (16.2)
Median	120.0	-8.0	119.5	-6.5
Min - Max	102 - 128	-20 - 10	90 - 140	-30 - 30
AFTER PAC INFUSION				
n	10	10	19	19
Mean (SD)	114.9 (12.6)	-8.4 (9.6)	122.3 (14.8)	4.2 (16.2)
Median	114.0	-7.0	123.0	0.0
Min - Max	92 - 132	-24 - 8	91 - 150	-17 - 40
Cycle 19 Day 8				
PRE PAC INFUSION				
n	9	9	20	20
Mean (SD)	116.4 (12.1)	-5.6 (11.4)	116.6 (12.1)	-2.4 (15.3)
Median	120.0	-7.0	119.5	-2.5
Min - Max	100 - 134	-20 - 10	89 - 132	-29 - 30

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	9	9	19	19
Mean (SD)	117.3 (11.1)	-4.7 (9.1)	117.4 (13.3)	-0.9 (13.6)
Median	118.0	-3.0	119.0	-7.0
Min - Max	100 - 134	-20 - 9	88 - 139	-26 - 20
Cycle 19 Day 15				
PRE PAC INFUSION				
n	10	10	20	20
Mean (SD)	116.6 (11.8)	-6.7 (11.9)	115.5 (14.2)	-2.4 (16.5)
Median	117.5	-9.0	111.5	0.0
Min - Max	103 - 130	-20 - 19	91 - 152	-28 - 26
AFTER PAC INFUSION				
n	9	9	19	19
Mean (SD)	120.8 (10.2)	-2.7 (7.7)	116.7 (13.7)	-0.4 (14.2)
Median	123.0	-1.0	118.0	3.0
Min - Max	100 - 134	-20 - 9	91 - 138	-35 - 20
Cycle 20 Day 1				
PRE PAC INFUSION				
n	11	11	23	23
Mean (SD)	117.9 (8.6)	-4.2 (6.8)	121.6 (15.6)	-0.4 (15.1)
Median	119.0	-5.0	122.0	0.0
Min - Max	107 - 131	-11 - 10	84 - 147	-25 - 26
AFTER PAC INFUSION				
n	10	10	17	17
Mean (SD)	118.4 (9.7)	-4.9 (8.6)	121.8 (20.7)	3.5 (22.3)
Median	120.0	-5.5	122.0	2.0
Min - Max	102 - 132	-20 - 9	85 - 178	-29 - 60
Cycle 20 Day 8				
PRE PAC INFUSION				
n	9	9	16	16
Mean (SD)	115.4 (13.3)	-6.8 (12.5)	117.1 (12.9)	-2.0 (16.4)
Median	115.0	-7.0	112.0	-3.0
Min - Max	100 - 137	-26 - 13	97 - 153	-29 - 32
AFTER PAC INFUSION				
n	9	9	16	16
Mean (SD)	114.2 (10.8)	-8.0 (10.3)	120.3 (13.3)	1.2 (14.8)
Median	111.0	-13.0	117.5	-2.0
Min - Max	100 - 135	-20 - 11	97 - 145	-25 - 24
Cycle 20 Day 15				
PRE PAC INFUSION				
n	10	10	16	16
Mean (SD)	121.0 (9.3)	-2.3 (10.0)	115.6 (12.0)	-3.4 (16.3)
Median	121.0	-2.5	116.0	-4.5
Min - Max	104 - 133	-15 - 16	91 - 135	-34 - 30

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	10	10	16	16
Mean (SD)	120.5 (9.9)	-2.8 (5.8)	115.3 (14.2)	-3.6 (14.4)
Median	118.5	-1.5	115.5	-5.0
Min - Max	110 - 137	-14 - 5	90 - 140	-29 - 20
Cycle 21 Day 1				
PRE PAC INFUSION				
n	9	9	21	21
Mean (SD)	116.3 (8.1)	-5.0 (11.8)	123.0 (14.6)	1.0 (20.7)
Median	119.0	-6.0	125.0	2.0
Min - Max	104 - 128	-27 - 10	91 - 150	-41 - 40
AFTER PAC INFUSION				
n	6	6	15	15
Mean (SD)	118.8 (19.4)	-3.2 (14.1)	124.5 (11.7)	5.4 (21.8)
Median	111.5	-5.0	126.0	5.0
Min - Max	100 - 155	-20 - 22	97 - 140	-35 - 50
Cycle 21 Day 8				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	117.3 (7.5)	-5.7 (9.9)	118.5 (11.8)	-0.7 (19.5)
Median	119.0	-5.0	121.0	0.0
Min - Max	106 - 128	-27 - 9	98 - 142	-37 - 40
AFTER PAC INFUSION				
n	9	9	14	14
Mean (SD)	118.9 (9.1)	-4.1 (9.2)	120.6 (10.9)	1.4 (17.0)
Median	120.0	-2.0	120.5	0.0
Min - Max	102 - 135	-20 - 9	98 - 138	-25 - 31
Cycle 21 Day 15				
PRE PAC INFUSION				
n	9	9	15	15
Mean (SD)	118.7 (8.1)	-4.8 (5.6)	119.3 (10.1)	0.1 (18.5)
Median	117.0	-3.0	120.0	-2.0
Min - Max	110 - 136	-16 - 1	102 - 136	-33 - 45
AFTER PAC INFUSION				
n	8	8	15	15
Mean (SD)	121.4 (9.6)	-1.8 (9.0)	119.7 (11.3)	0.6 (17.6)
Median	123.0	-0.5	119.0	-2.0
Min - Max	107 - 136	-15 - 12	94 - 140	-30 - 35
Cycle 22 Day 1				
PRE PAC INFUSION				
n	10	10	21	21
Mean (SD)	116.7 (9.4)	-4.1 (12.4)	119.4 (11.7)	-2.6 (18.6)
Median	116.0	-3.0	118.0	0.0
Min - Max	101 - 130	-20 - 15	104 - 143	-36 - 40

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	7	7	15	15
Mean (SD)	117.1 (11.6)	-5.1 (7.7)	124.1 (10.0)	4.9 (16.8)
Median	111.0	-1.0	125.0	2.0
Min - Max	102 - 132	-17 - 5	102 - 137	-27 - 45
Cycle 22 Day 8				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	118.7 (7.2)	-4.3 (5.6)	120.9 (12.0)	1.7 (16.7)
Median	120.0	-6.0	121.5	0.0
Min - Max	109 - 129	-10 - 9	100 - 143	-27 - 33
AFTER PAC INFUSION				
n	9	9	14	14
Mean (SD)	122.2 (20.0)	-0.8 (15.5)	124.5 (11.9)	5.3 (16.2)
Median	120.0	-1.0	123.5	5.0
Min - Max	100 - 163	-20 - 30	98 - 148	-21 - 40
Cycle 22 Day 15				
PRE PAC INFUSION				
n	7	7	14	14
Mean (SD)	117.4 (10.8)	-4.0 (5.8)	119.2 (13.2)	1.6 (18.2)
Median	120.0	-3.0	118.0	0.0
Min - Max	104 - 135	-15 - 2	95 - 141	-22 - 50
AFTER PAC INFUSION				
n	7	7	14	14
Mean (SD)	115.1 (9.4)	-6.3 (5.1)	122.5 (14.1)	4.9 (19.0)
Median	110.0	-7.0	122.5	4.5
Min - Max	102 - 126	-14 - -1	95 - 149	-24 - 50
Cycle 23 Day 1				
PRE PAC INFUSION				
n	9	9	19	19
Mean (SD)	112.8 (9.9)	-9.2 (11.2)	120.5 (16.0)	-1.6 (16.7)
Median	110.0	-7.0	120.0	-2.0
Min - Max	100 - 130	-28 - 8	95 - 148	-28 - 40
AFTER PAC INFUSION				
n	7	7	13	13
Mean (SD)	113.9 (7.1)	-8.4 (6.1)	121.4 (15.4)	2.5 (19.0)
Median	110.0	-10.0	117.0	-4.0
Min - Max	107 - 125	-17 - -1	99 - 149	-34 - 45
Cycle 23 Day 8				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	114.4 (10.2)	-7.1 (7.9)	117.3 (14.8)	-4.3 (16.2)
Median	110.0	-7.0	119.0	-5.0
Min - Max	100 - 127	-20 - 5	88 - 137	-29 - 22

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	122.5 (12.5)	1.0 (9.8)	118.2 (12.9)	-3.4 (17.8)
Median	123.0	1.0	114.0	-7.0
Min - Max	101 - 135	-15 - 12	93 - 140	-23 - 24
Cycle 23 Day 15				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	116.8 (10.7)	-4.8 (11.4)	115.8 (11.1)	0.1 (12.3)
Median	118.0	-3.5	116.0	1.0
Min - Max	100 - 133	-20 - 11	102 - 138	-27 - 17
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	119.0 (13.6)	-2.5 (10.2)	121.9 (13.7)	6.2 (15.7)
Median	119.5	-2.5	120.0	0.0
Min - Max	100 - 142	-20 - 9	96 - 140	-21 - 32
Cycle 24 Day 1				
PRE PAC INFUSION				
n	9	9	17	17
Mean (SD)	122.9 (16.8)	0.9 (15.6)	119.1 (12.6)	-3.9 (17.7)
Median	125.0	-2.0	119.0	-9.0
Min - Max	100 - 155	-20 - 33	95 - 137	-30 - 40
AFTER PAC INFUSION				
n	7	7	12	12
Mean (SD)	122.9 (11.3)	0.6 (12.5)	122.6 (13.4)	2.1 (18.7)
Median	123.0	7.0	124.5	-3.0
Min - Max	100 - 133	-20 - 14	95 - 140	-30 - 45
Cycle 24 Day 8				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	116.4 (9.0)	-5.1 (9.4)	118.8 (13.1)	-1.9 (17.2)
Median	119.0	-4.5	120.0	0.0
Min - Max	100 - 125	-20 - 9	100 - 140	-35 - 30
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	116.8 (14.1)	-4.8 (14.2)	120.3 (11.6)	-0.5 (16.9)
Median	119.0	-3.5	123.0	-8.0
Min - Max	90 - 130	-30 - 19	101 - 140	-27 - 34
Cycle 24 Day 15				
PRE PAC INFUSION				
n	8	8	12	12
Mean (SD)	115.8 (6.0)	-5.8 (9.7)	117.0 (16.0)	-3.5 (21.0)
Median	116.0	-4.5	114.0	-6.0
Min - Max	108 - 124	-25 - 9	91 - 135	-40 - 40

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	8	8	12	12
Mean (SD)	119.6 (11.0)	-1.9 (8.9)	120.4 (14.7)	-0.1 (22.9)
Median	123.5	-1.0	120.5	-3.5
Min - Max	100 - 133	-20 - 11	96 - 140	-41 - 50
Cycle 25 Day 1				
PRE PAC INFUSION				
n	8	8	14	14
Mean (SD)	112.6 (19.1)	-9.1 (22.2)	122.4 (17.8)	-2.1 (15.9)
Median	109.0	-14.0	124.0	-0.5
Min - Max	79 - 137	-43 - 21	88 - 150	-33 - 30
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	117.7 (8.4)	-3.4 (6.6)	118.6 (17.1)	-4.9 (11.6)
Median	113.0	-5.0	117.0	-7.0
Min - Max	110 - 130	-10 - 9	85 - 144	-20 - 12
Cycle 25 Day 8				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	122.0 (13.0)	0.9 (10.4)	120.1 (10.9)	-5.2 (8.7)
Median	117.0	-1.0	120.0	-6.0
Min - Max	110 - 140	-10 - 20	103 - 138	-18 - 6
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	117.7 (11.3)	-3.4 (8.1)	123.8 (13.9)	-1.6 (11.8)
Median	116.0	-1.0	121.0	1.0
Min - Max	100 - 133	-20 - 6	104 - 144	-23 - 20
Cycle 25 Day 15				
PRE PAC INFUSION				
n	7	7	10	10
Mean (SD)	114.0 (10.7)	-7.1 (10.7)	116.0 (14.1)	-8.6 (12.4)
Median	114.0	-10.0	117.0	-8.5
Min - Max	100 - 129	-20 - 9	88 - 134	-33 - 14
AFTER PAC INFUSION				
n	7	7	10	10
Mean (SD)	123.9 (13.9)	2.7 (14.4)	121.4 (14.5)	-3.2 (13.2)
Median	123.0	4.0	120.0	-2.0
Min - Max	100 - 142	-20 - 26	92 - 140	-23 - 20
Cycle 26 Day 1				
PRE PAC INFUSION				
n	8	8	14	14
Mean (SD)	118.4 (10.3)	-3.4 (12.2)	115.9 (13.7)	-10.6 (13.5)
Median	121.0	-3.0	116.0	-11.0
Min - Max	100 - 131	-20 - 15	86 - 137	-36 - 17

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	126.6 (15.3)	5.4 (13.9)	120.3 (15.3)	-4.8 (12.2)
Median	128.0	5.0	123.0	-6.0
Min - Max	100 - 147	-20 - 25	94 - 140	-21 - 20
Cycle 26 Day 8				
PRE PAC INFUSION				
n	7	7	7	7
Mean (SD)	116.6 (11.0)	-4.6 (11.9)	117.1 (16.0)	-8.0 (14.8)
Median	119.0	3.0	121.0	-10.0
Min - Max	100 - 130	-20 - 9	90 - 136	-33 - 16
AFTER PAC INFUSION				
n	7	7	7	7
Mean (SD)	119.1 (14.3)	-2.0 (9.5)	121.0 (11.3)	-4.1 (16.6)
Median	113.0	-1.0	120.0	-7.0
Min - Max	100 - 139	-20 - 8	106 - 140	-31 - 20
Cycle 26 Day 15				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	117.6 (10.6)	-3.6 (10.9)	115.4 (10.2)	-9.7 (10.0)
Median	112.0	-7.0	117.0	-7.0
Min - Max	106 - 133	-16 - 17	99 - 130	-26 - 0
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	118.9 (9.5)	-2.3 (4.9)	125.2 (17.1)	0.1 (12.0)
Median	117.0	-1.0	123.0	1.0
Min - Max	110 - 133	-10 - 4	88 - 148	-15 - 21
Cycle 27 Day 1				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	118.6 (7.1)	-4.7 (6.6)	117.0 (15.2)	-9.5 (14.3)
Median	118.0	-6.0	111.5	-9.0
Min - Max	110 - 130	-13 - 9	91 - 142	-36 - 12
AFTER PAC INFUSION				
n	8	8	8	8
Mean (SD)	117.4 (11.8)	-5.5 (8.6)	114.9 (15.0)	-8.4 (13.1)
Median	117.0	-7.0	114.5	-9.5
Min - Max	96 - 132	-20 - 9	86 - 140	-22 - 20
Cycle 27 Day 8				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	116.7 (8.5)	-2.5 (9.7)	115.9 (12.4)	-10.1 (9.2)
Median	115.0	-4.5	112.5	-9.5
Min - Max	108 - 128	-12 - 9	96 - 136	-22 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	6	6	8	8
Mean (SD)	115.7 (8.1)	-3.5 (7.9)	122.6 (13.7)	-3.4 (11.8)
Median	115.0	-4.0	123.0	-3.5
Min - Max	106 - 128	-13 - 9	98 - 140	-23 - 13
Cycle 27 Day 15				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	118.6 (14.2)	-2.9 (10.6)	119.9 (13.9)	-5.2 (14.0)
Median	119.0	-1.0	124.0	-5.0
Min - Max	100 - 139	-20 - 12	93 - 134	-33 - 10
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	117.4 (9.2)	-4.0 (3.8)	122.6 (12.3)	-2.6 (14.3)
Median	114.0	-5.0	123.0	-2.0
Min - Max	110 - 132	-10 - 2	105 - 140	-24 - 20
Cycle 28 Day 1				
PRE PAC INFUSION				
n	7	7	13	13
Mean (SD)	114.9 (9.9)	-5.3 (10.8)	114.2 (13.8)	-12.5 (19.1)
Median	113.0	-9.0	115.0	-18.0
Min - Max	100 - 132	-20 - 9	96 - 139	-43 - 23
AFTER PAC INFUSION				
n	6	6	6	6
Mean (SD)	120.2 (10.7)	1.0 (8.6)	112.5 (16.1)	-9.2 (8.1)
Median	116.5	2.0	116.0	-10.5
Min - Max	110 - 136	-10 - 9	89 - 129	-20 - 5
Cycle 28 Day 8				
PRE PAC INFUSION				
n	6	6	7	7
Mean (SD)	117.7 (9.1)	-1.5 (9.8)	113.9 (16.7)	-13.0 (19.4)
Median	120.0	1.5	121.0	-16.0
Min - Max	105 - 130	-14 - 9	90 - 137	-45 - 13
AFTER PAC INFUSION				
n	6	6	7	7
Mean (SD)	119.8 (10.3)	0.7 (9.4)	118.3 (9.9)	-8.6 (10.4)
Median	116.5	2.5	120.0	-13.0
Min - Max	110 - 136	-10 - 9	100 - 130	-20 - 6
Cycle 28 Day 15				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	113.8 (12.7)	-5.3 (12.9)	115.9 (11.8)	-9.9 (12.4)
Median	112.5	-2.5	120.5	-10.0
Min - Max	100 - 129	-21 - 12	94 - 128	-30 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	6	6	8	8
Mean (SD)	116.2 (12.4)	-3.0 (8.9)	116.0 (14.9)	-9.8 (16.2)
Median	111.5	-3.5	124.5	-8.5
Min - Max	105 - 135	-14 - 8	91 - 129	-35 - 9
Cycle 29 Day 1				
PRE PAC INFUSION				
n	7	7	11	11
Mean (SD)	120.3 (7.6)	-2.0 (7.3)	119.4 (9.4)	-6.7 (16.6)
Median	120.0	-4.0	118.0	-3.0
Min - Max	110 - 134	-10 - 9	108 - 135	-37 - 15
AFTER PAC INFUSION				
n	6	6	6	6
Mean (SD)	124.2 (7.9)	2.5 (4.0)	117.5 (11.3)	-6.2 (11.6)
Median	121.0	0.0	120.5	-6.5
Min - Max	116 - 135	0 - 9	99 - 130	-22 - 10
Cycle 29 Day 8				
PRE PAC INFUSION				
n	6	6	5	5
Mean (SD)	121.7 (13.5)	0.0 (11.5)	113.2 (14.2)	-9.4 (10.7)
Median	128.0	0.5	112.0	-8.0
Min - Max	100 - 134	-19 - 12	92 - 131	-20 - 7
AFTER PAC INFUSION				
n	6	6	5	5
Mean (SD)	124.5 (7.9)	2.8 (9.0)	107.8 (15.0)	-14.8 (14.6)
Median	125.5	0.0	110.0	-10.0
Min - Max	113 - 134	-6 - 19	90 - 127	-36 - 3
Cycle 29 Day 15				
PRE PAC INFUSION				
n	6	6	7	7
Mean (SD)	122.3 (7.8)	0.7 (8.7)	121.0 (10.8)	-2.7 (16.2)
Median	122.5	2.5	118.0	0.0
Min - Max	110 - 132	-12 - 9	110 - 140	-22 - 20
AFTER PAC INFUSION				
n	6	6	7	7
Mean (SD)	117.7 (14.9)	-4.0 (11.5)	116.3 (17.1)	-7.4 (17.5)
Median	119.5	0.5	122.0	-2.0
Min - Max	93 - 136	-23 - 9	90 - 134	-31 - 13
Cycle 30 Day 1				
PRE PAC INFUSION				
n	7	7	12	12
Mean (SD)	120.6 (6.8)	-1.7 (6.0)	117.7 (15.0)	-8.3 (15.6)
Median	120.0	-4.0	115.0	-7.0
Min - Max	112 - 130	-7 - 9	94 - 140	-34 - 20

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
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Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	5	5	7	7
Mean (SD)	128.4 (14.1)	6.2 (15.7)	116.4 (11.0)	-7.3 (8.9)
Median	132.0	9.0	115.0	-5.0
Min - Max	109 - 145	-13 - 29	99 - 131	-22 - 5
Cycle 30 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	125.6 (8.9)	3.4 (11.2)	108.6 (9.8)	-17.0 (16.5)
Median	130.0	3.0	104.0	-27.0
Min - Max	113 - 135	-9 - 19	101 - 125	-32 - 1
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	117.4 (13.0)	-4.8 (11.3)	117.0 (13.1)	-8.6 (15.9)
Median	120.0	-8.0	114.0	-8.0
Min - Max	102 - 132	-16 - 9	104 - 134	-26 - 10
Cycle 30 Day 15				
PRE PAC INFUSION				
n	4	4	7	7
Mean (SD)	120.5 (4.7)	-0.5 (7.1)	112.3 (12.7)	-11.4 (17.0)
Median	119.5	-1.5	120.0	-2.0
Min - Max	116 - 127	-8 - 9	98 - 127	-37 - 4
AFTER PAC INFUSION				
n	4	4	7	7
Mean (SD)	121.5 (7.1)	0.5 (6.2)	115.3 (16.1)	-8.4 (16.4)
Median	118.5	-1.0	116.0	-2.0
Min - Max	117 - 132	-5 - 9	95 - 136	-36 - 7
Cycle 31 Day 1				
PRE PAC INFUSION				
n	6	6	12	12
Mean (SD)	116.3 (11.5)	-5.2 (7.2)	114.3 (16.6)	-11.7 (17.9)
Median	116.0	-2.5	112.5	-17.5
Min - Max	101 - 132	-15 - 3	85 - 140	-35 - 16
AFTER PAC INFUSION				
n	4	4	6	6
Mean (SD)	124.3 (8.1)	3.3 (6.1)	118.3 (13.9)	-6.0 (13.8)
Median	125.0	3.5	117.0	-6.0
Min - Max	115 - 132	-3 - 9	101 - 137	-29 - 13
Cycle 31 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	117.0 (11.1)	-5.2 (4.4)	112.6 (13.0)	-13.0 (15.3)
Median	115.0	-3.0	107.0	-12.0
Min - Max	104 - 132	-12 - -1	100 - 128	-29 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	118.2 (13.9)	-4.0 (9.1)	115.6 (15.8)	-10.0 (15.8)
Median	114.0	-1.0	109.0	-5.0
Min - Max	102 - 135	-20 - 3	97 - 134	-29 - 10
Cycle 31 Day 15				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	129.0 (5.5)	4.0 (5.8)	114.3 (14.4)	-10.0 (12.1)
Median	131.0	4.0	116.0	-13.5
Min - Max	121 - 133	-3 - 11	90 - 134	-22 - 10
AFTER PAC INFUSION				
n	4	4	6	6
Mean (SD)	129.8 (10.9)	4.8 (10.3)	112.7 (16.9)	-11.7 (11.6)
Median	133.5	6.0	113.5	-11.5
Min - Max	114 - 138	-8 - 15	84 - 129	-30 - 5
Cycle 32 Day 1				
PRE PAC INFUSION				
n	7	7	11	11
Mean (SD)	128.4 (13.6)	6.1 (13.6)	113.0 (12.8)	-13.5 (13.1)
Median	132.0	6.0	119.0	-12.0
Min - Max	104 - 147	-15 - 25	96 - 130	-31 - 5
AFTER PAC INFUSION				
n	5	5	6	6
Mean (SD)	121.2 (12.2)	-1.0 (4.3)	116.8 (12.9)	-7.5 (12.9)
Median	118.0	-1.0	112.5	-3.0
Min - Max	110 - 136	-6 - 5	103 - 140	-26 - 5
Cycle 32 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	126.0 (15.3)	3.8 (13.2)	113.8 (17.7)	-11.8 (15.4)
Median	130.0	7.0	114.0	-9.0
Min - Max	103 - 143	-13 - 21	92 - 134	-31 - 10
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	125.0 (12.7)	2.8 (10.3)	114.8 (11.4)	-10.8 (13.6)
Median	130.0	8.0	114.0	-12.0
Min - Max	105 - 135	-11 - 13	101 - 129	-25 - 5
Cycle 32 Day 15				
PRE PAC INFUSION				
n	4	4	5	5
Mean (SD)	123.5 (13.5)	4.5 (11.1)	110.6 (19.9)	-11.6 (19.0)
Median	124.0	5.0	108.0	-16.0
Min - Max	107 - 139	-9 - 17	84 - 137	-29 - 13

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	4	4	5	5
Mean (SD)	129.8 (13.0)	10.8 (6.9)	110.4 (10.3)	-11.8 (15.4)
Median	128.0	11.5	107.0	-2.0
Min - Max	118 - 145	2 - 18	98 - 122	-30 - 2
Cycle 33 Day 1				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	122.9 (10.9)	0.6 (10.7)	122.1 (11.0)	-4.3 (13.7)
Median	129.0	1.0	120.0	-1.0
Min - Max	106 - 130	-11 - 19	103 - 141	-24 - 17
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	121.0 (13.1)	-1.2 (8.7)	126.0 (13.3)	4.2 (7.9)
Median	120.0	1.0	132.0	3.0
Min - Max	102 - 136	-14 - 9	103 - 135	-6 - 14
Cycle 33 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	124.3 (10.9)	3.3 (7.9)	112.5 (17.2)	-10.3 (20.3)
Median	126.0	2.5	106.5	-11.5
Min - Max	110 - 135	-5 - 13	100 - 137	-31 - 13
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	126.8 (14.7)	5.8 (7.2)	119.3 (19.8)	-3.5 (6.6)
Median	125.5	9.0	127.0	-4.5
Min - Max	111 - 145	-5 - 10	90 - 133	-10 - 5
Cycle 33 Day 15				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	120.8 (10.9)	-1.4 (6.0)	107.2 (12.1)	-14.6 (15.7)
Median	126.0	-1.0	102.0	-16.0
Min - Max	108 - 130	-8 - 8	98 - 128	-34 - 4
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	121.8 (12.1)	-0.4 (5.1)	118.8 (20.5)	-3.0 (10.2)
Median	118.0	-1.0	120.0	-7.0
Min - Max	110 - 142	-5 - 7	93 - 148	-12 - 13
Cycle 34 Day 1				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	126.9 (7.6)	4.6 (7.5)	106.4 (13.0)	-20.0 (12.0)
Median	126.0	2.0	110.0	-19.0
Min - Max	120 - 141	-3 - 19	87 - 126	-42 - -4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	122.8 (9.7)	0.6 (5.4)	115.5 (12.8)	-3.0 (11.0)
Median	120.0	-2.0	113.5	-2.5
Min - Max	112 - 138	-4 - 9	104 - 131	-14 - 7
Cycle 34 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	122.5 (13.0)	-2.5 (7.8)	118.3 (19.9)	-4.5 (16.8)
Median	125.0	-3.0	113.5	1.0
Min - Max	105 - 135	-11 - 7	102 - 144	-29 - 9
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	117.0 (14.3)	-8.0 (6.5)	124.3 (27.1)	1.5 (18.3)
Median	118.0	-6.5	122.0	1.5
Min - Max	99 - 133	-17 - -2	95 - 158	-20 - 23
Cycle 34 Day 15				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	118.4 (12.8)	-3.8 (5.6)	114.6 (10.5)	-7.2 (17.9)
Median	126.0	-5.0	113.0	4.0
Min - Max	100 - 130	-11 - 4	102 - 128	-33 - 8
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	122.2 (7.4)	0.0 (11.2)	121.2 (10.0)	-0.6 (9.7)
Median	124.0	-3.0	124.0	0.0
Min - Max	110 - 130	-10 - 19	106 - 131	-15 - 10
Cycle 35 Day 1				
PRE PAC INFUSION				
n	7	7	8	8
Mean (SD)	118.7 (10.2)	-3.6 (5.5)	115.3 (15.7)	-12.3 (15.2)
Median	122.0	-4.0	114.0	-12.5
Min - Max	100 - 130	-11 - 5	94 - 145	-35 - 15
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	124.2 (8.5)	2.0 (5.0)	120.0 (6.3)	-2.8 (12.6)
Median	125.0	1.0	119.0	-4.5
Min - Max	113 - 136	-3 - 9	114 - 128	-16 - 14
Cycle 35 Day 8				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	120.4 (7.2)	-1.8 (7.5)	111.5 (14.0)	-11.3 (20.6)
Median	120.0	-2.0	106.5	-11.0
Min - Max	114 - 132	-12 - 9	101 - 132	-31 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	117.0 (11.6)	-5.2 (10.1)	121.0 (14.0)	-1.8 (13.8)
Median	120.0	-7.0	118.5	3.0
Min - Max	103 - 133	-19 - 9	109 - 138	-22 - 9
Cycle 35 Day 15				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	117.0 (10.0)	-5.2 (3.8)	118.3 (7.5)	-4.5 (19.3)
Median	113.0	-5.0	115.5	-7.0
Min - Max	107 - 130	-9 - -1	113 - 129	-22 - 18
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	129.0 (10.8)	6.8 (8.9)	118.5 (20.9)	-4.3 (16.3)
Median	125.0	9.0	117.0	2.0
Min - Max	120 - 145	-2 - 19	98 - 142	-28 - 7
Cycle 36 Day 1				
PRE PAC INFUSION				
n	7	7	8	8
Mean (SD)	119.3 (8.3)	-3.0 (6.5)	117.8 (13.8)	-9.8 (17.7)
Median	115.0	-2.0	116.5	-12.5
Min - Max	110 - 129	-14 - 7	100 - 139	-35 - 13
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	116.8 (12.5)	-5.4 (6.6)	121.3 (5.1)	-1.5 (15.3)
Median	114.0	-5.0	121.0	-4.0
Min - Max	101 - 130	-15 - 2	116 - 127	-16 - 18
Cycle 36 Day 8				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	119.0 (15.7)	-3.2 (15.4)	114.5 (9.8)	-8.3 (17.1)
Median	125.0	-2.0	110.5	-9.0
Min - Max	99 - 135	-23 - 19	108 - 129	-23 - 8
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	116.6 (16.4)	-5.6 (12.8)	125.3 (15.2)	2.5 (7.0)
Median	120.0	-1.0	131.0	3.5
Min - Max	98 - 137	-20 - 9	103 - 136	-7 - 10
Cycle 36 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	116.5 (11.5)	-4.5 (7.9)	118.3 (13.5)	-4.5 (21.7)
Median	114.0	-2.0	115.5	-1.0
Min - Max	106 - 132	-16 - 2	105 - 137	-30 - 14

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	115.5 (10.8)	-5.5 (10.0)	120.8 (14.0)	-2.0 (9.0)
Median	115.5	-9.0	124.5	-0.5
Min - Max	103 - 128	-13 - 9	102 - 132	-14 - 7
Cycle 37 Day 1				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	122.2 (6.1)	-0.2 (9.8)	115.8 (11.1)	-11.8 (13.2)
Median	122.0	-2.0	116.0	-10.0
Min - Max	114 - 130	-8 - 19	101 - 130	-33 - 3
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	119.8 (11.4)	-2.5 (2.4)	122.5 (17.8)	-0.3 (2.1)
Median	117.0	-2.5	128.0	0.0
Min - Max	110 - 135	-5 - 0	97 - 137	-3 - 2
Cycle 37 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	120.8 (11.8)	-1.5 (1.9)	113.8 (17.3)	-9.0 (18.4)
Median	118.5	-2.0	112.5	-4.5
Min - Max	110 - 136	-3 - 1	98 - 132	-35 - 8
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	123.0 (14.4)	0.8 (4.2)	121.8 (14.5)	-1.0 (4.5)
Median	120.0	-1.0	128.5	-2.0
Min - Max	110 - 142	-2 - 7	100 - 130	-5 - 5
Cycle 37 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	116.3 (10.6)	-6.0 (4.2)	110.0 (10.2)	-12.8 (17.9)
Median	116.0	-6.0	107.5	-10.5
Min - Max	105 - 128	-11 - -1	101 - 124	-34 - 4
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	114.8 (15.5)	-7.5 (8.5)	122.8 (19.3)	0.0 (5.4)
Median	114.0	-5.0	131.0	-0.5
Min - Max	97 - 134	-19 - -1	94 - 135	-6 - 7
Cycle 38 Day 1				
PRE PAC INFUSION				
n	5	5	8	8
Mean (SD)	123.0 (7.7)	3.2 (8.1)	116.6 (13.0)	-10.9 (10.2)
Median	120.0	7.0	118.0	-10.0
Min - Max	116 - 134	-10 - 9	90 - 135	-27 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	109.3 (24.0)	-8.7 (19.7)	119.8 (9.7)	-3.0 (6.2)
Median	110.0	-1.0	122.5	-5.5
Min - Max	85 - 133	-31 - 6	106 - 128	-7 - 6
Cycle 38 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	120.3 (7.3)	-2.0 (7.9)	107.0 (10.3)	-15.8 (18.6)
Median	122.5	-4.0	103.5	-14.5
Min - Max	110 - 126	-9 - 9	99 - 122	-36 - 2
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	122.3 (11.1)	0.0 (7.0)	118.8 (18.7)	-4.0 (4.1)
Median	123.5	-0.5	122.5	-5.5
Min - Max	108 - 134	-8 - 9	93 - 137	-7 - 2
Cycle 38 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	117.3 (10.2)	-5.0 (4.6)	108.5 (14.3)	-14.3 (17.6)
Median	118.0	-5.0	104.5	-15.0
Min - Max	107 - 126	-9 - -1	96 - 129	-32 - 5
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	120.3 (15.3)	-2.0 (10.9)	118.0 (21.5)	-4.8 (12.0)
Median	124.0	0.0	117.0	-5.0
Min - Max	99 - 134	-17 - 9	93 - 145	-19 - 10
Cycle 39 Day 1				
PRE PAC INFUSION				
n	5	5	8	8
Mean (SD)	121.2 (9.9)	-1.8 (7.2)	119.5 (9.2)	-8.0 (15.0)
Median	120.0	-3.0	118.0	-8.0
Min - Max	109 - 136	-9 - 9	106 - 131	-29 - 16
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	122.8 (12.7)	0.5 (1.9)	124.0 (16.7)	1.3 (14.8)
Median	121.5	0.0	122.0	8.5
Min - Max	110 - 138	-1 - 3	109 - 143	-21 - 9
Cycle 39 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	120.0 (13.0)	-2.3 (3.9)	110.0 (8.0)	-12.8 (18.5)
Median	119.0	-1.0	110.5	-12.0
Min - Max	108 - 134	-8 - 1	100 - 119	-35 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	118.3 (12.8)	-4.0 (4.8)	114.8 (13.4)	-8.0 (11.8)
Median	118.0	-2.0	115.5	-3.5
Min - Max	105 - 132	-11 - -1	100 - 128	-25 - 0
Cycle 39 Day 15				
PRE PAC INFUSION				
n	4	4	3	3
Mean (SD)	121.8 (9.3)	-0.5 (6.6)	107.3 (9.3)	-15.0 (17.1)
Median	122.5	-2.5	103.0	-17.0
Min - Max	110 - 132	-6 - 9	101 - 118	-31 - 3
AFTER PAC INFUSION				
n	4	4	3	3
Mean (SD)	122.8 (17.8)	0.5 (20.1)	117.0 (18.3)	-5.3 (11.8)
Median	126.5	-4.5	113.0	1.0
Min - Max	98 - 140	-18 - 29	101 - 137	-19 - 2
Cycle 40 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	116.3 (13.4)	-9.8 (8.1)	115.0 (11.9)	-12.5 (17.9)
Median	118.0	-11.5	113.5	-14.0
Min - Max	101 - 128	-17 - 1	97 - 136	-38 - 13
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	123.3 (7.6)	-2.7 (2.1)	110.3 (12.4)	-8.3 (5.1)
Median	125.0	-2.0	117.0	-7.0
Min - Max	115 - 130	-5 - -1	96 - 118	-14 - -4
Cycle 40 Day 8				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	122.7 (14.5)	-3.3 (7.6)	107.0 (14.3)	-15.8 (21.2)
Median	130.0	-5.0	102.0	-15.5
Min - Max	106 - 132	-10 - 5	96 - 128	-36 - 4
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	119.3 (20.8)	-6.7 (14.6)	114.8 (15.5)	-8.0 (7.5)
Median	126.0	-9.0	117.5	-5.5
Min - Max	96 - 136	-20 - 9	94 - 130	-19 - -2
Cycle 40 Day 15				
PRE PAC INFUSION				
n	2	2	4	4
Mean (SD)	115.5 (26.2)	-10.0 (12.7)	101.0 (15.8)	-21.8 (25.4)
Median	115.5	-10.0	99.0	-18.5
Min - Max	97 - 134	-19 - -1	84 - 122	-51 - 1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	4	4
Mean (SD)	120.5 (24.7)	-5.0 (11.3)	112.0 (12.5)	-10.8 (12.7)
Median	120.5	-5.0	111.0	-7.0
Min - Max	103 - 138	-13 - 3	100 - 126	-29 - 0
Cycle 41 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	121.5 (7.3)	-4.5 (1.9)	120.6 (10.9)	-6.9 (19.6)
Median	123.5	-4.0	121.0	-11.5
Min - Max	111 - 128	-7 - -3	109 - 139	-26 - 31
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	124.0 (8.5)	-2.0 (1.0)	116.3 (18.5)	-6.5 (9.5)
Median	125.0	-2.0	116.0	-5.5
Min - Max	115 - 132	-3 - -1	94 - 139	-19 - 4
Cycle 41 Day 8				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	126.3 (6.7)	0.3 (6.1)	109.8 (12.4)	-13.0 (18.5)
Median	123.0	-1.0	104.5	-13.0
Min - Max	122 - 134	-5 - 7	102 - 128	-30 - 4
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	121.0 (17.5)	-5.0 (8.0)	114.8 (11.8)	-8.0 (12.4)
Median	122.0	-5.0	110.5	-7.5
Min - Max	103 - 138	-13 - 3	106 - 132	-23 - 6
Cycle 41 Day 15				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	124.0 (13.5)	-2.0 (4.0)	107.5 (14.0)	-15.3 (17.5)
Median	125.0	-2.0	106.5	-9.5
Min - Max	110 - 137	-6 - 2	95 - 122	-40 - -2
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	125.0 (22.6)	-1.0 (13.1)	112.0 (7.0)	-10.8 (12.8)
Median	128.0	1.0	112.0	-11.5
Min - Max	101 - 146	-15 - 11	105 - 119	-25 - 5
Cycle 42 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	123.3 (9.2)	-2.8 (4.0)	125.1 (12.3)	-2.4 (13.8)
Median	126.5	-4.0	121.5	-7.5
Min - Max	110 - 130	-6 - 3	111 - 144	-21 - 15

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	121.7 (17.4)	-4.3 (8.4)	121.0 (9.3)	-1.8 (9.9)
Median	128.0	0.0	121.0	-1.5
Min - Max	102 - 135	-14 - 1	110 - 132	-14 - 10
Cycle 42 Day 8				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	120.5 (6.4)	-1.0 (1.4)	115.5 (21.9)	3.5 (4.9)
Median	120.5	-1.0	115.5	3.5
Min - Max	116 - 125	-2 - 0	100 - 131	0 - 7
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	124.5 (0.7)	3.0 (7.1)	119.0 (21.2)	7.0 (4.2)
Median	124.5	3.0	119.0	7.0
Min - Max	124 - 125	-2 - 8	104 - 134	4 - 10
Cycle 42 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	124.3 (7.1)	-1.7 (3.2)	119.0 (13.5)	-0.7 (16.8)
Median	123.0	-3.0	115.0	8.0
Min - Max	118 - 132	-4 - 2	108 - 134	-20 - 10
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	118.7 (13.1)	-7.3 (4.2)	127.0 (24.2)	7.3 (6.5)
Median	123.0	-6.0	131.0	7.0
Min - Max	104 - 129	-12 - -4	101 - 149	1 - 14
Cycle 43 Day 1				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	122.8 (10.5)	-3.3 (3.2)	121.8 (6.2)	-4.5 (15.7)
Median	123.0	-3.5	123.5	-1.5
Min - Max	110 - 135	-6 - 0	112 - 127	-23 - 18
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	120.0 (17.1)	-6.0 (7.8)	120.0 (14.4)	0.3 (3.5)
Median	125.0	-2.0	124.0	0.0
Min - Max	101 - 134	-15 - -1	104 - 132	-3 - 4
Cycle 43 Day 8				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	120.7 (13.3)	-5.3 (4.0)	113.3 (16.2)	-6.3 (21.5)
Median	124.0	-3.0	104.0	4.0
Min - Max	106 - 132	-10 - -3	104 - 132	-31 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	124.0 (8.7)	-2.0 (3.0)	113.3 (18.7)	-6.3 (2.9)
Median	128.0	-2.0	121.0	-8.0
Min - Max	114 - 130	-5 - 1	92 - 127	-8 - -3
Cycle 43 Day 15				
PRE PAC INFUSION				
n	3	3	1	1
Mean (SD)	125.7 (7.8)	-0.3 (2.3)	122.0 (NE)	-2.0 (NE)
Median	128.0	1.0	122.0	-2.0
Min - Max	117 - 132	-3 - 1	122 - 122	-2 - -2
AFTER PAC INFUSION				
n	3	3	1	1
Mean (SD)	119.0 (16.5)	-7.0 (8.2)	129.0 (NE)	5.0 (NE)
Median	127.0	-5.0	129.0	5.0
Min - Max	100 - 130	-16 - 0	129 - 129	5 - 5
Cycle 44 Day 1				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	123.8 (10.4)	-2.3 (3.1)	122.7 (10.9)	-3.7 (18.7)
Median	123.0	-3.0	126.0	2.5
Min - Max	112 - 137	-5 - 2	104 - 134	-31 - 16
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	126.3 (20.0)	0.3 (10.7)	126.3 (13.0)	6.7 (5.5)
Median	125.0	-2.0	127.0	4.0
Min - Max	107 - 147	-9 - 12	113 - 139	3 - 13
Cycle 44 Day 8				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	123.3 (10.1)	-2.7 (2.1)	112.0 (14.7)	-7.7 (21.1)
Median	122.0	-2.0	104.0	4.0
Min - Max	114 - 134	-5 - -1	103 - 129	-32 - 5
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	124.0 (5.6)	-2.0 (4.4)	124.0 (17.5)	4.3 (2.9)
Median	123.0	-4.0	125.0	6.0
Min - Max	119 - 130	-5 - 3	106 - 141	1 - 6
Cycle 44 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	127.0 (14.1)	1.0 (4.6)	107.0 (14.8)	-12.7 (19.4)
Median	129.0	2.0	100.0	-3.0
Min - Max	112 - 140	-4 - 5	97 - 124	-35 - 0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	124.3 (19.4)	-1.7 (11.0)	117.0 (19.1)	-2.7 (2.5)
Median	134.0	2.0	119.0	-3.0
Min - Max	102 - 137	-14 - 7	97 - 135	-5 - 0
Cycle 45 Day 1				
PRE PAC INFUSION				
n	4	4	5	5
Mean (SD)	124.3 (12.5)	-1.8 (6.9)	115.2 (19.1)	-11.6 (24.4)
Median	127.0	-3.5	117.0	0.0
Min - Max	108 - 135	-8 - 8	92 - 143	-43 - 13
AFTER PAC INFUSION				
n	3	3	1	1
Mean (SD)	129.7 (13.2)	3.7 (4.7)	106.0 (NE)	6.0 (NE)
Median	127.0	2.0	106.0	6.0
Min - Max	118 - 144	0 - 9	106 - 106	6 - 6
Cycle 45 Day 8				
PRE PAC INFUSION				
n	3	3	2	2
Mean (SD)	122.3 (12.7)	-3.7 (4.0)	97.5 (2.1)	-20.0 (26.9)
Median	127.0	-3.0	97.5	-20.0
Min - Max	108 - 132	-8 - 0	96 - 99	-39 - -1
AFTER PAC INFUSION				
n	3	3	2	2
Mean (SD)	124.7 (17.9)	-1.3 (10.1)	126.5 (17.7)	9.0 (7.1)
Median	135.0	0.0	126.5	9.0
Min - Max	104 - 135	-12 - 8	114 - 139	4 - 14
Cycle 45 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	121.7 (13.6)	-4.3 (6.7)	115.3 (11.1)	-4.3 (14.5)
Median	129.0	-6.0	114.0	3.0
Min - Max	106 - 130	-10 - 3	105 - 127	-21 - 5
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	131.0 (14.1)	5.0 (5.2)	119.3 (22.1)	-0.3 (4.2)
Median	129.0	2.0	125.0	1.0
Min - Max	118 - 146	2 - 11	95 - 138	-5 - 3
Cycle 46 Day 1				
PRE PAC INFUSION				
n	3	3	6	6
Mean (SD)	117.7 (13.6)	-8.0 (9.5)	120.5 (8.7)	-5.8 (11.3)
Median	113.0	-3.0	122.0	0.0
Min - Max	107 - 133	-19 - -2	105 - 130	-23 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	124.5 (29.0)	-1.0 (15.6)	126.0 (15.6)	8.5 (9.2)
Median	124.5	-1.0	126.0	8.5
Min - Max	104 - 145	-12 - 10	115 - 137	2 - 15
Cycle 46 Day 8				
PRE PAC INFUSION				
n	2	2	3	3
Mean (SD)	129.5 (12.0)	4.0 (1.4)	106.0 (11.3)	-13.7 (19.5)
Median	129.5	4.0	100.0	-5.0
Min - Max	121 - 138	3 - 5	99 - 119	-36 - 0
AFTER PAC INFUSION				
n	2	2	3	3
Mean (SD)	125.5 (30.4)	0.0 (17.0)	121.3 (6.0)	1.7 (11.9)
Median	125.5	0.0	122.0	-2.0
Min - Max	104 - 147	-12 - 12	115 - 127	-8 - 15
Cycle 46 Day 15				
PRE PAC INFUSION				
n	2	2	3	3
Mean (SD)	123.5 (12.0)	-2.0 (1.4)	113.3 (9.3)	-6.3 (19.3)
Median	123.5	-2.0	109.0	0.0
Min - Max	115 - 132	-3 - -1	107 - 124	-28 - 9
AFTER PAC INFUSION				
n	2	2	3	3
Mean (SD)	126.5 (24.7)	1.0 (11.3)	117.3 (17.5)	-2.3 (4.0)
Median	126.5	1.0	117.0	0.0
Min - Max	109 - 144	-7 - 9	100 - 135	-7 - 0
Cycle 47 Day 1				
PRE PAC INFUSION				
n	3	3	6	6
Mean (SD)	124.7 (15.9)	-1.0 (6.9)	115.0 (20.2)	-11.3 (24.1)
Median	129.0	3.0	114.0	-4.5
Min - Max	107 - 138	-9 - 3	91 - 146	-51 - 16
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	115.0 (18.4)	-10.5 (4.9)	108.5 (13.4)	-3.5 (3.5)
Median	115.0	-10.5	108.5	-3.5
Min - Max	102 - 128	-14 - -7	99 - 118	-6 - -1
Cycle 47 Day 8				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	129.5 (20.5)	4.0 (7.1)	111.5 (29.0)	-0.5 (12.0)
Median	129.5	4.0	111.5	-0.5
Min - Max	115 - 144	-1 - 9	91 - 132	-9 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	120.0 (22.6)	-5.5 (9.2)	108.0 (18.4)	-4.0 (1.4)
Median	120.0	-5.5	108.0	-4.0
Min - Max	104 - 136	-12 - 1	95 - 121	-5 - -3
Cycle 47 Day 15				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	129.0 (18.4)	3.5 (4.9)	123.0 (8.5)	11.0 (8.5)
Median	129.0	3.5	123.0	11.0
Min - Max	116 - 142	0 - 7	117 - 129	5 - 17
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	111.5 (27.6)	-14.0 (14.1)	105.5 (26.2)	-6.5 (9.2)
Median	111.5	-14.0	105.5	-6.5
Min - Max	92 - 131	-24 - -4	87 - 124	-13 - 0
Cycle 48 Day 1				
PRE PAC INFUSION				
n	1	1	5	5
Mean (SD)	134.0 (NE)	-1.0 (NE)	120.6 (21.3)	-4.0 (8.7)
Median	134.0	-1.0	123.0	-9.0
Min - Max	134 - 134	-1 - -1	90 - 140	-10 - 10
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	149.0 (NE)	14.0 (NE)	113.5 (9.2)	1.5 (7.8)
Median	149.0	14.0	113.5	1.5
Min - Max	149 - 149	14 - 14	107 - 120	-4 - 7
Cycle 48 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	142.0 (NE)	7.0 (NE)	116.0 (15.6)	4.0 (1.4)
Median	142.0	7.0	116.0	4.0
Min - Max	142 - 142	7 - 7	105 - 127	3 - 5
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	145.0 (NE)	10.0 (NE)	108.0 (15.6)	-4.0 (1.4)
Median	145.0	10.0	108.0	-4.0
Min - Max	145 - 145	10 - 10	97 - 119	-5 - -3
Cycle 48 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	137.0 (NE)	2.0 (NE)	107.5 (16.3)	-4.5 (0.7)
Median	137.0	2.0	107.5	-4.5
Min - Max	137 - 137	2 - 2	96 - 119	-5 - -4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	148.0 (NE)	13.0 (NE)	104.0 (25.5)	-8.0 (8.5)
Median	148.0	13.0	104.0	-8.0
Min - Max	148 - 148	13 - 13	86 - 122	-14 - -2
Cycle 49 Day 1				
PRE PAC INFUSION				
n	1	1	3	3
Mean (SD)	132.0 (NE)	-3.0 (NE)	114.7 (16.6)	-3.3 (3.5)
Median	132.0	-3.0	117.0	-3.0
Min - Max	132 - 132	-3 - -3	97 - 130	-7 - 0
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	145.0 (NE)	10.0 (NE)	113.0 (2.8)	1.0 (14.1)
Median	145.0	10.0	113.0	1.0
Min - Max	145 - 145	10 - 10	111 - 115	-9 - 11
Cycle 49 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	138.0 (NE)	3.0 (NE)	121.0 (9.9)	9.0 (26.9)
Median	138.0	3.0	121.0	9.0
Min - Max	138 - 138	3 - 3	114 - 128	-10 - 28
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	142.0 (NE)	7.0 (NE)	120.5 (2.1)	8.5 (19.1)
Median	142.0	7.0	120.5	8.5
Min - Max	142 - 142	7 - 7	119 - 122	-5 - 22
Cycle 49 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	142.0 (NE)	7.0 (NE)	106.5 (14.8)	-5.5 (2.1)
Median	142.0	7.0	106.5	-5.5
Min - Max	142 - 142	7 - 7	96 - 117	-7 - -4
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	148.0 (NE)	13.0 (NE)	116.0 (8.5)	4.0 (8.5)
Median	148.0	13.0	116.0	4.0
Min - Max	148 - 148	13 - 13	110 - 122	-2 - 10
Cycle 50 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	145.0 (NE)	10.0 (NE)	105.0 (0.0)	-7.0 (17.0)
Median	145.0	10.0	105.0	-7.0
Min - Max	145 - 145	10 - 10	105 - 105	-19 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	139.0 (NE)	4.0 (NE)	127.0 (NE)	27.0 (NE)
Median	139.0	4.0	127.0	27.0
Min - Max	139 - 139	4 - 4	127 - 127	27 - 27
Cycle 50 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	149.0 (NE)	14.0 (NE)	120.0 (18.4)	8.0 (1.4)
Median	149.0	14.0	120.0	8.0
Min - Max	149 - 149	14 - 14	107 - 133	7 - 9
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	142.0 (NE)	7.0 (NE)	112.5 (12.0)	0.5 (4.9)
Median	142.0	7.0	112.5	0.5
Min - Max	142 - 142	7 - 7	104 - 121	-3 - 4
Cycle 50 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	138.0 (NE)	3.0 (NE)	114.5 (20.5)	2.5 (3.5)
Median	138.0	3.0	114.5	2.5
Min - Max	138 - 138	3 - 3	100 - 129	0 - 5
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	143.0 (NE)	8.0 (NE)	109.0 (21.2)	-3.0 (4.2)
Median	143.0	8.0	109.0	-3.0
Min - Max	143 - 143	8 - 8	94 - 124	-6 - 0
Cycle 51 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	134.0 (NE)	-1.0 (NE)	116.0 (9.9)	4.0 (7.1)
Median	134.0	-1.0	116.0	4.0
Min - Max	134 - 134	-1 - -1	109 - 123	-1 - 9
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	148.0 (NE)	13.0 (NE)	120.0 (2.8)	8.0 (19.8)
Median	148.0	13.0	120.0	8.0
Min - Max	148 - 148	13 - 13	118 - 122	-6 - 22
Cycle 51 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	145.0 (NE)	10.0 (NE)	122.0 (NE)	-2.0 (NE)
Median	145.0	10.0	122.0	-2.0
Min - Max	145 - 145	10 - 10	122 - 122	-2 - -2

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	152.0 (NE)	17.0 (NE)	NE (NE)	NE (NE)
Median	152.0	17.0	NE	NE
Min - Max	152 - 152	17 - 17	NE - NE	NE - NE
Cycle 51 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	140.0 (NE)	5.0 (NE)	113.5 (6.4)	1.5 (10.6)
Median	140.0	5.0	113.5	1.5
Min - Max	140 - 140	5 - 5	109 - 118	-6 - 9
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	148.0 (NE)	13.0 (NE)	113.0 (1.4)	1.0 (18.4)
Median	148.0	13.0	113.0	1.0
Min - Max	148 - 148	13 - 13	112 - 114	-12 - 14
Cycle 52 Day 1				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	118.0 (22.6)	6.0 (5.7)
Median	NE	NE	118.0	6.0
Min - Max	NE - NE	NE - NE	102 - 134	2 - 10
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	117.0 (9.9)	5.0 (7.1)
Median	NE	NE	117.0	5.0
Min - Max	NE - NE	NE - NE	110 - 124	0 - 10
Cycle 52 Day 8				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	120.5 (13.4)	8.5 (3.5)
Median	NE	NE	120.5	8.5
Min - Max	NE - NE	NE - NE	111 - 130	6 - 11
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	117.5 (20.5)	5.5 (3.5)
Median	NE	NE	117.5	5.5
Min - Max	NE - NE	NE - NE	103 - 132	3 - 8
Cycle 52 Day 15				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	128.5 (9.2)	16.5 (7.8)
Median	NE	NE	128.5	16.5
Min - Max	NE - NE	NE - NE	122 - 135	11 - 22

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	117.5 (6.4)	5.5 (10.6)
Median	NE	NE	117.5	5.5
Min - Max	NE - NE	NE - NE	113 - 122	-2 - 13
Cycle 53 Day 1				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	114.5 (23.3)	2.5 (6.4)
Median	NE	NE	114.5	2.5
Min - Max	NE - NE	NE - NE	98 - 131	-2 - 7
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	112.0 (9.9)	0.0 (7.1)
Median	NE	NE	112.0	0.0
Min - Max	NE - NE	NE - NE	105 - 119	-5 - 5
Cycle 53 Day 8				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	127.0 (NE)	3.0 (NE)
Median	NE	NE	127.0	3.0
Min - Max	NE - NE	NE - NE	127 - 127	3 - 3
AFTER PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	117.0 (NE)	-7.0 (NE)
Median	NE	NE	117.0	-7.0
Min - Max	NE - NE	NE - NE	117 - 117	-7 - -7
Cycle 53 Day 15				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	125.0 (NE)	1.0 (NE)
Median	NE	NE	125.0	1.0
Min - Max	NE - NE	NE - NE	125 - 125	1 - 1
Study Drug Discontinuation				
n	70	68	127	127
Mean (SD)	120.5 (13.6)	-2.6 (14.4)	121.1 (14.3)	-3.6 (16.3)
Median	122.0	0.5	122.0	-3.0
Min - Max	90 - 160	-43 - 30	88 - 160	-39 - 41
Post-Baseline Last				
n	69	69	128	128
Mean (SD)	120.3 (13.6)	-2.4 (14.4)	121.3 (14.1)	-3.4 (16.1)
Median	122.0	1.0	122.5	-3.0
Min - Max	90 - 160	-43 - 30	88 - 160	-39 - 41

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
PRE PAC INFUSION				
n	1	1	3	3
Mean (SD)	90.0 (NE)	-22.0 (NE)	116.0 (19.7)	2.7 (26.1)
Median	90.0	-22.0	110.0	0.0
Min - Max	90 - 90	-22 - -22	100 - 138	-22 - 30
AFTER PAC INFUSION				
n	2	2	13	13
Mean (SD)	124.0 (19.8)	4.0 (8.5)	122.3 (12.2)	6.3 (16.6)
Median	124.0	4.0	120.0	4.0
Min - Max	110 - 138	-2 - 10	100 - 140	-19 - 50
Post-Baseline Minimum				
n	4	4	15	15
Mean (SD)	110.5 (6.2)	-4.0 (9.7)	102.9 (13.4)	-20.3 (14.9)
Median	109.5	-3.5	102.0	-23.0
Min - Max	104 - 119	-15 - 6	80 - 125	-45 - 10
PRE PAC INFUSION				
n	52	52	85	85
Mean (SD)	101.6 (11.9)	-20.8 (12.9)	99.9 (11.8)	-24.4 (12.9)
Median	101.0	-20.5	99.0	-23.0
Min - Max	78 - 134	-49 - 10	78 - 130	-51 - 10
AFTER PAC INFUSION				
n	16	16	44	44
Mean (SD)	101.1 (12.6)	-23.8 (12.9)	104.1 (13.2)	-18.6 (14.8)
Median	100.0	-19.0	105.5	-19.0
Min - Max	83 - 125	-46 - -10	82 - 130	-51 - 10
Post-Baseline Maximum				
n	2	2	9	9
Mean (SD)	176.0 (62.2)	53.5 (58.7)	142.6 (8.0)	20.0 (15.1)
Median	176.0	53.5	140.0	20.0
Min - Max	132 - 220	12 - 95	132 - 160	-2 - 41
PRE PAC INFUSION				
n	28	28	57	57
Mean (SD)	141.2 (14.7)	19.4 (12.7)	142.4 (15.1)	16.4 (17.0)
Median	139.5	19.0	140.0	14.0
Min - Max	110 - 165	-19 - 45	120 - 189	-8 - 79
AFTER PAC INFUSION				
n	42	42	78	78
Mean (SD)	145.6 (16.8)	22.6 (18.5)	143.2 (17.0)	21.0 (17.0)
Median	142.0	17.0	139.5	19.0
Min - Max	108 - 186	-4 - 73	112 - 202	-10 - 82

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
Baseline				
n	72		144	
Mean (SD)	79.0 (9.8)		79.8 (11.2)	
Median	78.0		79.0	
Min - Max	58 - 112		58 - 108	
Cycle 1 Day 1				
PRE PAC INFUSION				
n	69	67	140	139
Mean (SD)	77.8 (12.0)	-1.4 (10.3)	77.3 (12.4)	-2.4 (11.6)
Median	77.0	0.0	76.0	-1.0
Min - Max	58 - 111	-30 - 31	54 - 121	-38 - 34
AFTER PAC INFUSION				
n	71	69	140	139
Mean (SD)	78.0 (10.4)	-0.7 (9.6)	76.6 (10.5)	-2.7 (10.8)
Median	78.0	-1.0	76.5	-2.0
Min - Max	53 - 104	-30 - 26	49 - 103	-33 - 25
Cycle 1 Day 8				
PRE PAC INFUSION				
n	72	69	135	135
Mean (SD)	79.6 (14.2)	0.7 (11.8)	80.2 (10.9)	0.2 (11.8)
Median	76.0	0.0	80.0	0.0
Min - Max	55 - 117	-31 - 30	54 - 112	-38 - 26
AFTER PAC INFUSION				
n	62	61	126	126
Mean (SD)	79.4 (12.4)	0.0 (11.1)	77.9 (9.9)	-1.5 (10.4)
Median	79.5	0.0	77.0	-1.0
Min - Max	60 - 111	-31 - 32	56 - 100	-40 - 23
Cycle 1 Day 15				
PRE PAC INFUSION				
n	70	67	130	130
Mean (SD)	79.8 (13.2)	0.5 (12.3)	80.0 (10.6)	0.0 (12.0)
Median	76.0	0.0	80.0	0.0
Min - Max	60 - 116	-33 - 46	55 - 109	-32 - 33
AFTER PAC INFUSION				
n	57	55	116	116
Mean (SD)	78.7 (12.0)	0.2 (10.4)	78.1 (10.0)	-1.9 (12.0)
Median	76.0	0.0	78.0	-2.0
Min - Max	58 - 112	-28 - 33	56 - 101	-33 - 22
Cycle 2 Day 1				
PRE PAC INFUSION				
n	73	71	129	128
Mean (SD)	78.5 (11.4)	-0.8 (11.0)	79.7 (11.1)	-0.1 (10.5)
Median	77.0	0.0	80.0	0.0
Min - Max	60 - 110	-25 - 28	58 - 119	-27 - 31

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	67	66	122	121
Mean (SD)	78.1 (11.5)	-1.5 (10.4)	77.3 (10.0)	-2.2 (11.0)
Median	77.0	-1.0	77.0	-1.0
Min - Max	52 - 103	-35 - 30	53 - 105	-32 - 26
Cycle 2 Day 8				
PRE PAC INFUSION				
n	72	70	127	126
Mean (SD)	80.4 (13.4)	0.8 (13.1)	81.0 (12.6)	1.3 (13.5)
Median	78.5	1.5	79.0	0.0
Min - Max	57 - 121	-35 - 36	60 - 129	-27 - 64
AFTER PAC INFUSION				
n	68	66	122	121
Mean (SD)	80.0 (11.1)	0.6 (10.4)	78.8 (10.0)	-0.9 (11.5)
Median	80.0	2.0	78.0	-1.0
Min - Max	60 - 107	-32 - 27	54 - 104	-42 - 30
Cycle 2 Day 15				
PRE PAC INFUSION				
n	69	67	123	122
Mean (SD)	80.0 (12.6)	0.3 (12.6)	80.6 (11.3)	1.1 (12.1)
Median	79.0	0.0	78.0	0.0
Min - Max	55 - 113	-37 - 33	57 - 112	-36 - 33
AFTER PAC INFUSION				
n	65	64	110	109
Mean (SD)	78.0 (10.9)	-1.8 (11.0)	79.8 (9.9)	0.1 (10.7)
Median	76.0	-0.5	78.5	0.0
Min - Max	57 - 109	-35 - 25	60 - 114	-33 - 27
Cycle 3 Day 1				
PRE PAC INFUSION				
n	70	68	121	121
Mean (SD)	79.9 (14.2)	0.6 (15.3)	80.8 (10.7)	1.2 (11.5)
Median	78.0	0.0	78.0	0.0
Min - Max	56 - 136	-36 - 72	57 - 111	-24 - 30
AFTER PAC INFUSION				
n	65	63	111	111
Mean (SD)	78.0 (12.4)	-0.8 (14.5)	79.5 (10.3)	-0.6 (11.1)
Median	78.0	-1.0	78.0	0.0
Min - Max	54 - 140	-38 - 76	54 - 106	-41 - 23
Cycle 3 Day 8				
PRE PAC INFUSION				
n	65	63	116	115
Mean (SD)	81.2 (12.0)	2.3 (11.4)	81.6 (11.7)	1.6 (12.5)
Median	79.0	2.0	80.0	1.0
Min - Max	60 - 120	-32 - 35	53 - 113	-33 - 38

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	59	57	105	104
Mean (SD)	79.1 (10.4)	0.5 (9.7)	80.0 (10.2)	-0.1 (10.6)
Median	79.0	0.0	80.0	0.5
Min - Max	60 - 103	-31 - 18	53 - 103	-33 - 23
Cycle 3 Day 15				
PRE PAC INFUSION				
n	64	62	116	115
Mean (SD)	80.3 (12.1)	1.3 (11.4)	81.8 (11.5)	1.9 (12.7)
Median	77.0	1.0	81.0	0.0
Min - Max	60 - 117	-32 - 32	56 - 112	-29 - 37
AFTER PAC INFUSION				
n	60	58	107	107
Mean (SD)	78.4 (10.2)	-1.1 (10.8)	79.0 (10.1)	-1.0 (11.2)
Median	78.0	2.0	78.0	0.0
Min - Max	57 - 102	-35 - 15	58 - 112	-36 - 21
Cycle 4 Day 1				
PRE PAC INFUSION				
n	62	60	114	113
Mean (SD)	79.3 (12.1)	-0.3 (12.3)	80.2 (11.4)	0.4 (13.0)
Median	80.0	0.0	80.0	0.0
Min - Max	55 - 114	-34 - 21	53 - 112	-34 - 31
AFTER PAC INFUSION				
n	60	58	105	105
Mean (SD)	77.1 (9.4)	-2.2 (10.8)	78.7 (10.0)	-0.7 (12.0)
Median	76.0	0.0	79.0	-1.0
Min - Max	59 - 108	-33 - 17	54 - 100	-33 - 35
Cycle 4 Day 8				
PRE PAC INFUSION				
n	62	60	114	114
Mean (SD)	80.6 (12.3)	1.7 (11.5)	81.3 (11.0)	1.3 (11.1)
Median	80.0	1.0	80.5	0.5
Min - Max	57 - 115	-29 - 23	59 - 110	-25 - 30
AFTER PAC INFUSION				
n	60	58	107	107
Mean (SD)	79.1 (10.1)	0.2 (9.5)	79.7 (10.1)	-0.2 (11.2)
Median	80.0	2.0	80.0	0.0
Min - Max	58 - 100	-34 - 16	53 - 110	-33 - 22
Cycle 4 Day 15				
PRE PAC INFUSION				
n	57	55	105	105
Mean (SD)	79.8 (12.1)	0.3 (10.3)	80.9 (11.2)	1.5 (12.5)
Median	78.0	2.0	80.0	2.0
Min - Max	58 - 110	-24 - 26	57 - 112	-40 - 33

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	53	51	98	98
Mean (SD)	79.4 (12.0)	-0.1 (11.5)	78.3 (9.3)	-0.8 (11.5)
Median	78.0	0.0	78.5	0.0
Min - Max	60 - 108	-31 - 19	59 - 105	-36 - 26
Cycle 5 Day 1				
PRE PAC INFUSION				
n	56	55	108	108
Mean (SD)	79.9 (10.0)	0.9 (10.2)	79.3 (10.8)	-0.4 (11.0)
Median	80.0	1.0	78.5	0.0
Min - Max	52 - 100	-30 - 26	54 - 106	-31 - 30
AFTER PAC INFUSION				
n	50	49	102	102
Mean (SD)	77.6 (9.7)	-1.3 (9.3)	76.9 (9.8)	-2.5 (10.6)
Median	79.0	0.0	76.0	-1.5
Min - Max	60 - 102	-24 - 19	45 - 100	-43 - 20
Cycle 5 Day 8				
PRE PAC INFUSION				
n	55	54	105	105
Mean (SD)	79.7 (11.6)	0.5 (11.7)	80.0 (11.4)	0.7 (11.3)
Median	78.0	1.0	79.0	0.0
Min - Max	57 - 109	-27 - 22	53 - 119	-27 - 34
AFTER PAC INFUSION				
n	52	51	101	101
Mean (SD)	79.0 (9.8)	-0.1 (9.9)	78.5 (9.8)	-0.6 (11.1)
Median	78.0	-1.0	78.0	0.0
Min - Max	60 - 108	-24 - 16	45 - 99	-41 - 37
Cycle 5 Day 15				
PRE PAC INFUSION				
n	51	50	100	100
Mean (SD)	79.5 (11.9)	0.7 (11.7)	80.2 (12.2)	1.1 (11.8)
Median	79.0	0.0	78.0	0.0
Min - Max	58 - 112	-28 - 21	51 - 118	-32 - 31
AFTER PAC INFUSION				
n	49	48	96	96
Mean (SD)	77.6 (10.5)	-1.0 (10.5)	77.8 (10.2)	-1.0 (10.4)
Median	77.0	0.0	77.0	0.0
Min - Max	60 - 110	-30 - 25	54 - 106	-37 - 23
Cycle 6 Day 1				
PRE PAC INFUSION				
n	52	51	101	101
Mean (SD)	78.8 (12.0)	0.2 (11.7)	79.4 (11.4)	0.6 (12.4)
Median	78.0	1.0	79.0	0.0
Min - Max	56 - 109	-36 - 24	53 - 118	-33 - 30

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	50	49	95	95
Mean (SD)	77.4 (11.0)	-1.2 (10.8)	76.5 (10.1)	-2.5 (11.6)
Median	77.5	0.0	77.0	-2.0
Min - Max	53 - 109	-39 - 25	54 - 105	-32 - 25
Cycle 6 Day 8				
PRE PAC INFUSION				
n	52	51	102	102
Mean (SD)	80.7 (12.9)	1.5 (13.0)	80.9 (12.2)	1.8 (12.8)
Median	79.0	1.0	80.0	0.0
Min - Max	56 - 108	-36 - 33	58 - 124	-27 - 36
AFTER PAC INFUSION				
n	48	47	96	96
Mean (SD)	79.1 (11.4)	0.9 (10.9)	78.8 (9.9)	-0.6 (11.6)
Median	80.0	1.0	78.0	0.0
Min - Max	56 - 110	-36 - 26	54 - 104	-37 - 28
Cycle 6 Day 15				
PRE PAC INFUSION				
n	51	50	98	98
Mean (SD)	79.2 (12.5)	0.1 (12.2)	80.8 (11.8)	1.6 (13.3)
Median	78.0	1.0	78.0	2.0
Min - Max	59 - 112	-33 - 21	49 - 115	-34 - 34
AFTER PAC INFUSION				
n	48	47	91	91
Mean (SD)	78.9 (11.3)	-0.2 (10.7)	78.1 (9.6)	-1.2 (11.3)
Median	76.5	1.0	78.0	-1.0
Min - Max	60 - 110	-29 - 24	48 - 104	-39 - 24
Cycle 7 Day 1				
PRE PAC INFUSION				
n	49	49	93	93
Mean (SD)	77.8 (12.6)	-1.0 (11.8)	80.1 (12.2)	0.6 (12.2)
Median	78.0	0.0	78.0	1.0
Min - Max	53 - 105	-32 - 35	55 - 112	-35 - 26
AFTER PAC INFUSION				
n	46	46	83	83
Mean (SD)	76.0 (10.3)	-2.3 (8.9)	76.5 (10.0)	-3.1 (11.7)
Median	77.0	-2.0	76.0	-2.0
Min - Max	58 - 102	-29 - 17	56 - 108	-34 - 23
Cycle 7 Day 8				
PRE PAC INFUSION				
n	48	48	85	85
Mean (SD)	78.1 (8.3)	-0.2 (10.0)	81.1 (13.0)	1.8 (13.7)
Median	78.0	-0.5	78.0	0.0
Min - Max	60 - 96	-30 - 22	58 - 121	-37 - 45

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	47	47	79	79
Mean (SD)	78.1 (9.2)	-0.1 (10.0)	77.8 (9.9)	-2.1 (12.1)
Median	77.0	0.0	76.0	-1.0
Min - Max	63 - 109	-27 - 25	59 - 105	-41 - 23
Cycle 7 Day 15				
PRE PAC INFUSION				
n	47	47	83	83
Mean (SD)	79.5 (11.5)	0.9 (12.3)	80.8 (11.4)	1.3 (13.1)
Median	78.0	0.0	79.0	1.0
Min - Max	53 - 109	-32 - 32	53 - 112	-31 - 32
AFTER PAC INFUSION				
n	42	42	80	80
Mean (SD)	76.8 (10.4)	-1.1 (10.2)	78.2 (9.7)	-1.6 (12.5)
Median	73.5	-2.0	78.0	0.0
Min - Max	63 - 104	-27 - 20	53 - 108	-42 - 23
Cycle 8 Day 1				
PRE PAC INFUSION				
n	47	47	90	90
Mean (SD)	80.4 (11.6)	1.7 (12.5)	80.4 (11.5)	0.1 (12.7)
Median	80.0	5.0	78.0	0.0
Min - Max	57 - 105	-35 - 28	56 - 120	-31 - 32
AFTER PAC INFUSION				
n	45	45	78	78
Mean (SD)	77.0 (9.5)	-1.6 (12.2)	79.2 (9.6)	-1.5 (11.8)
Median	78.0	1.0	78.0	-1.0
Min - Max	54 - 103	-38 - 20	55 - 112	-32 - 24
Cycle 8 Day 8				
PRE PAC INFUSION				
n	45	45	81	81
Mean (SD)	79.7 (10.7)	1.6 (12.3)	81.9 (11.3)	1.4 (13.6)
Median	78.0	2.0	80.0	2.0
Min - Max	59 - 105	-32 - 29	58 - 106	-45 - 34
AFTER PAC INFUSION				
n	39	39	76	76
Mean (SD)	77.6 (9.9)	-0.3 (10.2)	77.7 (9.7)	-2.6 (11.3)
Median	77.0	-1.0	78.0	-2.0
Min - Max	58 - 103	-32 - 23	60 - 102	-39 - 21
Cycle 8 Day 15				
PRE PAC INFUSION				
n	45	45	77	77
Mean (SD)	80.3 (12.9)	2.1 (12.1)	83.1 (10.4)	2.3 (14.2)
Median	78.0	2.0	81.0	4.0
Min - Max	56 - 116	-36 - 34	60 - 104	-35 - 35

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	43	43	69	69
Mean (SD)	77.1 (11.4)	-1.1 (9.7)	78.5 (10.3)	-2.3 (12.4)
Median	77.0	1.0	79.0	-1.0
Min - Max	56 - 103	-33 - 17	54 - 102	-40 - 21
Cycle 9 Day 1				
PRE PAC INFUSION				
n	37	37	77	77
Mean (SD)	78.6 (12.1)	2.3 (9.1)	80.9 (10.8)	0.5 (12.8)
Median	78.0	3.0	80.0	0.0
Min - Max	60 - 109	-18 - 19	53 - 110	-33 - 26
AFTER PAC INFUSION				
n	35	35	65	65
Mean (SD)	75.5 (10.3)	-1.2 (7.7)	78.0 (9.2)	-2.9 (13.1)
Median	76.0	0.0	78.0	-2.0
Min - Max	58 - 100	-17 - 12	58 - 101	-42 - 28
Cycle 9 Day 8				
PRE PAC INFUSION				
n	39	39	66	66
Mean (SD)	79.6 (11.3)	2.6 (8.6)	80.7 (12.5)	-0.2 (14.8)
Median	78.0	2.0	78.0	0.0
Min - Max	58 - 106	-18 - 23	56 - 112	-41 - 32
AFTER PAC INFUSION				
n	39	39	61	61
Mean (SD)	77.7 (11.5)	0.7 (9.1)	77.0 (11.4)	-3.7 (13.6)
Median	78.0	1.0	75.0	-2.0
Min - Max	58 - 113	-28 - 21	58 - 101	-43 - 26
Cycle 9 Day 15				
PRE PAC INFUSION				
n	39	39	62	62
Mean (SD)	79.7 (10.6)	2.7 (8.0)	82.4 (11.9)	1.4 (14.7)
Median	80.0	1.0	81.0	0.5
Min - Max	60 - 108	-11 - 20	58 - 116	-32 - 34
AFTER PAC INFUSION				
n	37	37	55	55
Mean (SD)	77.8 (11.2)	1.5 (8.6)	78.6 (10.3)	-2.4 (12.9)
Median	78.0	2.0	78.0	-2.0
Min - Max	60 - 113	-21 - 21	55 - 107	-43 - 25
Cycle 10 Day 1				
PRE PAC INFUSION				
n	39	39	70	70
Mean (SD)	79.8 (11.7)	2.8 (10.0)	80.8 (13.7)	0.1 (14.1)
Median	81.0	2.0	79.0	-1.0
Min - Max	57 - 101	-20 - 24	57 - 133	-32 - 39

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	37	37	58	58
Mean (SD)	75.6 (9.8)	-1.2 (8.5)	77.6 (10.3)	-3.5 (12.0)
Median	74.0	0.0	77.5	-1.5
Min - Max	59 - 97	-20 - 15	57 - 100	-30 - 21
Cycle 10 Day 8				
PRE PAC INFUSION				
n	38	38	61	61
Mean (SD)	79.1 (13.2)	2.4 (10.2)	81.6 (13.9)	0.7 (14.8)
Median	76.0	3.0	80.0	1.0
Min - Max	59 - 110	-19 - 25	52 - 120	-34 - 44
AFTER PAC INFUSION				
n	37	37	57	57
Mean (SD)	75.6 (10.5)	-1.2 (9.0)	79.2 (11.5)	-1.4 (13.0)
Median	75.0	-1.0	77.0	-1.0
Min - Max	60 - 106	-24 - 22	56 - 104	-28 - 28
Cycle 10 Day 15				
PRE PAC INFUSION				
n	36	36	59	59
Mean (SD)	80.5 (10.0)	3.8 (8.6)	82.1 (14.0)	1.1 (15.0)
Median	80.0	3.5	80.0	0.0
Min - Max	61 - 101	-16 - 20	53 - 119	-50 - 35
AFTER PAC INFUSION				
n	35	35	52	52
Mean (SD)	77.4 (9.6)	0.5 (7.0)	79.4 (10.9)	-1.9 (12.3)
Median	78.0	-1.0	78.0	-2.0
Min - Max	61 - 102	-16 - 15	59 - 102	-33 - 27
Cycle 11 Day 1				
PRE PAC INFUSION				
n	35	35	64	64
Mean (SD)	78.5 (10.9)	1.5 (8.3)	82.5 (11.5)	1.2 (12.8)
Median	77.0	0.0	80.5	0.0
Min - Max	60 - 106	-13 - 22	57 - 113	-26 - 30
AFTER PAC INFUSION				
n	34	34	49	49
Mean (SD)	77.5 (10.7)	0.8 (8.1)	78.7 (10.0)	-3.0 (11.2)
Median	75.0	-0.5	79.0	-1.0
Min - Max	60 - 102	-12 - 18	60 - 100	-28 - 21
Cycle 11 Day 8				
PRE PAC INFUSION				
n	33	33	48	48
Mean (SD)	78.1 (11.2)	1.3 (9.3)	85.3 (11.8)	3.7 (12.7)
Median	76.0	0.0	85.0	0.0
Min - Max	57 - 106	-19 - 24	57 - 113	-30 - 34

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	31	31	46	46
Mean (SD)	77.6 (10.4)	1.5 (7.4)	82.1 (10.3)	0.3 (11.3)
Median	76.0	0.0	82.5	2.0
Min - Max	60 - 102	-11 - 18	56 - 104	-33 - 25
Cycle 11 Day 15				
PRE PAC INFUSION				
n	34	34	44	44
Mean (SD)	80.4 (12.3)	3.7 (8.9)	82.3 (11.0)	1.5 (14.2)
Median	78.5	4.5	82.0	1.5
Min - Max	58 - 102	-14 - 20	60 - 101	-36 - 26
AFTER PAC INFUSION				
n	31	31	44	44
Mean (SD)	79.5 (11.9)	3.7 (8.6)	78.2 (10.3)	-2.6 (11.7)
Median	79.0	2.0	78.5	0.0
Min - Max	59 - 108	-7 - 24	59 - 102	-32 - 18
Cycle 12 Day 1				
PRE PAC INFUSION				
n	33	33	57	57
Mean (SD)	78.6 (12.5)	1.6 (8.4)	80.3 (12.1)	-0.7 (12.3)
Median	80.0	2.0	78.0	0.0
Min - Max	58 - 104	-14 - 22	54 - 110	-30 - 22
AFTER PAC INFUSION				
n	30	30	43	43
Mean (SD)	77.0 (10.7)	0.5 (9.0)	78.6 (10.1)	-3.6 (11.5)
Median	76.5	1.0	78.0	-1.0
Min - Max	62 - 104	-26 - 20	59 - 106	-33 - 13
Cycle 12 Day 8				
PRE PAC INFUSION				
n	30	30	42	42
Mean (SD)	79.6 (10.7)	2.4 (6.6)	82.3 (13.0)	0.1 (12.5)
Median	78.5	2.0	80.5	-0.5
Min - Max	62 - 102	-10 - 15	58 - 109	-29 - 28
AFTER PAC INFUSION				
n	24	24	40	40
Mean (SD)	75.4 (10.1)	0.4 (8.6)	79.0 (11.9)	-2.6 (11.7)
Median	75.5	-1.5	76.5	-2.0
Min - Max	60 - 97	-11 - 26	60 - 107	-33 - 16
Cycle 12 Day 15				
PRE PAC INFUSION				
n	30	30	43	43
Mean (SD)	79.6 (11.8)	3.2 (8.3)	81.3 (9.7)	-0.7 (10.6)
Median	78.5	2.0	81.0	1.0
Min - Max	61 - 109	-11 - 25	60 - 107	-30 - 23

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	26	26	40	40
Mean (SD)	78.0 (10.6)	2.4 (7.9)	78.7 (10.2)	-3.3 (10.4)
Median	75.5	2.0	78.0	-1.0
Min - Max	62 - 110	-10 - 26	58 - 100	-27 - 17
Cycle 13 Day 1				
PRE PAC INFUSION				
n	28	28	49	49
Mean (SD)	76.5 (10.3)	0.0 (8.6)	82.0 (12.3)	-0.2 (15.0)
Median	76.0	0.0	80.0	0.0
Min - Max	57 - 96	-22 - 14	59 - 106	-34 - 32
AFTER PAC INFUSION				
n	25	25	36	36
Mean (SD)	76.4 (11.1)	0.4 (10.4)	79.9 (10.2)	-3.9 (14.8)
Median	74.0	0.0	80.5	-4.0
Min - Max	60 - 106	-20 - 20	60 - 109	-31 - 30
Cycle 13 Day 8				
PRE PAC INFUSION				
n	26	26	36	36
Mean (SD)	79.8 (12.1)	3.9 (7.8)	84.8 (12.3)	0.6 (13.9)
Median	78.5	4.5	86.5	1.0
Min - Max	62 - 101	-11 - 19	61 - 117	-35 - 37
AFTER PAC INFUSION				
n	25	25	36	36
Mean (SD)	77.0 (11.2)	1.3 (7.4)	81.9 (9.4)	-2.3 (11.6)
Median	78.0	1.0	81.0	-2.5
Min - Max	58 - 103	-10 - 19	65 - 99	-36 - 28
Cycle 13 Day 15				
PRE PAC INFUSION				
n	25	25	35	35
Mean (SD)	79.2 (10.5)	3.6 (8.3)	84.6 (8.9)	0.0 (11.6)
Median	78.0	3.0	84.0	0.0
Min - Max	60 - 102	-12 - 27	70 - 100	-23 - 24
AFTER PAC INFUSION				
n	23	23	35	35
Mean (SD)	77.0 (10.7)	2.6 (6.9)	80.7 (9.0)	-3.9 (11.1)
Median	77.0	2.0	80.0	-4.0
Min - Max	61 - 102	-8 - 19	60 - 101	-28 - 16
Cycle 14 Day 1				
PRE PAC INFUSION				
n	26	26	42	42
Mean (SD)	80.0 (10.8)	3.4 (10.1)	82.4 (12.7)	-0.6 (12.9)
Median	78.0	3.5	80.0	-0.5
Min - Max	63 - 101	-13 - 35	55 - 115	-26 - 27

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	24	24	33	33
Mean (SD)	75.3 (9.4)	0.3 (9.2)	78.4 (10.0)	-6.2 (11.9)
Median	75.0	2.0	78.0	-4.0
Min - Max	51 - 95	-16 - 15	61 - 103	-29 - 15
Cycle 14 Day 8				
PRE PAC INFUSION				
n	25	25	32	32
Mean (SD)	77.7 (13.7)	1.9 (11.4)	84.4 (10.4)	-1.4 (8.8)
Median	76.0	1.0	82.5	-1.0
Min - Max	57 - 116	-19 - 25	68 - 107	-16 - 16
AFTER PAC INFUSION				
n	24	24	31	31
Mean (SD)	76.1 (11.1)	0.6 (10.0)	80.8 (9.8)	-5.1 (9.6)
Median	75.5	1.5	79.0	-4.0
Min - Max	63 - 108	-19 - 20	65 - 103	-29 - 12
Cycle 14 Day 15				
PRE PAC INFUSION				
n	25	25	29	29
Mean (SD)	80.3 (12.1)	4.6 (8.9)	84.6 (11.1)	0.2 (9.9)
Median	78.0	4.0	84.0	-2.0
Min - Max	63 - 105	-9 - 23	63 - 117	-19 - 19
AFTER PAC INFUSION				
n	24	24	28	28
Mean (SD)	74.8 (10.0)	-0.8 (9.7)	81.1 (8.7)	-3.2 (10.1)
Median	74.0	-1.5	82.0	-3.0
Min - Max	60 - 101	-29 - 17	64 - 96	-26 - 18
Cycle 15 Day 1				
PRE PAC INFUSION				
n	20	20	35	35
Mean (SD)	75.4 (10.4)	0.3 (5.8)	80.9 (12.3)	-2.1 (9.3)
Median	74.0	0.0	79.0	-3.0
Min - Max	58 - 96	-11 - 11	64 - 106	-28 - 15
AFTER PAC INFUSION				
n	19	19	25	25
Mean (SD)	78.1 (9.5)	2.6 (5.5)	80.0 (11.1)	-6.0 (11.2)
Median	78.0	1.0	81.0	-6.0
Min - Max	65 - 101	-6 - 12	60 - 105	-33 - 26
Cycle 15 Day 8				
PRE PAC INFUSION				
n	18	18	27	27
Mean (SD)	78.2 (12.8)	3.2 (9.7)	84.7 (11.2)	-1.4 (9.9)
Median	76.0	2.0	83.0	0.0
Min - Max	61 - 114	-16 - 22	68 - 100	-30 - 15

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	18	18	27	27
Mean (SD)	78.7 (9.9)	3.8 (5.2)	81.4 (10.7)	-4.6 (11.8)
Median	77.5	4.0	81.0	-6.0
Min - Max	63 - 100	-4 - 17	66 - 101	-35 - 17
Cycle 15 Day 15				
PRE PAC INFUSION				
n	19	19	25	25
Mean (SD)	76.5 (13.8)	1.5 (12.1)	85.6 (9.2)	0.2 (8.7)
Median	75.0	0.0	87.0	-2.0
Min - Max	58 - 110	-21 - 30	72 - 101	-12 - 21
AFTER PAC INFUSION				
n	19	19	25	25
Mean (SD)	76.1 (10.3)	1.1 (8.0)	82.0 (8.4)	-3.5 (8.0)
Median	74.0	3.0	82.0	-4.0
Min - Max	60 - 97	-19 - 13	68 - 96	-19 - 11
Cycle 16 Day 1				
PRE PAC INFUSION				
n	21	21	32	32
Mean (SD)	76.4 (12.4)	1.9 (8.1)	81.2 (11.4)	-2.9 (10.0)
Median	72.0	2.0	78.0	-2.0
Min - Max	60 - 112	-10 - 20	66 - 106	-30 - 12
AFTER PAC INFUSION				
n	20	20	24	24
Mean (SD)	76.7 (10.3)	1.9 (6.4)	79.3 (11.5)	-6.3 (8.0)
Median	74.0	1.0	77.5	-6.0
Min - Max	62 - 104	-10 - 14	60 - 101	-28 - 7
Cycle 16 Day 8				
PRE PAC INFUSION				
n	20	20	23	23
Mean (SD)	76.5 (10.6)	1.7 (10.2)	85.2 (11.6)	-0.3 (9.0)
Median	75.0	0.5	88.0	0.0
Min - Max	60 - 104	-24 - 18	62 - 104	-23 - 13
AFTER PAC INFUSION				
n	19	19	23	23
Mean (SD)	75.8 (10.0)	0.8 (7.3)	80.5 (10.4)	-5.0 (10.3)
Median	76.0	1.0	80.0	-4.0
Min - Max	60 - 100	-11 - 13	62 - 98	-24 - 15
Cycle 16 Day 15				
PRE PAC INFUSION				
n	18	18	25	25
Mean (SD)	77.4 (10.0)	3.0 (9.7)	84.6 (11.6)	-0.4 (10.3)
Median	78.0	1.0	84.0	1.0
Min - Max	58 - 101	-8 - 26	63 - 103	-26 - 16

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	17	17	24	24
Mean (SD)	77.5 (8.8)	2.9 (6.3)	79.6 (10.3)	-5.6 (9.8)
Median	76.0	4.0	81.0	-4.0
Min - Max	63 - 97	-10 - 11	56 - 96	-21 - 18
Cycle 17 Day 1				
PRE PAC INFUSION				
n	18	18	31	31
Mean (SD)	79.2 (12.4)	4.5 (9.5)	82.5 (9.9)	0.2 (11.6)
Median	78.0	4.5	81.0	0.0
Min - Max	61 - 103	-16 - 20	68 - 101	-26 - 26
AFTER PAC INFUSION				
n	17	17	23	23
Mean (SD)	76.0 (12.8)	0.9 (9.5)	80.0 (10.0)	-4.0 (10.8)
Median	76.0	2.0	81.0	-6.0
Min - Max	56 - 110	-18 - 18	63 - 99	-28 - 17
Cycle 17 Day 8				
PRE PAC INFUSION				
n	16	16	20	20
Mean (SD)	79.9 (8.8)	5.4 (6.6)	86.0 (9.6)	2.1 (11.0)
Median	78.5	6.0	84.5	0.5
Min - Max	65 - 95	-7 - 16	68 - 102	-24 - 17
AFTER PAC INFUSION				
n	16	16	20	20
Mean (SD)	77.7 (10.9)	3.2 (7.4)	79.2 (9.3)	-4.7 (9.1)
Median	76.5	4.0	78.5	-3.0
Min - Max	62 - 98	-12 - 14	64 - 97	-24 - 10
Cycle 17 Day 15				
PRE PAC INFUSION				
n	17	17	21	21
Mean (SD)	77.6 (10.7)	2.9 (9.4)	81.0 (11.1)	-1.8 (13.4)
Median	75.0	1.0	79.0	-2.0
Min - Max	59 - 97	-9 - 19	61 - 102	-37 - 22
AFTER PAC INFUSION				
n	17	17	22	22
Mean (SD)	77.2 (10.9)	2.5 (7.9)	79.2 (10.6)	-3.8 (12.3)
Median	76.0	3.0	78.0	-3.5
Min - Max	63 - 101	-10 - 20	65 - 102	-26 - 33
Cycle 18 Day 1				
PRE PAC INFUSION				
n	16	16	24	24
Mean (SD)	78.1 (12.1)	3.3 (7.7)	79.0 (11.1)	-3.1 (10.3)
Median	75.0	3.5	77.5	0.5
Min - Max	64 - 103	-10 - 17	63 - 102	-27 - 12

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	14	14	21	21
Mean (SD)	78.3 (10.5)	2.4 (7.1)	77.0 (9.8)	-6.5 (10.2)
Median	78.0	2.5	78.0	-8.0
Min - Max	65 - 97	-11 - 13	63 - 96	-27 - 8
Cycle 18 Day 8				
PRE PAC INFUSION				
n	14	14	21	21
Mean (SD)	79.8 (12.2)	4.9 (8.5)	81.1 (7.9)	-2.0 (9.6)
Median	77.0	6.0	79.0	0.0
Min - Max	61 - 103	-10 - 18	68 - 96	-20 - 13
AFTER PAC INFUSION				
n	14	14	20	20
Mean (SD)	77.0 (9.4)	2.1 (6.3)	78.6 (9.7)	-4.4 (8.9)
Median	76.0	2.0	78.5	-1.0
Min - Max	66 - 99	-13 - 10	60 - 95	-21 - 8
Cycle 18 Day 15				
PRE PAC INFUSION				
n	15	15	20	20
Mean (SD)	79.1 (10.1)	4.0 (8.1)	85.1 (8.4)	1.3 (11.9)
Median	79.0	1.0	85.0	0.5
Min - Max	57 - 100	-6 - 19	71 - 100	-23 - 31
AFTER PAC INFUSION				
n	15	15	19	19
Mean (SD)	77.8 (12.5)	2.7 (9.1)	80.8 (10.0)	-2.8 (8.8)
Median	75.0	2.0	81.0	-4.0
Min - Max	58 - 109	-13 - 17	62 - 100	-18 - 10
Cycle 19 Day 1				
PRE PAC INFUSION				
n	11	11	26	26
Mean (SD)	76.5 (13.0)	2.6 (7.8)	79.2 (10.8)	-3.0 (10.6)
Median	74.0	4.0	76.5	-0.5
Min - Max	55 - 103	-8 - 17	58 - 98	-22 - 13
AFTER PAC INFUSION				
n	10	10	19	19
Mean (SD)	75.5 (7.7)	1.6 (6.6)	75.6 (8.2)	-6.2 (7.4)
Median	75.5	-1.0	75.0	-5.0
Min - Max	60 - 84	-5 - 17	65 - 90	-24 - 7
Cycle 19 Day 8				
PRE PAC INFUSION				
n	9	9	20	20
Mean (SD)	80.9 (10.7)	7.4 (9.9)	84.3 (9.5)	1.9 (9.2)
Median	78.0	10.0	81.0	1.0
Min - Max	70 - 103	-7 - 23	68 - 101	-17 - 21

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	9	9	19	19
Mean (SD)	77.0 (8.5)	3.6 (7.1)	80.8 (8.1)	-1.3 (8.7)
Median	73.0	5.0	80.0	-2.0
Min - Max	69 - 96	-6 - 14	63 - 96	-20 - 13
Cycle 19 Day 15				
PRE PAC INFUSION				
n	10	10	20	20
Mean (SD)	71.4 (13.9)	-2.5 (13.0)	82.3 (11.0)	0.4 (11.1)
Median	70.5	-3.0	78.5	0.0
Min - Max	56 - 106	-27 - 20	65 - 100	-27 - 19
AFTER PAC INFUSION				
n	9	9	19	19
Mean (SD)	73.2 (8.3)	-1.7 (11.3)	77.4 (10.4)	-4.1 (8.6)
Median	72.0	-3.0	77.0	-1.0
Min - Max	62 - 88	-22 - 17	64 - 105	-24 - 10
Cycle 20 Day 1				
PRE PAC INFUSION				
n	11	11	23	23
Mean (SD)	75.7 (11.4)	1.8 (9.4)	82.1 (10.1)	-0.2 (9.9)
Median	76.0	2.0	79.0	1.0
Min - Max	60 - 96	-19 - 14	65 - 106	-19 - 16
AFTER PAC INFUSION				
n	10	10	17	17
Mean (SD)	77.6 (10.4)	3.7 (9.4)	79.3 (10.0)	-3.9 (8.8)
Median	77.5	4.0	79.0	-3.0
Min - Max	61 - 97	-13 - 15	63 - 97	-17 - 13
Cycle 20 Day 8				
PRE PAC INFUSION				
n	9	9	16	16
Mean (SD)	79.3 (16.3)	3.7 (15.1)	83.1 (9.7)	0.6 (11.6)
Median	79.0	5.0	83.0	3.0
Min - Max	57 - 116	-27 - 30	68 - 98	-24 - 16
AFTER PAC INFUSION				
n	9	9	16	16
Mean (SD)	76.6 (10.7)	0.9 (7.3)	80.8 (10.7)	-1.6 (7.7)
Median	74.0	-3.0	81.0	-2.5
Min - Max	58 - 96	-7 - 14	65 - 96	-12 - 10
Cycle 20 Day 15				
PRE PAC INFUSION				
n	10	10	16	16
Mean (SD)	73.2 (10.0)	-0.7 (11.9)	82.0 (11.7)	-0.1 (13.6)
Median	74.5	1.0	79.5	-0.5
Min - Max	58 - 94	-26 - 13	68 - 101	-29 - 25

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	10	10	16	16
Mean (SD)	72.7 (8.2)	-1.2 (9.4)	77.9 (11.9)	-4.2 (11.8)
Median	71.5	1.0	78.0	-1.5
Min - Max	62 - 86	-22 - 10	61 - 101	-35 - 14
Cycle 21 Day 1				
PRE PAC INFUSION				
n	9	9	21	21
Mean (SD)	68.7 (7.7)	-3.4 (6.7)	79.0 (10.6)	-2.7 (9.1)
Median	68.0	-2.0	77.0	-2.0
Min - Max	58 - 82	-16 - 4	61 - 100	-16 - 13
AFTER PAC INFUSION				
n	6	6	15	15
Mean (SD)	67.8 (5.7)	-3.5 (6.4)	74.9 (10.2)	-6.9 (9.0)
Median	68.0	-3.5	74.0	-6.0
Min - Max	62 - 76	-13 - 7	60 - 94	-17 - 8
Cycle 21 Day 8				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	75.0 (13.2)	-0.1 (10.5)	83.4 (8.6)	1.4 (12.6)
Median	71.0	5.0	84.0	0.0
Min - Max	60 - 94	-17 - 11	70 - 100	-17 - 25
AFTER PAC INFUSION				
n	9	9	14	14
Mean (SD)	71.9 (7.2)	-3.2 (7.1)	78.9 (9.1)	-3.1 (11.3)
Median	72.0	-3.0	81.5	-3.5
Min - Max	62 - 84	-12 - 10	65 - 95	-19 - 23
Cycle 21 Day 15				
PRE PAC INFUSION				
n	9	9	15	15
Mean (SD)	75.4 (12.4)	0.6 (12.5)	82.1 (10.5)	0.2 (12.6)
Median	74.0	-4.0	80.0	-1.0
Min - Max	61 - 98	-21 - 14	68 - 105	-17 - 25
AFTER PAC INFUSION				
n	8	8	15	15
Mean (SD)	69.9 (12.8)	-6.5 (14.4)	77.3 (9.9)	-4.6 (9.3)
Median	67.5	-3.0	78.0	-5.0
Min - Max	50 - 92	-34 - 8	64 - 95	-19 - 9
Cycle 22 Day 1				
PRE PAC INFUSION				
n	10	10	20	20
Mean (SD)	74.1 (10.9)	0.6 (9.2)	78.5 (9.8)	-3.0 (11.9)
Median	74.0	-0.5	77.5	-2.5
Min - Max	57 - 98	-13 - 12	62 - 98	-24 - 26

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	7	7	15	15
Mean (SD)	72.1 (7.5)	-1.0 (7.4)	80.2 (12.5)	-1.7 (12.6)
Median	76.0	-1.0	82.0	-6.0
Min - Max	63 - 83	-12 - 10	58 - 98	-15 - 34
Cycle 22 Day 8				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	77.0 (8.2)	1.9 (6.7)	83.1 (8.8)	1.1 (11.6)
Median	78.0	2.0	81.0	0.5
Min - Max	64 - 88	-8 - 11	69 - 100	-25 - 16
AFTER PAC INFUSION				
n	9	9	14	14
Mean (SD)	76.8 (9.2)	1.7 (10.3)	79.6 (10.3)	-2.4 (10.9)
Median	76.0	0.0	78.5	-3.5
Min - Max	65 - 96	-11 - 18	61 - 98	-20 - 22
Cycle 22 Day 15				
PRE PAC INFUSION				
n	7	7	14	14
Mean (SD)	77.0 (15.6)	0.9 (11.3)	78.6 (12.0)	-2.6 (15.1)
Median	70.0	2.0	74.5	-3.5
Min - Max	63 - 101	-12 - 15	68 - 107	-26 - 27
AFTER PAC INFUSION				
n	7	7	14	14
Mean (SD)	71.1 (12.0)	-5.0 (12.4)	77.2 (11.5)	-4.1 (9.3)
Median	66.0	-1.0	73.0	-4.0
Min - Max	55 - 89	-29 - 5	65 - 97	-21 - 12
Cycle 23 Day 1				
PRE PAC INFUSION				
n	9	9	19	19
Mean (SD)	76.6 (12.4)	3.1 (9.1)	80.7 (10.6)	-0.5 (10.8)
Median	74.0	3.0	78.0	-1.0
Min - Max	62 - 105	-6 - 19	68 - 109	-20 - 19
AFTER PAC INFUSION				
n	7	7	13	13
Mean (SD)	74.3 (6.2)	1.1 (8.6)	74.6 (10.8)	-6.6 (10.1)
Median	76.0	0.0	72.0	-10.0
Min - Max	66 - 84	-9 - 18	60 - 95	-24 - 10
Cycle 23 Day 8				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	77.3 (9.4)	2.5 (7.3)	81.6 (10.5)	-0.2 (15.5)
Median	76.0	2.5	80.0	0.0
Min - Max	67 - 93	-8 - 11	70 - 100	-27 - 36

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	70.5 (11.7)	-4.3 (12.1)	79.3 (12.1)	-2.5 (13.3)
Median	70.5	-0.5	82.0	-8.0
Min - Max	50 - 90	-29 - 9	64 - 96	-14 - 32
Cycle 23 Day 15				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	76.1 (10.5)	1.4 (10.9)	80.8 (10.4)	-1.5 (13.8)
Median	75.0	4.5	82.0	-1.0
Min - Max	64 - 92	-15 - 15	65 - 96	-33 - 18
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	71.3 (9.2)	-3.5 (8.7)	80.0 (10.1)	-2.4 (10.7)
Median	67.5	-1.0	80.0	-4.0
Min - Max	60 - 85	-19 - 10	63 - 93	-18 - 13
Cycle 24 Day 1				
PRE PAC INFUSION				
n	9	9	17	17
Mean (SD)	74.7 (12.5)	1.2 (7.2)	80.8 (9.4)	-1.7 (10.9)
Median	70.0	2.0	80.0	-2.0
Min - Max	59 - 95	-12 - 10	68 - 102	-18 - 22
AFTER PAC INFUSION				
n	7	7	12	12
Mean (SD)	71.7 (9.1)	-1.4 (6.5)	75.9 (9.8)	-6.7 (10.9)
Median	67.0	-1.0	73.5	-6.5
Min - Max	60 - 83	-12 - 7	62 - 91	-31 - 11
Cycle 24 Day 8				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	80.3 (11.2)	5.5 (14.1)	83.6 (11.4)	0.8 (13.8)
Median	80.0	9.5	86.0	0.0
Min - Max	59 - 95	-25 - 22	68 - 102	-19 - 26
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	76.3 (9.6)	1.5 (5.0)	81.9 (12.2)	-0.9 (14.4)
Median	75.5	0.0	85.0	-8.0
Min - Max	62 - 91	-4 - 10	63 - 96	-17 - 30
Cycle 24 Day 15				
PRE PAC INFUSION				
n	8	8	12	12
Mean (SD)	75.1 (12.9)	0.4 (14.6)	81.8 (10.0)	-0.8 (10.2)
Median	73.5	5.0	84.0	-3.5
Min - Max	56 - 94	-28 - 17	67 - 96	-12 - 20

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	8	8	12	12
Mean (SD)	73.1 (9.4)	-1.6 (12.2)	77.7 (10.9)	-4.9 (10.8)
Median	71.5	1.5	76.0	-5.5
Min - Max	60 - 90	-24 - 13	59 - 99	-20 - 19
Cycle 25 Day 1				
PRE PAC INFUSION				
n	8	8	14	14
Mean (SD)	81.4 (15.9)	9.3 (11.0)	83.4 (9.7)	-0.1 (14.7)
Median	76.0	4.0	82.0	-2.0
Min - Max	67 - 113	-5 - 27	68 - 100	-22 - 36
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	75.6 (9.4)	2.1 (7.7)	78.8 (11.2)	-4.7 (14.6)
Median	71.0	4.0	78.0	-12.0
Min - Max	64 - 90	-9 - 14	60 - 94	-16 - 30
Cycle 25 Day 8				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	78.4 (14.8)	5.0 (9.7)	81.9 (8.5)	-1.2 (13.6)
Median	78.0	4.0	81.0	-1.0
Min - Max	62 - 101	-13 - 15	72 - 93	-22 - 26
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	75.3 (14.5)	1.9 (7.2)	81.6 (11.3)	-1.6 (15.2)
Median	71.0	5.0	78.0	-4.0
Min - Max	58 - 94	-8 - 10	63 - 94	-20 - 30
Cycle 25 Day 15				
PRE PAC INFUSION				
n	7	7	10	10
Mean (SD)	79.7 (14.7)	6.3 (7.8)	80.9 (9.7)	-1.9 (10.5)
Median	75.0	7.0	80.0	-4.0
Min - Max	65 - 104	-4 - 18	68 - 98	-14 - 16
AFTER PAC INFUSION				
n	7	7	10	10
Mean (SD)	77.4 (13.5)	4.0 (4.9)	79.4 (12.8)	-3.4 (12.0)
Median	79.0	3.0	77.0	-7.5
Min - Max	63 - 96	-2 - 12	64 - 101	-17 - 20
Cycle 26 Day 1				
PRE PAC INFUSION				
n	8	8	14	14
Mean (SD)	76.6 (17.2)	4.5 (10.0)	79.1 (9.6)	-3.8 (9.7)
Median	69.0	5.0	78.0	-4.5
Min - Max	57 - 105	-13 - 21	68 - 96	-24 - 10

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	71.9 (7.3)	-1.6 (5.2)	73.6 (10.7)	-9.8 (9.7)
Median	75.0	-4.0	74.0	-9.0
Min - Max	60 - 80	-6 - 8	60 - 93	-24 - 6
Cycle 26 Day 8				
PRE PAC INFUSION				
n	7	7	7	7
Mean (SD)	82.0 (10.4)	8.6 (9.0)	78.6 (12.9)	-2.0 (11.5)
Median	80.0	6.0	73.0	0.0
Min - Max	65 - 98	-1 - 20	66 - 101	-19 - 11
AFTER PAC INFUSION				
n	7	7	7	7
Mean (SD)	73.7 (9.4)	0.3 (4.6)	73.6 (6.2)	-7.0 (9.4)
Median	74.0	0.0	74.0	-6.0
Min - Max	65 - 90	-5 - 7	65 - 84	-24 - 6
Cycle 26 Day 15				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	82.3 (14.1)	8.9 (11.3)	81.4 (12.5)	-1.9 (12.5)
Median	78.0	13.0	80.0	0.0
Min - Max	66 - 103	-13 - 17	64 - 101	-18 - 16
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	74.7 (11.6)	1.3 (7.8)	77.6 (11.2)	-5.8 (10.9)
Median	69.0	4.0	77.0	-11.0
Min - Max	65 - 95	-13 - 11	65 - 94	-17 - 13
Cycle 27 Day 1				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	75.1 (10.1)	2.3 (8.6)	80.9 (11.6)	-2.1 (10.1)
Median	74.0	4.0	79.5	-2.0
Min - Max	61 - 93	-18 - 11	66 - 102	-19 - 16
AFTER PAC INFUSION				
n	8	8	8	8
Mean (SD)	69.6 (9.0)	-4.4 (8.8)	73.9 (13.1)	-8.6 (10.7)
Median	68.5	-4.0	70.0	-12.0
Min - Max	59 - 84	-17 - 8	60 - 95	-20 - 10
Cycle 27 Day 8				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	79.3 (11.6)	3.3 (10.2)	84.0 (13.8)	0.3 (16.1)
Median	78.5	8.0	81.5	3.5
Min - Max	64 - 97	-15 - 11	70 - 105	-26 - 20

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	6	6	8	8
Mean (SD)	74.0 (8.8)	-2.0 (6.4)	78.5 (11.7)	-5.3 (10.2)
Median	73.0	-0.5	76.5	-8.0
Min - Max	64 - 88	-12 - 4	67 - 96	-17 - 12
Cycle 27 Day 15				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	81.4 (11.9)	5.1 (7.3)	87.7 (13.1)	4.3 (13.1)
Median	76.0	6.0	84.0	-2.0
Min - Max	67 - 100	-5 - 16	75 - 110	-14 - 23
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	78.1 (11.8)	1.9 (5.9)	79.2 (12.7)	-4.1 (9.4)
Median	84.0	3.0	73.0	-4.0
Min - Max	58 - 89	-7 - 8	64 - 102	-20 - 11
Cycle 28 Day 1				
PRE PAC INFUSION				
n	7	7	13	13
Mean (SD)	77.3 (8.9)	3.1 (6.3)	82.2 (10.6)	0.5 (10.7)
Median	73.0	6.0	80.0	0.0
Min - Max	70 - 94	-6 - 8	67 - 105	-23 - 15
AFTER PAC INFUSION				
n	6	6	6	6
Mean (SD)	73.8 (7.8)	-2.2 (6.8)	75.8 (11.5)	-7.8 (9.9)
Median	73.0	-3.0	78.5	-2.5
Min - Max	65 - 84	-11 - 8	61 - 90	-22 - 0
Cycle 28 Day 8				
PRE PAC INFUSION				
n	6	6	7	7
Mean (SD)	83.5 (16.3)	7.5 (12.9)	84.3 (15.4)	-2.3 (15.5)
Median	82.0	8.5	83.0	-6.0
Min - Max	65 - 107	-14 - 23	70 - 114	-23 - 24
AFTER PAC INFUSION				
n	6	6	7	7
Mean (SD)	75.3 (10.7)	-0.7 (6.1)	78.9 (11.0)	-7.7 (6.8)
Median	76.0	-1.5	80.0	-9.0
Min - Max	62 - 88	-9 - 8	64 - 93	-17 - 2
Cycle 28 Day 15				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	83.5 (11.1)	7.5 (8.2)	83.3 (16.4)	-2.5 (15.0)
Median	85.0	8.5	80.5	-8.0
Min - Max	66 - 97	-3 - 20	66 - 117	-18 - 27

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	6	6	8	8
Mean (SD)	77.0 (9.7)	1.0 (6.0)	77.3 (14.1)	-8.5 (13.9)
Median	77.5	1.5	73.5	-10.0
Min - Max	66 - 87	-8 - 10	61 - 102	-24 - 12
Cycle 29 Day 1				
PRE PAC INFUSION				
n	7	7	11	11
Mean (SD)	77.6 (11.7)	1.7 (8.4)	74.9 (7.1)	-7.7 (7.5)
Median	76.0	3.0	74.0	-6.0
Min - Max	68 - 100	-11 - 16	65 - 89	-25 - 4
AFTER PAC INFUSION				
n	6	6	6	6
Mean (SD)	74.5 (11.2)	-3.5 (7.6)	71.3 (8.5)	-11.7 (7.4)
Median	79.0	-3.0	72.5	-12.0
Min - Max	58 - 84	-16 - 6	61 - 84	-22 - -2
Cycle 29 Day 8				
PRE PAC INFUSION				
n	6	6	5	5
Mean (SD)	80.0 (12.4)	2.0 (12.6)	83.6 (9.8)	-4.2 (17.6)
Median	78.5	5.0	80.0	-2.0
Min - Max	63 - 100	-16 - 14	74 - 99	-24 - 19
AFTER PAC INFUSION				
n	6	6	5	5
Mean (SD)	77.7 (12.8)	-0.3 (8.9)	77.6 (11.5)	-10.2 (12.4)
Median	78.5	-1.0	76.0	-10.0
Min - Max	61 - 99	-10 - 15	63 - 91	-27 - 7
Cycle 29 Day 15				
PRE PAC INFUSION				
n	6	6	7	7
Mean (SD)	81.7 (13.7)	3.7 (10.5)	76.3 (11.6)	-8.9 (18.1)
Median	76.5	4.5	74.0	-8.0
Min - Max	66 - 100	-13 - 16	61 - 92	-45 - 12
AFTER PAC INFUSION				
n	6	6	7	7
Mean (SD)	78.2 (7.7)	0.2 (5.8)	70.0 (6.5)	-15.1 (9.5)
Median	79.0	1.0	72.0	-15.0
Min - Max	67 - 88	-7 - 8	62 - 78	-30 - -2
Cycle 30 Day 1				
PRE PAC INFUSION				
n	7	7	12	12
Mean (SD)	83.7 (11.3)	7.9 (6.3)	78.3 (7.1)	-5.6 (8.6)
Median	84.0	6.0	80.5	-3.0
Min - Max	67 - 103	0 - 19	66 - 89	-23 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	7	7
Mean (SD)	74.0 (9.3)	-3.8 (6.2)	74.7 (13.5)	-10.4 (7.8)
Median	78.0	-4.0	72.0	-12.0
Min - Max	58 - 80	-12 - 4	58 - 94	-18 - 6
Cycle 30 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	89.6 (7.6)	11.8 (11.6)	80.0 (12.3)	-6.8 (13.9)
Median	87.0	8.0	83.0	-10.0
Min - Max	82 - 100	1 - 30	63 - 96	-24 - 11
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	85.2 (8.3)	7.4 (5.8)	75.0 (10.3)	-11.8 (9.5)
Median	84.0	6.0	72.0	-11.0
Min - Max	78 - 98	2 - 14	66 - 91	-26 - -1
Cycle 30 Day 15				
PRE PAC INFUSION				
n	4	4	7	7
Mean (SD)	84.3 (12.3)	6.0 (6.7)	78.4 (8.3)	-6.7 (14.5)
Median	82.0	6.0	79.0	-8.0
Min - Max	73 - 100	-2 - 14	69 - 90	-34 - 11
AFTER PAC INFUSION				
n	4	4	7	7
Mean (SD)	80.5 (2.6)	2.3 (9.7)	76.3 (10.0)	-8.9 (4.4)
Median	80.0	0.0	74.0	-9.0
Min - Max	78 - 84	-7 - 16	64 - 93	-14 - -1
Cycle 31 Day 1				
PRE PAC INFUSION				
n	6	6	12	12
Mean (SD)	78.3 (9.5)	2.5 (10.9)	78.3 (6.4)	-5.7 (9.1)
Median	78.0	6.0	80.5	-7.5
Min - Max	66 - 93	-18 - 13	66 - 84	-22 - 11
AFTER PAC INFUSION				
n	4	4	6	6
Mean (SD)	73.5 (5.9)	-4.8 (9.4)	73.0 (11.3)	-12.7 (7.3)
Median	73.0	-3.5	73.5	-15.0
Min - Max	68 - 80	-16 - 4	60 - 87	-19 - 1
Cycle 31 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	85.8 (9.0)	8.0 (11.2)	78.6 (9.9)	-8.2 (16.1)
Median	82.0	6.0	79.0	-14.0
Min - Max	78 - 100	-4 - 24	63 - 90	-23 - 17

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	79.6 (11.4)	1.8 (7.4)	76.8 (11.8)	-10.0 (12.5)
Median	76.0	0.0	79.0	-10.0
Min - Max	68 - 98	-4 - 14	64 - 88	-27 - 8
Cycle 31 Day 15				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	85.3 (10.4)	9.0 (9.6)	86.5 (8.8)	0.8 (17.8)
Median	81.5	8.0	85.0	0.0
Min - Max	78 - 100	0 - 20	75 - 98	-25 - 25
AFTER PAC INFUSION				
n	4	4	6	6
Mean (SD)	78.3 (7.8)	2.0 (0.8)	75.0 (13.2)	-10.7 (7.7)
Median	79.0	2.0	73.0	-12.0
Min - Max	68 - 87	1 - 3	63 - 94	-17 - 4
Cycle 32 Day 1				
PRE PAC INFUSION				
n	7	7	11	11
Mean (SD)	84.4 (11.8)	8.6 (16.6)	77.7 (8.4)	-6.4 (8.7)
Median	80.0	2.0	78.0	-6.0
Min - Max	74 - 109	-4 - 44	65 - 91	-19 - 6
AFTER PAC INFUSION				
n	5	5	6	6
Mean (SD)	78.0 (11.0)	0.2 (7.2)	73.8 (9.9)	-11.8 (3.5)
Median	78.0	0.0	69.0	-11.0
Min - Max	60 - 88	-8 - 10	65 - 90	-16 - -8
Cycle 32 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	84.8 (6.3)	7.0 (7.8)	81.8 (8.0)	-5.0 (12.3)
Median	85.0	4.0	82.0	-7.0
Min - Max	78 - 94	0 - 20	70 - 91	-16 - 14
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	78.8 (6.3)	1.0 (5.0)	77.2 (11.1)	-9.6 (4.7)
Median	79.0	2.0	76.0	-9.0
Min - Max	69 - 86	-7 - 6	65 - 89	-17 - -4
Cycle 32 Day 15				
PRE PAC INFUSION				
n	4	4	5	5
Mean (SD)	88.8 (9.0)	11.0 (5.8)	79.4 (7.4)	-8.0 (12.0)
Median	87.0	11.0	79.0	-10.0
Min - Max	81 - 100	6 - 16	70 - 89	-19 - 11

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	4	4	5	5
Mean (SD)	82.0 (14.0)	4.3 (8.5)	76.8 (11.8)	-10.6 (5.1)
Median	81.0	2.5	77.0	-12.0
Min - Max	66 - 100	-4 - 16	64 - 94	-17 - -3
Cycle 33 Day 1				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	83.3 (9.9)	7.4 (5.3)	75.1 (5.5)	-10.1 (11.3)
Median	82.0	7.0	78.0	-8.0
Min - Max	70 - 98	0 - 14	64 - 80	-27 - 6
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	78.6 (7.4)	0.8 (8.4)	71.4 (10.7)	-16.8 (9.4)
Median	78.0	4.0	70.0	-17.0
Min - Max	71 - 88	-14 - 6	60 - 86	-28 - -2
Cycle 33 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	84.0 (10.7)	5.8 (4.8)	84.5 (9.0)	-5.8 (11.7)
Median	83.0	6.0	86.0	-8.5
Min - Max	73 - 97	0 - 11	73 - 93	-16 - 10
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	79.3 (9.7)	1.0 (8.1)	81.0 (13.3)	-9.3 (10.3)
Median	79.5	4.5	77.0	-6.5
Min - Max	68 - 90	-11 - 6	70 - 100	-24 - 0
Cycle 33 Day 15				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	83.0 (12.1)	5.2 (10.5)	82.6 (11.2)	-5.6 (9.0)
Median	82.0	3.0	81.0	-6.0
Min - Max	69 - 101	-7 - 17	69 - 100	-19 - 4
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	74.2 (9.7)	-3.6 (9.5)	79.2 (16.3)	-9.0 (7.0)
Median	70.0	1.0	79.0	-8.0
Min - Max	66 - 89	-19 - 5	60 - 100	-20 - -1
Cycle 34 Day 1				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	80.7 (9.1)	4.9 (7.2)	81.0 (7.5)	-4.2 (8.2)
Median	78.0	2.0	79.0	-8.0
Min - Max	73 - 100	-3 - 14	68 - 93	-13 - 14

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	77.8 (8.2)	0.0 (3.7)	78.0 (12.2)	-13.0 (7.6)
Median	78.0	0.0	81.0	-15.5
Min - Max	69 - 89	-5 - 4	61 - 89	-19 - -2
Cycle 34 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	82.0 (9.6)	5.8 (10.9)	81.8 (13.9)	-8.5 (13.3)
Median	82.5	4.5	87.5	-13.5
Min - Max	70 - 93	-6 - 20	61 - 91	-18 - 11
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	74.0 (8.2)	-2.3 (1.7)	82.8 (15.9)	-7.5 (11.4)
Median	75.5	-2.5	84.5	-10.5
Min - Max	63 - 82	-4 - 0	62 - 100	-17 - 8
Cycle 34 Day 15				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	84.4 (9.4)	6.6 (8.4)	83.8 (8.8)	-4.4 (13.4)
Median	82.0	4.0	82.0	-3.0
Min - Max	75 - 100	-1 - 16	74 - 96	-17 - 16
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	81.2 (10.3)	3.4 (4.7)	82.0 (6.0)	-6.2 (9.1)
Median	82.0	4.0	84.0	-3.0
Min - Max	69 - 94	-3 - 10	74 - 89	-17 - 5
Cycle 35 Day 1				
PRE PAC INFUSION				
n	7	7	8	8
Mean (SD)	80.6 (9.1)	4.7 (3.9)	76.9 (5.4)	-9.0 (11.6)
Median	84.0	6.0	76.0	-9.0
Min - Max	69 - 92	-4 - 8	69 - 86	-24 - 6
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	78.2 (11.7)	0.4 (8.6)	81.5 (8.8)	-8.8 (10.0)
Median	77.0	2.0	81.5	-10.0
Min - Max	67 - 97	-9 - 13	71 - 92	-19 - 4
Cycle 35 Day 8				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	81.8 (7.3)	4.0 (10.1)	83.0 (11.0)	-7.3 (17.7)
Median	82.0	0.0	81.5	-12.5
Min - Max	72 - 91	-4 - 21	72 - 97	-21 - 17

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	78.0 (7.6)	0.2 (1.1)	80.5 (10.5)	-9.8 (8.8)
Median	78.0	0.0	82.5	-13.0
Min - Max	67 - 86	-1 - 2	66 - 91	-16 - 3
Cycle 35 Day 15				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	82.0 (10.2)	4.2 (12.5)	86.8 (11.4)	-3.5 (14.9)
Median	82.0	-2.0	89.0	-8.0
Min - Max	72 - 95	-6 - 24	71 - 98	-16 - 18
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	76.2 (6.3)	-1.6 (5.2)	80.8 (12.6)	-9.5 (11.7)
Median	78.0	-4.0	84.5	-14.5
Min - Max	69 - 82	-6 - 4	63 - 91	-17 - 8
Cycle 36 Day 1				
PRE PAC INFUSION				
n	7	7	8	8
Mean (SD)	77.9 (5.9)	2.0 (6.4)	81.0 (11.6)	-4.9 (13.4)
Median	77.0	-2.0	76.5	-7.0
Min - Max	70 - 88	-3 - 14	70 - 99	-21 - 19
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	78.2 (6.6)	0.4 (4.6)	80.0 (6.6)	-10.3 (15.1)
Median	78.0	1.0	80.0	-11.0
Min - Max	68 - 84	-6 - 6	72 - 88	-27 - 8
Cycle 36 Day 8				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	89.4 (13.3)	11.6 (15.0)	84.8 (14.4)	-5.5 (14.7)
Median	98.0	12.0	88.5	-10.5
Min - Max	72 - 100	-4 - 34	66 - 96	-17 - 16
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	80.4 (14.0)	2.6 (12.3)	84.5 (10.5)	-5.8 (12.1)
Median	75.0	4.0	83.5	-6.0
Min - Max	69 - 104	-11 - 20	74 - 97	-20 - 9
Cycle 36 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	89.8 (9.2)	11.5 (14.0)	86.5 (9.7)	-3.8 (7.6)
Median	91.5	7.5	88.5	-6.0
Min - Max	78 - 98	0 - 31	73 - 96	-10 - 7

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	79.0 (8.8)	0.8 (2.6)	82.5 (10.8)	-7.8 (5.9)
Median	80.5	1.0	82.0	-8.5
Min - Max	68 - 87	-2 - 3	70 - 96	-14 - 0
Cycle 37 Day 1				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	79.0 (12.5)	1.3 (9.9)	80.8 (9.2)	-5.1 (9.3)
Median	73.5	1.5	79.5	-7.0
Min - Max	68 - 100	-13 - 14	69 - 97	-19 - 11
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	77.0 (9.1)	-4.0 (8.0)	83.0 (11.5)	-7.3 (8.2)
Median	74.5	-2.5	82.0	-7.5
Min - Max	69 - 90	-15 - 4	70 - 98	-17 - 3
Cycle 37 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	82.8 (15.0)	1.8 (10.3)	72.5 (25.5)	-17.8 (17.3)
Median	82.0	1.0	78.5	-12.0
Min - Max	67 - 100	-9 - 14	37 - 96	-43 - -4
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	82.0 (12.1)	1.0 (8.9)	83.5 (13.9)	-6.8 (16.9)
Median	80.0	-2.0	83.5	-8.0
Min - Max	70 - 98	-6 - 14	71 - 96	-26 - 15
Cycle 37 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	85.8 (16.0)	4.8 (11.4)	85.5 (13.0)	-4.8 (15.6)
Median	86.5	4.5	87.0	-8.0
Min - Max	70 - 100	-6 - 16	71 - 97	-20 - 17
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	78.3 (9.9)	-2.8 (7.4)	86.8 (13.1)	-3.5 (13.9)
Median	75.5	-5.5	88.5	-6.5
Min - Max	70 - 92	-8 - 8	71 - 99	-17 - 16
Cycle 38 Day 1				
PRE PAC INFUSION				
n	5	5	8	8
Mean (SD)	82.6 (12.0)	5.0 (11.5)	77.5 (9.1)	-8.4 (6.0)
Median	76.0	11.0	77.0	-9.0
Min - Max	71 - 100	-13 - 14	66 - 97	-18 - -1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	80.3 (7.1)	-1.7 (5.5)	81.3 (13.9)	-9.0 (13.1)
Median	79.0	-2.0	81.0	-10.0
Min - Max	74 - 88	-7 - 4	66 - 97	-24 - 8
Cycle 38 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	84.0 (5.9)	3.0 (2.0)	88.0 (17.6)	-2.3 (22.5)
Median	84.0	4.0	85.0	-7.0
Min - Max	78 - 90	0 - 4	73 - 109	-24 - 29
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	83.3 (6.2)	2.3 (4.9)	86.5 (10.7)	-3.8 (14.9)
Median	83.0	2.0	86.0	-3.0
Min - Max	76 - 91	-2 - 7	76 - 98	-22 - 13
Cycle 38 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	86.8 (9.8)	5.8 (5.9)	83.0 (11.2)	-7.3 (10.7)
Median	87.5	6.5	82.0	-7.5
Min - Max	76 - 96	-2 - 12	71 - 97	-20 - 6
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	85.3 (9.1)	4.3 (7.1)	81.0 (11.0)	-9.3 (11.6)
Median	85.5	4.5	82.5	-12.0
Min - Max	74 - 96	-4 - 12	67 - 92	-20 - 7
Cycle 39 Day 1				
PRE PAC INFUSION				
n	5	5	8	8
Mean (SD)	79.8 (6.1)	2.4 (8.0)	77.9 (7.1)	-8.0 (11.9)
Median	79.0	0.0	75.0	-7.0
Min - Max	71 - 86	-5 - 16	70 - 89	-23 - 17
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	78.5 (5.0)	-2.5 (5.7)	78.5 (10.7)	-11.8 (10.9)
Median	79.0	-5.0	76.0	-10.5
Min - Max	72 - 84	-6 - 6	69 - 93	-26 - 0
Cycle 39 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	81.0 (8.0)	0.0 (3.6)	83.0 (14.0)	-7.3 (21.1)
Median	82.5	1.0	80.0	-11.5
Min - Max	71 - 88	-5 - 3	71 - 101	-27 - 21

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	81.3 (4.4)	0.3 (5.9)	84.3 (7.8)	-6.0 (11.0)
Median	81.0	-0.5	82.0	-5.0
Min - Max	77 - 86	-6 - 8	78 - 95	-19 - 5
Cycle 39 Day 15				
PRE PAC INFUSION				
n	4	4	3	3
Mean (SD)	76.5 (9.1)	-4.5 (7.4)	85.3 (12.1)	-2.3 (6.0)
Median	73.0	-4.0	84.0	-3.0
Min - Max	70 - 90	-14 - 4	74 - 98	-8 - 4
AFTER PAC INFUSION				
n	4	4	3	3
Mean (SD)	76.5 (4.5)	-4.5 (4.4)	82.7 (11.4)	-5.0 (10.1)
Median	78.0	-6.5	86.0	-7.0
Min - Max	70 - 80	-7 - 2	70 - 92	-14 - 6
Cycle 40 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	78.8 (13.9)	3.0 (8.0)	78.6 (4.0)	-7.3 (11.5)
Median	76.0	4.5	77.0	-7.0
Min - Max	66 - 97	-8 - 11	75 - 87	-24 - 7
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	78.7 (8.1)	-1.3 (3.1)	84.7 (5.7)	-10.0 (11.4)
Median	74.0	-2.0	83.0	-15.0
Min - Max	74 - 88	-4 - 2	80 - 91	-18 - 3
Cycle 40 Day 8				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	79.3 (9.5)	-0.7 (4.2)	85.0 (11.4)	-5.3 (21.3)
Median	76.0	-2.0	80.0	-9.0
Min - Max	72 - 90	-4 - 4	78 - 102	-25 - 22
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	77.3 (5.0)	-2.7 (4.2)	79.3 (12.1)	-11.0 (10.1)
Median	78.0	-4.0	80.0	-13.0
Min - Max	72 - 82	-6 - 2	64 - 93	-21 - 3
Cycle 40 Day 15				
PRE PAC INFUSION				
n	2	2	4	4
Mean (SD)	79.0 (1.4)	-3.0 (4.2)	92.3 (9.6)	2.0 (19.1)
Median	79.0	-3.0	94.5	3.0
Min - Max	78 - 80	-6 - 0	79 - 101	-19 - 21

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	2	2	4	4
Mean (SD)	75.5 (2.1)	-6.5 (3.5)	81.5 (8.0)	-8.8 (10.3)
Median	75.5	-6.5	81.5	-10.0
Min - Max	74 - 77	-9 - -4	72 - 91	-19 - 4
Cycle 41 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	76.8 (4.3)	1.0 (7.3)	74.5 (6.7)	-11.4 (9.0)
Median	75.5	-2.5	76.0	-10.5
Min - Max	73 - 83	-3 - 12	65 - 84	-24 - 0
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	81.3 (2.9)	1.3 (5.1)	79.3 (10.8)	-11.0 (9.6)
Median	83.0	0.0	79.5	-12.5
Min - Max	78 - 83	-3 - 7	66 - 92	-21 - 2
Cycle 41 Day 8				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	83.3 (15.0)	3.3 (10.0)	85.3 (7.6)	-5.0 (12.9)
Median	82.0	4.0	87.0	-8.0
Min - Max	69 - 99	-7 - 13	75 - 92	-16 - 12
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	81.3 (2.3)	1.3 (6.4)	83.3 (10.5)	-7.0 (10.2)
Median	80.0	4.0	84.0	-9.0
Min - Max	80 - 84	-6 - 6	70 - 95	-17 - 7
Cycle 41 Day 15				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	79.7 (7.2)	-0.3 (2.1)	87.0 (13.8)	-3.3 (9.7)
Median	76.0	-1.0	89.5	-7.0
Min - Max	75 - 88	-2 - 2	68 - 101	-10 - 11
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	82.3 (4.0)	2.3 (8.5)	83.5 (12.0)	-6.8 (12.1)
Median	80.0	2.0	84.5	-9.0
Min - Max	80 - 87	-6 - 11	69 - 96	-19 - 10
Cycle 42 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	76.5 (7.9)	0.8 (2.2)	76.8 (10.2)	-9.1 (4.0)
Median	76.5	0.0	74.5	-9.0
Min - Max	67 - 86	-1 - 4	65 - 95	-14 - -2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	81.3 (9.0)	1.3 (4.6)	84.3 (9.9)	-6.0 (4.7)
Median	82.0	4.0	82.5	-5.5
Min - Max	72 - 90	-4 - 4	75 - 97	-11 - -2
Cycle 42 Day 8				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	78.5 (13.4)	-2.5 (6.4)	88.5 (2.1)	-0.5 (14.8)
Median	78.5	-2.5	88.5	-0.5
Min - Max	69 - 88	-7 - 2	87 - 90	-11 - 10
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	76.0 (8.5)	-5.0 (1.4)	81.5 (0.7)	-7.5 (13.4)
Median	76.0	-5.0	81.5	-7.5
Min - Max	70 - 82	-6 - -4	81 - 82	-17 - 2
Cycle 42 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	79.3 (6.4)	-0.7 (4.2)	75.0 (5.2)	-10.0 (14.2)
Median	82.0	-2.0	72.0	-5.0
Min - Max	72 - 84	-4 - 4	72 - 81	-26 - 1
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	75.7 (8.5)	-4.3 (4.0)	79.7 (2.3)	-5.3 (10.1)
Median	76.0	-2.0	81.0	0.0
Min - Max	67 - 84	-9 - -2	77 - 81	-17 - 1
Cycle 43 Day 1				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	75.5 (4.7)	-0.3 (5.1)	74.7 (10.8)	-9.2 (12.9)
Median	76.5	-0.5	72.0	-10.5
Min - Max	69 - 80	-6 - 6	64 - 94	-24 - 14
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	77.3 (6.4)	-2.7 (4.2)	76.0 (9.5)	-9.0 (8.9)
Median	80.0	-4.0	81.0	-12.0
Min - Max	70 - 82	-6 - 2	65 - 82	-16 - 1
Cycle 43 Day 8				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	81.0 (13.5)	1.0 (8.5)	80.7 (7.1)	-4.3 (6.5)
Median	80.0	2.0	82.0	-4.0
Min - Max	68 - 95	-8 - 9	73 - 87	-11 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	82.3 (5.7)	2.3 (3.2)	73.0 (8.2)	-12.0 (14.5)
Median	84.0	1.0	71.0	-11.0
Min - Max	76 - 87	0 - 6	66 - 82	-27 - 2
Cycle 43 Day 15				
PRE PAC INFUSION				
n	3	3	1	1
Mean (SD)	87.0 (11.3)	7.0 (6.2)	84.0 (NE)	-14.0 (NE)
Median	81.0	5.0	84.0	-14.0
Min - Max	80 - 100	2 - 14	84 - 84	-14 - -14
AFTER PAC INFUSION				
n	3	3	1	1
Mean (SD)	82.3 (6.7)	2.3 (3.5)	81.0 (NE)	-17.0 (NE)
Median	84.0	2.0	81.0	-17.0
Min - Max	75 - 88	-1 - 6	81 - 81	-17 - -17
Cycle 44 Day 1				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	77.5 (10.6)	1.8 (3.9)	74.0 (8.8)	-9.8 (7.3)
Median	77.0	3.5	71.5	-10.5
Min - Max	66 - 90	-4 - 4	66 - 88	-20 - 1
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	82.0 (8.7)	2.0 (7.2)	73.3 (6.4)	-11.7 (9.0)
Median	86.0	0.0	77.0	-11.0
Min - Max	72 - 88	-4 - 10	66 - 77	-21 - -3
Cycle 44 Day 8				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	86.0 (12.2)	6.0 (7.2)	77.0 (10.4)	-8.0 (8.7)
Median	80.0	4.0	82.0	-12.0
Min - Max	78 - 100	0 - 14	65 - 84	-14 - 2
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	80.7 (6.7)	0.7 (3.2)	80.7 (8.5)	-4.3 (7.6)
Median	79.0	2.0	84.0	-6.0
Min - Max	75 - 88	-3 - 3	71 - 87	-11 - 4
Cycle 44 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	79.7 (3.5)	-0.3 (2.5)	82.7 (18.6)	-2.3 (17.8)
Median	80.0	0.0	88.0	-10.0
Min - Max	76 - 83	-3 - 2	62 - 98	-15 - 18

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	80.3 (4.7)	0.3 (3.2)	76.0 (10.4)	-9.0 (10.6)
Median	82.0	-1.0	81.0	-13.0
Min - Max	75 - 84	-2 - 4	64 - 83	-17 - 3
Cycle 45 Day 1				
PRE PAC INFUSION				
n	4	4	5	5
Mean (SD)	79.3 (13.6)	3.5 (5.6)	82.0 (10.8)	1.0 (12.3)
Median	78.0	2.5	82.0	-2.0
Min - Max	64 - 97	-2 - 11	69 - 98	-14 - 18
AFTER PAC INFUSION				
n	3	3	1	1
Mean (SD)	77.3 (4.7)	-2.7 (4.9)	84.0 (NE)	4.0 (NE)
Median	79.0	-5.0	84.0	4.0
Min - Max	72 - 81	-6 - 3	84 - 84	4 - 4
Cycle 45 Day 8				
PRE PAC INFUSION				
n	3	3	2	2
Mean (SD)	81.7 (10.7)	1.7 (6.7)	78.0 (12.7)	-0.5 (10.6)
Median	84.0	5.0	78.0	-0.5
Min - Max	70 - 91	-6 - 6	69 - 87	-8 - 7
AFTER PAC INFUSION				
n	3	3	2	2
Mean (SD)	82.0 (4.0)	2.0 (2.0)	73.0 (8.5)	-5.5 (6.4)
Median	82.0	2.0	73.0	-5.5
Min - Max	78 - 86	0 - 4	67 - 79	-10 - -1
Cycle 45 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	81.0 (6.9)	1.0 (2.0)	84.3 (15.5)	-0.7 (18.1)
Median	77.0	1.0	84.0	-8.0
Min - Max	77 - 89	-1 - 3	69 - 100	-14 - 20
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	83.0 (7.0)	3.0 (6.1)	75.3 (11.4)	-9.7 (17.0)
Median	86.0	0.0	72.0	-11.0
Min - Max	75 - 88	-1 - 10	66 - 88	-26 - 8
Cycle 46 Day 1				
PRE PAC INFUSION				
n	3	3	6	6
Mean (SD)	81.7 (11.6)	6.0 (3.5)	76.3 (9.1)	-7.5 (16.7)
Median	80.0	8.0	76.0	-5.5
Min - Max	71 - 94	2 - 8	65 - 91	-33 - 11

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	85.0 (1.4)	3.0 (7.1)	75.5 (6.4)	-3.0 (4.2)
Median	85.0	3.0	75.5	-3.0
Min - Max	84 - 86	-2 - 8	71 - 80	-6 - 0
Cycle 46 Day 8				
PRE PAC INFUSION				
n	2	2	3	3
Mean (SD)	85.5 (10.6)	3.5 (4.9)	83.0 (11.5)	-2.0 (15.7)
Median	85.5	3.5	82.0	-5.0
Min - Max	78 - 93	0 - 7	72 - 95	-16 - 15
AFTER PAC INFUSION				
n	2	2	3	3
Mean (SD)	87.5 (7.8)	5.5 (2.1)	74.3 (4.9)	-10.7 (6.4)
Median	87.5	5.5	72.0	-8.0
Min - Max	82 - 93	4 - 7	71 - 80	-18 - -6
Cycle 46 Day 15				
PRE PAC INFUSION				
n	2	2	3	3
Mean (SD)	90.5 (21.9)	8.5 (16.3)	80.7 (17.0)	-4.3 (19.5)
Median	90.5	8.5	80.0	-13.0
Min - Max	75 - 106	-3 - 20	64 - 98	-18 - 18
AFTER PAC INFUSION				
n	2	2	3	3
Mean (SD)	84.5 (2.1)	2.5 (7.8)	73.3 (7.0)	-11.7 (12.0)
Median	84.5	2.5	74.0	-11.0
Min - Max	83 - 86	-3 - 8	66 - 80	-24 - 0
Cycle 47 Day 1				
PRE PAC INFUSION				
n	3	3	6	6
Mean (SD)	81.7 (22.0)	6.0 (14.5)	81.8 (9.7)	-2.0 (12.1)
Median	70.0	5.0	85.0	0.5
Min - Max	68 - 107	-8 - 21	70 - 92	-17 - 11
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	86.0 (8.5)	4.0 (2.8)	76.5 (6.4)	-12.5 (19.1)
Median	86.0	4.0	76.5	-12.5
Min - Max	80 - 92	2 - 6	72 - 81	-26 - 1
Cycle 47 Day 8				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	91.0 (17.0)	9.0 (11.3)	83.0 (12.7)	-6.0 (25.5)
Median	91.0	9.0	83.0	-6.0
Min - Max	79 - 103	1 - 17	74 - 92	-24 - 12

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	83.5 (0.7)	1.5 (6.4)	82.5 (6.4)	-6.5 (19.1)
Median	83.5	1.5	82.5	-6.5
Min - Max	83 - 84	-3 - 6	78 - 87	-20 - 7
Cycle 47 Day 15				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	90.5 (12.0)	8.5 (6.4)	95.0 (9.9)	6.0 (22.6)
Median	90.5	8.5	95.0	6.0
Min - Max	82 - 99	4 - 13	88 - 102	-10 - 22
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	87.0 (1.4)	5.0 (4.2)	81.0 (5.7)	-8.0 (18.4)
Median	87.0	5.0	81.0	-8.0
Min - Max	86 - 88	2 - 8	77 - 85	-21 - 5
Cycle 48 Day 1				
PRE PAC INFUSION				
n	1	1	5	5
Mean (SD)	75.0 (NE)	-3.0 (NE)	82.4 (11.2)	-2.8 (12.9)
Median	75.0	-3.0	84.0	0.0
Min - Max	75 - 75	-3 - -3	71 - 96	-16 - 16
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	80.0 (NE)	2.0 (NE)	80.5 (4.9)	-8.5 (17.7)
Median	80.0	2.0	80.5	-8.5
Min - Max	80 - 80	2 - 2	77 - 84	-21 - 4
Cycle 48 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	82.0 (NE)	4.0 (NE)	93.0 (4.2)	4.0 (17.0)
Median	82.0	4.0	93.0	4.0
Min - Max	82 - 82	4 - 4	90 - 96	-8 - 16
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	86.0 (NE)	8.0 (NE)	82.0 (2.8)	-7.0 (9.9)
Median	86.0	8.0	82.0	-7.0
Min - Max	86 - 86	8 - 8	80 - 84	-14 - 0
Cycle 48 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	80.0 (NE)	2.0 (NE)	96.5 (12.0)	7.5 (24.7)
Median	80.0	2.0	96.5	7.5
Min - Max	80 - 80	2 - 2	88 - 105	-10 - 25

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	82.0 (NE)	4.0 (NE)	84.0 (4.2)	-5.0 (17.0)
Median	82.0	4.0	84.0	-5.0
Min - Max	82 - 82	4 - 4	81 - 87	-17 - 7
Cycle 49 Day 1				
PRE PAC INFUSION				
n	1	1	3	3
Mean (SD)	75.0 (NE)	-3.0 (NE)	88.3 (10.5)	-1.0 (17.3)
Median	75.0	-3.0	88.0	-10.0
Min - Max	75 - 75	-3 - -3	78 - 99	-12 - 19
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	86.0 (NE)	8.0 (NE)	81.0 (2.8)	-8.0 (15.6)
Median	86.0	8.0	81.0	-8.0
Min - Max	86 - 86	8 - 8	79 - 83	-19 - 3
Cycle 49 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	72.0 (NE)	-6.0 (NE)	93.5 (20.5)	4.5 (33.2)
Median	72.0	-6.0	93.5	4.5
Min - Max	72 - 72	-6 - -6	79 - 108	-19 - 28
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	80.0 (NE)	2.0 (NE)	77.5 (9.2)	-11.5 (21.9)
Median	80.0	2.0	77.5	-11.5
Min - Max	80 - 80	2 - 2	71 - 84	-27 - 4
Cycle 49 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	76.0 (NE)	-2.0 (NE)	90.5 (3.5)	1.5 (16.3)
Median	76.0	-2.0	90.5	1.5
Min - Max	76 - 76	-2 - -2	88 - 93	-10 - 13
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	82.0 (NE)	4.0 (NE)	78.5 (0.7)	-10.5 (12.0)
Median	82.0	4.0	78.5	-10.5
Min - Max	82 - 82	4 - 4	78 - 79	-19 - -2
Cycle 50 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	72.0 (NE)	-6.0 (NE)	80.5 (16.3)	-8.5 (29.0)
Median	72.0	-6.0	80.5	-8.5
Min - Max	72 - 72	-6 - -6	69 - 92	-29 - 12

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	84.0 (NE)	6.0 (NE)	84.0 (NE)	4.0 (NE)
Median	84.0	6.0	84.0	4.0
Min - Max	84 - 84	6 - 6	84 - 84	4 - 4
Cycle 50 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	80.0 (NE)	2.0 (NE)	85.5 (6.4)	-3.5 (19.1)
Median	80.0	2.0	85.5	-3.5
Min - Max	80 - 80	2 - 2	81 - 90	-17 - 10
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	79.0 (NE)	1.0 (NE)	80.5 (2.1)	-8.5 (14.8)
Median	79.0	1.0	80.5	-8.5
Min - Max	79 - 79	1 - 1	79 - 82	-19 - 2
Cycle 50 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	70.0 (NE)	-8.0 (NE)	89.5 (7.8)	0.5 (20.5)
Median	70.0	-8.0	89.5	0.5
Min - Max	70 - 70	-8 - -8	84 - 95	-14 - 15
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	72.0 (NE)	-6.0 (NE)	82.5 (3.5)	-6.5 (16.3)
Median	72.0	-6.0	82.5	-6.5
Min - Max	72 - 72	-6 - -6	80 - 85	-18 - 5
Cycle 51 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	79.0 (NE)	1.0 (NE)	84.0 (14.1)	-5.0 (26.9)
Median	79.0	1.0	84.0	-5.0
Min - Max	79 - 79	1 - 1	74 - 94	-24 - 14
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	82.0 (NE)	4.0 (NE)	78.0 (1.4)	-11.0 (14.1)
Median	82.0	4.0	78.0	-11.0
Min - Max	82 - 82	4 - 4	77 - 79	-21 - -1
Cycle 51 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	88.0 (NE)	10.0 (NE)	70.0 (NE)	-28.0 (NE)
Median	88.0	10.0	70.0	-28.0
Min - Max	88 - 88	10 - 10	70 - 70	-28 - -28

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	86.0 (NE)	8.0 (NE)	NE (NE)	NE (NE)
Median	86.0	8.0	NE	NE
Min - Max	86 - 86	8 - 8	NE - NE	NE - NE
Cycle 51 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	82.0 (NE)	4.0 (NE)	88.0 (15.6)	-1.0 (28.3)
Median	82.0	4.0	88.0	-1.0
Min - Max	82 - 82	4 - 4	77 - 99	-21 - 19
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	84.0 (NE)	6.0 (NE)	76.5 (6.4)	-12.5 (6.4)
Median	84.0	6.0	76.5	-12.5
Min - Max	84 - 84	6 - 6	72 - 81	-17 - -8
Cycle 52 Day 1				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	84.0 (17.0)	-5.0 (29.7)
Median	NE	NE	84.0	-5.0
Min - Max	NE - NE	NE - NE	72 - 96	-26 - 16
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	80.5 (13.4)	-8.5 (26.2)
Median	NE	NE	80.5	-8.5
Min - Max	NE - NE	NE - NE	71 - 90	-27 - 10
Cycle 52 Day 8				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	80.5 (12.0)	-8.5 (24.7)
Median	NE	NE	80.5	-8.5
Min - Max	NE - NE	NE - NE	72 - 89	-26 - 9
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	82.0 (5.7)	-7.0 (18.4)
Median	NE	NE	82.0	-7.0
Min - Max	NE - NE	NE - NE	78 - 86	-20 - 6
Cycle 52 Day 15				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	90.0 (19.8)	1.0 (32.5)
Median	NE	NE	90.0	1.0
Min - Max	NE - NE	NE - NE	76 - 104	-22 - 24

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	80.5 (6.4)	-8.5 (19.1)
Median	NE	NE	80.5	-8.5
Min - Max	NE - NE	NE - NE	76 - 85	-22 - 5
Cycle 53 Day 1				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	88.0 (5.7)	-1.0 (18.4)
Median	NE	NE	88.0	-1.0
Min - Max	NE - NE	NE - NE	84 - 92	-14 - 12
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	76.5 (3.5)	-12.5 (16.3)
Median	NE	NE	76.5	-12.5
Min - Max	NE - NE	NE - NE	74 - 79	-24 - -1
Cycle 53 Day 8				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	75.0 (NE)	-23.0 (NE)
Median	NE	NE	75.0	-23.0
Min - Max	NE - NE	NE - NE	75 - 75	-23 - -23
AFTER PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	78.0 (NE)	-20.0 (NE)
Median	NE	NE	78.0	-20.0
Min - Max	NE - NE	NE - NE	78 - 78	-20 - -20
Cycle 53 Day 15				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	87.0 (NE)	-11.0 (NE)
Median	NE	NE	87.0	-11.0
Min - Max	NE - NE	NE - NE	87 - 87	-11 - -11
Study Drug Discontinuation				
n	70	68	127	127
Mean (SD)	83.7 (14.4)	4.5 (14.4)	81.0 (13.1)	1.7 (15.0)
Median	81.0	3.0	78.0	0.0
Min - Max	56 - 126	-24 - 54	54 - 136	-54 - 68
Post-Baseline Last				
n	69	69	128	128
Mean (SD)	83.1 (14.0)	4.1 (14.7)	81.2 (13.2)	1.9 (15.0)
Median	81.0	3.0	78.0	0.0
Min - Max	56 - 126	-25 - 54	54 - 136	-54 - 68

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
PRE PAC INFUSION				
n	1	1	3	3
Mean (SD)	85.0 (NE)	-5.0 (NE)	97.7 (5.5)	9.3 (6.0)
Median	85.0	-5.0	98.0	10.0
Min - Max	85 - 85	-5 - -5	92 - 103	3 - 15
AFTER PAC INFUSION				
n	2	2	13	13
Mean (SD)	88.5 (9.2)	14.5 (14.8)	80.3 (7.1)	-3.1 (12.2)
Median	88.5	14.5	80.0	-2.0
Min - Max	82 - 95	4 - 25	70 - 94	-25 - 19
Post-Baseline Minimum				
n	6	6	16	16
Mean (SD)	66.0 (9.1)	-16.3 (6.0)	70.7 (8.4)	-8.9 (14.5)
Median	64.0	-17.0	70.0	-6.0
Min - Max	56 - 82	-24 - -8	54 - 92	-54 - 15
PRE PAC INFUSION				
n	39	39	79	79
Mean (SD)	66.8 (9.0)	-12.7 (9.8)	64.8 (7.6)	-16.3 (11.7)
Median	68.0	-12.0	66.0	-15.0
Min - Max	52 - 94	-34 - 20	37 - 83	-50 - 2
AFTER PAC INFUSION				
n	27	27	49	49
Mean (SD)	61.7 (7.2)	-15.7 (10.4)	65.1 (9.2)	-12.7 (10.1)
Median	62.0	-14.0	65.0	-11.0
Min - Max	50 - 76	-39 - 0	45 - 89	-33 - 8
Post-Baseline Maximum				
n	12	12	22	22
Mean (SD)	100.5 (14.9)	23.3 (13.5)	101.6 (12.3)	21.4 (15.3)
Median	104.0	22.0	99.5	20.5
Min - Max	78 - 126	9 - 54	86 - 136	0 - 68
PRE PAC INFUSION				
n	42	42	92	92
Mean (SD)	97.3 (11.8)	19.1 (10.7)	98.0 (11.8)	18.3 (13.2)
Median	93.5	18.0	97.0	19.0
Min - Max	78 - 121	-4 - 46	78 - 133	-8 - 64
AFTER PAC INFUSION				
n	18	18	30	30
Mean (SD)	93.9 (15.1)	11.9 (17.6)	91.5 (10.7)	11.6 (10.7)
Median	88.0	9.0	90.5	13.0
Min - Max	80 - 140	-6 - 76	76 - 114	-20 - 37

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
Baseline				
n	73		143	
Mean (SD)	17.0 (2.1)		16.9 (2.1)	
Median	17.0		17.0	
Min - Max	12 - 22		10 - 22	
Cycle 1 Day 1				
PRE PAC INFUSION				
n	69	67	139	138
Mean (SD)	17.0 (2.0)	0.0 (1.8)	17.0 (2.3)	0.0 (1.8)
Median	17.0	0.0	16.0	0.0
Min - Max	11 - 20	-5 - 4	11 - 22	-9 - 4
AFTER PAC INFUSION				
n	70	70	139	138
Mean (SD)	17.1 (1.6)	0.2 (1.8)	17.1 (2.2)	0.2 (1.8)
Median	17.0	0.0	17.0	0.0
Min - Max	13 - 20	-5 - 5	12 - 22	-7 - 5
Cycle 1 Day 8				
PRE PAC INFUSION				
n	72	70	133	133
Mean (SD)	17.0 (2.3)	0.0 (2.4)	17.1 (2.4)	0.2 (1.9)
Median	17.0	0.0	17.0	0.0
Min - Max	10 - 25	-6 - 11	12 - 24	-8 - 6
AFTER PAC INFUSION				
n	62	61	125	125
Mean (SD)	16.9 (2.0)	-0.1 (2.2)	17.0 (2.3)	0.2 (1.8)
Median	17.0	0.0	17.0	0.0
Min - Max	12 - 20	-6 - 5	11 - 22	-4 - 6
Cycle 1 Day 15				
PRE PAC INFUSION				
n	70	68	126	126
Mean (SD)	17.2 (2.5)	0.1 (2.7)	17.0 (2.2)	0.1 (1.6)
Median	18.0	0.0	16.5	0.0
Min - Max	9 - 23	-8 - 11	12 - 24	-6 - 5
AFTER PAC INFUSION				
n	57	56	114	114
Mean (SD)	16.9 (2.2)	-0.1 (2.9)	17.2 (2.1)	0.4 (2.0)
Median	16.0	0.0	17.0	0.0
Min - Max	11 - 22	-6 - 10	12 - 22	-4 - 8
Cycle 2 Day 1				
PRE PAC INFUSION				
n	73	72	126	125
Mean (SD)	16.9 (2.0)	-0.1 (2.4)	17.0 (2.2)	0.1 (2.0)
Median	17.0	0.0	17.0	0.0
Min - Max	12 - 24	-6 - 10	11 - 22	-8 - 6

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	66	66	120	119
Mean (SD)	17.1 (2.6)	0.2 (2.9)	16.9 (2.5)	0.0 (2.6)
Median	17.0	0.0	17.0	0.0
Min - Max	11 - 30	-8 - 13	6 - 22	-11 - 7
Cycle 2 Day 8				
PRE PAC INFUSION				
n	72	71	127	125
Mean (SD)	16.9 (2.0)	-0.1 (2.2)	16.9 (2.4)	0.1 (2.1)
Median	17.0	0.0	17.0	0.0
Min - Max	13 - 24	-6 - 10	10 - 24	-8 - 9
AFTER PAC INFUSION				
n	68	67	120	118
Mean (SD)	16.9 (2.4)	0.0 (2.2)	17.1 (2.4)	0.3 (2.0)
Median	17.0	0.0	17.0	0.0
Min - Max	10 - 27	-5 - 10	10 - 24	-4 - 8
Cycle 2 Day 15				
PRE PAC INFUSION				
n	69	68	120	118
Mean (SD)	17.0 (2.3)	0.0 (2.4)	17.0 (2.3)	0.1 (2.0)
Median	17.0	0.0	17.0	0.0
Min - Max	11 - 25	-6 - 11	11 - 24	-6 - 6
AFTER PAC INFUSION				
n	66	65	108	106
Mean (SD)	16.9 (2.2)	-0.1 (2.1)	17.1 (2.4)	0.2 (2.1)
Median	17.0	0.0	17.0	0.0
Min - Max	12 - 22	-6 - 6	12 - 24	-8 - 6
Cycle 3 Day 1				
PRE PAC INFUSION				
n	70	69	120	119
Mean (SD)	16.7 (2.3)	-0.3 (2.6)	17.0 (2.3)	0.2 (2.2)
Median	16.5	0.0	17.0	0.0
Min - Max	12 - 23	-6 - 9	12 - 25	-7 - 7
AFTER PAC INFUSION				
n	65	64	108	107
Mean (SD)	17.0 (2.1)	0.0 (2.2)	17.1 (2.2)	0.2 (1.9)
Median	17.0	0.0	16.0	0.0
Min - Max	11 - 24	-5 - 6	11 - 22	-4 - 7
Cycle 3 Day 8				
PRE PAC INFUSION				
n	64	63	115	113
Mean (SD)	16.8 (1.9)	-0.3 (2.1)	17.0 (2.3)	0.0 (2.0)
Median	17.0	0.0	17.0	0.0
Min - Max	12 - 20	-6 - 4	10 - 24	-6 - 6

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
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Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	59	58	104	102
Mean (SD)	17.2 (2.0)	0.2 (2.0)	17.1 (2.4)	0.2 (2.0)
Median	17.0	0.0	17.0	0.0
Min - Max	13 - 21	-5 - 7	11 - 24	-6 - 5
Cycle 3 Day 15				
PRE PAC INFUSION				
n	64	63	115	113
Mean (SD)	17.0 (2.1)	-0.1 (2.4)	17.0 (2.3)	0.1 (2.1)
Median	17.0	0.0	16.0	0.0
Min - Max	12 - 25	-6 - 11	10 - 24	-8 - 6
AFTER PAC INFUSION				
n	60	59	105	104
Mean (SD)	16.9 (2.3)	-0.2 (2.2)	17.2 (2.1)	0.1 (1.9)
Median	17.0	0.0	17.0	0.0
Min - Max	12 - 24	-6 - 6	11 - 22	-5 - 4
Cycle 4 Day 1				
PRE PAC INFUSION				
n	62	61	111	109
Mean (SD)	17.0 (2.1)	-0.1 (2.3)	17.1 (2.2)	0.1 (1.9)
Median	17.0	0.0	17.0	0.0
Min - Max	11 - 23	-6 - 9	12 - 24	-7 - 5
AFTER PAC INFUSION				
n	60	59	104	103
Mean (SD)	17.0 (1.9)	-0.1 (2.1)	17.3 (2.3)	0.3 (2.1)
Median	17.0	0.0	17.0	0.0
Min - Max	12 - 20	-6 - 4	12 - 24	-7 - 8
Cycle 4 Day 8				
PRE PAC INFUSION				
n	62	61	111	110
Mean (SD)	17.2 (2.3)	0.1 (2.5)	17.1 (2.3)	0.3 (2.1)
Median	17.0	0.0	17.0	0.0
Min - Max	11 - 25	-4 - 11	10 - 24	-7 - 6
AFTER PAC INFUSION				
n	60	59	106	105
Mean (SD)	17.3 (2.0)	0.3 (2.2)	17.0 (2.2)	0.1 (2.3)
Median	17.0	0.0	16.0	0.0
Min - Max	13 - 25	-4 - 9	10 - 23	-9 - 9
Cycle 4 Day 15				
PRE PAC INFUSION				
n	56	55	104	103
Mean (SD)	17.0 (2.4)	-0.2 (2.6)	16.8 (2.2)	-0.1 (2.2)
Median	17.0	0.0	16.0	0.0
Min - Max	12 - 23	-6 - 9	11 - 22	-10 - 8

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	52	51	97	96
Mean (SD)	17.0 (2.4)	-0.1 (2.1)	16.9 (2.3)	-0.1 (2.2)
Median	16.5	0.0	17.0	0.0
Min - Max	13 - 24	-6 - 6	12 - 26	-10 - 6
Cycle 5 Day 1				
PRE PAC INFUSION				
n	55	54	107	106
Mean (SD)	16.8 (2.1)	-0.3 (2.2)	17.2 (2.3)	0.3 (2.1)
Median	16.0	0.0	17.0	0.0
Min - Max	11 - 21	-6 - 5	12 - 24	-5 - 8
AFTER PAC INFUSION				
n	50	49	100	99
Mean (SD)	16.8 (1.8)	-0.3 (2.0)	17.0 (2.6)	0.2 (2.5)
Median	16.0	0.0	17.0	0.0
Min - Max	14 - 21	-6 - 4	10 - 24	-9 - 8
Cycle 5 Day 8				
PRE PAC INFUSION				
n	55	54	103	102
Mean (SD)	16.8 (1.9)	-0.4 (2.1)	17.0 (2.4)	0.2 (1.9)
Median	16.0	0.0	17.0	0.0
Min - Max	13 - 21	-8 - 4	12 - 24	-5 - 7
AFTER PAC INFUSION				
n	52	51	99	98
Mean (SD)	16.8 (2.0)	-0.3 (2.1)	17.1 (2.3)	0.0 (2.0)
Median	17.0	0.0	17.0	0.0
Min - Max	12 - 22	-5 - 5	12 - 22	-6 - 7
Cycle 5 Day 15				
PRE PAC INFUSION				
n	51	50	99	98
Mean (SD)	16.9 (2.2)	-0.3 (2.5)	17.0 (2.2)	0.0 (2.1)
Median	16.0	0.0	16.0	0.0
Min - Max	12 - 23	-8 - 9	12 - 24	-7 - 7
AFTER PAC INFUSION				
n	49	48	96	95
Mean (SD)	16.9 (2.2)	-0.2 (2.4)	17.2 (2.3)	0.2 (2.2)
Median	17.0	0.0	17.0	0.0
Min - Max	12 - 24	-7 - 7	12 - 24	-7 - 8
Cycle 6 Day 1				
PRE PAC INFUSION				
n	51	50	99	98
Mean (SD)	17.2 (2.2)	0.0 (2.4)	17.1 (2.2)	0.1 (1.9)
Median	17.0	0.0	17.0	0.0
Min - Max	14 - 23	-6 - 9	12 - 24	-6 - 5

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	49	49	94	93
Mean (SD)	17.4 (2.2)	0.1 (2.2)	17.1 (2.4)	0.1 (2.6)
Median	17.0	0.0	17.0	0.0
Min - Max	13 - 24	-5 - 8	10 - 24	-9 - 12
Cycle 6 Day 8				
PRE PAC INFUSION				
n	52	51	101	100
Mean (SD)	17.2 (2.1)	-0.1 (2.4)	16.7 (2.2)	-0.2 (2.0)
Median	17.0	0.0	16.0	0.0
Min - Max	14 - 22	-6 - 8	12 - 24	-4 - 6
AFTER PAC INFUSION				
n	48	47	93	92
Mean (SD)	17.0 (2.1)	-0.2 (2.2)	17.0 (2.3)	0.1 (2.2)
Median	17.0	0.0	16.0	0.0
Min - Max	12 - 20	-6 - 5	12 - 24	-4 - 8
Cycle 6 Day 15				
PRE PAC INFUSION				
n	51	50	97	96
Mean (SD)	17.0 (2.0)	-0.2 (2.1)	17.0 (2.3)	0.0 (2.0)
Median	16.0	0.0	17.0	0.0
Min - Max	14 - 22	-5 - 5	12 - 28	-4 - 6
AFTER PAC INFUSION				
n	48	47	90	89
Mean (SD)	16.7 (2.1)	-0.4 (2.5)	17.1 (2.3)	0.1 (1.9)
Median	16.0	0.0	17.0	0.0
Min - Max	12 - 21	-7 - 7	12 - 26	-4 - 6
Cycle 7 Day 1				
PRE PAC INFUSION				
n	48	48	91	90
Mean (SD)	17.0 (2.0)	-0.1 (2.3)	16.8 (2.1)	-0.2 (2.1)
Median	16.5	0.0	17.0	0.0
Min - Max	13 - 21	-6 - 5	11 - 22	-7 - 5
AFTER PAC INFUSION				
n	45	45	80	79
Mean (SD)	17.2 (2.0)	-0.1 (2.3)	17.1 (2.2)	0.1 (2.1)
Median	17.0	0.0	17.0	0.0
Min - Max	13 - 20	-5 - 5	12 - 24	-5 - 6
Cycle 7 Day 8				
PRE PAC INFUSION				
n	48	48	84	83
Mean (SD)	16.8 (1.8)	-0.4 (2.1)	16.5 (2.0)	-0.5 (1.9)
Median	16.5	0.0	16.0	0.0
Min - Max	12 - 20	-6 - 3	12 - 21	-6 - 5

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
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Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	47	47	78	77
Mean (SD)	17.3 (2.9)	0.2 (2.8)	17.1 (2.1)	0.1 (2.1)
Median	17.0	0.0	16.0	0.0
Min - Max	12 - 32	-6 - 12	12 - 23	-6 - 7
Cycle 7 Day 15				
PRE PAC INFUSION				
n	47	47	82	81
Mean (SD)	16.9 (1.9)	-0.4 (2.6)	16.9 (2.2)	-0.1 (2.1)
Median	16.0	0.0	16.0	0.0
Min - Max	14 - 22	-6 - 8	11 - 24	-6 - 6
AFTER PAC INFUSION				
n	42	42	79	78
Mean (SD)	17.1 (2.0)	-0.1 (2.3)	17.5 (2.4)	0.5 (2.6)
Median	17.0	0.0	18.0	0.0
Min - Max	14 - 21	-7 - 6	12 - 25	-6 - 13
Cycle 8 Day 1				
PRE PAC INFUSION				
n	46	46	89	88
Mean (SD)	17.2 (2.1)	0.1 (2.6)	16.9 (2.0)	-0.2 (1.9)
Median	17.0	0.0	17.0	0.0
Min - Max	14 - 26	-6 - 12	12 - 24	-6 - 5
AFTER PAC INFUSION				
n	44	44	77	76
Mean (SD)	16.8 (2.0)	-0.4 (2.0)	17.2 (2.2)	0.3 (1.8)
Median	17.0	0.0	17.0	0.0
Min - Max	12 - 20	-6 - 3	12 - 24	-4 - 5
Cycle 8 Day 8				
PRE PAC INFUSION				
n	44	44	81	80
Mean (SD)	16.8 (2.3)	-0.3 (2.8)	16.9 (2.3)	0.0 (2.1)
Median	17.0	0.0	17.0	0.0
Min - Max	12 - 23	-8 - 9	10 - 24	-7 - 8
AFTER PAC INFUSION				
n	39	39	76	75
Mean (SD)	16.9 (2.5)	-0.1 (2.1)	16.7 (2.4)	-0.2 (2.2)
Median	17.0	0.0	16.0	0.0
Min - Max	12 - 24	-6 - 4	11 - 24	-11 - 6
Cycle 8 Day 15				
PRE PAC INFUSION				
n	45	45	76	75
Mean (SD)	17.0 (2.2)	0.0 (2.4)	16.9 (1.9)	-0.2 (1.7)
Median	16.0	0.0	17.0	0.0
Min - Max	12 - 23	-6 - 9	12 - 22	-6 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	43	43	69	68
Mean (SD)	17.1 (2.0)	0.0 (2.1)	16.9 (2.3)	0.0 (2.2)
Median	18.0	0.0	16.0	0.0
Min - Max	13 - 20	-5 - 5	12 - 23	-6 - 6
Cycle 9 Day 1				
PRE PAC INFUSION				
n	37	37	76	75
Mean (SD)	17.0 (1.9)	0.0 (1.9)	17.2 (2.2)	0.3 (1.7)
Median	17.0	0.0	17.0	0.0
Min - Max	12 - 22	-6 - 4	12 - 24	-3 - 5
AFTER PAC INFUSION				
n	35	35	64	63
Mean (SD)	16.9 (1.9)	-0.2 (1.7)	17.1 (2.3)	0.2 (1.7)
Median	16.0	0.0	17.0	0.0
Min - Max	13 - 22	-5 - 4	12 - 22	-4 - 5
Cycle 9 Day 8				
PRE PAC INFUSION				
n	39	39	66	65
Mean (SD)	17.3 (2.0)	0.3 (2.2)	17.3 (1.9)	0.2 (1.8)
Median	16.0	0.0	17.5	0.0
Min - Max	15 - 22	-3 - 8	13 - 23	-4 - 4
AFTER PAC INFUSION				
n	39	39	61	60
Mean (SD)	17.2 (2.0)	0.2 (2.1)	17.3 (2.1)	0.2 (1.9)
Median	17.0	0.0	17.0	0.0
Min - Max	14 - 22	-3 - 6	12 - 24	-5 - 6
Cycle 9 Day 15				
PRE PAC INFUSION				
n	39	39	60	59
Mean (SD)	17.1 (1.9)	0.1 (2.2)	17.0 (1.8)	0.0 (1.5)
Median	16.0	0.0	17.0	0.0
Min - Max	14 - 22	-6 - 7	12 - 20	-5 - 4
AFTER PAC INFUSION				
n	37	37	53	52
Mean (SD)	17.2 (2.0)	0.2 (2.1)	17.2 (1.9)	0.3 (1.8)
Median	17.0	0.0	17.0	0.0
Min - Max	14 - 22	-4 - 5	12 - 20	-4 - 5
Cycle 10 Day 1				
PRE PAC INFUSION				
n	39	39	70	69
Mean (SD)	17.5 (1.9)	0.5 (2.4)	17.1 (2.1)	0.3 (1.7)
Median	18.0	0.0	17.0	0.0
Min - Max	14 - 23	-6 - 9	12 - 24	-4 - 6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	37	37	56	55
Mean (SD)	17.5 (2.0)	0.4 (2.5)	17.0 (2.2)	0.2 (1.9)
Median	18.0	0.0	17.0	0.0
Min - Max	14 - 21	-8 - 7	12 - 24	-4 - 6
Cycle 10 Day 8				
PRE PAC INFUSION				
n	37	37	61	60
Mean (SD)	17.1 (2.2)	0.1 (2.6)	16.9 (2.0)	0.1 (1.7)
Median	16.0	0.0	17.0	0.0
Min - Max	15 - 25	-6 - 11	12 - 20	-4 - 5
AFTER PAC INFUSION				
n	36	36	57	56
Mean (SD)	17.3 (2.2)	0.2 (2.5)	16.8 (2.1)	0.0 (1.9)
Median	17.5	0.0	17.0	0.0
Min - Max	13 - 22	-8 - 5	12 - 20	-7 - 4
Cycle 10 Day 15				
PRE PAC INFUSION				
n	36	36	58	57
Mean (SD)	17.2 (2.2)	0.3 (2.4)	17.0 (2.2)	0.2 (1.9)
Median	17.0	0.0	17.0	0.0
Min - Max	14 - 22	-6 - 8	12 - 22	-4 - 6
AFTER PAC INFUSION				
n	35	35	52	51
Mean (SD)	16.7 (2.2)	-0.3 (2.4)	16.8 (2.6)	0.0 (2.2)
Median	16.0	0.0	17.0	0.0
Min - Max	12 - 22	-9 - 5	12 - 25	-5 - 7
Cycle 11 Day 1				
PRE PAC INFUSION				
n	34	34	63	62
Mean (SD)	16.9 (2.4)	-0.1 (2.7)	17.4 (2.2)	0.5 (2.0)
Median	17.0	-0.5	18.0	0.0
Min - Max	12 - 22	-8 - 7	12 - 24	-6 - 6
AFTER PAC INFUSION				
n	34	34	49	48
Mean (SD)	17.2 (2.4)	0.2 (2.8)	17.2 (2.5)	0.1 (2.8)
Median	17.0	0.0	17.0	0.0
Min - Max	12 - 22	-10 - 5	12 - 24	-7 - 12
Cycle 11 Day 8				
PRE PAC INFUSION				
n	32	32	47	46
Mean (SD)	17.4 (2.3)	0.4 (2.7)	17.4 (2.1)	0.3 (1.9)
Median	17.5	0.0	18.0	0.0
Min - Max	14 - 24	-6 - 10	12 - 21	-4 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	31	31	45	44
Mean (SD)	16.3 (2.2)	-0.6 (2.2)	17.2 (2.0)	0.1 (1.9)
Median	16.0	-1.0	18.0	0.0
Min - Max	12 - 22	-6 - 4	12 - 20	-5 - 6
Cycle 11 Day 15				
PRE PAC INFUSION				
n	34	34	44	43
Mean (SD)	17.1 (2.1)	0.1 (2.6)	17.3 (2.1)	0.3 (2.0)
Median	17.0	0.0	18.0	0.0
Min - Max	14 - 22	-7 - 8	12 - 21	-5 - 6
AFTER PAC INFUSION				
n	31	31	43	42
Mean (SD)	17.1 (2.1)	0.1 (2.2)	17.1 (2.3)	0.1 (2.2)
Median	18.0	0.0	17.0	0.0
Min - Max	12 - 22	-5 - 4	12 - 22	-4 - 5
Cycle 12 Day 1				
PRE PAC INFUSION				
n	33	33	56	55
Mean (SD)	16.8 (2.2)	-0.1 (2.0)	17.3 (2.4)	0.6 (2.1)
Median	16.0	0.0	17.5	0.0
Min - Max	13 - 22	-4 - 6	12 - 23	-5 - 5
AFTER PAC INFUSION				
n	30	30	42	41
Mean (SD)	16.9 (1.8)	0.0 (1.9)	17.2 (2.6)	0.3 (2.2)
Median	17.0	0.0	18.0	0.0
Min - Max	14 - 20	-4 - 4	12 - 24	-6 - 6
Cycle 12 Day 8				
PRE PAC INFUSION				
n	29	29	42	41
Mean (SD)	17.0 (2.0)	0.1 (1.8)	17.3 (2.5)	0.2 (2.3)
Median	17.0	0.0	17.0	0.0
Min - Max	14 - 22	-4 - 4	11 - 24	-4 - 6
AFTER PAC INFUSION				
n	24	24	40	39
Mean (SD)	16.6 (1.8)	-0.4 (1.8)	17.2 (2.2)	0.1 (2.0)
Median	16.0	0.0	18.0	0.0
Min - Max	13 - 20	-3 - 4	11 - 22	-7 - 4
Cycle 12 Day 15				
PRE PAC INFUSION				
n	30	30	43	42
Mean (SD)	16.7 (1.6)	-0.2 (1.9)	17.4 (2.6)	0.4 (2.3)
Median	16.0	0.0	18.0	0.0
Min - Max	14 - 20	-6 - 4	10 - 23	-4 - 7

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	26	26	40	39
Mean (SD)	16.9 (1.9)	0.0 (2.0)	17.5 (3.8)	0.7 (3.1)
Median	17.0	0.0	17.0	0.0
Min - Max	13 - 20	-5 - 4	12 - 37	-3 - 17
Cycle 13 Day 1				
PRE PAC INFUSION				
n	27	27	49	48
Mean (SD)	16.9 (2.1)	-0.1 (2.1)	17.0 (2.2)	0.0 (2.2)
Median	16.0	0.0	17.0	0.0
Min - Max	13 - 21	-4 - 5	12 - 23	-8 - 5
AFTER PAC INFUSION				
n	24	24	36	35
Mean (SD)	16.8 (2.4)	-0.3 (2.2)	17.2 (2.6)	0.3 (1.8)
Median	16.0	0.0	17.0	0.0
Min - Max	12 - 21	-6 - 3	12 - 24	-3 - 5
Cycle 13 Day 8				
PRE PAC INFUSION				
n	25	25	36	35
Mean (SD)	16.8 (1.7)	-0.2 (1.7)	17.5 (2.3)	0.4 (2.1)
Median	17.0	0.0	18.0	0.0
Min - Max	14 - 20	-4 - 2	14 - 22	-3 - 6
AFTER PAC INFUSION				
n	24	24	36	35
Mean (SD)	16.5 (2.0)	-0.5 (2.3)	17.3 (2.6)	0.3 (2.2)
Median	16.0	0.0	18.0	0.0
Min - Max	12 - 20	-6 - 4	12 - 22	-5 - 5
Cycle 13 Day 15				
PRE PAC INFUSION				
n	25	25	35	34
Mean (SD)	17.0 (1.9)	0.0 (2.1)	17.4 (2.3)	0.3 (2.1)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 21	-4 - 3	12 - 23	-3 - 6
AFTER PAC INFUSION				
n	23	23	35	34
Mean (SD)	16.0 (1.8)	-0.9 (2.0)	17.2 (2.5)	0.1 (1.9)
Median	16.0	0.0	17.0	0.0
Min - Max	12 - 20	-5 - 3	10 - 22	-4 - 4
Cycle 14 Day 1				
PRE PAC INFUSION				
n	26	26	41	40
Mean (SD)	17.1 (2.0)	0.0 (2.2)	17.0 (2.3)	0.1 (1.8)
Median	16.5	0.0	16.0	0.0
Min - Max	12 - 20	-6 - 4	12 - 23	-4 - 6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	24	24	33	32
Mean (SD)	17.3 (2.2)	0.2 (1.5)	17.1 (2.3)	0.1 (1.8)
Median	17.0	0.0	17.0	0.0
Min - Max	14 - 24	-3 - 4	12 - 23	-3 - 5
Cycle 14 Day 8				
PRE PAC INFUSION				
n	25	25	32	31
Mean (SD)	16.8 (1.8)	-0.2 (1.9)	17.3 (2.4)	0.2 (2.4)
Median	17.0	0.0	17.0	0.0
Min - Max	13 - 20	-6 - 2	12 - 23	-4 - 6
AFTER PAC INFUSION				
n	24	24	31	30
Mean (SD)	16.5 (2.0)	-0.5 (2.2)	16.9 (2.2)	0.0 (1.8)
Median	16.0	0.0	17.0	0.0
Min - Max	12 - 20	-6 - 4	12 - 22	-3 - 4
Cycle 14 Day 15				
PRE PAC INFUSION				
n	25	25	29	28
Mean (SD)	16.7 (1.9)	-0.4 (2.2)	17.6 (2.3)	0.4 (1.9)
Median	16.0	0.0	17.0	0.0
Min - Max	14 - 22	-6 - 6	14 - 23	-3 - 5
AFTER PAC INFUSION				
n	24	24	28	27
Mean (SD)	17.0 (2.2)	0.0 (1.9)	17.5 (2.4)	0.5 (2.2)
Median	17.0	0.0	17.5	0.0
Min - Max	12 - 24	-4 - 4	13 - 22	-3 - 6
Cycle 15 Day 1				
PRE PAC INFUSION				
n	20	20	35	34
Mean (SD)	17.4 (1.9)	0.5 (2.4)	17.0 (2.3)	0.1 (1.8)
Median	17.5	0.0	18.0	0.0
Min - Max	14 - 22	-4 - 6	12 - 22	-3 - 4
AFTER PAC INFUSION				
n	19	19	25	24
Mean (SD)	16.6 (1.5)	-0.4 (2.3)	17.2 (2.5)	0.2 (2.4)
Median	16.0	0.0	16.0	0.0
Min - Max	14 - 20	-8 - 2	13 - 22	-4 - 6
Cycle 15 Day 8				
PRE PAC INFUSION				
n	18	18	27	26
Mean (SD)	16.8 (1.8)	0.0 (2.0)	17.3 (2.2)	0.2 (2.0)
Median	16.0	0.0	17.0	0.0
Min - Max	14 - 21	-4 - 5	13 - 23	-3 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	18	18	27	26
Mean (SD)	16.0 (2.1)	-0.8 (2.6)	17.3 (2.5)	0.2 (2.2)
Median	16.0	-0.5	18.0	0.0
Min - Max	12 - 20	-9 - 2	12 - 24	-3 - 6
Cycle 15 Day 15				
PRE PAC INFUSION				
n	19	19	25	24
Mean (SD)	16.2 (1.9)	-0.8 (1.5)	17.0 (2.4)	-0.3 (1.6)
Median	16.0	0.0	18.0	0.0
Min - Max	12 - 20	-4 - 2	12 - 22	-3 - 4
AFTER PAC INFUSION				
n	19	19	25	24
Mean (SD)	16.5 (2.0)	-0.5 (1.7)	16.6 (2.5)	-0.5 (2.0)
Median	16.0	0.0	17.0	-1.0
Min - Max	12 - 21	-4 - 3	12 - 22	-4 - 4
Cycle 16 Day 1				
PRE PAC INFUSION				
n	21	21	32	31
Mean (SD)	17.1 (2.1)	0.1 (2.4)	16.8 (2.3)	0.0 (1.6)
Median	17.0	0.0	17.0	0.0
Min - Max	14 - 20	-6 - 4	12 - 22	-3 - 4
AFTER PAC INFUSION				
n	20	20	24	23
Mean (SD)	16.9 (2.0)	-0.2 (2.3)	17.1 (3.0)	-0.1 (3.3)
Median	16.5	0.0	16.5	0.0
Min - Max	12 - 20	-4 - 4	10 - 24	-9 - 9
Cycle 16 Day 8				
PRE PAC INFUSION				
n	20	20	23	22
Mean (SD)	16.4 (1.1)	-0.7 (1.4)	17.3 (2.1)	0.1 (1.8)
Median	16.0	0.0	18.0	0.0
Min - Max	14 - 18	-4 - 2	13 - 22	-4 - 4
AFTER PAC INFUSION				
n	19	19	23	22
Mean (SD)	17.0 (1.5)	-0.2 (1.9)	17.6 (2.4)	0.3 (2.5)
Median	17.0	0.0	18.0	0.0
Min - Max	15 - 20	-5 - 3	12 - 24	-3 - 9
Cycle 16 Day 15				
PRE PAC INFUSION				
n	18	18	25	24
Mean (SD)	16.7 (1.9)	-0.3 (2.2)	17.2 (2.2)	0.0 (1.5)
Median	16.0	0.0	17.0	0.0
Min - Max	14 - 22	-4 - 6	12 - 20	-3 - 3

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	17	17	24	23
Mean (SD)	16.9 (2.1)	-0.2 (2.2)	17.1 (2.4)	-0.2 (2.1)
Median	17.0	0.0	17.0	-1.0
Min - Max	14 - 22	-4 - 5	12 - 22	-3 - 6
Cycle 17 Day 1				
PRE PAC INFUSION				
n	18	18	31	30
Mean (SD)	17.1 (1.5)	-0.2 (2.2)	17.1 (2.3)	0.1 (1.8)
Median	17.0	0.0	18.0	0.0
Min - Max	14 - 20	-6 - 4	12 - 24	-3 - 6
AFTER PAC INFUSION				
n	17	17	23	22
Mean (SD)	17.1 (1.9)	-0.3 (2.1)	17.5 (2.3)	0.3 (2.0)
Median	18.0	0.0	18.0	0.0
Min - Max	12 - 20	-4 - 4	13 - 23	-3 - 5
Cycle 17 Day 8				
PRE PAC INFUSION				
n	16	16	20	19
Mean (SD)	16.7 (1.7)	-0.8 (2.2)	17.7 (2.3)	0.3 (2.2)
Median	16.5	0.0	18.0	0.0
Min - Max	12 - 19	-6 - 2	14 - 24	-3 - 6
AFTER PAC INFUSION				
n	16	16	20	19
Mean (SD)	16.7 (1.9)	-0.8 (2.3)	17.5 (2.5)	-0.1 (2.7)
Median	16.5	0.0	18.0	0.0
Min - Max	12 - 20	-6 - 3	12 - 22	-7 - 4
Cycle 17 Day 15				
PRE PAC INFUSION				
n	17	17	21	21
Mean (SD)	16.6 (1.9)	-0.5 (2.5)	17.8 (1.9)	0.4 (1.7)
Median	17.0	0.0	18.0	0.0
Min - Max	12 - 20	-6 - 3	14 - 22	-2 - 4
AFTER PAC INFUSION				
n	17	17	22	22
Mean (SD)	16.4 (2.3)	-0.7 (2.8)	17.5 (2.3)	0.0 (2.7)
Median	16.0	0.0	18.0	0.0
Min - Max	12 - 20	-6 - 4	12 - 23	-7 - 7
Cycle 18 Day 1				
PRE PAC INFUSION				
n	16	16	24	24
Mean (SD)	16.8 (2.1)	-0.4 (3.0)	17.2 (2.0)	-0.1 (1.5)
Median	17.0	0.0	17.0	0.0
Min - Max	13 - 20	-8 - 4	12 - 22	-3 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	14	14	21	21
Mean (SD)	17.1 (1.1)	0.1 (1.4)	17.4 (2.3)	-0.1 (2.6)
Median	17.5	0.0	17.0	0.0
Min - Max	15 - 18	-2 - 2	12 - 23	-7 - 5
Cycle 18 Day 8				
PRE PAC INFUSION				
n	14	14	21	21
Mean (SD)	16.9 (1.5)	-0.6 (2.0)	17.7 (1.9)	0.0 (2.0)
Median	17.5	-0.5	18.0	0.0
Min - Max	14 - 18	-4 - 3	15 - 22	-3 - 4
AFTER PAC INFUSION				
n	14	14	20	20
Mean (SD)	17.4 (1.4)	-0.1 (2.5)	18.0 (1.9)	0.3 (1.9)
Median	17.5	0.0	18.0	0.0
Min - Max	14 - 20	-6 - 4	16 - 23	-3 - 5
Cycle 18 Day 15				
PRE PAC INFUSION				
n	15	15	20	20
Mean (SD)	16.8 (1.0)	-0.5 (2.1)	17.5 (2.4)	-0.1 (2.1)
Median	17.0	0.0	17.5	0.0
Min - Max	15 - 18	-6 - 2	14 - 23	-5 - 5
AFTER PAC INFUSION				
n	15	15	19	19
Mean (SD)	17.7 (1.4)	0.3 (2.5)	17.3 (2.0)	-0.4 (1.8)
Median	18.0	1.0	16.0	-1.0
Min - Max	15 - 20	-6 - 4	15 - 22	-3 - 4
Cycle 19 Day 1				
PRE PAC INFUSION				
n	11	11	26	26
Mean (SD)	16.9 (1.0)	-0.6 (2.0)	16.8 (1.9)	-0.4 (1.5)
Median	17.0	0.0	16.0	0.0
Min - Max	16 - 19	-6 - 2	12 - 21	-3 - 2
AFTER PAC INFUSION				
n	10	10	19	19
Mean (SD)	17.0 (1.5)	-0.6 (1.3)	16.9 (1.9)	-0.8 (1.8)
Median	16.5	-0.5	16.0	-1.0
Min - Max	15 - 20	-2 - 1	14 - 20	-4 - 2
Cycle 19 Day 8				
PRE PAC INFUSION				
n	9	9	20	20
Mean (SD)	17.1 (1.2)	-0.8 (1.9)	17.4 (2.1)	-0.3 (2.0)
Median	18.0	-1.0	17.0	0.0
Min - Max	15 - 18	-4 - 3	14 - 22	-3 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	9	9	19	19
Mean (SD)	16.8 (1.6)	-1.1 (2.3)	17.5 (2.4)	-0.2 (2.3)
Median	17.0	-1.0	16.0	0.0
Min - Max	14 - 19	-6 - 2	14 - 24	-5 - 6
Cycle 19 Day 15				
PRE PAC INFUSION				
n	10	10	20	20
Mean (SD)	17.0 (1.1)	-0.6 (2.2)	17.4 (2.2)	-0.1 (1.8)
Median	17.0	0.0	16.5	0.0
Min - Max	16 - 18	-6 - 2	14 - 23	-2 - 5
AFTER PAC INFUSION				
n	9	9	19	19
Mean (SD)	16.1 (2.0)	-1.0 (1.4)	17.2 (1.9)	-0.4 (1.7)
Median	16.0	-1.0	17.0	0.0
Min - Max	12 - 19	-4 - 1	14 - 22	-3 - 4
Cycle 20 Day 1				
PRE PAC INFUSION				
n	11	11	23	23
Mean (SD)	17.0 (1.3)	-0.5 (2.3)	16.5 (2.1)	-0.4 (1.8)
Median	18.0	0.0	16.0	0.0
Min - Max	15 - 18	-6 - 2	12 - 22	-4 - 4
AFTER PAC INFUSION				
n	10	10	17	17
Mean (SD)	16.7 (1.3)	-0.9 (2.1)	17.2 (2.0)	-0.2 (2.0)
Median	16.5	-0.5	16.0	0.0
Min - Max	15 - 19	-6 - 2	14 - 21	-5 - 3
Cycle 20 Day 8				
PRE PAC INFUSION				
n	9	9	16	16
Mean (SD)	17.1 (1.4)	-0.7 (1.6)	17.1 (1.9)	-0.4 (1.6)
Median	18.0	0.0	17.5	-1.0
Min - Max	15 - 19	-4 - 1	14 - 21	-2 - 3
AFTER PAC INFUSION				
n	9	9	16	16
Mean (SD)	17.2 (1.5)	-0.6 (1.4)	16.8 (2.2)	-0.8 (2.3)
Median	17.0	-1.0	16.0	-1.0
Min - Max	15 - 20	-2 - 2	13 - 22	-6 - 4
Cycle 20 Day 15				
PRE PAC INFUSION				
n	10	10	16	16
Mean (SD)	17.6 (1.3)	0.0 (2.4)	17.5 (1.8)	0.0 (1.7)
Median	18.0	0.0	18.0	0.0
Min - Max	15 - 20	-4 - 4	15 - 21	-3 - 3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	10	10	16	16
Mean (SD)	17.4 (1.3)	-0.2 (2.8)	17.1 (2.5)	-0.4 (2.8)
Median	17.5	-1.0	17.5	-0.5
Min - Max	15 - 19	-6 - 4	11 - 22	-8 - 4
Cycle 21 Day 1				
PRE PAC INFUSION				
n	9	9	20	20
Mean (SD)	17.7 (1.0)	-0.1 (1.9)	17.2 (2.6)	0.1 (1.9)
Median	18.0	0.0	16.0	0.0
Min - Max	16 - 19	-4 - 2	12 - 23	-2 - 5
AFTER PAC INFUSION				
n	6	6	15	15
Mean (SD)	18.5 (1.9)	0.3 (2.6)	17.8 (2.5)	0.3 (2.5)
Median	19.0	-0.5	18.0	0.0
Min - Max	15 - 20	-2 - 4	14 - 24	-3 - 6
Cycle 21 Day 8				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	17.1 (1.3)	-0.3 (2.1)	17.6 (2.1)	0.1 (2.1)
Median	17.0	0.0	18.0	0.0
Min - Max	15 - 19	-5 - 2	14 - 22	-3 - 4
AFTER PAC INFUSION				
n	9	9	14	14
Mean (SD)	16.6 (1.6)	-0.9 (1.8)	16.9 (2.2)	-0.7 (1.9)
Median	16.0	-1.0	16.5	-1.0
Min - Max	14 - 19	-4 - 1	14 - 20	-5 - 2
Cycle 21 Day 15				
PRE PAC INFUSION				
n	9	9	15	15
Mean (SD)	17.4 (0.9)	0.3 (1.7)	17.5 (2.3)	0.1 (2.2)
Median	18.0	0.0	18.0	0.0
Min - Max	16 - 18	-2 - 3	14 - 22	-3 - 3
AFTER PAC INFUSION				
n	8	8	15	15
Mean (SD)	17.1 (1.2)	0.3 (1.7)	16.9 (2.6)	-0.6 (2.5)
Median	17.0	0.0	16.0	-1.0
Min - Max	15 - 19	-2 - 3	12 - 22	-7 - 4
Cycle 22 Day 1				
PRE PAC INFUSION				
n	10	10	20	20
Mean (SD)	17.4 (1.3)	-0.4 (1.8)	17.3 (2.4)	0.2 (2.0)
Median	18.0	0.0	16.5	0.0
Min - Max	15 - 19	-4 - 3	13 - 24	-2 - 6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	7	7	15	15
Mean (SD)	16.3 (2.6)	-1.4 (4.2)	17.7 (2.6)	0.3 (2.9)
Median	18.0	-1.0	18.0	0.0
Min - Max	12 - 19	-10 - 3	12 - 23	-7 - 5
Cycle 22 Day 8				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	17.2 (2.0)	-0.2 (2.7)	17.4 (2.2)	-0.2 (2.0)
Median	17.0	0.0	17.0	-0.5
Min - Max	14 - 20	-6 - 3	14 - 22	-3 - 4
AFTER PAC INFUSION				
n	9	9	14	14
Mean (SD)	16.8 (2.6)	-0.7 (4.3)	17.4 (2.1)	-0.2 (1.9)
Median	18.0	0.0	16.5	-0.5
Min - Max	11 - 19	-11 - 3	14 - 22	-3 - 4
Cycle 22 Day 15				
PRE PAC INFUSION				
n	7	7	14	14
Mean (SD)	16.9 (1.6)	-0.3 (1.1)	17.4 (2.0)	0.0 (2.0)
Median	17.0	-1.0	17.5	0.0
Min - Max	15 - 19	-1 - 2	14 - 22	-2 - 4
AFTER PAC INFUSION				
n	7	7	14	14
Mean (SD)	15.6 (2.2)	-1.6 (1.5)	17.5 (2.4)	0.1 (2.1)
Median	16.0	-2.0	16.0	0.0
Min - Max	12 - 19	-4 - 1	15 - 24	-2 - 6
Cycle 23 Day 1				
PRE PAC INFUSION				
n	9	9	19	19
Mean (SD)	17.8 (1.3)	-0.1 (2.6)	16.9 (1.8)	-0.3 (1.5)
Median	18.0	-1.0	17.0	0.0
Min - Max	15 - 20	-4 - 4	13 - 20	-3 - 2
AFTER PAC INFUSION				
n	7	7	13	13
Mean (SD)	17.7 (1.8)	0.0 (3.1)	17.2 (2.5)	-0.5 (2.3)
Median	18.0	-1.0	16.0	-1.0
Min - Max	15 - 20	-4 - 5	14 - 22	-4 - 4
Cycle 23 Day 8				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	17.1 (1.6)	-0.6 (1.8)	17.5 (2.0)	-0.4 (2.0)
Median	18.0	-0.5	18.0	0.0
Min - Max	14 - 19	-4 - 2	14 - 20	-3 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	16.3 (2.3)	-1.5 (3.5)	17.0 (1.7)	-0.8 (1.6)
Median	17.5	-1.0	17.0	-1.0
Min - Max	13 - 18	-9 - 2	14 - 20	-3 - 2
Cycle 23 Day 15				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	17.0 (1.1)	-0.8 (1.6)	18.1 (2.6)	0.3 (2.3)
Median	17.0	0.0	18.0	0.0
Min - Max	16 - 18	-4 - 1	15 - 22	-3 - 4
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	17.0 (2.7)	-0.8 (1.9)	18.2 (1.8)	0.4 (1.9)
Median	17.5	-1.5	18.0	0.0
Min - Max	13 - 20	-3 - 2	16 - 22	-2 - 4
Cycle 24 Day 1				
PRE PAC INFUSION				
n	9	9	17	17
Mean (SD)	16.9 (1.7)	-1.0 (2.1)	17.2 (2.6)	0.1 (1.9)
Median	16.0	0.0	16.0	0.0
Min - Max	15 - 20	-6 - 1	12 - 22	-2 - 4
AFTER PAC INFUSION				
n	7	7	12	12
Mean (SD)	16.4 (2.5)	-1.3 (1.7)	17.0 (2.0)	-0.8 (1.7)
Median	17.0	-2.0	16.0	-1.0
Min - Max	13 - 20	-3 - 2	14 - 20	-3 - 2
Cycle 24 Day 8				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	17.1 (1.2)	-0.6 (2.4)	17.7 (2.5)	-0.3 (2.5)
Median	17.0	0.0	18.0	-1.0
Min - Max	16 - 19	-6 - 2	14 - 23	-3 - 5
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	16.8 (2.2)	-1.0 (2.8)	18.0 (2.8)	0.0 (2.8)
Median	18.0	-1.0	18.0	-1.0
Min - Max	12 - 18	-5 - 3	14 - 23	-5 - 5
Cycle 24 Day 15				
PRE PAC INFUSION				
n	8	8	12	12
Mean (SD)	17.1 (1.4)	-0.6 (1.8)	18.2 (2.3)	0.3 (2.0)
Median	17.5	0.0	18.0	0.0
Min - Max	15 - 19	-4 - 2	15 - 22	-2 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	8	8	12	12
Mean (SD)	16.4 (1.6)	-1.4 (2.3)	17.2 (2.9)	-0.7 (2.9)
Median	16.5	-1.5	16.5	-1.0
Min - Max	14 - 18	-6 - 2	12 - 23	-7 - 5
Cycle 25 Day 1				
PRE PAC INFUSION				
n	8	8	14	14
Mean (SD)	16.8 (2.1)	-1.5 (3.6)	17.5 (1.8)	0.2 (2.0)
Median	18.0	-0.5	18.0	0.0
Min - Max	12 - 18	-10 - 2	14 - 20	-3 - 4
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	17.6 (1.4)	-0.6 (1.9)	15.9 (3.0)	-1.9 (3.4)
Median	18.0	0.0	17.0	-2.0
Min - Max	16 - 20	-4 - 2	10 - 20	-9 - 2
Cycle 25 Day 8				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	16.0 (2.5)	-2.1 (2.3)	17.9 (2.6)	0.1 (2.6)
Median	17.0	-2.0	18.0	-1.0
Min - Max	12 - 18	-6 - 0	14 - 22	-3 - 4
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	17.1 (2.2)	-1.0 (1.3)	16.8 (2.6)	-1.0 (2.9)
Median	18.0	0.0	16.0	-1.0
Min - Max	13 - 20	-3 - 0	13 - 20	-6 - 4
Cycle 25 Day 15				
PRE PAC INFUSION				
n	7	7	10	10
Mean (SD)	17.0 (1.8)	-1.1 (1.5)	17.3 (2.1)	-0.3 (1.6)
Median	18.0	-1.0	17.5	-0.5
Min - Max	14 - 19	-4 - 0	14 - 20	-3 - 2
AFTER PAC INFUSION				
n	7	7	10	10
Mean (SD)	17.1 (1.6)	-1.0 (1.6)	17.1 (2.4)	-0.5 (2.5)
Median	17.0	-1.0	17.0	-0.5
Min - Max	14 - 19	-4 - 1	14 - 20	-5 - 4
Cycle 26 Day 1				
PRE PAC INFUSION				
n	8	8	14	14
Mean (SD)	17.6 (1.7)	-0.6 (1.8)	17.1 (1.6)	0.1 (1.7)
Median	18.0	0.0	17.0	0.5
Min - Max	14 - 20	-4 - 2	14 - 20	-2 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	17.0 (1.4)	-1.1 (1.2)	16.7 (2.0)	-1.1 (1.8)
Median	17.0	-1.0	16.0	-1.0
Min - Max	15 - 19	-3 - 0	14 - 20	-4 - 2
Cycle 26 Day 8				
PRE PAC INFUSION				
n	7	7	7	7
Mean (SD)	16.4 (1.8)	-1.7 (2.5)	18.3 (3.0)	0.6 (3.0)
Median	16.0	-2.0	18.0	-1.0
Min - Max	13 - 18	-6 - 2	15 - 24	-3 - 6
AFTER PAC INFUSION				
n	7	7	7	7
Mean (SD)	16.6 (1.9)	-1.6 (1.4)	18.0 (2.8)	0.3 (3.2)
Median	18.0	-2.0	18.0	0.0
Min - Max	14 - 18	-4 - 0	14 - 22	-4 - 4
Cycle 26 Day 15				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	17.3 (1.7)	-0.9 (1.9)	18.0 (1.7)	0.2 (2.0)
Median	18.0	-1.0	18.0	0.0
Min - Max	14 - 19	-4 - 2	16 - 20	-2 - 4
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	16.9 (1.9)	-1.3 (1.8)	17.9 (2.0)	0.1 (2.0)
Median	18.0	-1.0	17.0	0.0
Min - Max	13 - 18	-4 - 1	16 - 20	-2 - 4
Cycle 27 Day 1				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	16.8 (1.4)	-1.1 (2.2)	16.9 (2.1)	-0.1 (2.5)
Median	17.0	-1.0	16.0	0.0
Min - Max	14 - 18	-6 - 2	14 - 20	-6 - 4
AFTER PAC INFUSION				
n	8	8	8	8
Mean (SD)	17.8 (2.9)	0.0 (1.5)	17.1 (2.4)	-0.5 (3.2)
Median	17.5	0.0	16.0	-1.5
Min - Max	14 - 24	-2 - 2	14 - 21	-4 - 5
Cycle 27 Day 8				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	16.3 (2.0)	-2.2 (3.0)	17.6 (2.5)	-0.4 (2.7)
Median	17.0	-1.5	18.0	0.0
Min - Max	14 - 18	-8 - 0	14 - 20	-5 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	6	6	8	8
Mean (SD)	17.3 (1.2)	-1.2 (1.6)	17.5 (1.8)	-0.5 (1.9)
Median	18.0	-0.5	17.5	-0.5
Min - Max	15 - 18	-4 - 0	15 - 20	-3 - 2
Cycle 27 Day 15				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	17.0 (1.2)	-1.0 (2.5)	17.6 (2.4)	-0.2 (2.9)
Median	17.0	0.0	18.0	0.0
Min - Max	15 - 18	-6 - 2	14 - 20	-5 - 4
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	16.6 (1.4)	-1.4 (2.8)	17.6 (1.9)	-0.2 (1.6)
Median	17.0	0.0	18.0	0.0
Min - Max	14 - 18	-6 - 2	15 - 20	-3 - 2
Cycle 28 Day 1				
PRE PAC INFUSION				
n	7	7	13	13
Mean (SD)	17.4 (1.6)	-1.1 (1.5)	17.0 (1.6)	0.0 (2.6)
Median	18.0	-1.0	18.0	0.0
Min - Max	14 - 19	-4 - 0	14 - 20	-5 - 4
AFTER PAC INFUSION				
n	6	6	6	6
Mean (SD)	16.7 (1.8)	-1.8 (2.2)	17.3 (1.8)	-0.8 (2.1)
Median	16.5	-1.5	16.5	-1.5
Min - Max	14 - 19	-6 - 0	16 - 20	-3 - 3
Cycle 28 Day 8				
PRE PAC INFUSION				
n	6	6	7	7
Mean (SD)	17.5 (2.0)	-1.0 (1.7)	16.9 (1.7)	-1.1 (2.3)
Median	18.0	0.0	18.0	0.0
Min - Max	14 - 20	-4 - 0	14 - 18	-4 - 2
AFTER PAC INFUSION				
n	6	6	7	7
Mean (SD)	16.7 (2.3)	-1.8 (2.8)	16.6 (2.5)	-1.4 (2.4)
Median	17.5	-0.5	16.0	0.0
Min - Max	13 - 19	-7 - 0	13 - 21	-6 - 1
Cycle 28 Day 15				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	16.8 (1.8)	-1.7 (2.3)	16.5 (1.4)	-1.3 (1.8)
Median	17.0	-1.0	16.0	-0.5
Min - Max	14 - 19	-6 - 0	14 - 18	-5 - 0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	6	6	8	8
Mean (SD)	16.2 (2.2)	-2.3 (2.3)	16.0 (3.1)	-1.8 (3.8)
Median	16.5	-1.5	16.5	-1.0
Min - Max	12 - 18	-6 - 0	10 - 20	-9 - 4
Cycle 29 Day 1				
PRE PAC INFUSION				
n	7	7	11	11
Mean (SD)	18.0 (1.0)	-0.4 (1.4)	16.4 (1.8)	-0.4 (2.5)
Median	18.0	0.0	16.0	0.0
Min - Max	17 - 20	-2 - 2	13 - 20	-3 - 4
AFTER PAC INFUSION				
n	6	6	6	6
Mean (SD)	17.7 (1.4)	-0.7 (1.5)	16.2 (3.1)	-1.5 (2.3)
Median	17.5	-1.0	16.5	-1.5
Min - Max	16 - 20	-2 - 2	12 - 21	-4 - 1
Cycle 29 Day 8				
PRE PAC INFUSION				
n	6	6	5	5
Mean (SD)	17.8 (1.2)	-0.5 (1.6)	17.6 (2.6)	-0.6 (2.6)
Median	18.0	-0.5	18.0	-1.0
Min - Max	16 - 19	-3 - 2	14 - 20	-4 - 2
AFTER PAC INFUSION				
n	6	6	5	5
Mean (SD)	17.3 (0.8)	-1.0 (2.4)	16.4 (2.2)	-1.8 (1.5)
Median	17.5	-0.5	16.0	-2.0
Min - Max	16 - 18	-5 - 2	14 - 20	-4 - 0
Cycle 29 Day 15				
PRE PAC INFUSION				
n	6	6	7	7
Mean (SD)	17.3 (1.0)	-1.0 (1.8)	17.0 (2.0)	-0.6 (2.5)
Median	18.0	-0.5	16.0	-1.0
Min - Max	16 - 18	-4 - 1	15 - 20	-4 - 3
AFTER PAC INFUSION				
n	6	6	7	7
Mean (SD)	17.8 (1.2)	-0.5 (1.6)	17.3 (1.8)	-0.3 (2.0)
Median	18.0	-0.5	17.0	-1.0
Min - Max	16 - 19	-3 - 2	15 - 20	-3 - 2
Cycle 30 Day 1				
PRE PAC INFUSION				
n	7	7	11	11
Mean (SD)	17.6 (0.8)	-0.9 (1.9)	16.2 (1.3)	-0.6 (1.5)
Median	18.0	-1.0	16.0	0.0
Min - Max	16 - 18	-4 - 2	14 - 18	-3 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	7	7
Mean (SD)	16.8 (0.8)	-1.6 (2.9)	16.6 (1.6)	-1.0 (1.8)
Median	17.0	-1.0	16.0	-1.0
Min - Max	16 - 18	-6 - 2	14 - 19	-4 - 2
Cycle 30 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	18.0 (1.2)	-0.4 (2.2)	17.2 (1.8)	-0.6 (0.9)
Median	18.0	0.0	16.0	0.0
Min - Max	17 - 20	-4 - 2	16 - 20	-2 - 0
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	17.2 (0.8)	-1.2 (2.2)	17.0 (1.4)	-0.8 (0.8)
Median	17.0	-1.0	16.0	-1.0
Min - Max	16 - 18	-4 - 2	16 - 19	-2 - 0
Cycle 30 Day 15				
PRE PAC INFUSION				
n	4	4	7	7
Mean (SD)	18.5 (1.3)	-0.3 (1.7)	17.4 (2.0)	-0.1 (2.4)
Median	18.5	-0.5	18.0	0.0
Min - Max	17 - 20	-2 - 2	14 - 20	-4 - 4
AFTER PAC INFUSION				
n	4	4	7	7
Mean (SD)	18.0 (0.8)	-0.8 (2.5)	16.7 (2.1)	-0.9 (2.6)
Median	18.0	-0.5	16.0	-1.0
Min - Max	17 - 19	-4 - 2	14 - 20	-4 - 4
Cycle 31 Day 1				
PRE PAC INFUSION				
n	6	6	12	12
Mean (SD)	17.5 (1.2)	-1.2 (2.5)	17.3 (2.1)	0.6 (2.0)
Median	18.0	-0.5	17.0	0.0
Min - Max	16 - 19	-6 - 1	14 - 20	-3 - 4
AFTER PAC INFUSION				
n	4	4	6	6
Mean (SD)	17.5 (1.3)	-1.3 (3.4)	18.0 (1.9)	0.5 (2.3)
Median	17.5	-0.5	18.0	0.0
Min - Max	16 - 19	-6 - 2	16 - 21	-1 - 5
Cycle 31 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	18.0 (1.6)	-0.4 (1.5)	17.6 (1.3)	-0.2 (1.3)
Median	18.0	-1.0	17.0	0.0
Min - Max	16 - 20	-2 - 2	16 - 19	-2 - 1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	18.6 (3.4)	0.2 (1.3)	17.8 (1.5)	0.0 (0.0)
Median	17.0	0.0	18.0	0.0
Min - Max	16 - 24	-1 - 2	16 - 20	0 - 0
Cycle 31 Day 15				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	17.5 (1.0)	-0.5 (2.9)	16.5 (1.5)	-1.0 (1.3)
Median	18.0	-0.5	16.5	-1.5
Min - Max	16 - 18	-4 - 3	14 - 18	-2 - 1
AFTER PAC INFUSION				
n	4	4	6	6
Mean (SD)	19.0 (3.4)	1.0 (1.2)	16.5 (1.2)	-1.0 (0.9)
Median	17.5	1.0	16.0	-1.0
Min - Max	17 - 24	0 - 2	16 - 19	-2 - 0
Cycle 32 Day 1				
PRE PAC INFUSION				
n	7	7	11	11
Mean (SD)	17.9 (1.2)	-0.6 (1.4)	17.5 (2.0)	0.9 (1.9)
Median	18.0	-1.0	18.0	0.0
Min - Max	16 - 20	-2 - 2	14 - 20	-2 - 4
AFTER PAC INFUSION				
n	5	5	6	6
Mean (SD)	18.2 (2.2)	-0.2 (1.5)	17.3 (1.8)	-0.2 (1.5)
Median	17.0	0.0	16.5	-0.5
Min - Max	17 - 22	-2 - 2	16 - 20	-2 - 2
Cycle 32 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	17.6 (1.7)	-0.8 (1.3)	17.2 (2.3)	-0.6 (3.0)
Median	18.0	-1.0	18.0	-1.0
Min - Max	16 - 20	-2 - 1	14 - 20	-4 - 4
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	17.6 (1.1)	-0.8 (1.9)	16.6 (1.3)	-1.2 (0.8)
Median	18.0	0.0	16.0	-1.0
Min - Max	16 - 19	-4 - 1	16 - 19	-2 - 0
Cycle 32 Day 15				
PRE PAC INFUSION				
n	4	4	5	5
Mean (SD)	17.5 (1.3)	-1.8 (2.9)	16.6 (0.9)	-1.2 (1.8)
Median	17.5	-0.5	16.0	0.0
Min - Max	16 - 19	-6 - 0	16 - 18	-4 - 0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	4	4	5	5
Mean (SD)	16.8 (1.0)	-2.5 (2.4)	16.0 (2.5)	-1.8 (2.4)
Median	16.5	-1.5	16.0	-1.0
Min - Max	16 - 18	-6 - -1	12 - 19	-6 - 0
Cycle 33 Day 1				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	17.3 (1.0)	-1.1 (2.5)	16.4 (1.9)	0.1 (1.3)
Median	18.0	-1.0	16.0	0.0
Min - Max	16 - 18	-6 - 2	12 - 18	-2 - 2
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	17.2 (1.1)	-1.2 (1.9)	17.4 (1.3)	0.0 (1.2)
Median	18.0	-1.0	18.0	0.0
Min - Max	16 - 18	-4 - 1	16 - 19	-1 - 2
Cycle 33 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	17.8 (1.3)	-1.0 (2.2)	17.0 (1.4)	-0.8 (1.0)
Median	18.0	-0.5	17.5	-0.5
Min - Max	16 - 19	-4 - 1	15 - 18	-2 - 0
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	18.0 (1.8)	-0.8 (1.9)	18.3 (2.1)	0.5 (2.4)
Median	18.0	-1.5	18.5	-0.5
Min - Max	16 - 20	-2 - 2	16 - 20	-1 - 4
Cycle 33 Day 15				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	17.2 (1.1)	-1.2 (1.9)	17.2 (1.1)	-0.2 (1.5)
Median	18.0	-1.0	18.0	0.0
Min - Max	16 - 18	-4 - 1	16 - 18	-2 - 2
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	17.2 (1.6)	-1.2 (2.2)	17.8 (1.5)	0.4 (1.5)
Median	18.0	-2.0	18.0	0.0
Min - Max	15 - 19	-4 - 1	16 - 20	-1 - 2
Cycle 34 Day 1				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	17.6 (1.6)	-0.9 (1.2)	16.1 (2.7)	-0.2 (1.9)
Median	18.0	-1.0	16.0	0.0
Min - Max	15 - 20	-2 - 1	12 - 20	-2 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	16.8 (1.3)	-1.6 (1.8)	17.8 (2.1)	0.0 (2.7)
Median	17.0	-2.0	17.5	-1.0
Min - Max	15 - 18	-4 - 1	16 - 20	-2 - 4
Cycle 34 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	17.0 (1.4)	-1.0 (2.6)	16.5 (1.0)	-1.3 (1.0)
Median	17.5	-1.0	16.0	-1.5
Min - Max	15 - 18	-4 - 2	16 - 18	-2 - 0
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	16.8 (1.5)	-1.3 (2.2)	17.3 (1.9)	-0.5 (1.0)
Median	17.0	-1.0	16.5	0.0
Min - Max	15 - 18	-4 - 1	16 - 20	-2 - 0
Cycle 34 Day 15				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	17.4 (1.7)	-1.0 (3.0)	16.8 (1.3)	-0.6 (0.9)
Median	17.0	0.0	17.0	0.0
Min - Max	16 - 20	-6 - 2	15 - 18	-2 - 0
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	16.8 (1.3)	-1.6 (2.2)	16.8 (2.3)	-0.6 (0.9)
Median	17.0	-2.0	16.0	0.0
Min - Max	15 - 18	-4 - 2	14 - 20	-2 - 0
Cycle 35 Day 1				
PRE PAC INFUSION				
n	7	7	8	8
Mean (SD)	17.0 (1.3)	-1.4 (2.3)	17.0 (1.8)	0.6 (2.1)
Median	18.0	-1.0	17.0	0.5
Min - Max	15 - 18	-6 - 1	14 - 20	-3 - 4
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	18.0 (2.5)	-0.4 (1.7)	17.0 (1.2)	-0.8 (1.0)
Median	18.0	0.0	17.0	-0.5
Min - Max	15 - 22	-2 - 2	16 - 18	-2 - 0
Cycle 35 Day 8				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	16.8 (1.3)	-1.6 (3.0)	16.5 (1.9)	-1.3 (1.0)
Median	17.0	-2.0	17.0	-1.5
Min - Max	15 - 18	-6 - 2	14 - 18	-2 - 0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	17.4 (1.9)	-1.0 (1.4)	16.5 (1.7)	-1.3 (0.5)
Median	18.0	-2.0	16.0	-1.0
Min - Max	15 - 20	-2 - 1	15 - 19	-2 - -1
Cycle 35 Day 15				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	16.8 (1.3)	-1.6 (3.0)	17.0 (1.4)	-0.8 (1.0)
Median	17.0	-2.0	17.5	-0.5
Min - Max	15 - 18	-6 - 2	15 - 18	-2 - 0
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	17.2 (1.6)	-1.2 (1.6)	17.5 (1.0)	-0.3 (1.0)
Median	18.0	-2.0	17.0	-0.5
Min - Max	15 - 19	-3 - 1	17 - 19	-1 - 1
Cycle 36 Day 1				
PRE PAC INFUSION				
n	7	7	8	8
Mean (SD)	17.0 (1.3)	-1.4 (2.3)	16.6 (1.6)	0.3 (1.2)
Median	18.0	-1.0	16.0	0.0
Min - Max	15 - 18	-6 - 1	14 - 19	-1 - 2
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	18.4 (3.3)	0.0 (1.6)	17.5 (1.9)	-0.3 (0.5)
Median	18.0	0.0	17.0	0.0
Min - Max	16 - 24	-2 - 2	16 - 20	-1 - 0
Cycle 36 Day 8				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	16.6 (1.3)	-1.8 (2.7)	16.3 (2.9)	-1.5 (1.9)
Median	16.0	-2.0	17.5	-1.0
Min - Max	15 - 18	-6 - 1	12 - 18	-4 - 0
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	17.0 (1.4)	-1.4 (1.9)	17.0 (2.6)	-0.8 (1.0)
Median	18.0	-2.0	17.0	-0.5
Min - Max	15 - 18	-4 - 1	14 - 20	-2 - 0
Cycle 36 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	17.0 (1.2)	-1.8 (3.1)	16.3 (2.4)	-1.5 (1.3)
Median	17.0	-1.0	17.0	-1.5
Min - Max	16 - 18	-6 - 1	13 - 18	-3 - 0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	17.3 (1.5)	-1.5 (3.1)	17.3 (1.5)	-0.5 (0.6)
Median	17.0	-0.5	17.0	-0.5
Min - Max	16 - 19	-6 - 1	16 - 19	-1 - 0
Cycle 37 Day 1				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	17.2 (1.3)	-0.7 (1.2)	16.3 (1.7)	-0.1 (1.6)
Median	18.0	-0.5	16.0	0.0
Min - Max	15 - 18	-2 - 1	14 - 18	-2 - 2
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	16.3 (1.3)	-1.3 (1.5)	17.3 (1.5)	-0.5 (1.7)
Median	16.0	-2.0	17.0	-1.0
Min - Max	15 - 18	-2 - 1	16 - 19	-2 - 2
Cycle 37 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	17.3 (1.5)	-0.3 (1.0)	16.8 (1.9)	-1.0 (1.2)
Median	17.0	-0.5	17.5	-1.0
Min - Max	16 - 19	-1 - 1	14 - 18	-2 - 0
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	17.0 (1.2)	-0.5 (1.3)	17.5 (2.1)	-0.3 (0.5)
Median	17.0	-0.5	17.5	0.0
Min - Max	16 - 18	-2 - 1	15 - 20	-1 - 0
Cycle 37 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	17.3 (1.0)	-0.3 (1.7)	17.0 (1.2)	-0.8 (1.0)
Median	17.5	-0.5	17.0	-0.5
Min - Max	16 - 18	-2 - 2	16 - 18	-2 - 0
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	16.8 (1.5)	-0.8 (1.5)	17.3 (2.2)	-0.5 (0.6)
Median	17.0	-1.0	17.0	-0.5
Min - Max	15 - 18	-2 - 1	15 - 20	-1 - 0
Cycle 38 Day 1				
PRE PAC INFUSION				
n	5	5	8	8
Mean (SD)	17.6 (0.9)	-0.8 (0.8)	16.8 (1.6)	0.4 (1.5)
Median	18.0	-1.0	17.5	0.0
Min - Max	16 - 18	-2 - 0	14 - 18	-2 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	16.7 (1.5)	-1.7 (0.6)	17.3 (2.5)	-0.5 (1.0)
Median	17.0	-2.0	17.5	0.0
Min - Max	15 - 18	-2 - -1	14 - 20	-2 - 0
Cycle 38 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	17.3 (1.5)	-0.3 (1.0)	18.0 (0.8)	0.3 (1.3)
Median	17.0	-0.5	18.0	0.0
Min - Max	16 - 19	-1 - 1	17 - 19	-1 - 2
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	17.0 (1.8)	-0.5 (1.3)	17.5 (1.3)	-0.3 (1.7)
Median	17.0	-0.5	17.5	-0.5
Min - Max	15 - 19	-2 - 1	16 - 19	-2 - 2
Cycle 38 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	17.3 (1.5)	-0.3 (1.0)	16.8 (1.5)	-1.0 (0.8)
Median	17.0	-0.5	17.0	-1.0
Min - Max	16 - 19	-1 - 1	15 - 18	-2 - 0
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	16.8 (2.1)	-0.8 (1.5)	18.3 (1.7)	0.5 (2.4)
Median	16.5	-1.0	18.5	-0.5
Min - Max	15 - 19	-2 - 1	16 - 20	-1 - 4
Cycle 39 Day 1				
PRE PAC INFUSION				
n	5	5	8	8
Mean (SD)	17.0 (1.4)	-0.8 (1.3)	16.1 (1.6)	-0.3 (1.8)
Median	18.0	-1.0	16.0	0.0
Min - Max	15 - 18	-2 - 1	14 - 18	-3 - 2
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	17.0 (1.4)	-0.5 (1.9)	17.0 (1.2)	-0.8 (1.0)
Median	17.5	-1.0	17.0	-0.5
Min - Max	15 - 18	-2 - 2	16 - 18	-2 - 0
Cycle 39 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	16.8 (1.5)	-0.8 (1.5)	17.0 (2.6)	-0.8 (1.9)
Median	17.0	-1.0	17.0	-1.5
Min - Max	15 - 18	-2 - 1	14 - 20	-2 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	16.8 (1.5)	-0.8 (1.5)	17.3 (1.5)	-0.5 (0.6)
Median	17.0	-1.0	17.0	-0.5
Min - Max	15 - 18	-2 - 1	16 - 19	-1 - 0
Cycle 39 Day 15				
PRE PAC INFUSION				
n	4	4	3	3
Mean (SD)	17.0 (1.2)	-0.5 (1.3)	16.3 (3.8)	-1.7 (2.1)
Median	17.0	-0.5	18.0	-1.0
Min - Max	16 - 18	-2 - 1	12 - 19	-4 - 0
AFTER PAC INFUSION				
n	4	4	3	3
Mean (SD)	17.0 (1.2)	-0.5 (1.3)	19.3 (1.2)	1.3 (2.3)
Median	17.0	-0.5	20.0	0.0
Min - Max	16 - 18	-2 - 1	18 - 20	0 - 4
Cycle 40 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	17.0 (1.2)	-0.3 (1.0)	16.8 (1.9)	0.4 (1.2)
Median	17.0	-0.5	16.5	0.0
Min - Max	16 - 18	-1 - 1	14 - 20	-1 - 2
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	16.3 (1.5)	-0.3 (1.5)	17.3 (1.2)	-1.0 (1.0)
Median	16.0	0.0	18.0	-1.0
Min - Max	15 - 18	-2 - 1	16 - 18	-2 - 0
Cycle 40 Day 8				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	16.3 (1.5)	-0.3 (1.5)	17.0 (1.2)	-0.8 (2.5)
Median	16.0	0.0	17.0	-0.5
Min - Max	15 - 18	-2 - 1	16 - 18	-4 - 2
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	16.0 (1.0)	-0.7 (0.6)	18.8 (2.5)	1.0 (3.4)
Median	16.0	-1.0	18.5	-0.5
Min - Max	15 - 17	-1 - 0	16 - 22	-1 - 6
Cycle 40 Day 15				
PRE PAC INFUSION				
n	2	2	4	4
Mean (SD)	17.0 (1.4)	0.5 (0.7)	18.0 (1.6)	0.3 (2.6)
Median	17.0	0.5	18.0	-0.5
Min - Max	16 - 18	0 - 1	16 - 20	-2 - 4

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	Placebo + Paclitaxel (N=75) Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	Ipatasertib + Paclitaxel (N=145) Change from Baseline
AFTER PAC INFUSION				
n	2	2	4	4
Mean (SD)	17.0 (1.4)	0.5 (0.7)	17.0 (2.6)	-0.8 (1.0)
Median	17.0	0.5	17.0	-0.5
Min - Max	16 - 18	0 - 1	14 - 20	-2 - 0
Cycle 41 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	17.3 (1.0)	0.0 (1.4)	16.9 (1.8)	0.5 (2.1)
Median	17.5	-0.5	16.5	0.0
Min - Max	16 - 18	-1 - 2	14 - 20	-3 - 4
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	17.7 (2.1)	1.0 (1.7)	17.0 (1.2)	-0.8 (1.0)
Median	17.0	2.0	17.0	-0.5
Min - Max	16 - 20	-1 - 2	16 - 18	-2 - 0
Cycle 41 Day 8				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	16.3 (1.5)	-0.3 (1.5)	16.8 (1.0)	-1.0 (1.4)
Median	16.0	0.0	16.5	-0.5
Min - Max	15 - 18	-2 - 1	16 - 18	-3 - 0
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	16.3 (0.6)	-0.3 (2.1)	17.3 (1.5)	-0.5 (0.6)
Median	16.0	-1.0	17.0	-0.5
Min - Max	16 - 17	-2 - 2	16 - 19	-1 - 0
Cycle 41 Day 15				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	16.0 (1.7)	-0.7 (1.2)	16.5 (1.0)	-1.3 (2.5)
Median	15.0	0.0	16.0	-1.5
Min - Max	15 - 18	-2 - 0	16 - 18	-4 - 2
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	16.0 (1.0)	-0.7 (1.5)	17.8 (1.7)	0.0 (1.4)
Median	16.0	-1.0	17.5	-0.5
Min - Max	15 - 17	-2 - 1	16 - 20	-1 - 2
Cycle 42 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	16.8 (1.5)	-0.5 (0.6)	16.4 (1.6)	0.0 (2.1)
Median	17.0	-0.5	16.0	0.0
Min - Max	15 - 18	-1 - 0	14 - 19	-4 - 3

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	16.3 (1.5)	-0.3 (1.5)	17.0 (1.2)	-0.8 (1.0)
Median	16.0	0.0	17.0	-0.5
Min - Max	15 - 18	-2 - 1	16 - 18	-2 - 0
Cycle 42 Day 8				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	17.0 (1.4)	-0.5 (0.7)
Median	17.0	-0.5	17.0	-0.5
Min - Max	16 - 18	-1 - 0	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	17.0 (1.4)	-0.5 (0.7)	17.0 (1.4)	-0.5 (0.7)
Median	17.0	-0.5	17.0	-0.5
Min - Max	16 - 18	-1 - 0	16 - 18	-1 - 0
Cycle 42 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	16.3 (1.5)	-0.3 (1.5)	16.7 (1.2)	-0.3 (0.6)
Median	16.0	0.0	16.0	0.0
Min - Max	15 - 18	-2 - 1	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	15.7 (2.1)	-1.0 (1.7)	18.0 (2.0)	1.0 (2.6)
Median	15.0	0.0	18.0	0.0
Min - Max	14 - 18	-3 - 0	16 - 20	-1 - 4
Cycle 43 Day 1				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	16.5 (1.7)	-0.8 (1.0)	16.0 (1.8)	0.2 (1.6)
Median	16.5	-0.5	16.0	0.0
Min - Max	15 - 18	-2 - 0	14 - 18	-2 - 2
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	16.3 (1.5)	-0.3 (0.6)	16.7 (1.2)	-0.3 (2.1)
Median	16.0	0.0	16.0	-1.0
Min - Max	15 - 18	-1 - 0	16 - 18	-2 - 2
Cycle 43 Day 8				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	16.3 (1.5)	-0.3 (0.6)	16.7 (1.2)	-0.3 (0.6)
Median	16.0	0.0	16.0	0.0
Min - Max	15 - 18	-1 - 0	16 - 18	-1 - 0

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	16.3 (1.5)	-0.3 (1.5)	18.0 (2.0)	1.0 (2.6)
Median	16.0	0.0	18.0	0.0
Min - Max	15 - 18	-2 - 1	16 - 20	-1 - 4
Cycle 43 Day 15				
PRE PAC INFUSION				
n	3	3	1	1
Mean (SD)	16.3 (1.5)	-0.3 (0.6)	17.0 (NE)	0.0 (NE)
Median	16.0	0.0	17.0	0.0
Min - Max	15 - 18	-1 - 0	17 - 17	0 - 0
AFTER PAC INFUSION				
n	3	3	1	1
Mean (SD)	16.3 (1.5)	-0.3 (1.5)	16.0 (NE)	-1.0 (NE)
Median	16.0	0.0	16.0	-1.0
Min - Max	15 - 18	-2 - 1	16 - 16	-1 - -1
Cycle 44 Day 1				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	16.5 (1.7)	-0.8 (1.0)	16.5 (1.8)	0.7 (1.5)
Median	16.5	-0.5	17.0	1.0
Min - Max	15 - 18	-2 - 0	14 - 18	-1 - 2
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	16.0 (0.0)	-0.7 (1.5)	16.0 (0.0)	-1.0 (1.0)
Median	16.0	-1.0	16.0	-1.0
Min - Max	16 - 16	-2 - 1	16 - 16	-2 - 0
Cycle 44 Day 8				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	16.0 (1.7)	-0.7 (1.2)	16.7 (1.2)	-0.3 (0.6)
Median	15.0	0.0	16.0	0.0
Min - Max	15 - 18	-2 - 0	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	16.3 (1.5)	-0.3 (1.5)	16.0 (2.0)	-1.0 (1.0)
Median	16.0	0.0	16.0	-1.0
Min - Max	15 - 18	-2 - 1	14 - 18	-2 - 0
Cycle 44 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	16.0 (1.7)	-0.7 (1.2)	16.0 (2.0)	-1.0 (1.0)
Median	15.0	0.0	16.0	-1.0
Min - Max	15 - 18	-2 - 0	14 - 18	-2 - 0

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	17.3 (2.3)	0.7 (1.5)	16.7 (1.2)	-0.3 (0.6)
Median	16.0	1.0	16.0	0.0
Min - Max	16 - 20	-1 - 2	16 - 18	-1 - 0
Cycle 45 Day 1				
PRE PAC INFUSION				
n	4	4	5	5
Mean (SD)	16.5 (1.7)	-0.8 (1.0)	16.4 (1.8)	0.8 (1.3)
Median	16.5	-0.5	17.0	1.0
Min - Max	15 - 18	-2 - 0	14 - 18	-1 - 2
AFTER PAC INFUSION				
n	3	3	1	1
Mean (SD)	16.3 (1.5)	-0.3 (0.6)	18.0 (NE)	0.0 (NE)
Median	16.0	0.0	18.0	0.0
Min - Max	15 - 18	-1 - 0	18 - 18	0 - 0
Cycle 45 Day 8				
PRE PAC INFUSION				
n	3	3	2	2
Mean (SD)	16.0 (1.7)	-0.7 (1.2)	17.5 (0.7)	0.5 (0.7)
Median	15.0	0.0	17.5	0.5
Min - Max	15 - 18	-2 - 0	17 - 18	0 - 1
AFTER PAC INFUSION				
n	3	3	2	2
Mean (SD)	17.0 (2.6)	0.3 (2.1)	17.0 (1.4)	0.0 (0.0)
Median	16.0	1.0	17.0	0.0
Min - Max	15 - 20	-2 - 2	16 - 18	0 - 0
Cycle 45 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	16.3 (1.5)	-0.3 (0.6)	16.7 (1.2)	-0.3 (0.6)
Median	16.0	0.0	16.0	0.0
Min - Max	15 - 18	-1 - 0	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	16.7 (1.2)	0.0 (1.0)	16.0 (2.0)	-1.0 (1.0)
Median	16.0	0.0	16.0	-1.0
Min - Max	16 - 18	-1 - 1	14 - 18	-2 - 0
Cycle 46 Day 1				
PRE PAC INFUSION				
n	3	3	6	6
Mean (SD)	17.0 (1.7)	-0.3 (0.6)	17.0 (2.1)	1.2 (1.8)
Median	18.0	0.0	17.0	1.0
Min - Max	15 - 18	-1 - 0	14 - 20	-1 - 4

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	17.5 (2.1)	1.0 (0.0)	18.0 (0.0)	1.0 (1.4)
Median	17.5	1.0	18.0	1.0
Min - Max	16 - 19	1 - 1	18 - 18	0 - 2
Cycle 46 Day 8				
PRE PAC INFUSION				
n	2	2	3	3
Mean (SD)	16.5 (2.1)	0.0 (0.0)	16.7 (1.2)	-0.3 (0.6)
Median	16.5	0.0	16.0	0.0
Min - Max	15 - 18	0 - 0	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	2	2	3	3
Mean (SD)	17.0 (1.4)	0.5 (0.7)	15.3 (1.2)	-1.7 (0.6)
Median	17.0	0.5	16.0	-2.0
Min - Max	16 - 18	0 - 1	14 - 16	-2 - -1
Cycle 46 Day 15				
PRE PAC INFUSION				
n	2	2	3	3
Mean (SD)	16.5 (2.1)	0.0 (0.0)	15.7 (2.5)	-1.3 (1.5)
Median	16.5	0.0	16.0	-1.0
Min - Max	15 - 18	0 - 0	13 - 18	-3 - 0
AFTER PAC INFUSION				
n	2	2	3	3
Mean (SD)	16.5 (2.1)	0.0 (0.0)	16.7 (1.2)	-0.3 (0.6)
Median	16.5	0.0	16.0	0.0
Min - Max	15 - 18	0 - 0	16 - 18	-1 - 0
Cycle 47 Day 1				
PRE PAC INFUSION				
n	3	3	6	6
Mean (SD)	17.0 (1.7)	-0.3 (0.6)	16.3 (1.5)	0.5 (1.2)
Median	18.0	0.0	16.0	0.0
Min - Max	15 - 18	-1 - 0	14 - 18	-1 - 2
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	17.5 (3.5)	1.0 (1.4)	17.0 (1.4)	-0.5 (0.7)
Median	17.5	1.0	17.0	-0.5
Min - Max	15 - 20	0 - 2	16 - 18	-1 - 0
Cycle 47 Day 8				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	16.5 (2.1)	0.0 (0.0)	17.0 (1.4)	-0.5 (0.7)
Median	16.5	0.0	17.0	-0.5
Min - Max	15 - 18	0 - 0	16 - 18	-1 - 0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	17.0 (1.4)	0.5 (0.7)	17.0 (1.4)	-0.5 (0.7)
Median	17.0	0.5	17.0	-0.5
Min - Max	16 - 18	0 - 1	16 - 18	-1 - 0
Cycle 47 Day 15				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	16.5 (2.1)	0.0 (0.0)	17.0 (1.4)	-0.5 (0.7)
Median	16.5	0.0	17.0	-0.5
Min - Max	15 - 18	0 - 0	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	15.5 (0.7)	-1.0 (1.4)	17.0 (1.4)	-0.5 (0.7)
Median	15.5	-1.0	17.0	-0.5
Min - Max	15 - 16	-2 - 0	16 - 18	-1 - 0
Cycle 48 Day 1				
PRE PAC INFUSION				
n	1	1	5	5
Mean (SD)	16.0 (NE)	1.0 (NE)	16.4 (1.7)	0.6 (1.3)
Median	16.0	1.0	16.0	0.0
Min - Max	16 - 16	1 - 1	14 - 18	-1 - 2
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	15.0 (NE)	0.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	15.0	0.0	17.0	-0.5
Min - Max	15 - 15	0 - 0	16 - 18	-1 - 0
Cycle 48 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	16.0 (NE)	1.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	16.0	1.0	17.0	-0.5
Min - Max	16 - 16	1 - 1	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	15.0 (NE)	0.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	15.0	0.0	17.0	-0.5
Min - Max	15 - 15	0 - 0	16 - 18	-1 - 0
Cycle 48 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	15.0 (NE)	0.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	15.0	0.0	17.0	-0.5
Min - Max	15 - 15	0 - 0	16 - 18	-1 - 0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	15.0 (NE)	0.0 (NE)	16.0 (0.0)	-1.5 (0.7)
Median	15.0	0.0	16.0	-1.5
Min - Max	15 - 15	0 - 0	16 - 16	-2 - -1
Cycle 49 Day 1				
PRE PAC INFUSION				
n	1	1	3	3
Mean (SD)	16.0 (NE)	1.0 (NE)	16.7 (1.2)	-0.3 (0.6)
Median	16.0	1.0	16.0	0.0
Min - Max	16 - 16	1 - 1	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	16.0 (NE)	1.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	16.0	1.0	17.0	-0.5
Min - Max	16 - 16	1 - 1	16 - 18	-1 - 0
Cycle 49 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	16.0 (NE)	1.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	16.0	1.0	17.0	-0.5
Min - Max	16 - 16	1 - 1	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	16.0 (NE)	1.0 (NE)	16.0 (0.0)	-1.5 (0.7)
Median	16.0	1.0	16.0	-1.5
Min - Max	16 - 16	1 - 1	16 - 16	-2 - -1
Cycle 49 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	15.0 (NE)	0.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	15.0	0.0	17.0	-0.5
Min - Max	15 - 15	0 - 0	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	16.0 (NE)	1.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	16.0	1.0	17.0	-0.5
Min - Max	16 - 16	1 - 1	16 - 18	-1 - 0
Cycle 50 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	15.0 (NE)	0.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	15.0	0.0	17.0	-0.5
Min - Max	15 - 15	0 - 0	16 - 18	-1 - 0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)	16.0 (NE)	-2.0 (NE)
Median	15.0	0.0	16.0	-2.0
Min - Max	15 - 15	0 - 0	16 - 16	-2 - -2
Cycle 50 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	15.0 (NE)	0.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	15.0	0.0	17.0	-0.5
Min - Max	15 - 15	0 - 0	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	16.0 (NE)	1.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	16.0	1.0	17.0	-0.5
Min - Max	16 - 16	1 - 1	16 - 18	-1 - 0
Cycle 50 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	15.0 (NE)	0.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	15.0	0.0	17.0	-0.5
Min - Max	15 - 15	0 - 0	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	15.0 (NE)	0.0 (NE)	16.0 (0.0)	-1.5 (0.7)
Median	15.0	0.0	16.0	-1.5
Min - Max	15 - 15	0 - 0	16 - 16	-2 - -1
Cycle 51 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	15.0 (NE)	0.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	15.0	0.0	17.0	-0.5
Min - Max	15 - 15	0 - 0	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	16.0 (NE)	1.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	16.0	1.0	17.0	-0.5
Min - Max	16 - 16	1 - 1	16 - 18	-1 - 0
Cycle 51 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)	16.0 (NE)	-1.0 (NE)
Median	15.0	0.0	16.0	-1.0
Min - Max	15 - 15	0 - 0	16 - 16	-1 - -1

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	16.0 (NE)	1.0 (NE)	NE (NE)	NE (NE)
Median	16.0	1.0	NE	NE
Min - Max	16 - 16	1 - 1	NE - NE	NE - NE
Cycle 51 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	15.0 (NE)	0.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	15.0	0.0	17.0	-0.5
Min - Max	15 - 15	0 - 0	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	15.0 (NE)	0.0 (NE)	17.0 (1.4)	-0.5 (0.7)
Median	15.0	0.0	17.0	-0.5
Min - Max	15 - 15	0 - 0	16 - 18	-1 - 0
Cycle 52 Day 1				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	17.0 (1.4)	-0.5 (0.7)
Median	NE	NE	17.0	-0.5
Min - Max	NE - NE	NE - NE	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	17.0 (1.4)	-0.5 (0.7)
Median	NE	NE	17.0	-0.5
Min - Max	NE - NE	NE - NE	16 - 18	-1 - 0
Cycle 52 Day 8				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	17.0 (1.4)	-0.5 (0.7)
Median	NE	NE	17.0	-0.5
Min - Max	NE - NE	NE - NE	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	17.0 (1.4)	-0.5 (0.7)
Median	NE	NE	17.0	-0.5
Min - Max	NE - NE	NE - NE	16 - 18	-1 - 0
Cycle 52 Day 15				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	17.0 (1.4)	-0.5 (0.7)
Median	NE	NE	17.0	-0.5
Min - Max	NE - NE	NE - NE	16 - 18	-1 - 0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	17.0 (1.4)	-0.5 (0.7)
Median	NE	NE	17.0	-0.5
Min - Max	NE - NE	NE - NE	16 - 18	-1 - 0
Cycle 53 Day 1				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	17.0 (1.4)	-0.5 (0.7)
Median	NE	NE	17.0	-0.5
Min - Max	NE - NE	NE - NE	16 - 18	-1 - 0
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	17.0 (1.4)	-0.5 (0.7)
Median	NE	NE	17.0	-0.5
Min - Max	NE - NE	NE - NE	16 - 18	-1 - 0
Cycle 53 Day 8				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	16.0 (NE)	-1.0 (NE)
Median	NE	NE	16.0	-1.0
Min - Max	NE - NE	NE - NE	16 - 16	-1 - -1
AFTER PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	16.0 (NE)	-1.0 (NE)
Median	NE	NE	16.0	-1.0
Min - Max	NE - NE	NE - NE	16 - 16	-1 - -1
Cycle 53 Day 15				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	16.0 (NE)	-1.0 (NE)
Median	NE	NE	16.0	-1.0
Min - Max	NE - NE	NE - NE	16 - 16	-1 - -1
Study Drug Discontinuation				
n	68	67	121	120
Mean (SD)	17.2 (2.3)	0.1 (2.3)	17.1 (2.7)	0.1 (2.1)
Median	17.0	0.0	16.0	0.0
Min - Max	12 - 25	-5 - 11	11 - 30	-6 - 10
Post-Baseline Last				
n	68	68	121	121
Mean (SD)	17.3 (2.3)	0.1 (2.3)	17.1 (2.8)	0.1 (2.1)
Median	17.0	0.0	16.0	0.0
Min - Max	12 - 25	-5 - 11	11 - 30	-6 - 10

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
PRE PAC INFUSION				
n	1	1	5	5
Mean (SD)	19.0 (NE)	2.0 (NE)	15.8 (2.7)	0.6 (1.9)
Median	19.0	2.0	16.0	0.0
Min - Max	19 - 19	2 - 2	13 - 20	-2 - 3
AFTER PAC INFUSION				
n	4	4	16	16
Mean (SD)	16.5 (0.6)	1.3 (1.7)	17.7 (2.5)	0.9 (1.9)
Median	16.5	1.5	18.0	1.0
Min - Max	16 - 17	-1 - 3	14 - 23	-2 - 5
Post-Baseline Minimum				
n	1	1	6	6
Mean (SD)	15.0 (NE)	-1.0 (NE)	15.3 (2.5)	-1.7 (2.6)
Median	15.0	-1.0	15.5	-1.5
Min - Max	15 - 15	-1 - -1	12 - 18	-5 - 2
PRE PAC INFUSION				
n	39	39	83	83
Mean (SD)	14.8 (2.3)	-1.8 (2.1)	14.7 (2.2)	-2.1 (2.3)
Median	14.0	-2.0	15.0	-2.0
Min - Max	9 - 19	-8 - 1	8 - 19	-10 - 1
AFTER PAC INFUSION				
n	33	33	53	53
Mean (SD)	14.2 (2.3)	-3.2 (2.5)	14.5 (2.8)	-2.5 (2.9)
Median	14.0	-3.0	14.0	-2.0
Min - Max	10 - 18	-11 - 2	6 - 19	-11 - 1
Post-Baseline Maximum				
n	7	7	6	6
Mean (SD)	21.4 (6.9)	5.6 (7.0)	21.8 (6.0)	4.2 (3.7)
Median	18.0	2.0	21.0	3.0
Min - Max	15 - 35	1 - 21	15 - 30	1 - 10
PRE PAC INFUSION				
n	36	36	79	79
Mean (SD)	19.3 (2.0)	2.1 (2.8)	19.2 (2.6)	2.3 (2.2)
Median	20.0	1.5	20.0	2.0
Min - Max	15 - 23	-4 - 11	14 - 28	-2 - 9
AFTER PAC INFUSION				
n	30	30	57	57
Mean (SD)	20.3 (3.8)	3.2 (3.2)	20.1 (3.7)	3.3 (3.4)
Median	20.0	2.0	20.0	2.0
Min - Max	14 - 32	0 - 13	14 - 37	-2 - 17

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
Baseline				
n	72		144	
Mean (SD)	36.45 (0.59)		36.47 (0.37)	
Median	36.60		36.50	
Min - Max	33.8 - 37.4		35.0 - 37.3	
Cycle 1 Day 1				
PRE PAC INFUSION				
n	69	66	140	139
Mean (SD)	36.47 (0.57)	0.00 (0.42)	36.50 (0.42)	0.02 (0.37)
Median	36.60	0.00	36.60	0.00
Min - Max	33.9 - 37.3	-0.8 - 1.4	35.2 - 37.5	-1.4 - 1.1
AFTER PAC INFUSION				
n	71	69	139	138
Mean (SD)	36.48 (0.55)	0.03 (0.43)	36.56 (0.40)	0.08 (0.35)
Median	36.60	0.00	36.60	0.00
Min - Max	34.0 - 37.2	-1.4 - 1.5	35.1 - 37.6	-0.9 - 1.2
Cycle 1 Day 8				
PRE PAC INFUSION				
n	72	69	134	134
Mean (SD)	36.48 (0.61)	0.01 (0.42)	36.52 (0.39)	0.02 (0.36)
Median	36.60	0.00	36.50	0.00
Min - Max	33.8 - 37.9	-1.0 - 1.7	34.7 - 37.6	-1.0 - 1.1
AFTER PAC INFUSION				
n	61	60	126	126
Mean (SD)	36.46 (0.57)	0.03 (0.46)	36.60 (0.37)	0.09 (0.37)
Median	36.60	0.00	36.60	0.00
Min - Max	33.9 - 37.1	-1.3 - 1.7	35.2 - 37.8	-0.7 - 1.5
Cycle 1 Day 15				
PRE PAC INFUSION				
n	70	67	128	128
Mean (SD)	36.51 (0.59)	0.04 (0.45)	36.47 (0.40)	-0.03 (0.41)
Median	36.60	0.00	36.50	0.00
Min - Max	33.9 - 37.4	-1.0 - 1.6	35.0 - 37.3	-1.5 - 1.1
AFTER PAC INFUSION				
n	57	55	115	115
Mean (SD)	36.60 (0.61)	0.14 (0.51)	36.54 (0.36)	0.03 (0.38)
Median	36.70	0.00	36.60	0.00
Min - Max	34.0 - 37.6	-0.7 - 1.8	35.4 - 37.7	-1.2 - 1.2
Cycle 2 Day 1				
PRE PAC INFUSION				
n	73	71	128	127
Mean (SD)	36.40 (0.61)	-0.05 (0.42)	36.49 (0.39)	-0.01 (0.36)
Median	36.40	0.00	36.50	0.00
Min - Max	33.9 - 38.1	-1.1 - 1.3	35.0 - 37.8	-1.1 - 1.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	67	66	120	119
Mean (SD)	36.43 (0.60)	-0.02 (0.45)	36.54 (0.35)	0.04 (0.35)
Median	36.50	0.00	36.50	0.00
Min - Max	33.9 - 37.5	-1.1 - 1.4	35.2 - 37.5	-1.0 - 1.0
Cycle 2 Day 8				
PRE PAC INFUSION				
n	72	70	127	126
Mean (SD)	36.45 (0.61)	-0.01 (0.49)	36.48 (0.38)	-0.02 (0.34)
Median	36.50	0.00	36.50	0.00
Min - Max	33.8 - 37.7	-1.4 - 1.7	35.0 - 37.4	-1.1 - 1.2
AFTER PAC INFUSION				
n	67	65	119	118
Mean (SD)	36.49 (0.63)	0.04 (0.49)	36.54 (0.37)	0.03 (0.34)
Median	36.60	0.00	36.50	0.00
Min - Max	34.0 - 37.5	-1.6 - 1.5	35.0 - 37.4	-0.9 - 1.5
Cycle 2 Day 15				
PRE PAC INFUSION				
n	69	67	122	121
Mean (SD)	36.51 (0.61)	0.06 (0.45)	36.47 (0.39)	-0.03 (0.35)
Median	36.60	0.00	36.50	0.00
Min - Max	33.9 - 37.4	-0.8 - 1.6	35.0 - 37.4	-1.1 - 0.8
AFTER PAC INFUSION				
n	65	63	107	107
Mean (SD)	36.56 (0.64)	0.10 (0.49)	36.51 (0.40)	0.00 (0.40)
Median	36.60	0.10	36.50	0.00
Min - Max	34.0 - 37.9	-1.1 - 1.5	35.1 - 37.5	-1.1 - 1.7
Cycle 3 Day 1				
PRE PAC INFUSION				
n	70	68	120	120
Mean (SD)	36.48 (0.56)	0.05 (0.41)	36.50 (0.40)	0.01 (0.37)
Median	36.60	0.00	36.50	0.00
Min - Max	33.8 - 37.5	-0.7 - 1.7	35.2 - 37.7	-0.9 - 1.1
AFTER PAC INFUSION				
n	65	63	108	108
Mean (SD)	36.46 (0.63)	0.02 (0.46)	36.54 (0.42)	0.03 (0.39)
Median	36.60	0.00	36.50	0.00
Min - Max	33.9 - 37.4	-1.0 - 1.3	35.6 - 38.0	-0.9 - 1.5
Cycle 3 Day 8				
PRE PAC INFUSION				
n	65	63	115	114
Mean (SD)	36.48 (0.59)	0.04 (0.45)	36.51 (0.39)	0.02 (0.39)
Median	36.60	0.00	36.50	0.00
Min - Max	33.7 - 37.3	-1.2 - 1.7	35.3 - 38.4	-1.0 - 1.5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	59	57	102	101
Mean (SD)	36.49 (0.63)	0.08 (0.55)	36.48 (0.30)	-0.02 (0.35)
Median	36.60	0.00	36.50	0.00
Min - Max	33.8 - 37.6	-1.6 - 1.5	35.5 - 37.1	-1.0 - 1.3
Cycle 3 Day 15				
PRE PAC INFUSION				
n	64	62	115	114
Mean (SD)	36.50 (0.58)	0.10 (0.40)	36.53 (0.35)	0.02 (0.38)
Median	36.60	0.00	36.60	0.00
Min - Max	33.9 - 37.4	-0.7 - 1.3	35.6 - 37.6	-0.9 - 1.4
AFTER PAC INFUSION				
n	59	57	106	106
Mean (SD)	36.47 (0.63)	0.05 (0.43)	36.53 (0.38)	0.01 (0.41)
Median	36.60	0.00	36.50	-0.10
Min - Max	33.8 - 37.4	-0.9 - 1.2	35.4 - 37.8	-1.0 - 1.8
Cycle 4 Day 1				
PRE PAC INFUSION				
n	62	61	113	112
Mean (SD)	36.48 (0.56)	0.06 (0.43)	36.53 (0.41)	0.03 (0.36)
Median	36.60	0.00	36.60	0.00
Min - Max	33.8 - 37.3	-0.8 - 1.5	35.0 - 37.6	-1.1 - 1.2
AFTER PAC INFUSION				
n	59	58	100	100
Mean (SD)	36.52 (0.62)	0.11 (0.40)	36.55 (0.35)	0.05 (0.39)
Median	36.60	0.10	36.50	0.00
Min - Max	33.8 - 37.5	-0.7 - 1.3	35.5 - 37.6	-1.3 - 1.3
Cycle 4 Day 8				
PRE PAC INFUSION				
n	62	61	113	113
Mean (SD)	36.40 (0.59)	-0.01 (0.48)	36.49 (0.40)	0.00 (0.43)
Median	36.55	0.00	36.50	0.00
Min - Max	33.8 - 37.1	-1.7 - 1.1	35.2 - 37.5	-1.5 - 1.2
AFTER PAC INFUSION				
n	60	59	106	106
Mean (SD)	36.45 (0.63)	0.03 (0.47)	36.56 (0.32)	0.06 (0.33)
Median	36.60	0.10	36.60	0.10
Min - Max	33.8 - 37.3	-1.3 - 1.3	35.0 - 37.2	-1.0 - 0.9
Cycle 4 Day 15				
PRE PAC INFUSION				
n	57	56	104	104
Mean (SD)	36.45 (0.67)	0.04 (0.47)	36.49 (0.40)	-0.01 (0.45)
Median	36.60	0.00	36.60	0.00
Min - Max	33.7 - 37.5	-1.6 - 1.1	35.2 - 37.4	-1.4 - 1.5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	52	51	96	96
Mean (SD)	36.42 (0.69)	0.01 (0.53)	36.52 (0.40)	0.01 (0.39)
Median	36.50	0.00	36.55	0.00
Min - Max	33.8 - 37.4	-1.7 - 1.2	35.1 - 37.4	-1.1 - 1.3
Cycle 5 Day 1				
PRE PAC INFUSION				
n	56	55	108	108
Mean (SD)	36.41 (0.67)	-0.01 (0.43)	36.51 (0.38)	0.01 (0.38)
Median	36.50	0.00	36.50	0.00
Min - Max	33.7 - 37.4	-1.1 - 1.0	35.3 - 37.5	-1.2 - 1.2
AFTER PAC INFUSION				
n	50	49	100	100
Mean (SD)	36.50 (0.68)	0.07 (0.43)	36.54 (0.38)	0.06 (0.42)
Median	36.60	0.00	36.50	0.10
Min - Max	33.8 - 37.6	-1.1 - 1.2	35.4 - 37.8	-1.0 - 2.0
Cycle 5 Day 8				
PRE PAC INFUSION				
n	55	54	105	105
Mean (SD)	36.47 (0.65)	0.04 (0.43)	36.43 (0.46)	-0.05 (0.47)
Median	36.60	0.00	36.50	0.00
Min - Max	33.8 - 37.7	-1.1 - 1.3	35.0 - 37.5	-1.4 - 1.7
AFTER PAC INFUSION				
n	52	51	99	99
Mean (SD)	36.41 (0.66)	-0.01 (0.46)	36.47 (0.46)	-0.02 (0.45)
Median	36.55	0.00	36.50	0.00
Min - Max	33.8 - 37.5	-1.7 - 1.1	35.0 - 37.9	-1.1 - 2.1
Cycle 5 Day 15				
PRE PAC INFUSION				
n	51	50	100	100
Mean (SD)	36.45 (0.64)	0.02 (0.41)	36.45 (0.41)	-0.02 (0.45)
Median	36.60	0.00	36.50	0.00
Min - Max	33.7 - 37.6	-1.0 - 1.2	35.0 - 37.4	-1.2 - 1.5
AFTER PAC INFUSION				
n	49	48	95	95
Mean (SD)	36.44 (0.67)	0.01 (0.45)	36.51 (0.42)	0.02 (0.43)
Median	36.50	0.00	36.50	0.00
Min - Max	33.7 - 37.6	-1.1 - 1.2	35.0 - 38.4	-1.0 - 1.5
Cycle 6 Day 1				
PRE PAC INFUSION				
n	52	51	100	100
Mean (SD)	36.43 (0.67)	0.01 (0.47)	36.47 (0.41)	0.00 (0.46)
Median	36.60	0.00	36.50	0.00
Min - Max	33.8 - 37.5	-1.3 - 0.9	35.2 - 37.8	-0.9 - 1.3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	49	49	94	94
Mean (SD)	36.45 (0.67)	0.02 (0.46)	36.48 (0.41)	-0.01 (0.37)
Median	36.60	0.00	36.50	0.00
Min - Max	33.8 - 37.3	-1.6 - 1.0	35.0 - 37.3	-0.9 - 1.2
Cycle 6 Day 8				
PRE PAC INFUSION				
n	52	51	102	102
Mean (SD)	36.36 (0.70)	-0.07 (0.47)	36.49 (0.36)	0.01 (0.38)
Median	36.50	0.00	36.60	0.00
Min - Max	33.7 - 37.4	-1.7 - 0.9	34.8 - 37.5	-1.3 - 0.9
AFTER PAC INFUSION				
n	48	47	96	96
Mean (SD)	36.42 (0.68)	-0.01 (0.49)	36.52 (0.37)	0.02 (0.42)
Median	36.50	0.00	36.50	0.00
Min - Max	33.8 - 37.3	-1.7 - 0.9	35.4 - 37.4	-1.1 - 1.4
Cycle 6 Day 15				
PRE PAC INFUSION				
n	51	50	98	98
Mean (SD)	36.43 (0.66)	-0.03 (0.41)	36.48 (0.40)	0.00 (0.37)
Median	36.60	0.00	36.50	0.00
Min - Max	33.8 - 37.2	-1.3 - 0.8	35.0 - 37.7	-1.0 - 1.3
AFTER PAC INFUSION				
n	48	47	90	90
Mean (SD)	36.45 (0.66)	-0.01 (0.32)	36.50 (0.38)	0.01 (0.39)
Median	36.60	0.00	36.50	0.00
Min - Max	33.8 - 37.4	-1.1 - 1.0	35.6 - 37.3	-1.2 - 1.0
Cycle 7 Day 1				
PRE PAC INFUSION				
n	49	49	93	93
Mean (SD)	36.52 (0.59)	0.03 (0.46)	36.44 (0.47)	-0.02 (0.40)
Median	36.60	0.00	36.50	0.00
Min - Max	33.7 - 37.3	-1.2 - 0.9	34.5 - 37.5	-1.6 - 0.8
AFTER PAC INFUSION				
n	45	45	80	80
Mean (SD)	36.47 (0.54)	0.00 (0.40)	36.47 (0.47)	0.03 (0.41)
Median	36.50	0.00	36.50	0.10
Min - Max	33.8 - 37.4	-1.0 - 1.0	34.5 - 37.6	-1.1 - 1.2
Cycle 7 Day 8				
PRE PAC INFUSION				
n	49	49	85	85
Mean (SD)	36.49 (0.53)	0.00 (0.45)	36.42 (0.37)	-0.02 (0.40)
Median	36.60	0.00	36.50	0.00
Min - Max	33.8 - 37.7	-1.2 - 1.3	35.3 - 37.1	-1.3 - 1.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	47	47	78	78
Mean (SD)	36.47 (0.53)	0.00 (0.38)	36.49 (0.39)	0.03 (0.39)
Median	36.60	0.00	36.50	0.00
Min - Max	33.7 - 37.2	-0.9 - 0.9	35.5 - 37.4	-0.7 - 1.0
Cycle 7 Day 15				
PRE PAC INFUSION				
n	47	47	83	83
Mean (SD)	36.49 (0.60)	0.00 (0.46)	36.43 (0.39)	-0.01 (0.38)
Median	36.50	0.00	36.50	0.00
Min - Max	33.7 - 37.4	-1.5 - 1.0	35.1 - 37.5	-1.0 - 1.3
AFTER PAC INFUSION				
n	41	41	80	80
Mean (SD)	36.42 (0.55)	-0.03 (0.43)	36.43 (0.47)	-0.03 (0.42)
Median	36.50	0.00	36.50	0.00
Min - Max	33.9 - 37.2	-1.5 - 0.8	33.9 - 37.2	-1.3 - 1.0
Cycle 8 Day 1				
PRE PAC INFUSION				
n	47	47	90	90
Mean (SD)	36.48 (0.57)	0.00 (0.38)	36.47 (0.40)	0.01 (0.43)
Median	36.60	0.00	36.60	0.00
Min - Max	33.7 - 37.3	-0.9 - 0.8	35.0 - 37.3	-1.6 - 1.4
AFTER PAC INFUSION				
n	45	45	78	78
Mean (SD)	36.41 (0.59)	-0.06 (0.42)	36.48 (0.44)	0.05 (0.37)
Median	36.50	0.00	36.55	0.00
Min - Max	33.6 - 37.3	-1.5 - 0.9	34.8 - 37.5	-1.0 - 1.0
Cycle 8 Day 8				
PRE PAC INFUSION				
n	45	45	81	81
Mean (SD)	36.45 (0.55)	0.00 (0.44)	36.46 (0.38)	0.02 (0.40)
Median	36.60	0.00	36.50	0.00
Min - Max	33.8 - 37.3	-1.6 - 0.8	35.0 - 37.3	-1.6 - 1.2
AFTER PAC INFUSION				
n	39	39	76	76
Mean (SD)	36.47 (0.53)	0.03 (0.37)	36.51 (0.39)	0.08 (0.44)
Median	36.60	0.00	36.50	0.00
Min - Max	33.9 - 37.2	-0.7 - 1.4	35.3 - 37.5	-0.8 - 1.3
Cycle 8 Day 15				
PRE PAC INFUSION				
n	45	45	77	77
Mean (SD)	36.46 (0.63)	0.00 (0.56)	36.47 (0.37)	0.02 (0.40)
Median	36.60	0.00	36.50	0.00
Min - Max	33.7 - 37.4	-1.7 - 1.3	35.2 - 37.4	-0.9 - 1.2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	43	43	69	69
Mean (SD)	36.46 (0.62)	-0.01 (0.56)	36.43 (0.49)	-0.01 (0.42)
Median	36.50	0.00	36.50	0.00
Min - Max	33.8 - 37.5	-1.6 - 1.1	33.9 - 37.5	-1.3 - 1.1
Cycle 9 Day 1				
PRE PAC INFUSION				
n	37	37	77	77
Mean (SD)	36.51 (0.55)	0.09 (0.35)	36.46 (0.36)	0.05 (0.41)
Median	36.60	0.10	36.50	0.00
Min - Max	33.7 - 37.1	-0.9 - 0.9	35.7 - 37.2	-0.9 - 1.2
AFTER PAC INFUSION				
n	34	34	65	65
Mean (SD)	36.47 (0.59)	0.06 (0.38)	36.52 (0.39)	0.09 (0.39)
Median	36.50	0.05	36.50	0.00
Min - Max	33.8 - 37.4	-0.9 - 1.0	35.8 - 37.6	-0.7 - 1.1
Cycle 9 Day 8				
PRE PAC INFUSION				
n	39	39	66	66
Mean (SD)	36.43 (0.62)	-0.02 (0.50)	36.45 (0.38)	0.02 (0.36)
Median	36.50	0.00	36.50	0.00
Min - Max	33.8 - 37.6	-1.2 - 1.2	35.3 - 37.2	-1.0 - 1.2
AFTER PAC INFUSION				
n	39	39	60	60
Mean (SD)	36.46 (0.65)	0.01 (0.53)	36.47 (0.43)	0.05 (0.37)
Median	36.50	-0.10	36.50	0.00
Min - Max	33.9 - 37.8	-1.1 - 1.3	34.8 - 37.1	-0.6 - 1.5
Cycle 9 Day 15				
PRE PAC INFUSION				
n	39	39	62	62
Mean (SD)	36.39 (0.65)	-0.06 (0.57)	36.42 (0.38)	-0.03 (0.43)
Median	36.50	0.00	36.50	0.00
Min - Max	33.7 - 37.4	-1.6 - 1.0	35.5 - 37.3	-1.1 - 1.1
AFTER PAC INFUSION				
n	36	36	54	54
Mean (SD)	36.44 (0.58)	0.01 (0.43)	36.46 (0.44)	0.03 (0.42)
Median	36.50	0.00	36.60	0.00
Min - Max	33.9 - 37.4	-0.7 - 1.0	35.0 - 37.2	-0.8 - 1.2
Cycle 10 Day 1				
PRE PAC INFUSION				
n	39	39	70	70
Mean (SD)	36.39 (0.58)	-0.05 (0.46)	36.39 (0.42)	-0.04 (0.44)
Median	36.50	0.00	36.50	0.00
Min - Max	33.8 - 37.2	-1.3 - 0.9	34.9 - 37.1	-1.3 - 0.9

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	37	37	56	56
Mean (SD)	36.43 (0.58)	0.00 (0.47)	36.55 (0.43)	0.14 (0.50)
Median	36.50	0.00	36.60	0.05
Min - Max	33.9 - 37.3	-1.1 - 1.3	35.2 - 37.6	-0.9 - 1.6
Cycle 10 Day 8				
PRE PAC INFUSION				
n	38	38	61	61
Mean (SD)	36.41 (0.72)	-0.02 (0.48)	36.44 (0.43)	0.02 (0.43)
Median	36.60	0.00	36.50	0.00
Min - Max	33.7 - 37.5	-1.4 - 1.1	35.1 - 37.2	-1.2 - 1.3
AFTER PAC INFUSION				
n	37	37	57	57
Mean (SD)	36.43 (0.64)	0.00 (0.45)	36.45 (0.46)	0.04 (0.42)
Median	36.50	0.00	36.50	0.00
Min - Max	33.8 - 37.3	-1.0 - 0.9	35.2 - 37.4	-1.4 - 1.1
Cycle 10 Day 15				
PRE PAC INFUSION				
n	36	36	59	59
Mean (SD)	36.46 (0.62)	0.04 (0.43)	36.44 (0.42)	0.03 (0.41)
Median	36.60	0.10	36.50	0.00
Min - Max	33.8 - 37.5	-1.0 - 1.1	35.0 - 37.3	-0.8 - 1.0
AFTER PAC INFUSION				
n	34	34	51	51
Mean (SD)	36.42 (0.68)	0.03 (0.47)	36.44 (0.52)	0.02 (0.47)
Median	36.60	0.10	36.50	0.00
Min - Max	33.9 - 37.2	-1.3 - 0.8	34.5 - 37.2	-1.1 - 1.3
Cycle 11 Day 1				
PRE PAC INFUSION				
n	35	35	64	64
Mean (SD)	36.41 (0.62)	-0.06 (0.41)	36.46 (0.39)	0.03 (0.48)
Median	36.50	0.00	36.50	0.00
Min - Max	33.8 - 37.4	-1.0 - 0.8	35.0 - 37.4	-1.6 - 2.2
AFTER PAC INFUSION				
n	34	34	48	48
Mean (SD)	36.39 (0.69)	-0.05 (0.53)	36.50 (0.48)	0.09 (0.47)
Median	36.45	0.05	36.60	0.10
Min - Max	33.8 - 37.4	-1.3 - 1.0	35.0 - 37.3	-1.6 - 1.0
Cycle 11 Day 8				
PRE PAC INFUSION				
n	33	33	48	48
Mean (SD)	36.41 (0.71)	-0.03 (0.56)	36.50 (0.43)	0.05 (0.43)
Median	36.60	0.10	36.55	0.10
Min - Max	33.8 - 37.7	-1.5 - 1.2	35.6 - 37.4	-1.0 - 1.2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	31	31	46	46
Mean (SD)	36.29 (0.65)	-0.12 (0.52)	36.61 (0.38)	0.16 (0.41)
Median	36.40	-0.10	36.70	0.10
Min - Max	33.8 - 37.3	-1.4 - 0.9	35.6 - 37.6	-0.5 - 1.2
Cycle 11 Day 15				
PRE PAC INFUSION				
n	34	34	44	44
Mean (SD)	36.40 (0.69)	-0.04 (0.53)	36.44 (0.35)	0.00 (0.39)
Median	36.50	0.00	36.50	0.00
Min - Max	33.8 - 37.5	-1.6 - 0.7	35.3 - 37.4	-0.8 - 1.0
AFTER PAC INFUSION				
n	31	31	42	42
Mean (SD)	36.45 (0.66)	0.04 (0.43)	36.36 (0.81)	-0.09 (0.76)
Median	36.70	0.10	36.50	-0.05
Min - Max	33.8 - 37.2	-1.0 - 0.8	32.1 - 37.3	-4.0 - 0.9
Cycle 12 Day 1				
PRE PAC INFUSION				
n	33	33	57	57
Mean (SD)	36.40 (0.69)	-0.02 (0.54)	36.48 (0.41)	0.04 (0.39)
Median	36.50	0.10	36.50	0.10
Min - Max	33.8 - 37.7	-1.5 - 1.1	35.4 - 37.4	-1.0 - 0.9
AFTER PAC INFUSION				
n	30	30	43	43
Mean (SD)	36.50 (0.70)	0.02 (0.46)	36.51 (0.32)	0.07 (0.30)
Median	36.60	0.10	36.50	0.10
Min - Max	33.8 - 37.3	-1.5 - 0.9	35.6 - 37.4	-0.7 - 0.7
Cycle 12 Day 8				
PRE PAC INFUSION				
n	30	30	42	42
Mean (SD)	36.44 (0.70)	-0.02 (0.50)	36.45 (0.40)	-0.01 (0.41)
Median	36.60	0.10	36.50	0.00
Min - Max	33.7 - 37.5	-1.3 - 1.1	34.9 - 37.0	-1.2 - 1.3
AFTER PAC INFUSION				
n	24	24	40	40
Mean (SD)	36.33 (0.68)	-0.09 (0.39)	36.46 (0.41)	-0.03 (0.41)
Median	36.60	0.00	36.55	0.00
Min - Max	33.9 - 37.0	-0.8 - 0.6	35.2 - 37.2	-0.9 - 0.8
Cycle 12 Day 15				
PRE PAC INFUSION				
n	30	30	43	43
Mean (SD)	36.43 (0.69)	-0.04 (0.54)	36.42 (0.37)	0.00 (0.39)
Median	36.60	0.00	36.40	0.00
Min - Max	33.8 - 37.2	-1.6 - 0.7	35.6 - 37.1	-0.9 - 0.8

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	25	25	40	40
Mean (SD)	36.38 (0.76)	-0.08 (0.55)	36.40 (0.36)	-0.02 (0.38)
Median	36.50	-0.10	36.40	-0.10
Min - Max	33.9 - 37.7	-1.4 - 1.3	35.5 - 37.2	-0.6 - 0.7
Cycle 13 Day 1				
PRE PAC INFUSION				
n	28	28	49	49
Mean (SD)	36.53 (0.60)	0.09 (0.39)	36.34 (0.51)	-0.10 (0.49)
Median	36.60	0.10	36.40	-0.10
Min - Max	33.9 - 37.4	-0.8 - 0.9	34.8 - 37.4	-1.4 - 0.7
AFTER PAC INFUSION				
n	25	25	36	36
Mean (SD)	36.50 (0.73)	0.03 (0.51)	36.46 (0.40)	0.01 (0.37)
Median	36.60	0.10	36.45	0.00
Min - Max	33.9 - 37.6	-1.4 - 1.2	35.8 - 37.6	-0.6 - 0.7
Cycle 13 Day 8				
PRE PAC INFUSION				
n	26	26	36	36
Mean (SD)	36.47 (0.64)	0.00 (0.44)	36.36 (0.47)	-0.09 (0.42)
Median	36.60	0.05	36.40	0.00
Min - Max	33.9 - 37.3	-0.9 - 0.8	35.0 - 37.0	-1.6 - 0.5
AFTER PAC INFUSION				
n	24	24	36	36
Mean (SD)	36.38 (0.65)	-0.08 (0.42)	36.45 (0.41)	-0.01 (0.37)
Median	36.50	-0.05	36.40	0.00
Min - Max	33.9 - 37.2	-0.9 - 0.7	35.7 - 37.3	-0.9 - 1.0
Cycle 13 Day 15				
PRE PAC INFUSION				
n	25	25	35	35
Mean (SD)	36.40 (0.60)	-0.07 (0.42)	36.44 (0.37)	-0.01 (0.38)
Median	36.50	-0.10	36.50	0.00
Min - Max	33.9 - 37.2	-1.1 - 0.7	35.6 - 37.1	-0.9 - 0.7
AFTER PAC INFUSION				
n	23	23	35	35
Mean (SD)	36.40 (0.64)	-0.04 (0.36)	36.48 (0.34)	0.03 (0.35)
Median	36.50	0.00	36.50	0.00
Min - Max	33.9 - 37.3	-0.8 - 0.9	35.7 - 37.3	-0.9 - 0.7
Cycle 14 Day 1				
PRE PAC INFUSION				
n	26	26	42	42
Mean (SD)	36.55 (0.67)	0.09 (0.42)	36.45 (0.47)	0.01 (0.48)
Median	36.60	0.10	36.50	0.05
Min - Max	34.0 - 37.3	-1.1 - 0.8	35.0 - 37.3	-1.2 - 0.9

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	24	24	33	33
Mean (SD)	36.36 (0.69)	-0.08 (0.49)	36.44 (0.42)	0.00 (0.37)
Median	36.50	-0.05	36.40	-0.10
Min - Max	34.0 - 37.4	-1.3 - 0.8	35.8 - 37.5	-0.8 - 0.8
Cycle 14 Day 8				
PRE PAC INFUSION				
n	25	25	32	32
Mean (SD)	36.45 (0.63)	-0.02 (0.38)	36.32 (0.48)	-0.12 (0.49)
Median	36.70	0.10	36.30	0.00
Min - Max	33.9 - 37.1	-1.2 - 0.5	35.0 - 37.3	-1.2 - 0.6
AFTER PAC INFUSION				
n	24	24	30	30
Mean (SD)	36.44 (0.66)	-0.02 (0.46)	36.47 (0.39)	0.02 (0.42)
Median	36.50	0.15	36.45	0.10
Min - Max	34.0 - 37.1	-1.1 - 0.7	35.4 - 37.5	-1.2 - 0.8
Cycle 14 Day 15				
PRE PAC INFUSION				
n	25	25	29	29
Mean (SD)	36.49 (0.65)	0.02 (0.48)	36.39 (0.52)	-0.04 (0.51)
Median	36.60	0.00	36.50	0.00
Min - Max	34.0 - 37.4	-1.2 - 0.9	35.2 - 37.2	-1.3 - 0.9
AFTER PAC INFUSION				
n	23	23	28	28
Mean (SD)	36.52 (0.68)	0.07 (0.47)	36.44 (0.40)	-0.01 (0.43)
Median	36.60	0.10	36.45	0.00
Min - Max	34.0 - 37.2	-1.5 - 0.8	35.5 - 37.2	-1.1 - 0.8
Cycle 15 Day 1				
PRE PAC INFUSION				
n	20	20	35	35
Mean (SD)	36.45 (0.67)	0.04 (0.40)	36.33 (0.49)	-0.09 (0.55)
Median	36.60	0.10	36.40	-0.10
Min - Max	33.9 - 37.0	-1.3 - 0.6	35.3 - 37.1	-1.3 - 0.8
AFTER PAC INFUSION				
n	19	19	25	25
Mean (SD)	36.33 (0.74)	-0.08 (0.61)	36.36 (0.36)	-0.10 (0.39)
Median	36.60	0.10	36.40	-0.10
Min - Max	34.0 - 37.1	-2.3 - 0.4	35.8 - 37.4	-0.8 - 1.0
Cycle 15 Day 8				
PRE PAC INFUSION				
n	18	18	27	27
Mean (SD)	36.48 (0.58)	0.07 (0.25)	36.34 (0.50)	-0.10 (0.52)
Median	36.60	0.10	36.30	-0.10
Min - Max	34.3 - 36.9	-0.4 - 0.5	35.2 - 37.3	-1.4 - 0.9

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	18	18	27	27
Mean (SD)	36.43 (0.60)	0.03 (0.32)	36.43 (0.39)	-0.01 (0.42)
Median	36.60	0.00	36.40	0.00
Min - Max	34.5 - 37.1	-0.4 - 0.7	35.5 - 37.2	-1.1 - 1.0
Cycle 15 Day 15				
PRE PAC INFUSION				
n	19	19	25	25
Mean (SD)	36.42 (0.74)	0.02 (0.51)	36.37 (0.50)	-0.07 (0.52)
Median	36.70	0.10	36.30	-0.20
Min - Max	34.2 - 37.2	-0.9 - 0.7	35.2 - 37.4	-1.0 - 1.2
AFTER PAC INFUSION				
n	19	19	25	25
Mean (SD)	36.37 (0.71)	-0.03 (0.47)	36.52 (0.39)	0.08 (0.45)
Median	36.50	0.00	36.40	0.10
Min - Max	34.1 - 37.4	-1.0 - 1.0	36.0 - 37.5	-0.7 - 1.2
Cycle 16 Day 1				
PRE PAC INFUSION				
n	21	21	32	32
Mean (SD)	36.40 (0.69)	-0.01 (0.47)	36.32 (0.54)	-0.11 (0.53)
Median	36.60	0.10	36.40	-0.10
Min - Max	33.9 - 37.1	-1.0 - 0.7	35.0 - 37.3	-1.6 - 0.8
AFTER PAC INFUSION				
n	20	20	24	24
Mean (SD)	36.32 (0.79)	-0.10 (0.61)	36.36 (0.51)	-0.09 (0.49)
Median	36.60	0.00	36.45	0.00
Min - Max	34.0 - 37.4	-1.4 - 1.0	35.0 - 37.2	-1.2 - 0.8
Cycle 16 Day 8				
PRE PAC INFUSION				
n	20	20	23	23
Mean (SD)	36.49 (0.44)	0.08 (0.38)	36.33 (0.62)	-0.13 (0.59)
Median	36.60	0.05	36.40	-0.10
Min - Max	34.9 - 36.9	-0.6 - 1.1	34.5 - 37.3	-1.6 - 0.9
AFTER PAC INFUSION				
n	19	19	23	23
Mean (SD)	36.31 (0.69)	-0.11 (0.39)	36.36 (0.42)	-0.10 (0.42)
Median	36.50	-0.10	36.40	0.00
Min - Max	33.9 - 36.9	-1.1 - 0.5	35.2 - 37.1	-0.8 - 0.6
Cycle 16 Day 15				
PRE PAC INFUSION				
n	18	18	25	25
Mean (SD)	36.46 (0.72)	0.06 (0.39)	36.38 (0.53)	-0.07 (0.55)
Median	36.60	0.10	36.40	-0.20
Min - Max	33.8 - 37.2	-0.9 - 0.8	34.9 - 37.4	-1.2 - 1.0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	17	17	24	24
Mean (SD)	36.35 (0.71)	-0.06 (0.42)	36.40 (0.39)	-0.07 (0.37)
Median	36.50	0.00	36.45	-0.05
Min - Max	34.0 - 37.2	-1.1 - 0.7	35.5 - 37.1	-0.7 - 0.6
Cycle 17 Day 1				
PRE PAC INFUSION				
n	18	18	31	31
Mean (SD)	36.42 (0.54)	0.02 (0.47)	36.35 (0.54)	-0.07 (0.56)
Median	36.55	0.00	36.30	0.00
Min - Max	34.8 - 37.0	-1.0 - 1.0	35.0 - 37.6	-1.6 - 1.3
AFTER PAC INFUSION				
n	17	17	23	23
Mean (SD)	36.32 (0.74)	-0.08 (0.39)	36.35 (0.46)	-0.07 (0.46)
Median	36.40	0.00	36.50	0.00
Min - Max	33.8 - 37.1	-1.0 - 0.4	35.1 - 37.0	-1.0 - 0.6
Cycle 17 Day 8				
PRE PAC INFUSION				
n	16	16	20	20
Mean (SD)	36.39 (0.75)	0.00 (0.39)	36.44 (0.48)	-0.02 (0.54)
Median	36.50	0.00	36.45	0.00
Min - Max	33.8 - 37.2	-0.8 - 0.8	35.3 - 37.4	-0.9 - 1.2
AFTER PAC INFUSION				
n	16	16	20	20
Mean (SD)	36.35 (0.80)	-0.04 (0.46)	36.41 (0.41)	-0.06 (0.46)
Median	36.55	0.00	36.40	0.00
Min - Max	33.8 - 37.4	-0.7 - 1.0	35.4 - 37.0	-1.2 - 0.5
Cycle 17 Day 15				
PRE PAC INFUSION				
n	17	17	21	21
Mean (SD)	36.42 (0.77)	0.02 (0.52)	36.42 (0.49)	0.00 (0.51)
Median	36.50	0.00	36.40	-0.10
Min - Max	33.8 - 37.3	-1.3 - 0.9	35.4 - 37.4	-1.2 - 1.2
AFTER PAC INFUSION				
n	17	17	22	22
Mean (SD)	36.29 (0.74)	-0.11 (0.43)	36.40 (0.32)	-0.04 (0.40)
Median	36.50	-0.10	36.40	0.00
Min - Max	33.9 - 37.2	-0.8 - 0.8	35.8 - 37.0	-0.7 - 0.8
Cycle 18 Day 1				
PRE PAC INFUSION				
n	16	16	24	24
Mean (SD)	36.31 (0.82)	-0.06 (0.50)	36.37 (0.51)	-0.04 (0.57)
Median	36.55	0.00	36.40	0.00
Min - Max	33.7 - 37.2	-1.0 - 0.7	34.6 - 37.3	-2.0 - 1.0

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	14	14	21	21
Mean (SD)	36.31 (0.88)	-0.09 (0.53)	36.40 (0.51)	-0.04 (0.58)
Median	36.60	0.00	36.60	0.10
Min - Max	33.8 - 37.2	-1.4 - 0.8	34.5 - 36.9	-2.1 - 0.6
Cycle 18 Day 8				
PRE PAC INFUSION				
n	14	14	21	21
Mean (SD)	36.36 (0.81)	0.00 (0.34)	36.41 (0.44)	-0.05 (0.43)
Median	36.60	0.05	36.30	-0.10
Min - Max	33.7 - 37.0	-0.8 - 0.6	35.5 - 37.4	-0.7 - 0.8
AFTER PAC INFUSION				
n	14	14	20	20
Mean (SD)	36.35 (0.93)	-0.01 (0.58)	36.44 (0.28)	-0.04 (0.33)
Median	36.55	0.10	36.40	0.00
Min - Max	33.8 - 37.6	-1.3 - 1.2	36.0 - 36.9	-0.6 - 0.5
Cycle 18 Day 15				
PRE PAC INFUSION				
n	15	15	20	20
Mean (SD)	36.47 (0.83)	0.10 (0.41)	36.45 (0.39)	0.01 (0.46)
Median	36.60	0.10	36.35	-0.05
Min - Max	33.7 - 37.4	-0.8 - 0.7	35.7 - 37.2	-0.6 - 0.9
AFTER PAC INFUSION				
n	15	15	19	19
Mean (SD)	36.39 (0.91)	0.01 (0.60)	36.49 (0.27)	0.03 (0.38)
Median	36.60	0.10	36.40	0.10
Min - Max	33.8 - 37.5	-1.2 - 1.1	36.1 - 37.0	-0.7 - 0.6
Cycle 19 Day 1				
PRE PAC INFUSION				
n	11	11	26	26
Mean (SD)	36.62 (0.29)	0.13 (0.34)	36.40 (0.39)	-0.02 (0.48)
Median	36.60	0.10	36.40	-0.10
Min - Max	36.1 - 37.1	-0.4 - 0.7	35.4 - 37.1	-1.2 - 0.9
AFTER PAC INFUSION				
n	10	10	19	19
Mean (SD)	36.58 (0.45)	0.10 (0.45)	36.43 (0.35)	-0.03 (0.44)
Median	36.65	0.10	36.50	-0.10
Min - Max	35.6 - 37.1	-0.9 - 0.7	35.5 - 37.0	-1.1 - 0.7
Cycle 19 Day 8				
PRE PAC INFUSION				
n	9	9	20	20
Mean (SD)	36.69 (0.51)	0.22 (0.54)	36.43 (0.41)	-0.03 (0.43)
Median	36.70	0.00	36.45	-0.05
Min - Max	36.0 - 37.8	-0.5 - 1.4	35.5 - 37.2	-0.8 - 0.8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	9	9	19	19
Mean (SD)	36.40 (0.74)	-0.07 (0.72)	36.46 (0.28)	0.01 (0.29)
Median	36.50	0.00	36.50	0.00
Min - Max	35.2 - 37.5	-1.3 - 1.1	35.9 - 37.0	-0.7 - 0.5
Cycle 19 Day 15				
PRE PAC INFUSION				
n	10	10	20	20
Mean (SD)	36.51 (0.54)	0.03 (0.56)	36.32 (0.37)	-0.14 (0.41)
Median	36.60	0.05	36.30	-0.10
Min - Max	35.1 - 37.0	-1.4 - 0.6	35.7 - 37.1	-0.9 - 0.7
AFTER PAC INFUSION				
n	9	9	19	19
Mean (SD)	36.56 (0.41)	0.03 (0.44)	36.45 (0.27)	0.00 (0.33)
Median	36.50	-0.10	36.40	-0.10
Min - Max	36.1 - 37.4	-0.4 - 1.0	36.0 - 37.0	-0.6 - 0.7
Cycle 20 Day 1				
PRE PAC INFUSION				
n	11	11	23	23
Mean (SD)	36.60 (0.38)	0.11 (0.42)	36.31 (0.46)	-0.11 (0.43)
Median	36.60	0.10	36.40	-0.10
Min - Max	35.7 - 37.2	-0.8 - 0.8	35.0 - 36.9	-1.1 - 0.5
AFTER PAC INFUSION				
n	10	10	17	17
Mean (SD)	36.45 (0.50)	-0.03 (0.53)	36.40 (0.35)	-0.04 (0.44)
Median	36.65	0.00	36.40	-0.10
Min - Max	35.5 - 36.9	-1.0 - 0.6	35.6 - 37.1	-1.0 - 0.8
Cycle 20 Day 8				
PRE PAC INFUSION				
n	9	9	16	16
Mean (SD)	36.58 (0.38)	0.07 (0.37)	36.33 (0.58)	-0.13 (0.57)
Median	36.50	0.00	36.35	-0.20
Min - Max	35.9 - 37.1	-0.6 - 0.6	35.0 - 37.6	-1.1 - 0.8
AFTER PAC INFUSION				
n	9	9	16	16
Mean (SD)	36.62 (0.53)	0.11 (0.51)	36.44 (0.39)	-0.03 (0.40)
Median	36.70	0.00	36.45	-0.10
Min - Max	35.6 - 37.3	-0.9 - 0.9	35.5 - 37.1	-0.6 - 0.7
Cycle 20 Day 15				
PRE PAC INFUSION				
n	10	10	16	16
Mean (SD)	36.52 (0.41)	0.04 (0.39)	36.38 (0.45)	-0.09 (0.53)
Median	36.50	0.00	36.25	-0.15
Min - Max	35.8 - 37.0	-0.7 - 0.6	35.6 - 37.3	-1.0 - 1.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	10	10	16	16
Mean (SD)	36.39 (0.59)	-0.09 (0.53)	36.38 (0.31)	-0.09 (0.36)
Median	36.60	0.00	36.40	-0.05
Min - Max	35.6 - 37.2	-0.9 - 0.8	35.9 - 36.9	-0.7 - 0.6
Cycle 21 Day 1				
PRE PAC INFUSION				
n	9	9	20	20
Mean (SD)	36.49 (0.44)	0.00 (0.46)	36.38 (0.39)	-0.08 (0.51)
Median	36.60	0.20	36.35	0.00
Min - Max	35.4 - 37.0	-1.1 - 0.4	35.3 - 37.2	-1.3 - 1.0
AFTER PAC INFUSION				
n	6	6	15	15
Mean (SD)	36.25 (0.33)	-0.23 (0.19)	36.39 (0.28)	-0.07 (0.41)
Median	36.25	-0.20	36.40	-0.10
Min - Max	35.9 - 36.6	-0.6 - -0.1	36.0 - 36.8	-0.7 - 0.8
Cycle 21 Day 8				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	36.33 (0.48)	-0.16 (0.43)	36.39 (0.28)	-0.09 (0.40)
Median	36.50	0.00	36.35	-0.05
Min - Max	35.5 - 36.8	-0.8 - 0.3	35.8 - 37.0	-0.8 - 0.5
AFTER PAC INFUSION				
n	9	9	14	14
Mean (SD)	36.54 (0.21)	0.06 (0.31)	36.35 (0.38)	-0.13 (0.44)
Median	36.50	0.10	36.35	-0.10
Min - Max	36.3 - 37.0	-0.4 - 0.6	35.7 - 36.9	-0.8 - 0.6
Cycle 21 Day 15				
PRE PAC INFUSION				
n	9	9	15	15
Mean (SD)	36.48 (0.50)	-0.04 (0.42)	36.37 (0.29)	-0.09 (0.41)
Median	36.60	0.10	36.40	0.00
Min - Max	35.6 - 37.2	-0.6 - 0.5	36.0 - 37.1	-0.8 - 0.5
AFTER PAC INFUSION				
n	8	8	15	15
Mean (SD)	36.60 (0.48)	0.06 (0.48)	36.37 (0.27)	-0.08 (0.35)
Median	36.55	0.05	36.40	0.00
Min - Max	35.9 - 37.4	-0.6 - 1.0	36.0 - 36.9	-0.8 - 0.4
Cycle 22 Day 1				
PRE PAC INFUSION				
n	10	10	20	20
Mean (SD)	36.42 (0.49)	-0.06 (0.50)	36.41 (0.42)	-0.04 (0.48)
Median	36.60	0.00	36.50	0.05
Min - Max	35.2 - 37.0	-1.3 - 0.6	35.4 - 37.0	-1.2 - 0.7

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	7	7	15	15
Mean (SD)	36.23 (0.53)	-0.26 (0.49)	36.49 (0.32)	0.03 (0.44)
Median	36.40	-0.30	36.50	0.00
Min - Max	35.6 - 37.0	-0.8 - 0.5	35.6 - 37.0	-1.0 - 0.7
Cycle 22 Day 8				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	36.53 (0.30)	0.04 (0.28)	36.43 (0.26)	-0.05 (0.35)
Median	36.60	0.10	36.40	-0.05
Min - Max	36.0 - 36.9	-0.5 - 0.5	36.1 - 37.0	-0.9 - 0.4
AFTER PAC INFUSION				
n	9	9	14	14
Mean (SD)	36.26 (0.69)	-0.23 (0.68)	36.41 (0.31)	-0.07 (0.36)
Median	36.50	-0.10	36.40	0.00
Min - Max	35.0 - 37.0	-1.5 - 0.5	35.9 - 37.1	-0.7 - 0.4
Cycle 22 Day 15				
PRE PAC INFUSION				
n	7	7	14	14
Mean (SD)	36.44 (0.24)	-0.09 (0.15)	36.26 (0.25)	-0.21 (0.38)
Median	36.50	0.00	36.20	-0.25
Min - Max	36.0 - 36.8	-0.3 - 0.1	35.9 - 36.8	-0.9 - 0.4
AFTER PAC INFUSION				
n	7	7	14	14
Mean (SD)	36.26 (0.61)	-0.27 (0.52)	36.48 (0.34)	0.01 (0.32)
Median	36.40	-0.30	36.45	0.05
Min - Max	35.4 - 37.0	-0.8 - 0.6	36.1 - 37.3	-0.5 - 0.5
Cycle 23 Day 1				
PRE PAC INFUSION				
n	9	9	19	19
Mean (SD)	36.33 (0.45)	-0.13 (0.42)	36.35 (0.39)	-0.07 (0.46)
Median	36.50	0.00	36.40	-0.10
Min - Max	35.4 - 36.8	-1.1 - 0.3	35.4 - 37.2	-1.2 - 0.7
AFTER PAC INFUSION				
n	7	7	13	13
Mean (SD)	36.23 (0.43)	-0.26 (0.44)	36.61 (0.28)	0.16 (0.46)
Median	36.40	-0.20	36.60	0.10
Min - Max	35.7 - 36.8	-0.8 - 0.4	36.2 - 37.1	-0.5 - 0.8
Cycle 23 Day 8				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	36.39 (0.49)	-0.09 (0.54)	36.47 (0.44)	0.05 (0.42)
Median	36.50	-0.10	36.50	0.10
Min - Max	35.3 - 36.9	-1.2 - 0.5	35.7 - 37.3	-0.8 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	36.33 (0.45)	-0.15 (0.45)	36.48 (0.50)	0.06 (0.49)
Median	36.30	-0.15	36.30	0.20
Min - Max	35.8 - 37.1	-0.7 - 0.7	35.8 - 37.3	-0.5 - 0.9
Cycle 23 Day 15				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	36.48 (0.30)	0.00 (0.33)	36.64 (0.31)	0.18 (0.36)
Median	36.50	0.05	36.70	0.20
Min - Max	35.9 - 36.8	-0.6 - 0.4	36.2 - 37.2	-0.3 - 0.7
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	36.38 (0.47)	-0.10 (0.40)	36.59 (0.33)	0.14 (0.30)
Median	36.30	-0.10	36.50	0.20
Min - Max	35.8 - 37.0	-0.7 - 0.6	36.2 - 37.1	-0.4 - 0.6
Cycle 24 Day 1				
PRE PAC INFUSION				
n	9	9	17	17
Mean (SD)	36.50 (0.58)	0.03 (0.61)	36.38 (0.39)	-0.05 (0.42)
Median	36.50	-0.10	36.40	0.00
Min - Max	35.6 - 37.7	-0.9 - 1.3	35.8 - 37.2	-1.0 - 0.5
AFTER PAC INFUSION				
n	7	7	12	12
Mean (SD)	36.24 (0.49)	-0.24 (0.48)	36.52 (0.29)	0.06 (0.38)
Median	36.30	-0.20	36.40	0.10
Min - Max	35.6 - 36.9	-0.9 - 0.3	36.2 - 37.1	-0.7 - 0.6
Cycle 24 Day 8				
PRE PAC INFUSION				
n	8	8	11	11
Mean (SD)	36.53 (0.51)	0.05 (0.56)	36.56 (0.37)	0.07 (0.37)
Median	36.50	-0.15	36.50	0.10
Min - Max	35.9 - 37.6	-0.5 - 1.2	36.1 - 37.3	-0.5 - 0.5
AFTER PAC INFUSION				
n	8	8	11	11
Mean (SD)	36.61 (0.45)	0.14 (0.40)	36.55 (0.49)	0.06 (0.53)
Median	36.55	0.05	36.40	0.10
Min - Max	36.1 - 37.4	-0.4 - 1.0	36.0 - 37.7	-0.6 - 0.9
Cycle 24 Day 15				
PRE PAC INFUSION				
n	8	8	12	12
Mean (SD)	36.46 (0.54)	-0.01 (0.59)	36.36 (0.36)	-0.10 (0.47)
Median	36.60	0.10	36.20	-0.10
Min - Max	35.3 - 37.0	-1.2 - 0.6	35.9 - 37.0	-1.0 - 0.8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	8	8	12	12
Mean (SD)	36.38 (0.59)	-0.10 (0.60)	36.48 (0.36)	0.03 (0.53)
Median	36.30	-0.05	36.40	0.05
Min - Max	35.2 - 37.2	-1.3 - 0.8	36.0 - 37.0	-0.9 - 0.8
Cycle 25 Day 1				
PRE PAC INFUSION				
n	8	8	14	14
Mean (SD)	36.53 (0.51)	0.06 (0.49)	36.39 (0.26)	0.02 (0.31)
Median	36.60	0.20	36.40	-0.05
Min - Max	35.5 - 37.2	-1.0 - 0.5	36.0 - 37.1	-0.4 - 0.6
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	36.41 (0.83)	-0.06 (0.70)	36.41 (0.40)	0.07 (0.34)
Median	36.60	-0.20	36.30	0.10
Min - Max	35.5 - 37.5	-0.9 - 1.1	36.0 - 37.4	-0.3 - 0.6
Cycle 25 Day 8				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	36.56 (0.37)	0.09 (0.51)	36.42 (0.40)	0.03 (0.47)
Median	36.60	0.10	36.40	-0.10
Min - Max	35.8 - 37.0	-0.7 - 0.6	35.9 - 37.0	-0.6 - 0.8
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	36.54 (0.53)	0.07 (0.48)	36.39 (0.28)	0.00 (0.32)
Median	36.50	0.00	36.30	0.00
Min - Max	36.0 - 37.4	-0.5 - 1.0	36.0 - 36.8	-0.5 - 0.5
Cycle 25 Day 15				
PRE PAC INFUSION				
n	7	7	10	10
Mean (SD)	36.57 (0.47)	0.10 (0.46)	36.47 (0.29)	0.11 (0.31)
Median	36.60	0.00	36.50	0.15
Min - Max	35.9 - 37.3	-0.6 - 0.9	36.1 - 37.1	-0.3 - 0.6
AFTER PAC INFUSION				
n	7	7	10	10
Mean (SD)	36.64 (0.57)	0.17 (0.64)	36.48 (0.35)	0.12 (0.36)
Median	36.60	0.10	36.45	0.10
Min - Max	35.6 - 37.5	-0.9 - 1.1	36.0 - 37.1	-0.5 - 0.6
Cycle 26 Day 1				
PRE PAC INFUSION				
n	8	8	14	14
Mean (SD)	36.78 (0.35)	0.31 (0.33)	36.24 (0.47)	-0.10 (0.57)
Median	36.85	0.35	36.20	-0.05
Min - Max	36.1 - 37.1	-0.2 - 0.7	35.0 - 36.9	-1.6 - 0.7

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	36.67 (0.39)	0.20 (0.36)	36.48 (0.37)	0.14 (0.37)
Median	36.70	0.20	36.30	0.20
Min - Max	36.1 - 37.3	-0.3 - 0.9	36.2 - 37.2	-0.4 - 0.6
Cycle 26 Day 8				
PRE PAC INFUSION				
n	7	7	7	7
Mean (SD)	36.63 (0.55)	0.16 (0.57)	36.44 (0.37)	0.10 (0.39)
Median	36.70	0.20	36.40	0.10
Min - Max	35.7 - 37.4	-0.8 - 1.0	36.0 - 36.9	-0.5 - 0.7
AFTER PAC INFUSION				
n	7	7	7	7
Mean (SD)	36.51 (0.56)	0.04 (0.45)	36.50 (0.37)	0.16 (0.45)
Median	36.60	-0.20	36.50	0.00
Min - Max	35.9 - 37.2	-0.5 - 0.8	36.0 - 37.2	-0.3 - 1.0
Cycle 26 Day 15				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	36.47 (0.38)	0.00 (0.43)	36.41 (0.34)	0.08 (0.38)
Median	36.60	0.00	36.50	0.10
Min - Max	35.8 - 37.0	-0.7 - 0.6	35.8 - 36.9	-0.7 - 0.5
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	36.37 (0.58)	-0.10 (0.50)	36.43 (0.32)	0.10 (0.37)
Median	36.60	0.00	36.40	0.00
Min - Max	35.6 - 37.1	-0.8 - 0.7	36.0 - 36.9	-0.4 - 0.6
Cycle 27 Day 1				
PRE PAC INFUSION				
n	9	9	14	14
Mean (SD)	36.49 (0.33)	0.01 (0.31)	36.39 (0.35)	0.04 (0.45)
Median	36.50	0.10	36.30	0.05
Min - Max	35.9 - 36.9	-0.6 - 0.5	35.8 - 37.1	-0.8 - 0.9
AFTER PAC INFUSION				
n	8	8	8	8
Mean (SD)	36.58 (0.61)	0.09 (0.57)	36.40 (0.33)	0.05 (0.34)
Median	36.60	0.20	36.25	0.10
Min - Max	35.6 - 37.4	-0.9 - 1.0	36.1 - 37.1	-0.4 - 0.6
Cycle 27 Day 8				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	36.50 (0.21)	-0.02 (0.21)	36.49 (0.38)	0.13 (0.48)
Median	36.55	0.00	36.40	0.05
Min - Max	36.2 - 36.7	-0.3 - 0.2	36.1 - 37.2	-0.5 - 1.0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	6	6	8	8
Mean (SD)	36.55 (0.58)	0.03 (0.60)	36.65 (0.32)	0.29 (0.29)
Median	36.60	0.05	36.70	0.35
Min - Max	35.7 - 37.4	-0.8 - 1.0	36.2 - 37.1	-0.3 - 0.7
Cycle 27 Day 15				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	36.61 (0.34)	0.09 (0.24)	36.46 (0.48)	0.12 (0.47)
Median	36.70	0.10	36.30	0.10
Min - Max	35.9 - 36.9	-0.2 - 0.5	36.0 - 37.2	-0.5 - 1.0
AFTER PAC INFUSION				
n	7	7	9	9
Mean (SD)	36.71 (0.32)	0.19 (0.41)	36.53 (0.41)	0.20 (0.32)
Median	36.70	0.20	36.50	0.30
Min - Max	36.1 - 37.1	-0.4 - 0.7	36.0 - 37.3	-0.4 - 0.7
Cycle 28 Day 1				
PRE PAC INFUSION				
n	7	7	13	13
Mean (SD)	36.67 (0.23)	0.17 (0.27)	36.29 (0.27)	-0.08 (0.32)
Median	36.60	0.20	36.30	-0.20
Min - Max	36.4 - 37.0	-0.3 - 0.5	35.7 - 36.7	-0.6 - 0.5
AFTER PAC INFUSION				
n	6	6	6	6
Mean (SD)	36.55 (0.56)	0.03 (0.50)	36.38 (0.47)	0.02 (0.37)
Median	36.60	0.00	36.35	0.05
Min - Max	35.9 - 37.2	-0.6 - 0.8	35.8 - 37.2	-0.5 - 0.4
Cycle 28 Day 8				
PRE PAC INFUSION				
n	6	6	7	7
Mean (SD)	36.50 (0.66)	-0.02 (0.75)	36.57 (0.34)	0.16 (0.49)
Median	36.70	0.05	36.50	0.00
Min - Max	35.2 - 37.0	-1.3 - 0.8	36.3 - 37.3	-0.3 - 1.1
AFTER PAC INFUSION				
n	6	6	7	7
Mean (SD)	36.65 (0.43)	0.13 (0.48)	36.66 (0.30)	0.24 (0.28)
Median	36.55	0.05	36.60	0.40
Min - Max	36.1 - 37.4	-0.3 - 1.0	36.3 - 37.2	-0.3 - 0.5
Cycle 28 Day 15				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	36.50 (0.46)	-0.02 (0.38)	36.54 (0.33)	0.16 (0.47)
Median	36.60	0.00	36.45	0.10
Min - Max	35.9 - 37.0	-0.5 - 0.5	36.1 - 37.2	-0.4 - 1.0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	6	6	8	8
Mean (SD)	36.65 (0.57)	0.13 (0.52)	36.49 (0.24)	0.11 (0.30)
Median	36.60	0.05	36.45	0.25
Min - Max	36.0 - 37.4	-0.4 - 1.0	36.2 - 37.0	-0.3 - 0.5
Cycle 29 Day 1				
PRE PAC INFUSION				
n	7	7	11	11
Mean (SD)	36.67 (0.30)	0.20 (0.30)	36.38 (0.31)	-0.04 (0.40)
Median	36.70	0.10	36.50	0.10
Min - Max	36.1 - 37.0	-0.2 - 0.6	35.6 - 36.6	-1.0 - 0.4
AFTER PAC INFUSION				
n	6	6	6	6
Mean (SD)	36.58 (0.43)	0.10 (0.34)	36.45 (0.48)	-0.02 (0.42)
Median	36.70	0.05	36.40	-0.10
Min - Max	35.8 - 37.1	-0.3 - 0.7	35.9 - 37.1	-0.6 - 0.6
Cycle 29 Day 8				
PRE PAC INFUSION				
n	6	6	5	5
Mean (SD)	36.68 (0.46)	0.20 (0.57)	36.42 (0.18)	-0.02 (0.19)
Median	36.70	0.10	36.50	0.00
Min - Max	35.9 - 37.3	-0.6 - 0.9	36.1 - 36.5	-0.3 - 0.2
AFTER PAC INFUSION				
n	6	6	5	5
Mean (SD)	36.45 (0.55)	-0.03 (0.50)	36.40 (0.29)	-0.04 (0.38)
Median	36.65	0.10	36.30	-0.20
Min - Max	35.5 - 36.9	-1.0 - 0.5	36.1 - 36.8	-0.4 - 0.5
Cycle 29 Day 15				
PRE PAC INFUSION				
n	6	6	7	7
Mean (SD)	36.63 (0.46)	0.15 (0.52)	36.54 (0.30)	0.14 (0.37)
Median	36.55	0.10	36.50	0.20
Min - Max	36.2 - 37.5	-0.3 - 1.1	36.2 - 37.0	-0.3 - 0.7
AFTER PAC INFUSION				
n	6	6	7	7
Mean (SD)	36.58 (0.31)	0.10 (0.32)	36.41 (0.25)	0.01 (0.35)
Median	36.70	0.15	36.40	0.00
Min - Max	36.0 - 36.9	-0.5 - 0.4	36.0 - 36.8	-0.5 - 0.5
Cycle 30 Day 1				
PRE PAC INFUSION				
n	7	7	12	12
Mean (SD)	36.51 (0.47)	0.04 (0.42)	36.34 (0.51)	-0.04 (0.60)
Median	36.60	0.10	36.40	-0.05
Min - Max	35.8 - 36.9	-0.7 - 0.5	35.0 - 37.0	-1.6 - 0.8

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	7	7
Mean (SD)	36.52 (0.67)	0.10 (0.67)	36.46 (0.40)	0.06 (0.42)
Median	36.70	0.10	36.60	0.10
Min - Max	35.6 - 37.4	-0.9 - 1.0	35.8 - 36.9	-0.4 - 0.7
Cycle 30 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	36.46 (0.50)	0.04 (0.55)	36.30 (0.20)	-0.12 (0.33)
Median	36.60	0.10	36.40	-0.10
Min - Max	35.6 - 36.9	-0.9 - 0.5	36.0 - 36.5	-0.5 - 0.4
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	36.64 (0.63)	0.22 (0.70)	36.34 (0.51)	-0.08 (0.66)
Median	36.80	0.20	36.40	-0.30
Min - Max	35.6 - 37.3	-0.9 - 0.9	35.6 - 37.0	-0.9 - 0.7
Cycle 30 Day 15				
PRE PAC INFUSION				
n	4	4	7	7
Mean (SD)	36.55 (0.58)	0.15 (0.57)	36.33 (0.32)	-0.07 (0.50)
Median	36.45	0.10	36.20	-0.20
Min - Max	36.0 - 37.3	-0.5 - 0.9	36.0 - 36.8	-0.6 - 0.8
AFTER PAC INFUSION				
n	4	4	7	7
Mean (SD)	36.38 (0.61)	-0.03 (0.63)	36.36 (0.33)	-0.04 (0.56)
Median	36.45	0.10	36.40	-0.20
Min - Max	35.6 - 37.0	-0.9 - 0.6	35.9 - 36.8	-0.8 - 0.7
Cycle 31 Day 1				
PRE PAC INFUSION				
n	6	6	12	12
Mean (SD)	36.62 (0.54)	0.15 (0.54)	36.16 (0.49)	-0.23 (0.57)
Median	36.75	0.10	36.25	-0.10
Min - Max	35.8 - 37.3	-0.7 - 0.9	35.1 - 36.9	-1.5 - 0.5
AFTER PAC INFUSION				
n	4	4	6	6
Mean (SD)	36.50 (0.62)	0.10 (0.62)	36.48 (0.42)	0.12 (0.56)
Median	36.50	0.15	36.35	0.00
Min - Max	35.8 - 37.2	-0.7 - 0.8	36.1 - 37.3	-0.4 - 1.0
Cycle 31 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	36.62 (0.29)	0.20 (0.39)	36.30 (0.33)	-0.12 (0.61)
Median	36.60	0.10	36.20	-0.30
Min - Max	36.2 - 37.0	-0.3 - 0.6	36.0 - 36.7	-0.8 - 0.7

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	36.44 (0.53)	0.02 (0.56)	36.68 (0.26)	0.26 (0.46)
Median	36.60	0.20	36.60	0.10
Min - Max	35.6 - 37.0	-0.9 - 0.6	36.4 - 37.1	-0.2 - 0.8
Cycle 31 Day 15				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	36.60 (0.29)	0.20 (0.20)	36.30 (0.28)	-0.07 (0.46)
Median	36.65	0.10	36.40	-0.15
Min - Max	36.2 - 36.9	0.1 - 0.5	35.8 - 36.5	-0.7 - 0.5
AFTER PAC INFUSION				
n	4	4	6	6
Mean (SD)	36.80 (0.50)	0.40 (0.48)	36.35 (0.34)	-0.02 (0.44)
Median	36.65	0.25	36.35	-0.25
Min - Max	36.4 - 37.5	0.0 - 1.1	35.9 - 36.8	-0.4 - 0.6
Cycle 32 Day 1				
PRE PAC INFUSION				
n	7	7	11	11
Mean (SD)	36.67 (0.42)	0.20 (0.41)	36.22 (0.48)	-0.15 (0.59)
Median	36.60	0.10	36.40	0.00
Min - Max	36.2 - 37.4	-0.3 - 1.0	35.0 - 36.8	-1.6 - 0.5
AFTER PAC INFUSION				
n	5	5	6	6
Mean (SD)	36.68 (0.36)	0.26 (0.31)	36.35 (0.08)	-0.02 (0.35)
Median	36.70	0.20	36.40	0.00
Min - Max	36.2 - 37.2	0.0 - 0.8	36.2 - 36.4	-0.5 - 0.4
Cycle 32 Day 8				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	36.42 (0.74)	0.00 (0.63)	36.38 (0.49)	-0.04 (0.55)
Median	36.60	0.00	36.50	0.10
Min - Max	35.3 - 37.3	-0.8 - 0.9	35.6 - 36.9	-0.9 - 0.5
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	36.56 (0.45)	0.14 (0.47)	36.22 (0.28)	-0.20 (0.40)
Median	36.60	0.20	36.20	-0.30
Min - Max	36.0 - 37.2	-0.5 - 0.8	35.9 - 36.5	-0.5 - 0.5
Cycle 32 Day 15				
PRE PAC INFUSION				
n	4	4	5	5
Mean (SD)	36.25 (0.97)	-0.13 (1.00)	36.28 (0.22)	-0.06 (0.46)
Median	36.35	0.05	36.30	0.10
Min - Max	35.0 - 37.3	-1.5 - 0.9	36.0 - 36.6	-0.8 - 0.3

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	4	4	5	5
Mean (SD)	36.45 (0.79)	0.08 (0.88)	36.44 (0.47)	0.10 (0.60)
Median	36.70	0.40	36.30	-0.20
Min - Max	35.3 - 37.1	-1.2 - 0.7	35.9 - 37.1	-0.5 - 0.8
Cycle 33 Day 1				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	36.56 (0.49)	0.09 (0.51)	36.34 (0.34)	0.00 (0.28)
Median	36.70	0.20	36.40	0.00
Min - Max	35.6 - 37.1	-0.9 - 0.7	35.6 - 36.7	-0.6 - 0.4
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	36.32 (0.64)	-0.10 (0.69)	36.38 (0.49)	0.00 (0.42)
Median	36.50	0.10	36.20	-0.30
Min - Max	35.2 - 36.8	-1.3 - 0.4	35.8 - 37.1	-0.3 - 0.6
Cycle 33 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.35 (0.97)	-0.05 (0.99)	36.45 (0.26)	0.00 (0.54)
Median	36.45	0.10	36.40	-0.25
Min - Max	35.1 - 37.4	-1.4 - 1.0	36.2 - 36.8	-0.3 - 0.8
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.35 (0.83)	-0.05 (0.82)	36.43 (0.26)	-0.03 (0.56)
Median	36.25	-0.10	36.40	-0.10
Min - Max	35.5 - 37.4	-1.0 - 1.0	36.2 - 36.7	-0.6 - 0.7
Cycle 33 Day 15				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	36.44 (0.69)	0.02 (0.68)	36.24 (0.28)	-0.14 (0.47)
Median	36.40	-0.10	36.30	-0.30
Min - Max	35.7 - 37.5	-0.8 - 1.1	35.9 - 36.5	-0.6 - 0.5
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	36.50 (0.55)	0.08 (0.54)	36.30 (0.12)	-0.08 (0.41)
Median	36.70	0.10	36.30	-0.30
Min - Max	35.8 - 37.2	-0.7 - 0.8	36.2 - 36.5	-0.5 - 0.5
Cycle 34 Day 1				
PRE PAC INFUSION				
n	7	7	9	9
Mean (SD)	36.63 (0.55)	0.16 (0.57)	36.26 (0.45)	-0.09 (0.45)
Median	36.60	0.20	36.30	-0.20
Min - Max	35.6 - 37.4	-0.9 - 1.0	35.5 - 36.8	-0.7 - 0.8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	36.38 (0.48)	-0.04 (0.50)	36.53 (0.44)	0.18 (0.46)
Median	36.50	0.10	36.50	0.10
Min - Max	35.6 - 36.8	-0.9 - 0.4	36.1 - 37.0	-0.3 - 0.8
Cycle 34 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.50 (0.55)	0.10 (0.48)	36.40 (0.36)	-0.05 (0.54)
Median	36.45	-0.10	36.50	-0.15
Min - Max	35.9 - 37.2	-0.2 - 0.8	35.9 - 36.7	-0.6 - 0.7
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.33 (0.80)	-0.08 (0.66)	36.53 (0.31)	0.08 (0.46)
Median	36.45	-0.10	36.60	0.00
Min - Max	35.3 - 37.1	-0.8 - 0.7	36.1 - 36.8	-0.4 - 0.7
Cycle 34 Day 15				
PRE PAC INFUSION				
n	5	5	5	5
Mean (SD)	36.56 (0.64)	0.14 (0.72)	36.50 (0.26)	0.12 (0.34)
Median	36.60	0.00	36.40	0.30
Min - Max	35.6 - 37.4	-0.9 - 1.0	36.2 - 36.9	-0.3 - 0.4
AFTER PAC INFUSION				
n	5	5	5	5
Mean (SD)	36.60 (0.46)	0.18 (0.47)	36.44 (0.32)	0.06 (0.42)
Median	36.60	0.20	36.40	0.10
Min - Max	36.1 - 37.3	-0.4 - 0.9	36.1 - 36.9	-0.4 - 0.6
Cycle 35 Day 1				
PRE PAC INFUSION				
n	7	7	8	8
Mean (SD)	36.54 (0.53)	0.07 (0.55)	36.38 (0.36)	0.00 (0.38)
Median	36.60	0.10	36.45	0.05
Min - Max	35.5 - 37.0	-1.0 - 0.6	35.7 - 36.8	-0.5 - 0.6
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	36.46 (0.89)	0.04 (0.93)	36.48 (0.55)	0.03 (0.56)
Median	36.60	0.10	36.35	0.00
Min - Max	35.1 - 37.6	-1.4 - 1.2	36.0 - 37.2	-0.5 - 0.6
Cycle 35 Day 8				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	36.70 (0.47)	0.28 (0.56)	36.20 (0.27)	-0.25 (0.58)
Median	36.70	0.10	36.10	-0.45
Min - Max	36.1 - 37.4	-0.4 - 1.0	36.0 - 36.6	-0.7 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	36.60 (0.34)	0.18 (0.30)	36.38 (0.22)	-0.08 (0.54)
Median	36.60	0.10	36.40	-0.10
Min - Max	36.2 - 37.1	-0.1 - 0.7	36.1 - 36.6	-0.7 - 0.6
Cycle 35 Day 15				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	36.42 (0.45)	0.00 (0.48)	36.65 (0.33)	0.20 (0.22)
Median	36.60	0.10	36.55	0.25
Min - Max	35.7 - 36.9	-0.8 - 0.5	36.4 - 37.1	-0.1 - 0.4
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	36.54 (0.61)	0.12 (0.69)	36.45 (0.49)	0.00 (0.45)
Median	36.70	0.10	36.40	0.10
Min - Max	35.5 - 37.1	-1.0 - 0.7	35.9 - 37.1	-0.6 - 0.4
Cycle 36 Day 1				
PRE PAC INFUSION				
n	7	7	8	8
Mean (SD)	36.56 (0.50)	0.09 (0.51)	36.43 (0.30)	0.05 (0.30)
Median	36.60	0.10	36.40	0.05
Min - Max	35.7 - 37.2	-0.8 - 0.8	36.0 - 36.9	-0.5 - 0.4
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	36.54 (0.70)	0.12 (0.72)	36.68 (0.44)	0.23 (0.36)
Median	36.70	0.20	36.70	0.35
Min - Max	35.5 - 37.4	-1.0 - 1.0	36.2 - 37.1	-0.3 - 0.5
Cycle 36 Day 8				
PRE PAC INFUSION				
n	5	5	4	4
Mean (SD)	36.52 (0.55)	0.10 (0.62)	36.43 (0.57)	-0.03 (0.67)
Median	36.60	0.10	36.45	-0.10
Min - Max	35.6 - 37.1	-0.9 - 0.7	35.8 - 37.0	-0.7 - 0.8
AFTER PAC INFUSION				
n	5	5	4	4
Mean (SD)	36.32 (0.81)	-0.10 (0.83)	36.73 (0.33)	0.28 (0.41)
Median	36.50	0.10	36.75	0.25
Min - Max	35.0 - 37.1	-1.5 - 0.7	36.3 - 37.1	-0.2 - 0.8
Cycle 36 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.48 (0.80)	0.08 (0.82)	36.83 (0.26)	0.38 (0.26)
Median	36.40	0.05	36.80	0.40
Min - Max	35.6 - 37.5	-0.9 - 1.1	36.6 - 37.1	0.1 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.43 (0.85)	0.03 (0.83)	36.68 (0.26)	0.23 (0.28)
Median	36.30	-0.05	36.70	0.25
Min - Max	35.6 - 37.5	-0.9 - 1.1	36.4 - 36.9	-0.1 - 0.5
Cycle 37 Day 1				
PRE PAC INFUSION				
n	6	6	8	8
Mean (SD)	36.55 (0.48)	0.02 (0.49)	36.43 (0.18)	0.05 (0.38)
Median	36.75	0.05	36.40	0.05
Min - Max	35.7 - 36.9	-0.8 - 0.5	36.1 - 36.7	-0.7 - 0.4
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.50 (0.65)	0.00 (0.68)	36.55 (0.24)	0.10 (0.26)
Median	36.45	-0.10	36.55	0.10
Min - Max	35.8 - 37.3	-0.7 - 0.9	36.3 - 36.8	-0.2 - 0.4
Cycle 37 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.58 (0.39)	0.08 (0.43)	36.60 (0.33)	0.15 (0.37)
Median	36.50	-0.05	36.60	0.15
Min - Max	36.2 - 37.1	-0.3 - 0.7	36.2 - 37.0	-0.3 - 0.6
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.68 (0.82)	0.18 (0.87)	36.55 (0.45)	0.10 (0.51)
Median	36.65	0.10	36.70	0.20
Min - Max	35.7 - 37.7	-0.8 - 1.3	35.9 - 36.9	-0.6 - 0.6
Cycle 37 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.45 (0.45)	-0.05 (0.47)	36.48 (0.54)	0.03 (0.67)
Median	36.60	0.05	36.40	0.00
Min - Max	35.8 - 36.8	-0.7 - 0.4	35.9 - 37.2	-0.6 - 0.7
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.45 (0.81)	-0.05 (0.83)	36.60 (0.26)	0.15 (0.35)
Median	36.65	0.10	36.60	0.15
Min - Max	35.3 - 37.2	-1.2 - 0.8	36.3 - 36.9	-0.2 - 0.5
Cycle 38 Day 1				
PRE PAC INFUSION				
n	5	5	8	8
Mean (SD)	36.74 (0.09)	0.22 (0.22)	36.63 (0.37)	0.25 (0.28)
Median	36.70	0.20	36.60	0.25
Min - Max	36.7 - 36.9	-0.1 - 0.5	36.0 - 37.1	-0.2 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	36.93 (0.42)	0.47 (0.47)	36.58 (0.28)	0.13 (0.32)
Median	36.80	0.30	36.55	0.15
Min - Max	36.6 - 37.4	0.1 - 1.0	36.3 - 36.9	-0.2 - 0.4
Cycle 38 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.33 (0.54)	-0.18 (0.57)	36.30 (0.20)	-0.15 (0.40)
Median	36.40	-0.15	36.40	-0.25
Min - Max	35.6 - 36.9	-0.9 - 0.5	36.0 - 36.4	-0.5 - 0.4
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.38 (0.99)	-0.13 (1.02)	36.65 (0.34)	0.20 (0.37)
Median	36.45	-0.10	36.70	0.25
Min - Max	35.1 - 37.5	-1.4 - 1.1	36.2 - 37.0	-0.3 - 0.6
Cycle 38 Day 15				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.33 (0.90)	-0.18 (0.91)	36.60 (0.08)	0.15 (0.25)
Median	36.65	0.10	36.60	0.10
Min - Max	35.0 - 37.0	-1.5 - 0.6	36.5 - 36.7	-0.1 - 0.5
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.35 (0.70)	-0.15 (0.71)	36.50 (0.24)	0.05 (0.33)
Median	36.50	-0.05	36.50	0.00
Min - Max	35.4 - 37.0	-1.1 - 0.6	36.2 - 36.8	-0.3 - 0.5
Cycle 39 Day 1				
PRE PAC INFUSION				
n	5	5	8	8
Mean (SD)	36.58 (0.38)	0.10 (0.43)	36.24 (0.47)	-0.14 (0.43)
Median	36.60	0.00	36.40	-0.05
Min - Max	36.2 - 37.0	-0.3 - 0.6	35.3 - 36.7	-0.9 - 0.4
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.43 (0.71)	-0.08 (0.75)	36.58 (0.36)	0.13 (0.44)
Median	36.40	-0.15	36.45	0.10
Min - Max	35.6 - 37.3	-0.9 - 0.9	36.3 - 37.1	-0.3 - 0.6
Cycle 39 Day 8				
PRE PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.33 (0.49)	-0.18 (0.51)	36.43 (0.36)	-0.03 (0.49)
Median	36.40	-0.15	36.55	-0.05
Min - Max	35.7 - 36.8	-0.8 - 0.4	35.9 - 36.7	-0.6 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	4	4	4	4
Mean (SD)	36.43 (0.63)	-0.08 (0.67)	36.50 (0.32)	0.05 (0.40)
Median	36.40	-0.15	36.45	-0.05
Min - Max	35.7 - 37.2	-0.8 - 0.8	36.2 - 36.9	-0.3 - 0.6
Cycle 39 Day 15				
PRE PAC INFUSION				
n	4	4	3	3
Mean (SD)	36.48 (0.19)	-0.03 (0.22)	36.63 (0.35)	0.03 (0.21)
Median	36.55	0.00	36.60	0.10
Min - Max	36.2 - 36.6	-0.3 - 0.2	36.3 - 37.0	-0.2 - 0.2
AFTER PAC INFUSION				
n	4	4	3	3
Mean (SD)	36.43 (0.64)	-0.08 (0.67)	36.63 (0.49)	0.03 (0.32)
Median	36.60	0.05	36.40	-0.10
Min - Max	35.5 - 37.0	-1.0 - 0.6	36.3 - 37.2	-0.2 - 0.4
Cycle 40 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	36.70 (0.08)	0.23 (0.17)	36.46 (0.38)	0.09 (0.43)
Median	36.70	0.25	36.60	0.10
Min - Max	36.6 - 36.8	0.0 - 0.4	35.8 - 36.8	-0.5 - 0.8
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	36.83 (0.42)	0.33 (0.51)	36.80 (0.26)	0.37 (0.15)
Median	36.70	0.20	36.90	0.40
Min - Max	36.5 - 37.3	-0.1 - 0.9	36.5 - 37.0	0.2 - 0.5
Cycle 40 Day 8				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	36.57 (0.06)	0.07 (0.06)	36.40 (0.68)	-0.05 (0.75)
Median	36.60	0.10	36.65	0.10
Min - Max	36.5 - 36.6	0.0 - 0.1	35.4 - 36.9	-1.1 - 0.7
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	36.90 (0.26)	0.40 (0.36)	36.58 (0.22)	0.13 (0.26)
Median	36.80	0.30	36.50	0.05
Min - Max	36.7 - 37.2	0.1 - 0.8	36.4 - 36.9	-0.1 - 0.5
Cycle 40 Day 15				
PRE PAC INFUSION				
n	2	2	4	4
Mean (SD)	37.00 (0.57)	0.50 (0.71)	36.35 (0.25)	-0.10 (0.50)
Median	37.00	0.50	36.40	-0.25
Min - Max	36.6 - 37.4	0.0 - 1.0	36.0 - 36.6	-0.5 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	4	4
Mean (SD)	37.00 (0.57)	0.50 (0.71)	36.33 (0.26)	-0.13 (0.56)
Median	37.00	0.50	36.30	-0.20
Min - Max	36.6 - 37.4	0.0 - 1.0	36.1 - 36.6	-0.7 - 0.6
Cycle 41 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	36.75 (0.24)	0.28 (0.32)	36.26 (0.42)	-0.11 (0.36)
Median	36.75	0.25	36.40	-0.05
Min - Max	36.5 - 37.0	0.0 - 0.6	35.4 - 36.6	-0.8 - 0.4
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	36.90 (0.70)	0.40 (0.78)	36.43 (0.21)	-0.03 (0.51)
Median	36.60	0.00	36.45	-0.05
Min - Max	36.4 - 37.7	-0.1 - 1.3	36.2 - 36.6	-0.6 - 0.6
Cycle 41 Day 8				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	36.67 (0.06)	0.17 (0.15)	36.38 (0.68)	-0.08 (0.73)
Median	36.70	0.20	36.55	0.10
Min - Max	36.6 - 36.7	0.0 - 0.3	35.4 - 37.0	-1.1 - 0.6
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	36.80 (0.17)	0.30 (0.26)	36.65 (0.21)	0.20 (0.36)
Median	36.70	0.20	36.65	0.15
Min - Max	36.7 - 37.0	0.1 - 0.6	36.4 - 36.9	-0.1 - 0.6
Cycle 41 Day 15				
PRE PAC INFUSION				
n	3	3	4	4
Mean (SD)	36.67 (0.21)	0.17 (0.29)	36.45 (0.30)	0.00 (0.42)
Median	36.60	0.00	36.40	-0.15
Min - Max	36.5 - 36.9	0.0 - 0.5	36.2 - 36.8	-0.3 - 0.6
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	36.63 (0.32)	0.13 (0.40)	36.60 (0.32)	0.15 (0.25)
Median	36.50	-0.10	36.55	0.20
Min - Max	36.4 - 37.0	-0.1 - 0.6	36.3 - 37.0	-0.2 - 0.4
Cycle 42 Day 1				
PRE PAC INFUSION				
n	4	4	8	8
Mean (SD)	36.78 (0.15)	0.30 (0.24)	36.30 (0.33)	-0.08 (0.39)
Median	36.80	0.35	36.30	-0.15
Min - Max	36.6 - 36.9	0.0 - 0.5	35.8 - 36.8	-0.5 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	4	4
Mean (SD)	36.90 (0.44)	0.40 (0.53)	36.53 (0.22)	0.08 (0.39)
Median	36.70	0.20	36.60	0.00
Min - Max	36.6 - 37.4	0.0 - 1.0	36.2 - 36.7	-0.3 - 0.6
Cycle 42 Day 8				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	36.65 (0.35)	0.20 (0.42)	36.55 (0.35)	0.15 (0.92)
Median	36.65	0.20	36.55	0.15
Min - Max	36.4 - 36.9	-0.1 - 0.5	36.3 - 36.8	-0.5 - 0.8
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	36.85 (0.49)	0.40 (0.57)	36.60 (0.28)	0.20 (0.85)
Median	36.85	0.40	36.60	0.20
Min - Max	36.5 - 37.2	0.0 - 0.8	36.4 - 36.8	-0.4 - 0.8
Cycle 42 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	36.60 (0.40)	0.10 (0.46)	36.23 (0.32)	-0.20 (0.70)
Median	36.60	0.00	36.10	-0.50
Min - Max	36.2 - 37.0	-0.3 - 0.6	36.0 - 36.6	-0.7 - 0.6
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	36.77 (0.21)	0.27 (0.29)	36.43 (0.29)	0.00 (0.53)
Median	36.70	0.10	36.60	-0.20
Min - Max	36.6 - 37.0	0.1 - 0.6	36.1 - 36.6	-0.4 - 0.6
Cycle 43 Day 1				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	36.75 (0.31)	0.28 (0.39)	36.25 (0.35)	-0.08 (0.41)
Median	36.75	0.25	36.20	0.00
Min - Max	36.4 - 37.1	-0.1 - 0.7	35.9 - 36.9	-0.6 - 0.4
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	36.87 (0.29)	0.37 (0.38)	36.67 (0.64)	0.23 (0.47)
Median	36.70	0.20	36.40	0.40
Min - Max	36.7 - 37.2	0.1 - 0.8	36.2 - 37.4	-0.3 - 0.6
Cycle 43 Day 8				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	36.77 (0.29)	0.27 (0.38)	36.30 (0.17)	-0.13 (0.57)
Median	36.60	0.10	36.20	-0.30
Min - Max	36.6 - 37.1	0.0 - 0.7	36.2 - 36.5	-0.6 - 0.5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	36.83 (0.49)	0.33 (0.59)	36.43 (0.50)	0.00 (0.56)
Median	36.60	0.10	36.50	0.10
Min - Max	36.5 - 37.4	-0.1 - 1.0	35.9 - 36.9	-0.6 - 0.5
Cycle 43 Day 15				
PRE PAC INFUSION				
n	3	3	1	1
Mean (SD)	36.80 (0.44)	0.30 (0.52)	36.60 (NE)	0.60 (NE)
Median	36.60	0.00	36.60	0.60
Min - Max	36.5 - 37.3	0.0 - 0.9	36.6 - 36.6	0.6 - 0.6
AFTER PAC INFUSION				
n	3	3	1	1
Mean (SD)	36.73 (0.32)	0.23 (0.42)	36.60 (NE)	0.60 (NE)
Median	36.60	0.10	36.60	0.60
Min - Max	36.5 - 37.1	-0.1 - 0.7	36.6 - 36.6	0.6 - 0.6
Cycle 44 Day 1				
PRE PAC INFUSION				
n	4	4	6	6
Mean (SD)	36.83 (0.36)	0.35 (0.44)	36.40 (0.46)	0.07 (0.48)
Median	36.75	0.25	36.45	0.05
Min - Max	36.5 - 37.3	0.0 - 0.9	35.7 - 37.0	-0.5 - 0.7
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	37.03 (0.68)	0.53 (0.76)	36.40 (0.96)	-0.03 (1.04)
Median	36.80	0.20	36.80	0.30
Min - Max	36.5 - 37.8	0.0 - 1.4	35.3 - 37.1	-1.2 - 0.8
Cycle 44 Day 8				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	36.83 (0.40)	0.33 (0.49)	36.53 (0.21)	0.10 (0.44)
Median	36.60	0.10	36.60	-0.10
Min - Max	36.6 - 37.3	0.0 - 0.9	36.3 - 36.7	-0.2 - 0.6
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	36.87 (0.50)	0.37 (0.57)	36.60 (0.00)	0.17 (0.40)
Median	36.80	0.20	36.60	0.10
Min - Max	36.4 - 37.4	-0.1 - 1.0	36.6 - 36.6	-0.2 - 0.6
Cycle 44 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	36.90 (0.62)	0.40 (0.70)	36.33 (0.40)	-0.10 (0.50)
Median	36.70	0.10	36.40	-0.10
Min - Max	36.4 - 37.6	-0.1 - 1.2	35.9 - 36.7	-0.6 - 0.4

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	37.07 (0.72)	0.57 (0.81)	36.67 (0.31)	0.23 (0.15)
Median	36.70	0.10	36.60	0.20
Min - Max	36.6 - 37.9	0.1 - 1.5	36.4 - 37.0	0.1 - 0.4
Cycle 45 Day 1				
PRE PAC INFUSION				
n	4	4	5	5
Mean (SD)	36.80 (0.18)	0.33 (0.28)	36.46 (0.38)	0.06 (0.35)
Median	36.80	0.35	36.70	0.00
Min - Max	36.6 - 37.0	0.0 - 0.6	36.0 - 36.8	-0.4 - 0.5
AFTER PAC INFUSION				
n	3	3	1	1
Mean (SD)	36.87 (0.21)	0.37 (0.31)	36.80 (NE)	0.00 (NE)
Median	36.80	0.30	36.80	0.00
Min - Max	36.7 - 37.1	0.1 - 0.7	36.8 - 36.8	0.0 - 0.0
Cycle 45 Day 8				
PRE PAC INFUSION				
n	3	3	2	2
Mean (SD)	36.70 (0.36)	0.20 (0.44)	36.35 (0.78)	-0.30 (0.57)
Median	36.60	0.00	36.35	-0.30
Min - Max	36.4 - 37.1	-0.1 - 0.7	35.8 - 36.9	-0.7 - 0.1
AFTER PAC INFUSION				
n	3	3	2	2
Mean (SD)	36.90 (0.35)	0.40 (0.44)	36.10 (0.42)	-0.55 (0.21)
Median	36.70	0.20	36.10	-0.55
Min - Max	36.7 - 37.3	0.1 - 0.9	35.8 - 36.4	-0.7 - -0.4
Cycle 45 Day 15				
PRE PAC INFUSION				
n	3	3	3	3
Mean (SD)	36.57 (0.12)	0.07 (0.21)	36.37 (0.40)	-0.07 (0.61)
Median	36.50	0.00	36.60	-0.20
Min - Max	36.5 - 36.7	-0.1 - 0.3	35.9 - 36.6	-0.6 - 0.6
AFTER PAC INFUSION				
n	3	3	3	3
Mean (SD)	36.93 (0.23)	0.43 (0.32)	36.40 (0.44)	-0.03 (0.60)
Median	36.80	0.30	36.60	-0.10
Min - Max	36.8 - 37.2	0.2 - 0.8	35.9 - 36.7	-0.6 - 0.6
Cycle 46 Day 1				
PRE PAC INFUSION				
n	3	3	6	6
Mean (SD)	36.80 (0.17)	0.33 (0.29)	36.23 (0.52)	-0.10 (0.53)
Median	36.90	0.50	36.40	0.00
Min - Max	36.6 - 36.9	0.0 - 0.5	35.3 - 36.7	-0.9 - 0.4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	36.95 (0.35)	0.45 (0.49)	36.55 (1.20)	-0.10 (0.99)
Median	36.95	0.45	36.55	-0.10
Min - Max	36.7 - 37.2	0.1 - 0.8	35.7 - 37.4	-0.8 - 0.6
Cycle 46 Day 8				
PRE PAC INFUSION				
n	2	2	3	3
Mean (SD)	36.70 (0.14)	0.20 (0.28)	36.40 (0.35)	-0.03 (0.57)
Median	36.70	0.20	36.60	-0.20
Min - Max	36.6 - 36.8	0.0 - 0.4	36.0 - 36.6	-0.5 - 0.6
AFTER PAC INFUSION				
n	2	2	3	3
Mean (SD)	36.85 (0.64)	0.35 (0.78)	36.47 (0.12)	0.03 (0.51)
Median	36.85	0.35	36.40	-0.10
Min - Max	36.4 - 37.3	-0.2 - 0.9	36.4 - 36.6	-0.4 - 0.6
Cycle 46 Day 15				
PRE PAC INFUSION				
n	2	2	3	3
Mean (SD)	36.60 (0.00)	0.10 (0.14)	36.33 (0.38)	-0.10 (0.62)
Median	36.60	0.10	36.50	-0.30
Min - Max	36.6 - 36.6	0.0 - 0.2	35.9 - 36.6	-0.6 - 0.6
AFTER PAC INFUSION				
n	2	2	3	3
Mean (SD)	36.85 (0.35)	0.35 (0.49)	36.40 (0.40)	-0.03 (0.45)
Median	36.85	0.35	36.40	0.00
Min - Max	36.6 - 37.1	0.0 - 0.7	36.0 - 36.8	-0.5 - 0.4
Cycle 47 Day 1				
PRE PAC INFUSION				
n	3	3	6	6
Mean (SD)	36.77 (0.15)	0.30 (0.26)	36.32 (0.50)	-0.02 (0.47)
Median	36.80	0.40	36.45	-0.05
Min - Max	36.6 - 36.9	0.0 - 0.5	35.5 - 36.9	-0.7 - 0.6
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	36.95 (0.35)	0.45 (0.49)	36.40 (0.28)	0.00 (0.85)
Median	36.95	0.45	36.40	0.00
Min - Max	36.7 - 37.2	0.1 - 0.8	36.2 - 36.6	-0.6 - 0.6
Cycle 47 Day 8				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	36.65 (0.07)	0.15 (0.07)	36.75 (0.07)	0.35 (0.64)
Median	36.65	0.15	36.75	0.35
Min - Max	36.6 - 36.7	0.1 - 0.2	36.7 - 36.8	-0.1 - 0.8

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	37.10 (0.42)	0.60 (0.57)	36.65 (0.07)	0.25 (0.49)
Median	37.10	0.60	36.65	0.25
Min - Max	36.8 - 37.4	0.2 - 1.0	36.6 - 36.7	-0.1 - 0.6
Cycle 47 Day 15				
PRE PAC INFUSION				
n	2	2	2	2
Mean (SD)	36.50 (0.14)	0.00 (0.00)	36.70 (0.28)	0.30 (0.28)
Median	36.50	0.00	36.70	0.30
Min - Max	36.4 - 36.6	0.0 - 0.0	36.5 - 36.9	0.1 - 0.5
AFTER PAC INFUSION				
n	2	2	2	2
Mean (SD)	36.85 (0.21)	0.35 (0.35)	36.45 (0.07)	0.05 (0.64)
Median	36.85	0.35	36.45	0.05
Min - Max	36.7 - 37.0	0.1 - 0.6	36.4 - 36.5	-0.4 - 0.5
Cycle 48 Day 1				
PRE PAC INFUSION				
n	1	1	5	5
Mean (SD)	36.60 (NE)	0.00 (NE)	36.46 (0.47)	0.16 (0.37)
Median	36.60	0.00	36.70	0.10
Min - Max	36.6 - 36.6	0.0 - 0.0	35.9 - 36.9	-0.3 - 0.7
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.80 (NE)	0.20 (NE)	36.75 (0.21)	0.35 (0.35)
Median	36.80	0.20	36.75	0.35
Min - Max	36.8 - 36.8	0.2 - 0.2	36.6 - 36.9	0.1 - 0.6
Cycle 48 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.70 (NE)	0.10 (NE)	36.75 (0.21)	0.35 (0.35)
Median	36.70	0.10	36.75	0.35
Min - Max	36.7 - 36.7	0.1 - 0.1	36.6 - 36.9	0.1 - 0.6
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.70 (NE)	0.10 (NE)	36.60 (0.00)	0.20 (0.57)
Median	36.70	0.10	36.60	0.20
Min - Max	36.7 - 36.7	0.1 - 0.1	36.6 - 36.6	-0.2 - 0.6
Cycle 48 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.70 (NE)	0.10 (NE)	36.60 (0.28)	0.20 (0.28)
Median	36.70	0.10	36.60	0.20
Min - Max	36.7 - 36.7	0.1 - 0.1	36.4 - 36.8	0.0 - 0.4

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.70 (NE)	0.10 (NE)	36.60 (0.28)	0.20 (0.28)
Median	36.70	0.10	36.60	0.20
Min - Max	36.7 - 36.7	0.1 - 0.1	36.4 - 36.8	0.0 - 0.4
Cycle 49 Day 1				
PRE PAC INFUSION				
n	1	1	3	3
Mean (SD)	36.60 (NE)	0.00 (NE)	36.60 (0.10)	0.17 (0.35)
Median	36.60	0.00	36.60	0.20
Min - Max	36.6 - 36.6	0.0 - 0.0	36.5 - 36.7	-0.2 - 0.5
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.80 (NE)	0.20 (NE)	36.85 (0.49)	0.45 (0.07)
Median	36.80	0.20	36.85	0.45
Min - Max	36.8 - 36.8	0.2 - 0.2	36.5 - 37.2	0.4 - 0.5
Cycle 49 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.50 (NE)	-0.10 (NE)	36.85 (0.07)	0.45 (0.49)
Median	36.50	-0.10	36.85	0.45
Min - Max	36.5 - 36.5	-0.1 - -0.1	36.8 - 36.9	0.1 - 0.8
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.70 (NE)	0.10 (NE)	37.05 (0.35)	0.65 (0.21)
Median	36.70	0.10	37.05	0.65
Min - Max	36.7 - 36.7	0.1 - 0.1	36.8 - 37.3	0.5 - 0.8
Cycle 49 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.70 (NE)	0.10 (NE)	36.60 (0.00)	0.20 (0.57)
Median	36.70	0.10	36.60	0.20
Min - Max	36.7 - 36.7	0.1 - 0.1	36.6 - 36.6	-0.2 - 0.6
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.70 (NE)	0.10 (NE)	36.70 (0.14)	0.30 (0.42)
Median	36.70	0.10	36.70	0.30
Min - Max	36.7 - 36.7	0.1 - 0.1	36.6 - 36.8	0.0 - 0.6
Cycle 50 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.70 (NE)	0.10 (NE)	36.60 (0.00)	0.20 (0.57)
Median	36.70	0.10	36.60	0.20
Min - Max	36.7 - 36.7	0.1 - 0.1	36.6 - 36.6	-0.2 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.80 (NE)	0.20 (NE)	36.40 (NE)	-0.40 (NE)
Median	36.80	0.20	36.40	-0.40
Min - Max	36.8 - 36.8	0.2 - 0.2	36.4 - 36.4	-0.4 - -0.4
Cycle 50 Day 8				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.50 (NE)	-0.10 (NE)	36.70 (0.00)	0.30 (0.57)
Median	36.50	-0.10	36.70	0.30
Min - Max	36.5 - 36.5	-0.1 - -0.1	36.7 - 36.7	-0.1 - 0.7
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.70 (NE)	0.10 (NE)	36.80 (0.28)	0.40 (0.28)
Median	36.70	0.10	36.80	0.40
Min - Max	36.7 - 36.7	0.1 - 0.1	36.6 - 37.0	0.2 - 0.6
Cycle 50 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.60 (NE)	0.00 (NE)	36.65 (0.07)	0.25 (0.64)
Median	36.60	0.00	36.65	0.25
Min - Max	36.6 - 36.6	0.0 - 0.0	36.6 - 36.7	-0.2 - 0.7
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.70 (NE)	0.10 (NE)	36.55 (0.07)	0.15 (0.64)
Median	36.70	0.10	36.55	0.15
Min - Max	36.7 - 36.7	0.1 - 0.1	36.5 - 36.6	-0.3 - 0.6
Cycle 51 Day 1				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.60 (NE)	0.00 (NE)	36.60 (0.14)	0.20 (0.71)
Median	36.60	0.00	36.60	0.20
Min - Max	36.6 - 36.6	0.0 - 0.0	36.5 - 36.7	-0.3 - 0.7
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.80 (NE)	0.20 (NE)	36.50 (0.14)	0.10 (0.71)
Median	36.80	0.20	36.50	0.10
Min - Max	36.8 - 36.8	0.2 - 0.2	36.4 - 36.6	-0.4 - 0.6
Cycle 51 Day 8				
PRE PAC INFUSION				
n	1	1	1	1
Mean (SD)	36.70 (NE)	0.10 (NE)	36.50 (NE)	0.50 (NE)
Median	36.70	0.10	36.50	0.50
Min - Max	36.7 - 36.7	0.1 - 0.1	36.5 - 36.5	0.5 - 0.5

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	1	1	0	0
Mean (SD)	36.80 (NE)	0.20 (NE)	NE (NE)	NE (NE)
Median	36.80	0.20	NE	NE
Min - Max	36.8 - 36.8	0.2 - 0.2	NE - NE	NE - NE
Cycle 51 Day 15				
PRE PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.80 (NE)	0.20 (NE)	36.65 (0.07)	0.25 (0.49)
Median	36.80	0.20	36.65	0.25
Min - Max	36.8 - 36.8	0.2 - 0.2	36.6 - 36.7	-0.1 - 0.6
AFTER PAC INFUSION				
n	1	1	2	2
Mean (SD)	36.80 (NE)	0.20 (NE)	36.45 (0.21)	0.05 (0.78)
Median	36.80	0.20	36.45	0.05
Min - Max	36.8 - 36.8	0.2 - 0.2	36.3 - 36.6	-0.5 - 0.6
Cycle 52 Day 1				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	36.55 (0.07)	0.15 (0.49)
Median	NE	NE	36.55	0.15
Min - Max	NE - NE	NE - NE	36.5 - 36.6	-0.2 - 0.5
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	36.50 (0.14)	0.10 (0.71)
Median	NE	NE	36.50	0.10
Min - Max	NE - NE	NE - NE	36.4 - 36.6	-0.4 - 0.6
Cycle 52 Day 8				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	36.55 (0.07)	0.15 (0.64)
Median	NE	NE	36.55	0.15
Min - Max	NE - NE	NE - NE	36.5 - 36.6	-0.3 - 0.6
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	36.60 (0.14)	0.20 (0.42)
Median	NE	NE	36.60	0.20
Min - Max	NE - NE	NE - NE	36.5 - 36.7	-0.1 - 0.5
Cycle 52 Day 15				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	36.80 (0.00)	0.40 (0.57)
Median	NE	NE	36.80	0.40
Min - Max	NE - NE	NE - NE	36.8 - 36.8	0.0 - 0.8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	36.90 (0.57)	0.50 (0.00)
Median	NE	NE	36.90	0.50
Min - Max	NE - NE	NE - NE	36.5 - 37.3	0.5 - 0.5
Cycle 53 Day 1				
PRE PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	36.75 (0.07)	0.35 (0.49)
Median	NE	NE	36.75	0.35
Min - Max	NE - NE	NE - NE	36.7 - 36.8	0.0 - 0.7
AFTER PAC INFUSION				
n	0	0	2	2
Mean (SD)	NE (NE)	NE (NE)	36.45 (0.35)	0.05 (0.92)
Median	NE	NE	36.45	0.05
Min - Max	NE - NE	NE - NE	36.2 - 36.7	-0.6 - 0.7
Cycle 53 Day 8				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	36.60 (NE)	0.60 (NE)
Median	NE	NE	36.60	0.60
Min - Max	NE - NE	NE - NE	36.6 - 36.6	0.6 - 0.6
AFTER PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	36.60 (NE)	0.60 (NE)
Median	NE	NE	36.60	0.60
Min - Max	NE - NE	NE - NE	36.6 - 36.6	0.6 - 0.6
Cycle 53 Day 15				
PRE PAC INFUSION				
n	0	0	1	1
Mean (SD)	NE (NE)	NE (NE)	36.70 (NE)	0.70 (NE)
Median	NE	NE	36.70	0.70
Min - Max	NE - NE	NE - NE	36.7 - 36.7	0.7 - 0.7
Study Drug Discontinuation				
n	70	68	124	124
Mean (SD)	36.35 (0.62)	-0.07 (0.48)	36.44 (0.40)	-0.03 (0.38)
Median	36.50	0.00	36.50	0.00
Min - Max	33.7 - 37.2	-2.4 - 1.1	35.0 - 37.4	-1.2 - 1.0
Post-Baseline Last				
n	69	69	125	125
Mean (SD)	36.37 (0.63)	-0.07 (0.48)	36.44 (0.40)	-0.03 (0.38)
Median	36.50	0.00	36.50	0.00
Min - Max	33.7 - 37.2	-2.4 - 1.1	35.0 - 37.4	-1.2 - 1.0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort B: HR+/HER2- Patients, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Placebo + Paclitaxel (N=75) Value at Visit	 Change from Baseline	Ipatasertib + Paclitaxel (N=145) Value at Visit	 Change from Baseline
PRE PAC INFUSION				
n	1	1	5	5
Mean (SD)	37.00 (NE)	-0.30 (NE)	36.94 (0.36)	0.42 (0.29)
Median	37.00	-0.30	36.90	0.40
Min - Max	37.0 - 37.0	-0.3 - -0.3	36.4 - 37.4	0.1 - 0.9
AFTER PAC INFUSION				
n	2	2	13	13
Mean (SD)	36.30 (0.14)	-0.20 (0.28)	36.55 (0.37)	-0.03 (0.39)
Median	36.30	-0.20	36.60	-0.10
Min - Max	36.2 - 36.4	-0.4 - 0.0	36.1 - 37.5	-0.9 - 0.8
Post-Baseline Minimum				
n	2	2	6	6
Mean (SD)	35.10 (0.85)	-1.65 (1.06)	35.90 (0.40)	-0.43 (0.52)
Median	35.10	-1.65	35.95	-0.40
Min - Max	34.5 - 35.7	-2.4 - -0.9	35.2 - 36.4	-1.2 - 0.2
PRE PAC INFUSION				
n	39	39	81	81
Mean (SD)	35.93 (0.56)	-0.42 (0.45)	35.91 (0.48)	-0.56 (0.46)
Median	36.00	-0.40	36.00	-0.50
Min - Max	33.7 - 36.6	-1.7 - 1.0	34.5 - 36.6	-1.6 - 0.1
AFTER PAC INFUSION				
n	31	31	56	56
Mean (SD)	35.78 (0.65)	-0.79 (0.50)	35.84 (0.71)	-0.65 (0.61)
Median	36.00	-0.70	36.00	-0.50
Min - Max	33.6 - 36.9	-2.3 - -0.1	32.1 - 36.8	-4.0 - 0.3
Post-Baseline Maximum				
n	3	3	10	10
Mean (SD)	37.07 (0.38)	0.43 (0.32)	37.31 (0.63)	0.69 (0.73)
Median	36.90	0.30	37.20	0.35
Min - Max	36.8 - 37.5	0.2 - 0.8	36.7 - 38.8	0.2 - 2.4
PRE PAC INFUSION				
n	32	32	65	65
Mean (SD)	36.99 (0.55)	0.59 (0.42)	37.07 (0.44)	0.61 (0.46)
Median	37.00	0.50	37.00	0.50
Min - Max	34.9 - 38.1	-0.2 - 1.7	36.1 - 38.4	-0.2 - 2.2
AFTER PAC INFUSION				
n	37	37	68	68
Mean (SD)	37.01 (0.63)	0.53 (0.47)	37.09 (0.40)	0.62 (0.48)
Median	37.10	0.40	37.00	0.50
Min - Max	34.0 - 37.9	-0.3 - 1.8	36.2 - 38.4	0.0 - 2.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_B_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Baseline		
n	102	
Mean (SD)	80.6 (13.2)	
Median	80.0	
Min - Max	55 - 160	
Cycle 1 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	97	97
Mean (SD)	77.5 (10.6)	-3.1 (15.2)
Median	79.0	0.0
Min - Max	57 - 103	-80 - 38
PRE PAC INFUSION		
n	78	78
Mean (SD)	77.4 (11.0)	-2.4 (13.0)
Median	78.0	-1.0
Min - Max	59 - 110	-54 - 27
AFTER PAC INFUSION		
n	95	95
Mean (SD)	78.4 (9.6)	-2.5 (14.6)
Median	79.0	0.0
Min - Max	60 - 99	-80 - 22
Cycle 1 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	16	16
Mean (SD)	76.0 (8.3)	-2.8 (9.9)
Median	75.5	-3.0
Min - Max	63 - 94	-19 - 14
PRE PAC INFUSION		
n	85	85
Mean (SD)	75.0 (8.1)	-5.7 (12.3)
Median	75.0	-3.0
Min - Max	59 - 94	-70 - 15
AFTER PAC INFUSION		
n	92	92
Mean (SD)	76.5 (9.4)	-4.3 (13.7)
Median	78.0	-1.0
Min - Max	51 - 110	-70 - 15
Cycle 1 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	92	92
Mean (SD)	73.6 (8.2)	-6.7 (13.4)
Median	73.0	-4.0
Min - Max	58 - 101	-80 - 24

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	68	68
Mean (SD)	73.0 (9.7)	-6.0 (11.8)
Median	71.5	-4.0
Min - Max	50 - 100	-49 - 17
AFTER PAC INFUSION		
n	78	78
Mean (SD)	74.5 (10.0)	-5.2 (14.7)
Median	73.0	-2.0
Min - Max	52 - 100	-70 - 20
Cycle 2 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	98	98
Mean (SD)	74.1 (8.9)	-6.0 (14.5)
Median	73.0	-2.5
Min - Max	50 - 94	-70 - 24
PRE PAC INFUSION		
n	79	79
Mean (SD)	74.1 (9.1)	-5.0 (11.9)
Median	75.0	-3.0
Min - Max	52 - 98	-60 - 20
AFTER PAC INFUSION		
n	90	90
Mean (SD)	76.6 (10.3)	-3.3 (14.3)
Median	77.0	-1.0
Min - Max	50 - 104	-70 - 25
Cycle 2 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	19	19
Mean (SD)	74.9 (9.9)	-3.7 (8.6)
Median	74.0	-2.0
Min - Max	55 - 90	-16 - 15
PRE PAC INFUSION		
n	79	79
Mean (SD)	74.1 (8.2)	-5.5 (11.4)
Median	75.0	-4.0
Min - Max	60 - 91	-53 - 20
AFTER PAC INFUSION		
n	87	87
Mean (SD)	75.4 (8.8)	-4.5 (11.6)
Median	76.0	-3.0
Min - Max	55 - 91	-54 - 18

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 2 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	88	88
Mean (SD)	73.3 (9.3)	-7.2 (15.7)
Median	73.0	-5.0
Min - Max	50 - 97	-100 - 24
PRE PAC INFUSION		
n	70	70
Mean (SD)	72.5 (9.1)	-6.6 (11.1)
Median	73.0	-5.5
Min - Max	50 - 90	-40 - 14
AFTER PAC INFUSION		
n	83	83
Mean (SD)	74.3 (9.2)	-6.3 (13.9)
Median	75.0	-5.0
Min - Max	50 - 97	-70 - 19
Cycle 3 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	86	86
Mean (SD)	74.7 (8.3)	-6.3 (13.9)
Median	76.0	-4.0
Min - Max	56 - 90	-80 - 21
PRE PAC INFUSION		
n	70	70
Mean (SD)	75.0 (8.6)	-4.3 (12.1)
Median	75.5	-2.5
Min - Max	56 - 97	-60 - 15
AFTER PAC INFUSION		
n	82	82
Mean (SD)	77.6 (9.3)	-4.0 (13.6)
Median	79.5	-1.0
Min - Max	57 - 100	-70 - 20
Cycle 3 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	15	15
Mean (SD)	76.9 (13.0)	-6.5 (18.9)
Median	76.0	-5.0
Min - Max	58 - 110	-50 - 20
PRE PAC INFUSION		
n	74	74
Mean (SD)	75.1 (9.5)	-5.5 (11.9)
Median	74.5	-4.0
Min - Max	56 - 120	-44 - 30

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
AFTER PAC INFUSION		
n	80	80
Mean (SD)	74.6 (8.8)	-6.6 (13.5)
Median	75.0	-5.0
Min - Max	50 - 100	-70 - 22
Cycle 3 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	78	78
Mean (SD)	74.7 (8.2)	-7.1 (14.8)
Median	75.0	-6.0
Min - Max	57 - 90	-90 - 20
PRE PAC INFUSION		
n	62	62
Mean (SD)	74.2 (8.2)	-5.8 (13.1)
Median	75.0	-2.5
Min - Max	59 - 90	-54 - 27
AFTER PAC INFUSION		
n	77	77
Mean (SD)	73.8 (9.4)	-7.6 (14.7)
Median	74.0	-5.0
Min - Max	50 - 100	-60 - 19
Cycle 4 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	79	79
Mean (SD)	74.3 (10.1)	-6.7 (15.5)
Median	75.0	-5.0
Min - Max	40 - 111	-70 - 27
PRE PAC INFUSION		
n	69	69
Mean (SD)	74.3 (8.6)	-4.5 (10.8)
Median	75.0	-4.0
Min - Max	55 - 100	-48 - 20
AFTER PAC INFUSION		
n	78	78
Mean (SD)	77.4 (9.1)	-3.6 (14.9)
Median	79.5	0.0
Min - Max	55 - 100	-70 - 21
Cycle 4 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	15	15
Mean (SD)	75.9 (16.0)	-2.0 (18.6)
Median	71.0	-5.0
Min - Max	57 - 120	-29 - 36

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	70	70
Mean (SD)	76.2 (8.6)	-5.2 (13.0)
Median	75.0	-3.5
Min - Max	60 - 100	-60 - 15
AFTER PAC INFUSION		
n	81	81
Mean (SD)	75.4 (10.1)	-5.6 (15.7)
Median	74.0	-1.0
Min - Max	43 - 100	-90 - 20
Cycle 4 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	79	79
Mean (SD)	72.9 (8.3)	-8.7 (14.8)
Median	73.0	-6.0
Min - Max	55 - 90	-90 - 27
PRE PAC INFUSION		
n	66	66
Mean (SD)	71.2 (8.4)	-9.4 (14.4)
Median	70.0	-7.0
Min - Max	57 - 90	-70 - 10
AFTER PAC INFUSION		
n	75	75
Mean (SD)	74.6 (8.5)	-5.9 (15.0)
Median	75.0	-5.0
Min - Max	60 - 93	-80 - 20
Cycle 5 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	65	65
Mean (SD)	74.2 (11.1)	-7.7 (16.2)
Median	76.0	-6.0
Min - Max	40 - 98	-80 - 25
PRE PAC INFUSION		
n	59	59
Mean (SD)	72.2 (8.9)	-8.6 (15.4)
Median	72.0	-7.0
Min - Max	60 - 100	-80 - 15
AFTER PAC INFUSION		
n	64	64
Mean (SD)	76.1 (8.7)	-4.9 (15.0)
Median	75.5	-4.0
Min - Max	60 - 104	-70 - 20

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 5 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	13	13
Mean (SD)	71.8 (8.2)	-5.0 (11.9)
Median	73.0	-9.0
Min - Max	60 - 90	-21 - 17
PRE PAC INFUSION		
n	55	55
Mean (SD)	72.9 (9.5)	-8.5 (14.2)
Median	74.0	-7.0
Min - Max	50 - 92	-70 - 12
AFTER PAC INFUSION		
n	59	59
Mean (SD)	74.9 (8.2)	-5.9 (14.2)
Median	76.0	-4.0
Min - Max	60 - 99	-80 - 19
Cycle 5 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	64	64
Mean (SD)	74.9 (11.7)	-7.0 (16.2)
Median	75.5	-5.5
Min - Max	40 - 113	-60 - 28
PRE PAC INFUSION		
n	56	56
Mean (SD)	73.3 (9.7)	-7.0 (17.4)
Median	72.0	-5.0
Min - Max	55 - 111	-80 - 26
AFTER PAC INFUSION		
n	58	58
Mean (SD)	77.2 (9.6)	-3.4 (15.2)
Median	77.5	-2.5
Min - Max	60 - 103	-80 - 20
Cycle 6 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	59	59
Mean (SD)	74.8 (8.1)	-6.3 (13.9)
Median	75.0	-3.0
Min - Max	57 - 92	-70 - 20
PRE PAC INFUSION		
n	57	57
Mean (SD)	75.6 (9.3)	-5.2 (15.8)
Median	76.0	-4.0
Min - Max	60 - 94	-90 - 22

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
AFTER PAC INFUSION		
n	58	58
Mean (SD)	78.7 (9.4)	-1.8 (12.1)
Median	77.0	-1.5
Min - Max	60 - 102	-60 - 25
Cycle 6 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	13	13
Mean (SD)	75.4 (12.4)	-2.8 (13.9)
Median	71.0	-5.0
Min - Max	63 - 106	-24 - 26
PRE PAC INFUSION		
n	49	49
Mean (SD)	74.3 (7.8)	-6.6 (16.0)
Median	74.0	-6.0
Min - Max	58 - 90	-90 - 17
AFTER PAC INFUSION		
n	58	58
Mean (SD)	76.5 (7.9)	-4.2 (13.5)
Median	78.0	-0.5
Min - Max	60 - 97	-70 - 18
Cycle 6 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	52	52
Mean (SD)	74.6 (9.1)	-6.0 (17.6)
Median	75.0	-5.0
Min - Max	60 - 95	-100 - 20
PRE PAC INFUSION		
n	49	49
Mean (SD)	74.8 (9.3)	-6.3 (17.2)
Median	72.0	-4.0
Min - Max	60 - 106	-90 - 22
AFTER PAC INFUSION		
n	49	49
Mean (SD)	77.9 (8.5)	-2.7 (14.5)
Median	78.0	0.0
Min - Max	60 - 102	-80 - 20
Cycle 7 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	53	53
Mean (SD)	74.2 (8.5)	-7.8 (15.1)
Median	76.0	-6.0
Min - Max	58 - 90	-70 - 16

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	46	46
Mean (SD)	76.0 (9.5)	-5.6 (16.4)
Median	77.0	-4.0
Min - Max	52 - 99	-70 - 28
AFTER PAC INFUSION		
n	50	50
Mean (SD)	78.9 (8.0)	-2.0 (15.4)
Median	80.0	0.0
Min - Max	60 - 95	-80 - 20
Cycle 7 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	74.6 (7.8)	-2.0 (12.5)
Median	76.5	-0.5
Min - Max	58 - 83	-24 - 18
PRE PAC INFUSION		
n	43	43
Mean (SD)	73.3 (6.7)	-8.5 (14.3)
Median	74.0	-6.0
Min - Max	60 - 87	-80 - 7
AFTER PAC INFUSION		
n	50	50
Mean (SD)	75.9 (8.9)	-4.9 (14.3)
Median	77.0	-3.0
Min - Max	60 - 106	-70 - 34
Cycle 7 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	49	49
Mean (SD)	75.4 (11.6)	-6.6 (13.1)
Median	76.0	-4.0
Min - Max	52 - 130	-51 - 15
PRE PAC INFUSION		
n	44	44
Mean (SD)	74.7 (8.9)	-5.6 (12.2)
Median	76.0	-2.5
Min - Max	52 - 96	-53 - 12
AFTER PAC INFUSION		
n	45	45
Mean (SD)	75.5 (8.1)	-2.9 (8.2)
Median	76.0	-2.0
Min - Max	60 - 90	-20 - 11

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 8 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	46	46
Mean (SD)	76.2 (8.8)	-3.6 (10.5)
Median	77.0	-4.0
Min - Max	55 - 94	-30 - 22
PRE PAC INFUSION		
n	42	42
Mean (SD)	75.2 (6.4)	-4.3 (10.0)
Median	77.0	-5.0
Min - Max	60 - 88	-34 - 18
AFTER PAC INFUSION		
n	45	45
Mean (SD)	75.8 (9.0)	-3.5 (9.9)
Median	77.0	-3.0
Min - Max	57 - 92	-40 - 21
Cycle 8 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	10	10
Mean (SD)	73.8 (10.0)	-3.0 (13.3)
Median	74.0	-2.5
Min - Max	60 - 88	-27 - 22
PRE PAC INFUSION		
n	34	34
Mean (SD)	73.2 (6.3)	-5.4 (10.0)
Median	72.5	-2.0
Min - Max	60 - 86	-30 - 14
AFTER PAC INFUSION		
n	42	42
Mean (SD)	74.5 (9.0)	-3.9 (10.7)
Median	75.0	-3.0
Min - Max	54 - 92	-30 - 19
Cycle 8 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	44	44
Mean (SD)	74.8 (10.5)	-4.8 (12.7)
Median	74.5	-2.5
Min - Max	47 - 100	-40 - 24
PRE PAC INFUSION		
n	33	33
Mean (SD)	74.0 (7.9)	-4.7 (10.1)
Median	73.0	-5.0
Min - Max	50 - 86	-20 - 24

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	39	39
Mean (SD)	76.3 (8.4)	-2.5 (9.0)
Median	78.0	-2.0
Min - Max	56 - 96	-20 - 15
Cycle 9 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	35	35
Mean (SD)	75.3 (7.3)	-2.6 (10.8)
Median	76.0	-2.0
Min - Max	59 - 90	-30 - 23
PRE PAC INFUSION		
n	30	30
Mean (SD)	74.4 (6.9)	-3.2 (11.2)
Median	75.0	-1.5
Min - Max	60 - 94	-30 - 24
AFTER PAC INFUSION		
n	32	32
Mean (SD)	75.3 (10.3)	-2.3 (11.7)
Median	76.0	0.0
Min - Max	40 - 99	-30 - 15
Cycle 9 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	7	7
Mean (SD)	73.1 (9.7)	1.7 (10.1)
Median	70.0	0.0
Min - Max	64 - 94	-14 - 18
PRE PAC INFUSION		
n	23	23
Mean (SD)	75.4 (5.6)	-3.7 (9.4)
Median	76.0	-3.0
Min - Max	60 - 84	-22 - 14
AFTER PAC INFUSION		
n	27	27
Mean (SD)	75.7 (6.7)	-1.9 (9.9)
Median	76.0	-1.0
Min - Max	62 - 93	-22 - 21
Cycle 9 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	33	33
Mean (SD)	72.8 (7.8)	-5.3 (11.2)
Median	72.0	-2.0
Min - Max	52 - 89	-46 - 13

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	29	29
Mean (SD)	73.8 (6.4)	-4.0 (8.6)
Median	74.0	-1.0
Min - Max	60 - 88	-30 - 13
AFTER PAC INFUSION		
n	26	26
Mean (SD)	75.4 (7.1)	-2.0 (8.8)
Median	75.0	-1.5
Min - Max	61 - 90	-26 - 11
Cycle 10 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	32	32
Mean (SD)	74.6 (8.7)	-3.0 (11.4)
Median	75.0	-4.5
Min - Max	51 - 98	-29 - 26
PRE PAC INFUSION		
n	31	31
Mean (SD)	75.1 (6.8)	-3.2 (9.9)
Median	77.0	-5.0
Min - Max	60 - 89	-29 - 14
AFTER PAC INFUSION		
n	28	28
Mean (SD)	77.2 (7.2)	-0.7 (12.5)
Median	77.5	-0.5
Min - Max	63 - 97	-29 - 25
Cycle 10 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	68.8 (11.3)	-2.3 (12.5)
Median	70.0	-4.5
Min - Max	52 - 81	-16 - 15
PRE PAC INFUSION		
n	21	21
Mean (SD)	76.9 (6.6)	-2.6 (10.7)
Median	78.0	-2.0
Min - Max	60 - 89	-30 - 13
AFTER PAC INFUSION		
n	23	23
Mean (SD)	75.4 (7.0)	-2.5 (8.8)
Median	76.0	0.0
Min - Max	60 - 88	-21 - 11

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 10 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	31	31
Mean (SD)	74.8 (7.4)	-2.7 (11.1)
Median	75.0	-3.0
Min - Max	60 - 92	-30 - 18
PRE PAC INFUSION		
n	28	28
Mean (SD)	74.7 (6.5)	-2.8 (9.6)
Median	74.5	-1.0
Min - Max	63 - 89	-29 - 14
AFTER PAC INFUSION		
n	24	24
Mean (SD)	77.0 (7.1)	0.7 (8.9)
Median	77.0	1.0
Min - Max	64 - 90	-17 - 14
Cycle 11 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	25	25
Mean (SD)	76.1 (7.4)	-2.5 (10.2)
Median	75.0	-2.0
Min - Max	63 - 88	-25 - 19
PRE PAC INFUSION		
n	22	22
Mean (SD)	75.8 (7.3)	-3.7 (11.2)
Median	78.0	-4.5
Min - Max	60 - 88	-24 - 15
AFTER PAC INFUSION		
n	21	21
Mean (SD)	75.0 (6.9)	-3.9 (13.2)
Median	75.0	-5.0
Min - Max	62 - 92	-33 - 21
Cycle 11 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	77.3 (11.4)	5.5 (8.3)
Median	73.0	7.5
Min - Max	69 - 94	-6 - 13
PRE PAC INFUSION		
n	16	16
Mean (SD)	72.6 (11.7)	-8.2 (11.2)
Median	77.0	-6.5
Min - Max	40 - 86	-33 - 11

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	18	18
Mean (SD)	73.8 (7.4)	-5.8 (10.3)
Median	74.0	-7.0
Min - Max	58 - 87	-20 - 18
Cycle 11 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	21	21
Mean (SD)	75.1 (9.5)	-3.8 (11.6)
Median	76.0	-3.0
Min - Max	54 - 92	-33 - 13
PRE PAC INFUSION		
n	21	21
Mean (SD)	76.8 (8.3)	-1.8 (10.9)
Median	78.0	0.0
Min - Max	59 - 93	-22 - 19
AFTER PAC INFUSION		
n	17	17
Mean (SD)	74.9 (8.6)	-2.6 (10.0)
Median	73.0	0.0
Min - Max	61 - 92	-20 - 13
Cycle 12 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	24	24
Mean (SD)	73.9 (8.8)	-4.9 (12.5)
Median	74.0	-2.5
Min - Max	59 - 90	-38 - 13
PRE PAC INFUSION		
n	21	21
Mean (SD)	77.5 (8.1)	-1.3 (12.7)
Median	78.0	0.0
Min - Max	63 - 94	-32 - 25
AFTER PAC INFUSION		
n	18	18
Mean (SD)	75.2 (8.8)	-2.9 (14.2)
Median	74.5	-1.0
Min - Max	60 - 90	-38 - 22
Cycle 12 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	71.5 (8.1)	-11.0 (15.4)
Median	72.5	-16.0
Min - Max	61 - 80	-23 - 11

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	15	15
Mean (SD)	76.6 (6.0)	-1.9 (9.7)
Median	76.0	0.0
Min - Max	68 - 90	-20 - 10
AFTER PAC INFUSION		
n	16	16
Mean (SD)	76.8 (6.4)	-2.5 (10.3)
Median	76.0	-1.0
Min - Max	64 - 90	-18 - 17
Cycle 12 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	23	23
Mean (SD)	76.4 (7.9)	-1.9 (10.5)
Median	76.0	-2.0
Min - Max	63 - 97	-31 - 23
PRE PAC INFUSION		
n	21	21
Mean (SD)	75.3 (7.7)	-3.5 (12.2)
Median	74.0	0.0
Min - Max	61 - 90	-37 - 10
AFTER PAC INFUSION		
n	17	17
Mean (SD)	75.5 (5.7)	-1.5 (10.6)
Median	76.0	0.0
Min - Max	66 - 91	-23 - 21
Cycle 13 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	21	21
Mean (SD)	77.4 (10.3)	-1.0 (12.4)
Median	77.0	0.0
Min - Max	56 - 100	-25 - 22
PRE PAC INFUSION		
n	20	20
Mean (SD)	77.0 (7.3)	-0.9 (10.1)
Median	78.0	0.0
Min - Max	65 - 91	-19 - 15
AFTER PAC INFUSION		
n	13	13
Mean (SD)	76.3 (6.5)	-1.0 (11.8)
Median	76.0	1.0
Min - Max	63 - 90	-25 - 17

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 13 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	69.5 (14.8)	7.0 (5.7)
Median	69.5	7.0
Min - Max	59 - 80	3 - 11
PRE PAC INFUSION		
n	14	14
Mean (SD)	75.8 (7.5)	-4.8 (11.9)
Median	75.0	-2.0
Min - Max	63 - 90	-35 - 10
AFTER PAC INFUSION		
n	15	15
Mean (SD)	76.3 (6.1)	-2.6 (11.8)
Median	77.0	-3.0
Min - Max	65 - 90	-20 - 13
Cycle 13 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	19	19
Mean (SD)	74.0 (8.9)	-3.3 (9.7)
Median	74.0	-1.0
Min - Max	57 - 90	-22 - 15
PRE PAC INFUSION		
n	19	19
Mean (SD)	73.6 (7.9)	-4.5 (10.6)
Median	75.0	-1.0
Min - Max	59 - 88	-39 - 7
AFTER PAC INFUSION		
n	15	15
Mean (SD)	75.4 (6.3)	-3.5 (7.9)
Median	76.0	-2.0
Min - Max	65 - 84	-17 - 9
Cycle 14 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	20	20
Mean (SD)	75.3 (7.8)	-2.6 (12.3)
Median	73.5	-3.0
Min - Max	62 - 89	-26 - 32
PRE PAC INFUSION		
n	18	18
Mean (SD)	75.2 (6.0)	-2.3 (10.2)
Median	74.0	0.0
Min - Max	66 - 92	-26 - 15

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	14	14
Mean (SD)	74.5 (7.1)	-3.6 (13.0)
Median	73.5	0.0
Min - Max	60 - 85	-30 - 20
Cycle 14 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	70.0 (12.3)	4.7 (11.2)
Median	65.0	9.0
Min - Max	61 - 84	-8 - 13
PRE PAC INFUSION		
n	10	10
Mean (SD)	78.5 (7.3)	-4.8 (10.3)
Median	80.5	-4.5
Min - Max	60 - 86	-20 - 12
AFTER PAC INFUSION		
n	12	12
Mean (SD)	76.4 (5.2)	-3.4 (9.1)
Median	77.0	-4.0
Min - Max	68 - 85	-16 - 12
Cycle 14 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	18	18
Mean (SD)	77.2 (8.4)	-1.5 (8.5)
Median	76.5	-1.5
Min - Max	61 - 91	-18 - 11
PRE PAC INFUSION		
n	16	16
Mean (SD)	79.6 (8.4)	-0.2 (7.5)
Median	80.0	0.5
Min - Max	65 - 94	-12 - 10
AFTER PAC INFUSION		
n	12	12
Mean (SD)	76.4 (7.1)	-4.6 (8.7)
Median	78.0	-4.0
Min - Max	63 - 86	-20 - 9
Cycle 15 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	17	17
Mean (SD)	75.3 (8.8)	-3.8 (8.4)
Median	76.0	-1.0
Min - Max	57 - 88	-19 - 7

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	16	16
Mean (SD)	77.6 (8.3)	-2.5 (7.7)
Median	78.0	-1.0
Min - Max	57 - 88	-13 - 12
AFTER PAC INFUSION		
n	10	10
Mean (SD)	79.7 (6.7)	-3.6 (8.1)
Median	79.5	-2.0
Min - Max	71 - 93	-16 - 9
Cycle 15 Day 8		
PRE PAC INFUSION		
n	10	10
Mean (SD)	72.9 (7.5)	-10.4 (10.1)
Median	71.5	-9.5
Min - Max	62 - 83	-30 - 3
AFTER PAC INFUSION		
n	10	10
Mean (SD)	77.7 (5.2)	-5.6 (10.1)
Median	80.0	-6.0
Min - Max	70 - 83	-18 - 14
Cycle 15 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	14	14
Mean (SD)	73.8 (9.6)	-3.9 (10.1)
Median	75.0	-3.0
Min - Max	55 - 90	-26 - 10
PRE PAC INFUSION		
n	13	13
Mean (SD)	77.8 (7.0)	-0.9 (8.0)
Median	80.0	0.0
Min - Max	63 - 88	-16 - 10
AFTER PAC INFUSION		
n	7	7
Mean (SD)	72.3 (7.7)	-7.7 (8.2)
Median	75.0	-11.0
Min - Max	58 - 80	-19 - 5
Cycle 16 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	74.8 (11.0)	-5.6 (12.2)
Median	77.5	-1.5
Min - Max	43 - 86	-35 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE PAC INFUSION		
n	12	12
Mean (SD)	78.6 (6.5)	-4.3 (12.1)
Median	77.5	-6.0
Min - Max	70 - 91	-26 - 15
AFTER PAC INFUSION		
n	7	7
Mean (SD)	82.4 (5.3)	-6.6 (10.6)
Median	81.0	-9.0
Min - Max	75 - 90	-20 - 10
Cycle 16 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	90.0 (NE)	0.0 (NE)
Median	90.0	0.0
Min - Max	90 - 90	0 - 0
PRE PAC INFUSION		
n	8	8
Mean (SD)	72.9 (9.2)	-12.5 (6.1)
Median	74.0	-13.5
Min - Max	57 - 84	-20 - -4
AFTER PAC INFUSION		
n	8	8
Mean (SD)	79.4 (9.6)	-6.0 (9.4)
Median	81.0	-4.5
Min - Max	66 - 90	-22 - 6
Cycle 16 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	14	14
Mean (SD)	78.3 (9.8)	-1.3 (10.4)
Median	79.0	0.0
Min - Max	58 - 93	-20 - 16
PRE PAC INFUSION		
n	14	14
Mean (SD)	72.6 (16.5)	-8.9 (16.9)
Median	75.0	-7.0
Min - Max	20 - 90	-60 - 10
AFTER PAC INFUSION		
n	7	7
Mean (SD)	78.9 (7.6)	-8.6 (8.0)
Median	77.0	-10.0
Min - Max	68 - 88	-18 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 17 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	75.3 (6.8)	-5.6 (9.6)
Median	75.0	-3.0
Min - Max	65 - 87	-21 - 7
PRE PAC INFUSION		
n	11	11
Mean (SD)	77.4 (7.8)	-4.2 (11.6)
Median	78.0	-5.0
Min - Max	64 - 94	-27 - 10
AFTER PAC INFUSION		
n	7	7
Mean (SD)	78.1 (8.4)	-8.0 (12.4)
Median	77.0	-4.0
Min - Max	66 - 92	-24 - 8
Cycle 17 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	79.0 (NE)	-19.0 (NE)
Median	79.0	-19.0
Min - Max	79 - 79	-19 - -19
PRE PAC INFUSION		
n	7	7
Mean (SD)	76.7 (7.9)	-6.9 (8.3)
Median	76.0	-4.0
Min - Max	67 - 90	-19 - 2
AFTER PAC INFUSION		
n	8	8
Mean (SD)	81.1 (8.4)	-4.3 (10.1)
Median	78.5	-3.0
Min - Max	72 - 94	-17 - 10
Cycle 17 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	75.3 (8.5)	-5.5 (8.9)
Median	75.5	-2.0
Min - Max	63 - 89	-18 - 5
PRE PAC INFUSION		
n	12	12
Mean (SD)	74.3 (7.2)	-7.0 (8.2)
Median	73.0	-7.5
Min - Max	64 - 85	-21 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	8	8
Mean (SD)	80.5 (5.8)	-4.9 (6.4)
Median	81.0	-2.5
Min - Max	68 - 86	-15 - 2
Cycle 18 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	73.4 (11.6)	-7.4 (12.3)
Median	73.0	-3.0
Min - Max	45 - 90	-33 - 6
PRE PAC INFUSION		
n	13	13
Mean (SD)	73.8 (7.4)	-7.5 (9.2)
Median	76.0	-10.0
Min - Max	58 - 86	-23 - 8
AFTER PAC INFUSION		
n	8	8
Mean (SD)	78.6 (5.7)	-6.8 (10.3)
Median	78.0	-7.0
Min - Max	73 - 90	-24 - 6
Cycle 18 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	71.0 (NE)	-27.0 (NE)
Median	71.0	-27.0
Min - Max	71 - 71	-27 - -27
PRE PAC INFUSION		
n	6	6
Mean (SD)	79.8 (6.8)	-6.2 (7.5)
Median	81.0	-8.0
Min - Max	71 - 89	-15 - 5
AFTER PAC INFUSION		
n	7	7
Mean (SD)	75.0 (4.3)	-12.7 (5.9)
Median	74.0	-11.0
Min - Max	70 - 83	-24 - -7
Cycle 18 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	75.5 (8.2)	-5.3 (11.7)
Median	76.0	-4.0
Min - Max	61 - 87	-26 - 14

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE PAC INFUSION		
n	11	11
Mean (SD)	76.0 (5.8)	-5.5 (10.6)
Median	78.0	-4.0
Min - Max	65 - 86	-28 - 10
AFTER PAC INFUSION		
n	7	7
Mean (SD)	76.9 (8.9)	-6.7 (9.2)
Median	78.0	-10.0
Min - Max	67 - 90	-19 - 10
Cycle 19 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	78.2 (7.1)	-2.6 (11.6)
Median	77.0	0.0
Min - Max	68 - 90	-30 - 9
PRE PAC INFUSION		
n	11	11
Mean (SD)	76.4 (9.7)	-5.1 (13.9)
Median	78.0	-1.0
Min - Max	63 - 91	-35 - 13
AFTER PAC INFUSION		
n	8	8
Mean (SD)	79.1 (7.1)	-6.3 (10.9)
Median	78.0	-5.5
Min - Max	71 - 93	-22 - 9
Cycle 19 Day 8		
PRE PAC INFUSION		
n	7	7
Mean (SD)	74.3 (8.4)	-9.3 (6.7)
Median	78.0	-9.0
Min - Max	60 - 85	-19 - -2
AFTER PAC INFUSION		
n	7	7
Mean (SD)	77.1 (7.2)	-6.4 (6.4)
Median	80.0	-7.0
Min - Max	62 - 83	-15 - 0
Cycle 19 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	74.6 (8.3)	-6.2 (8.2)
Median	75.0	-5.5
Min - Max	62 - 88	-24 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE PAC INFUSION		
n	11	11
Mean (SD)	75.9 (7.7)	-3.9 (8.0)
Median	75.0	-5.0
Min - Max	64 - 87	-20 - 7
AFTER PAC INFUSION		
n	7	7
Mean (SD)	75.7 (8.3)	-7.9 (8.2)
Median	74.0	-7.0
Min - Max	65 - 88	-23 - 2
Cycle 20 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	73.5 (9.6)	-7.3 (11.4)
Median	76.0	-3.5
Min - Max	52 - 89	-27 - 7
PRE PAC INFUSION		
n	10	10
Mean (SD)	74.9 (6.5)	-6.0 (7.4)
Median	74.0	-6.5
Min - Max	64 - 86	-18 - 5
AFTER PAC INFUSION		
n	7	7
Mean (SD)	78.7 (5.7)	-4.9 (6.7)
Median	80.0	-2.0
Min - Max	70 - 85	-16 - 1
Cycle 20 Day 8		
PRE PAC INFUSION		
n	7	7
Mean (SD)	75.9 (13.1)	-7.7 (10.2)
Median	80.0	-13.0
Min - Max	54 - 94	-19 - 10
AFTER PAC INFUSION		
n	7	7
Mean (SD)	74.6 (7.8)	-9.0 (7.9)
Median	76.0	-10.0
Min - Max	64 - 85	-24 - -2
Cycle 20 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	72.6 (8.0)	-8.2 (8.9)
Median	73.0	-8.0
Min - Max	59 - 82	-25 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	11	11
Mean (SD)	75.8 (5.8)	-4.0 (6.7)
Median	78.0	-4.0
Min - Max	63 - 82	-15 - 8
AFTER PAC INFUSION		
n	7	7
Mean (SD)	74.0 (7.9)	-9.6 (6.8)
Median	77.0	-8.0
Min - Max	63 - 83	-22 - 0
Cycle 21 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	76.8 (8.3)	-4.0 (9.8)
Median	76.5	-3.0
Min - Max	61 - 90	-23 - 10
PRE PAC INFUSION		
n	11	11
Mean (SD)	74.8 (7.9)	-5.0 (8.0)
Median	73.0	-4.0
Min - Max	60 - 86	-19 - 12
AFTER PAC INFUSION		
n	7	7
Mean (SD)	73.6 (6.3)	-10.0 (4.1)
Median	73.0	-10.0
Min - Max	62 - 81	-15 - -3
Cycle 21 Day 8		
PRE PAC INFUSION		
n	6	6
Mean (SD)	76.0 (11.7)	-8.2 (10.5)
Median	73.5	-10.0
Min - Max	64 - 91	-20 - 7
AFTER PAC INFUSION		
n	6	6
Mean (SD)	72.7 (7.2)	-11.5 (5.1)
Median	74.0	-9.5
Min - Max	60 - 82	-20 - -6
Cycle 21 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	71.7 (10.1)	-7.5 (9.3)
Median	72.0	-10.0
Min - Max	54 - 86	-19 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	9	9
Mean (SD)	72.9 (5.6)	-6.9 (10.5)
Median	74.0	-4.0
Min - Max	64 - 80	-24 - 6
AFTER PAC INFUSION		
n	6	6
Mean (SD)	72.5 (7.7)	-11.7 (6.6)
Median	73.5	-10.5
Min - Max	63 - 80	-22 - -5
Cycle 22 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	76.5 (7.1)	-4.3 (9.1)
Median	76.0	-3.5
Min - Max	65 - 91	-21 - 8
PRE PAC INFUSION		
n	10	10
Mean (SD)	76.2 (7.3)	-3.6 (7.0)
Median	79.5	-4.5
Min - Max	63 - 85	-14 - 11
AFTER PAC INFUSION		
n	6	6
Mean (SD)	77.5 (9.6)	-6.7 (6.8)
Median	82.0	-6.0
Min - Max	65 - 88	-15 - 4
Cycle 22 Day 8		
PRE PAC INFUSION		
n	4	4
Mean (SD)	79.3 (9.4)	-8.8 (9.4)
Median	80.5	-7.5
Min - Max	68 - 88	-20 - 0
AFTER PAC INFUSION		
n	4	4
Mean (SD)	77.8 (6.7)	-10.3 (7.4)
Median	76.5	-10.5
Min - Max	71 - 87	-19 - -1
Cycle 22 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	75.9 (8.4)	-4.9 (12.1)
Median	76.0	-5.0
Min - Max	64 - 90	-28 - 14

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	10	10
Mean (SD)	78.4 (8.0)	-1.4 (7.4)
Median	78.0	0.0
Min - Max	59 - 87	-13 - 7
AFTER PAC INFUSION		
n	6	6
Mean (SD)	78.3 (10.2)	-5.8 (5.9)
Median	82.0	-7.5
Min - Max	61 - 89	-12 - 5
Cycle 23 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	73.6 (10.7)	-3.8 (10.2)
Median	74.0	-3.0
Min - Max	57 - 89	-21 - 10
PRE PAC INFUSION		
n	9	9
Mean (SD)	77.1 (8.1)	-2.9 (7.5)
Median	78.0	-3.0
Min - Max	59 - 86	-15 - 10
AFTER PAC INFUSION		
n	6	6
Mean (SD)	78.3 (7.4)	-5.8 (4.3)
Median	80.5	-4.0
Min - Max	64 - 85	-13 - -2
Cycle 23 Day 8		
PRE PAC INFUSION		
n	5	5
Mean (SD)	79.0 (8.7)	-5.2 (7.9)
Median	82.0	-2.0
Min - Max	67 - 87	-14 - 4
AFTER PAC INFUSION		
n	5	5
Mean (SD)	76.4 (9.2)	-7.8 (4.3)
Median	81.0	-6.0
Min - Max	63 - 85	-14 - -3
Cycle 23 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	72.3 (8.3)	-7.2 (12.3)
Median	76.0	-4.0
Min - Max	59 - 84	-36 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	9	9
Mean (SD)	76.0 (5.8)	-4.0 (8.4)
Median	77.0	-3.0
Min - Max	68 - 86	-17 - 12
AFTER PAC INFUSION		
n	6	6
Mean (SD)	77.2 (4.9)	-7.0 (6.2)
Median	76.5	-8.5
Min - Max	72 - 85	-15 - 3
Cycle 24 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	10	10
Mean (SD)	75.6 (6.6)	-5.5 (9.6)
Median	75.5	-4.0
Min - Max	62 - 84	-22 - 7
PRE PAC INFUSION		
n	9	9
Mean (SD)	74.0 (5.9)	-6.0 (8.6)
Median	74.0	-7.0
Min - Max	62 - 82	-19 - 4
AFTER PAC INFUSION		
n	6	6
Mean (SD)	76.0 (8.6)	-8.2 (7.9)
Median	75.5	-5.5
Min - Max	62 - 88	-21 - 0
Cycle 24 Day 8		
PRE PAC INFUSION		
n	4	4
Mean (SD)	75.0 (11.4)	-6.5 (8.3)
Median	75.0	-4.0
Min - Max	62 - 88	-18 - 0
AFTER PAC INFUSION		
n	4	4
Mean (SD)	77.0 (7.4)	-4.5 (2.1)
Median	78.5	-4.5
Min - Max	67 - 84	-7 - -2
Cycle 24 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	10	10
Mean (SD)	77.7 (10.6)	-3.4 (9.8)
Median	77.0	-1.5
Min - Max	53 - 90	-24 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	9	9
Mean (SD)	75.8 (7.2)	-4.2 (8.5)
Median	74.0	-5.0
Min - Max	65 - 88	-16 - 11
AFTER PAC INFUSION		
n	6	6
Mean (SD)	77.5 (11.0)	-6.7 (5.5)
Median	81.5	-7.0
Min - Max	59 - 88	-14 - 0
Cycle 25 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	76.3 (6.7)	-6.2 (14.2)
Median	76.0	-8.0
Min - Max	67 - 88	-29 - 19
PRE PAC INFUSION		
n	10	10
Mean (SD)	73.1 (6.8)	-10.0 (8.6)
Median	74.5	-10.0
Min - Max	62 - 82	-23 - 3
AFTER PAC INFUSION		
n	4	4
Mean (SD)	74.0 (5.9)	-8.3 (6.6)
Median	72.5	-9.5
Min - Max	69 - 82	-14 - 0
Cycle 25 Day 8		
PRE PAC INFUSION		
n	3	3
Mean (SD)	79.7 (3.2)	-10.7 (7.2)
Median	81.0	-7.0
Min - Max	76 - 82	-19 - -6
AFTER PAC INFUSION		
n	3	3
Mean (SD)	77.3 (2.9)	-13.0 (6.9)
Median	79.0	-9.0
Min - Max	74 - 79	-21 - -9
Cycle 25 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	73.8 (11.8)	-10.3 (10.5)
Median	75.0	-7.0
Min - Max	54 - 89	-32 - 0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE PAC INFUSION		
n	8	8
Mean (SD)	76.6 (8.8)	-6.1 (3.6)
Median	78.5	-6.5
Min - Max	61 - 88	-10 - 1
AFTER PAC INFUSION		
n	5	5
Mean (SD)	80.4 (10.2)	-4.4 (4.9)
Median	80.0	-5.0
Min - Max	64 - 90	-8 - 4
Cycle 26 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	75.8 (7.0)	-8.5 (12.2)
Median	76.0	-9.0
Min - Max	68 - 89	-30 - 7
PRE PAC INFUSION		
n	8	8
Mean (SD)	76.0 (9.9)	-7.0 (11.9)
Median	75.0	-7.0
Min - Max	59 - 90	-22 - 10
AFTER PAC INFUSION		
n	4	4
Mean (SD)	76.5 (5.1)	-12.3 (6.8)
Median	78.5	-12.5
Min - Max	69 - 80	-19 - -5
Cycle 26 Day 8		
PRE PAC INFUSION		
n	5	5
Mean (SD)	76.8 (10.7)	-8.0 (8.9)
Median	81.0	-6.0
Min - Max	63 - 86	-20 - 2
AFTER PAC INFUSION		
n	5	5
Mean (SD)	77.8 (7.6)	-7.0 (9.6)
Median	78.0	-10.0
Min - Max	70 - 88	-18 - 4
Cycle 26 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	77.5 (6.4)	-6.8 (9.4)
Median	76.0	-3.5
Min - Max	70 - 88	-28 - 3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE PAC INFUSION		
n	8	8
Mean (SD)	77.4 (6.7)	-5.6 (6.7)
Median	77.0	-5.5
Min - Max	69 - 89	-14 - 7
AFTER PAC INFUSION		
n	4	4
Mean (SD)	78.5 (5.8)	-10.3 (3.2)
Median	77.5	-9.0
Min - Max	73 - 86	-15 - -8
Cycle 27 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	76.3 (8.6)	-8.0 (11.7)
Median	77.0	-3.0
Min - Max	61 - 88	-30 - 5
PRE PAC INFUSION		
n	8	8
Mean (SD)	76.1 (8.0)	-6.9 (10.3)
Median	78.0	-6.0
Min - Max	64 - 86	-24 - 7
AFTER PAC INFUSION		
n	4	4
Mean (SD)	79.3 (8.2)	-9.5 (10.5)
Median	79.5	-12.0
Min - Max	69 - 89	-19 - 5
Cycle 27 Day 8		
PRE PAC INFUSION		
n	3	3
Mean (SD)	86.0 (8.2)	-3.0 (10.6)
Median	88.0	-7.0
Min - Max	77 - 93	-11 - 9
AFTER PAC INFUSION		
n	3	3
Mean (SD)	85.7 (7.5)	-3.3 (8.6)
Median	90.0	-5.0
Min - Max	77 - 90	-11 - 6
Cycle 27 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	7	7
Mean (SD)	78.0 (4.0)	-6.7 (10.1)
Median	76.0	-4.0
Min - Max	73 - 84	-25 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	7	7
Mean (SD)	76.1 (6.1)	-7.1 (8.9)
Median	76.0	-8.0
Min - Max	67 - 86	-17 - 4
AFTER PAC INFUSION		
n	4	4
Mean (SD)	82.0 (3.6)	-6.8 (8.1)
Median	83.0	-5.0
Min - Max	77 - 85	-18 - 1
Cycle 28 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	74.3 (10.5)	-11.2 (17.0)
Median	75.0	-9.0
Min - Max	56 - 88	-42 - 8
PRE PAC INFUSION		
n	4	4
Mean (SD)	78.5 (7.9)	-4.3 (3.9)
Median	76.5	-5.0
Min - Max	72 - 89	-8 - 1
AFTER PAC INFUSION		
n	2	2
Mean (SD)	80.0 (12.7)	-11.5 (7.8)
Median	80.0	-11.5
Min - Max	71 - 89	-17 - -6
Cycle 28 Day 8		
PRE PAC INFUSION		
n	2	2
Mean (SD)	84.0 (4.2)	-7.5 (9.2)
Median	84.0	-7.5
Min - Max	81 - 87	-14 - -1
AFTER PAC INFUSION		
n	2	2
Mean (SD)	80.0 (0.0)	-11.5 (4.9)
Median	80.0	-11.5
Min - Max	80 - 80	-15 - -8
Cycle 28 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	80.0 (6.7)	-5.5 (10.3)
Median	78.0	-3.5
Min - Max	71 - 88	-21 - 7

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	4	4
Mean (SD)	84.5 (5.8)	1.8 (6.1)
Median	84.5	2.0
Min - Max	79 - 90	-6 - 9
AFTER PAC INFUSION		
n	2	2
Mean (SD)	86.0 (2.8)	-5.5 (2.1)
Median	86.0	-5.5
Min - Max	84 - 88	-7 - -4
Cycle 29 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	7	7
Mean (SD)	80.0 (9.9)	-4.9 (14.9)
Median	81.0	-2.0
Min - Max	61 - 90	-37 - 6
PRE PAC INFUSION		
n	4	4
Mean (SD)	79.5 (3.9)	-3.3 (7.4)
Median	78.5	-4.0
Min - Max	76 - 85	-10 - 5
AFTER PAC INFUSION		
n	2	2
Mean (SD)	85.0 (7.1)	-6.5 (2.1)
Median	85.0	-6.5
Min - Max	80 - 90	-8 - -5
Cycle 29 Day 8		
PRE PAC INFUSION		
n	2	2
Mean (SD)	80.5 (6.4)	-11.0 (11.3)
Median	80.5	-11.0
Min - Max	76 - 85	-19 - -3
AFTER PAC INFUSION		
n	2	2
Mean (SD)	81.0 (4.2)	-10.5 (9.2)
Median	81.0	-10.5
Min - Max	78 - 84	-17 - -4
Cycle 29 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	75.3 (8.3)	-9.0 (10.3)
Median	77.5	-9.0
Min - Max	62 - 86	-19 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	80.0 (7.5)	1.3 (1.2)
Median	79.0	2.0
Min - Max	73 - 88	0 - 2
AFTER PAC INFUSION		
n	1	1
Mean (SD)	82.0 (NE)	-6.0 (NE)
Median	82.0	-6.0
Min - Max	82 - 82	-6 - -6
Cycle 30 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	5	5
Mean (SD)	80.8 (8.7)	-2.8 (6.1)
Median	79.0	-2.0
Min - Max	75 - 96	-9 - 4
PRE PAC INFUSION		
n	3	3
Mean (SD)	78.7 (4.2)	0.0 (5.2)
Median	80.0	3.0
Min - Max	74 - 82	-6 - 3
AFTER PAC INFUSION		
n	1	1
Mean (SD)	88.0 (NE)	0.0 (NE)
Median	88.0	0.0
Min - Max	88 - 88	0 - 0
Cycle 30 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	84.0 (NE)	-4.0 (NE)
Median	84.0	-4.0
Min - Max	84 - 84	-4 - -4
AFTER PAC INFUSION		
n	1	1
Mean (SD)	86.0 (NE)	-2.0 (NE)
Median	86.0	-2.0
Min - Max	86 - 86	-2 - -2
Cycle 30 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	5	5
Mean (SD)	76.4 (8.3)	-7.2 (14.3)
Median	76.0	-1.0
Min - Max	68 - 90	-30 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	80.7 (3.1)	2.0 (5.6)
Median	80.0	3.0
Min - Max	78 - 84	-4 - 7
AFTER PAC INFUSION		
n	1	1
Mean (SD)	86.0 (NE)	-2.0 (NE)
Median	86.0	-2.0
Min - Max	86 - 86	-2 - -2
Cycle 31 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	81.5 (7.5)	1.5 (1.3)
Median	83.0	1.5
Min - Max	72 - 88	0 - 3
PRE PAC INFUSION		
n	3	3
Mean (SD)	81.0 (5.6)	2.3 (5.8)
Median	80.0	-1.0
Min - Max	76 - 87	-1 - 9
AFTER PAC INFUSION		
n	1	1
Mean (SD)	80.0 (NE)	-8.0 (NE)
Median	80.0	-8.0
Min - Max	80 - 80	-8 - -8
Cycle 31 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	88.0 (NE)	0.0 (NE)
Median	88.0	0.0
Min - Max	88 - 88	0 - 0
AFTER PAC INFUSION		
n	1	1
Mean (SD)	82.0 (NE)	-6.0 (NE)
Median	82.0	-6.0
Min - Max	82 - 82	-6 - -6
Cycle 31 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	80.8 (4.3)	0.8 (3.6)
Median	82.0	1.5
Min - Max	75 - 84	-4 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	78.7 (8.1)	0.0 (2.6)
Median	80.0	-1.0
Min - Max	70 - 86	-2 - 3
AFTER PAC INFUSION		
n	1	1
Mean (SD)	86.0 (NE)	-2.0 (NE)
Median	86.0	-2.0
Min - Max	86 - 86	-2 - -2
Cycle 32 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	83.0 (8.4)	3.0 (3.6)
Median	83.0	2.0
Min - Max	74 - 92	0 - 8
PRE PAC INFUSION		
n	3	3
Mean (SD)	78.3 (4.9)	-0.3 (4.7)
Median	76.0	-2.0
Min - Max	75 - 84	-4 - 5
AFTER PAC INFUSION		
n	1	1
Mean (SD)	80.0 (NE)	-8.0 (NE)
Median	80.0	-8.0
Min - Max	80 - 80	-8 - -8
Cycle 32 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	86.0 (NE)	-2.0 (NE)
Median	86.0	-2.0
Min - Max	86 - 86	-2 - -2
AFTER PAC INFUSION		
n	1	1
Mean (SD)	82.0 (NE)	-6.0 (NE)
Median	82.0	-6.0
Min - Max	82 - 82	-6 - -6
Cycle 32 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	80.5 (3.1)	0.5 (5.3)
Median	80.5	-1.0
Min - Max	77 - 84	-4 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	76.7 (8.1)	-2.0 (3.0)
Median	72.0	-2.0
Min - Max	72 - 86	-5 - 1
AFTER PAC INFUSION		
n	1	1
Mean (SD)	78.0 (NE)	-10.0 (NE)
Median	78.0	-10.0
Min - Max	78 - 78	-10 - -10
Cycle 33 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	76.0 (6.0)	-2.7 (2.9)
Median	76.0	-1.0
Min - Max	70 - 82	-6 - -1
PRE PAC INFUSION		
n	2	2
Mean (SD)	76.0 (2.8)	2.0 (1.4)
Median	76.0	2.0
Min - Max	74 - 78	1 - 3
Cycle 33 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	81.0 (NE)	-7.0 (NE)
Median	81.0	-7.0
Min - Max	81 - 81	-7 - -7
Cycle 33 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	78.5 (4.9)	-4.0 (2.8)
Median	78.5	-4.0
Min - Max	75 - 82	-6 - -2
PRE PAC INFUSION		
n	1	1
Mean (SD)	75.0 (NE)	-2.0 (NE)
Median	75.0	-2.0
Min - Max	75 - 75	-2 - -2
Cycle 34 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	78.0 (2.8)	4.0 (1.4)
Median	78.0	4.0
Min - Max	76 - 80	3 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE PAC INFUSION		
n	2	2
Mean (SD)	79.5 (0.7)	5.5 (4.9)
Median	79.5	5.5
Min - Max	79 - 80	2 - 9
AFTER PAC INFUSION		
n	1	1
Mean (SD)	79.0 (NE)	-9.0 (NE)
Median	79.0	-9.0
Min - Max	79 - 79	-9 - -9
Cycle 34 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	86.0 (NE)	-2.0 (NE)
Median	86.0	-2.0
Min - Max	86 - 86	-2 - -2
Cycle 34 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	79.5 (4.9)	-3.0 (2.8)
Median	79.5	-3.0
Min - Max	76 - 83	-5 - -1
PRE PAC INFUSION		
n	1	1
Mean (SD)	78.0 (NE)	1.0 (NE)
Median	78.0	1.0
Min - Max	78 - 78	1 - 1
Cycle 35 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	76.7 (2.1)	-2.0 (7.0)
Median	76.0	-2.0
Min - Max	75 - 79	-9 - 5
PRE PAC INFUSION		
n	2	2
Mean (SD)	78.0 (2.8)	4.0 (1.4)
Median	78.0	4.0
Min - Max	76 - 80	3 - 5
Cycle 35 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	83.0 (NE)	-5.0 (NE)
Median	83.0	-5.0
Min - Max	83 - 83	-5 - -5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 35 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	77.5 (2.1)	3.5 (2.1)
Median	77.5	3.5
Min - Max	76 - 79	2 - 5
PRE PAC INFUSION		
n	2	2
Mean (SD)	77.5 (3.5)	3.5 (0.7)
Median	77.5	3.5
Min - Max	75 - 80	3 - 4
Cycle 36 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	78.0 (0.0)	4.0 (4.2)
Median	78.0	4.0
Min - Max	78 - 78	1 - 7
PRE PAC INFUSION		
n	2	2
Mean (SD)	78.0 (5.7)	4.0 (1.4)
Median	78.0	4.0
Min - Max	74 - 82	3 - 5
Cycle 36 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	80.5 (0.7)	6.5 (3.5)
Median	80.5	6.5
Min - Max	80 - 81	4 - 9
PRE PAC INFUSION		
n	2	2
Mean (SD)	78.5 (3.5)	4.5 (0.7)
Median	78.5	4.5
Min - Max	76 - 81	4 - 5
Cycle 37 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	76.0 (0.0)	2.0 (4.2)
Median	76.0	2.0
Min - Max	76 - 76	-1 - 5
PRE PAC INFUSION		
n	2	2
Mean (SD)	74.0 (5.7)	0.0 (1.4)
Median	74.0	0.0
Min - Max	70 - 78	-1 - 1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 37 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	80.0 (0.0)	6.0 (4.2)
Median	80.0	6.0
Min - Max	80 - 80	3 - 9
PRE PAC INFUSION		
n	2	2
Mean (SD)	78.5 (4.9)	4.5 (0.7)
Median	78.5	4.5
Min - Max	75 - 82	4 - 5
Cycle 38 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	76.0 (0.0)	2.0 (4.2)
Median	76.0	2.0
Min - Max	76 - 76	-1 - 5
PRE PAC INFUSION		
n	2	2
Mean (SD)	74.5 (0.7)	0.5 (4.9)
Median	74.5	0.5
Min - Max	74 - 75	-3 - 4
Cycle 38 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	74.0 (1.4)	0.0 (2.8)
Median	74.0	0.0
Min - Max	73 - 75	-2 - 2
PRE PAC INFUSION		
n	2	2
Mean (SD)	75.0 (4.2)	1.0 (0.0)
Median	75.0	1.0
Min - Max	72 - 78	1 - 1
Cycle 39 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	79.0 (5.7)	5.0 (1.4)
Median	79.0	5.0
Min - Max	75 - 83	4 - 6
PRE PAC INFUSION		
n	2	2
Mean (SD)	77.0 (7.1)	3.0 (2.8)
Median	77.0	3.0
Min - Max	72 - 82	1 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 39 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	78.5 (3.5)	4.5 (0.7)
Median	78.5	4.5
Min - Max	76 - 81	4 - 5
PRE PAC INFUSION		
n	2	2
Mean (SD)	82.0 (0.0)	8.0 (4.2)
Median	82.0	8.0
Min - Max	82 - 82	5 - 11
Cycle 40 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	70.0 (NE)	-1.0 (NE)
Median	70.0	-1.0
Min - Max	70 - 70	-1 - -1
PRE PAC INFUSION		
n	1	1
Mean (SD)	76.0 (NE)	5.0 (NE)
Median	76.0	5.0
Min - Max	76 - 76	5 - 5
Cycle 40 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	68.0 (NE)	-3.0 (NE)
Median	68.0	-3.0
Min - Max	68 - 68	-3 - -3
PRE PAC INFUSION		
n	1	1
Mean (SD)	76.0 (NE)	5.0 (NE)
Median	76.0	5.0
Min - Max	76 - 76	5 - 5
Cycle 41 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	75.0 (NE)	4.0 (NE)
Median	75.0	4.0
Min - Max	75 - 75	4 - 4
PRE PAC INFUSION		
n	1	1
Mean (SD)	74.0 (NE)	3.0 (NE)
Median	74.0	3.0
Min - Max	74 - 74	3 - 3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 41 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	70.0 (NE)	-1.0 (NE)
Median	70.0	-1.0
Min - Max	70 - 70	-1 - -1
PRE PAC INFUSION		
n	1	1
Mean (SD)	65.0 (NE)	-6.0 (NE)
Median	65.0	-6.0
Min - Max	65 - 65	-6 - -6
Cycle 42 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	72.0 (NE)	1.0 (NE)
Median	72.0	1.0
Min - Max	72 - 72	1 - 1
PRE PAC INFUSION		
n	1	1
Mean (SD)	75.0 (NE)	4.0 (NE)
Median	75.0	4.0
Min - Max	75 - 75	4 - 4
Cycle 42 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	69.0 (NE)	-2.0 (NE)
Median	69.0	-2.0
Min - Max	69 - 69	-2 - -2
PRE PAC INFUSION		
n	1	1
Mean (SD)	70.0 (NE)	-1.0 (NE)
Median	70.0	-1.0
Min - Max	70 - 70	-1 - -1
Cycle 43 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	72.0 (NE)	1.0 (NE)
Median	72.0	1.0
Min - Max	72 - 72	1 - 1
PRE PAC INFUSION		
n	1	1
Mean (SD)	73.0 (NE)	2.0 (NE)
Median	73.0	2.0
Min - Max	73 - 73	2 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 43 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	78.0 (NE)	7.0 (NE)
Median	78.0	7.0
Min - Max	78 - 78	7 - 7
PRE PAC INFUSION		
n	1	1
Mean (SD)	70.0 (NE)	-1.0 (NE)
Median	70.0	-1.0
Min - Max	70 - 70	-1 - -1
Cycle 44 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	78.0 (NE)	7.0 (NE)
Median	78.0	7.0
Min - Max	78 - 78	7 - 7
PRE PAC INFUSION		
n	1	1
Mean (SD)	79.0 (NE)	8.0 (NE)
Median	79.0	8.0
Min - Max	79 - 79	8 - 8
Cycle 44 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	75.0 (NE)	4.0 (NE)
Median	75.0	4.0
Min - Max	75 - 75	4 - 4
PRE PAC INFUSION		
n	1	1
Mean (SD)	70.0 (NE)	-1.0 (NE)
Median	70.0	-1.0
Min - Max	70 - 70	-1 - -1
Study Drug Discontinuation		
n	89	89
Mean (SD)	75.4 (10.6)	-4.6 (13.2)
Median	76.0	-2.0
Min - Max	40 - 100	-60 - 24
Post-Baseline Last		
n	89	89
Mean (SD)	75.4 (10.6)	-4.6 (13.2)
Median	76.0	-2.0
Min - Max	40 - 100	-60 - 24

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	68.7 (9.1)	-17.3 (12.6)
Median	65.0	-19.0
Min - Max	62 - 79	-29 - -4
PRE PAC INFUSION		
n	3	3
Mean (SD)	69.7 (2.5)	-22.7 (26.4)
Median	70.0	-10.0
Min - Max	67 - 72	-53 - -5
AFTER PAC INFUSION		
n	7	7
Mean (SD)	77.3 (17.9)	-3.7 (19.3)
Median	75.0	-6.0
Min - Max	53 - 103	-33 - 20
Post-Baseline Minimum		
n	4	4
Mean (SD)	56.3 (9.2)	-22.3 (16.5)
Median	59.0	-24.5
Min - Max	43 - 64	-40 - 0
PRE ATEZO INFUSION (COHORT C)		
n	44	44
Mean (SD)	59.7 (7.8)	-21.1 (17.0)
Median	60.0	-20.0
Min - Max	40 - 73	-100 - 3
PRE PAC INFUSION		
n	36	36
Mean (SD)	60.4 (10.6)	-18.6 (14.3)
Median	60.0	-18.0
Min - Max	20 - 80	-62 - 0
AFTER PAC INFUSION		
n	18	18
Mean (SD)	62.1 (9.8)	-22.1 (12.1)
Median	65.0	-21.5
Min - Max	40 - 73	-40 - -2
Post-Baseline Maximum		
n	8	8
Mean (SD)	88.6 (7.4)	6.3 (12.0)
Median	90.0	8.0
Min - Max	74 - 98	-20 - 17
PRE ATEZO INFUSION (COHORT C)		
n	31	31
Mean (SD)	93.2 (10.9)	9.7 (16.5)
Median	90.0	10.0
Min - Max	78 - 130	-36 - 38

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Diastolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	27	27
Mean (SD)	90.3 (11.2)	11.4 (10.3)
Median	90.0	10.0
Min - Max	70 - 120	-10 - 30
AFTER PAC INFUSION		
n	36	36
Mean (SD)	90.0 (8.9)	11.0 (8.8)
Median	90.0	10.5
Min - Max	70 - 110	-9 - 34

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Baseline		
n	102	
Mean (SD)	129.1 (18.2)	
Median	129.0	
Min - Max	85 - 200	
Cycle 1 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	97	97
Mean (SD)	127.3 (17.3)	-2.4 (18.4)
Median	120.0	0.0
Min - Max	90 - 172	-70 - 45
PRE PAC INFUSION		
n	78	78
Mean (SD)	126.8 (15.4)	-1.3 (18.0)
Median	125.0	0.0
Min - Max	97 - 183	-57 - 45
AFTER PAC INFUSION		
n	95	95
Mean (SD)	130.2 (16.5)	0.4 (17.2)
Median	130.0	0.0
Min - Max	100 - 173	-52 - 39
Cycle 1 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	16	16
Mean (SD)	122.8 (14.9)	-12.8 (16.2)
Median	122.0	-10.0
Min - Max	100 - 146	-40 - 13
PRE PAC INFUSION		
n	85	85
Mean (SD)	121.1 (14.6)	-7.7 (19.4)
Median	120.0	-5.0
Min - Max	94 - 160	-79 - 45
AFTER PAC INFUSION		
n	92	92
Mean (SD)	124.6 (15.8)	-5.3 (18.0)
Median	123.0	-2.0
Min - Max	90 - 186	-60 - 40
Cycle 1 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	92	92
Mean (SD)	118.2 (12.5)	-10.4 (17.3)
Median	120.0	-10.0
Min - Max	90 - 151	-70 - 33

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	68	68
Mean (SD)	118.5 (13.7)	-8.3 (15.9)
Median	116.5	-5.5
Min - Max	90 - 148	-62 - 15
AFTER PAC INFUSION		
n	78	78
Mean (SD)	122.1 (14.7)	-6.2 (19.1)
Median	120.0	-4.5
Min - Max	90 - 168	-70 - 37
Cycle 2 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	98	98
Mean (SD)	120.8 (14.6)	-7.9 (18.9)
Median	120.0	-5.0
Min - Max	87 - 153	-65 - 30
PRE PAC INFUSION		
n	79	79
Mean (SD)	122.3 (14.6)	-5.0 (19.1)
Median	122.0	-5.0
Min - Max	97 - 188	-67 - 71
AFTER PAC INFUSION		
n	90	90
Mean (SD)	125.2 (15.8)	-3.6 (20.3)
Median	121.0	0.0
Min - Max	100 - 169	-80 - 49
Cycle 2 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	19	19
Mean (SD)	122.9 (17.5)	-12.4 (17.2)
Median	122.0	-12.0
Min - Max	94 - 151	-39 - 16
PRE PAC INFUSION		
n	79	79
Mean (SD)	119.6 (13.3)	-7.4 (14.8)
Median	120.0	-7.0
Min - Max	90 - 152	-55 - 19
AFTER PAC INFUSION		
n	87	87
Mean (SD)	121.2 (12.8)	-7.5 (17.1)
Median	120.0	-8.0
Min - Max	94 - 160	-72 - 26

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 2 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	88	88
Mean (SD)	118.9 (14.0)	-9.3 (19.6)
Median	118.5	-9.0
Min - Max	91 - 155	-90 - 26
PRE PAC INFUSION		
n	70	70
Mean (SD)	117.8 (15.2)	-9.6 (19.8)
Median	119.5	-9.0
Min - Max	90 - 168	-66 - 48
AFTER PAC INFUSION		
n	83	83
Mean (SD)	120.9 (13.9)	-7.8 (17.5)
Median	120.0	-5.0
Min - Max	89 - 148	-74 - 26
Cycle 3 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	86	86
Mean (SD)	123.5 (14.1)	-7.0 (16.8)
Median	120.5	-5.0
Min - Max	100 - 159	-80 - 31
PRE PAC INFUSION		
n	70	70
Mean (SD)	120.4 (12.4)	-8.0 (14.7)
Median	120.0	-6.5
Min - Max	100 - 150	-57 - 20
AFTER PAC INFUSION		
n	82	82
Mean (SD)	123.1 (15.4)	-8.0 (18.8)
Median	122.0	-7.5
Min - Max	99 - 170	-70 - 40
Cycle 3 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	15	15
Mean (SD)	122.5 (18.6)	-19.9 (25.1)
Median	122.0	-17.0
Min - Max	96 - 160	-73 - 17
PRE PAC INFUSION		
n	74	74
Mean (SD)	119.9 (13.3)	-7.7 (15.4)
Median	120.0	-5.5
Min - Max	96 - 160	-59 - 22

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
AFTER PAC INFUSION		
n	80	80
Mean (SD)	119.8 (14.9)	-9.8 (18.9)
Median	120.0	-6.0
Min - Max	90 - 165	-70 - 26
Cycle 3 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	78	78
Mean (SD)	121.8 (12.9)	-9.1 (18.5)
Median	120.0	-10.0
Min - Max	95 - 160	-70 - 30
PRE PAC INFUSION		
n	62	62
Mean (SD)	119.6 (11.4)	-9.2 (17.2)
Median	120.5	-6.5
Min - Max	93 - 142	-68 - 18
AFTER PAC INFUSION		
n	77	77
Mean (SD)	120.5 (13.7)	-9.6 (19.8)
Median	122.0	-4.0
Min - Max	85 - 156	-76 - 22
Cycle 4 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	79	79
Mean (SD)	120.0 (14.7)	-9.8 (18.5)
Median	120.0	-8.0
Min - Max	91 - 180	-61 - 36
PRE PAC INFUSION		
n	69	69
Mean (SD)	121.1 (15.5)	-5.4 (15.6)
Median	120.0	-3.0
Min - Max	97 - 180	-59 - 37
AFTER PAC INFUSION		
n	78	78
Mean (SD)	124.8 (13.5)	-4.2 (18.7)
Median	124.0	-2.5
Min - Max	99 - 165	-70 - 44
Cycle 4 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	15	15
Mean (SD)	119.7 (18.2)	-17.5 (24.5)
Median	116.0	-19.0
Min - Max	94 - 171	-58 - 36

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	70	70
Mean (SD)	121.8 (14.6)	-6.8 (14.9)
Median	120.5	-5.0
Min - Max	98 - 168	-62 - 16
AFTER PAC INFUSION		
n	81	81
Mean (SD)	123.1 (15.7)	-6.8 (19.6)
Median	124.0	-3.0
Min - Max	78 - 173	-70 - 38
Cycle 4 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	79	79
Mean (SD)	119.8 (11.7)	-10.2 (17.0)
Median	120.0	-7.0
Min - Max	91 - 148	-66 - 36
PRE PAC INFUSION		
n	66	66
Mean (SD)	117.8 (13.6)	-10.6 (18.1)
Median	120.0	-6.5
Min - Max	90 - 149	-66 - 14
AFTER PAC INFUSION		
n	75	75
Mean (SD)	121.7 (13.1)	-7.4 (18.2)
Median	120.0	-5.0
Min - Max	97 - 162	-80 - 27
Cycle 5 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	65	65
Mean (SD)	121.4 (14.8)	-9.3 (20.2)
Median	121.0	-5.0
Min - Max	81 - 170	-80 - 29
PRE PAC INFUSION		
n	59	59
Mean (SD)	120.2 (12.5)	-9.4 (18.4)
Median	120.0	-5.0
Min - Max	96 - 155	-70 - 17
AFTER PAC INFUSION		
n	64	64
Mean (SD)	124.9 (16.1)	-5.8 (20.0)
Median	124.0	-3.5
Min - Max	90 - 192	-69 - 57

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 5 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	13	13
Mean (SD)	125.3 (14.6)	-9.8 (21.7)
Median	124.0	-5.0
Min - Max	110 - 154	-52 - 20
PRE PAC INFUSION		
n	55	55
Mean (SD)	120.2 (14.0)	-9.1 (16.5)
Median	120.0	-7.0
Min - Max	90 - 158	-60 - 18
AFTER PAC INFUSION		
n	59	59
Mean (SD)	122.7 (13.4)	-7.3 (18.5)
Median	122.0	-7.0
Min - Max	100 - 172	-90 - 40
Cycle 5 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	64	64
Mean (SD)	121.3 (16.0)	-9.8 (17.8)
Median	120.0	-10.0
Min - Max	60 - 152	-60 - 26
PRE PAC INFUSION		
n	56	56
Mean (SD)	121.0 (14.6)	-7.6 (20.7)
Median	120.0	-4.5
Min - Max	100 - 184	-80 - 49
AFTER PAC INFUSION		
n	58	58
Mean (SD)	124.3 (13.5)	-5.0 (18.0)
Median	121.5	-6.5
Min - Max	100 - 173	-60 - 38
Cycle 6 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	59	59
Mean (SD)	121.7 (14.1)	-8.9 (17.9)
Median	122.0	-6.0
Min - Max	95 - 160	-50 - 25
PRE PAC INFUSION		
n	57	57
Mean (SD)	122.9 (13.6)	-6.9 (16.3)
Median	123.0	-5.0
Min - Max	90 - 162	-70 - 27

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	58	58
Mean (SD)	126.9 (15.6)	-3.4 (15.5)
Median	124.0	-2.5
Min - Max	90 - 183	-40 - 48
Cycle 6 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	13	13
Mean (SD)	126.2 (24.3)	-5.9 (23.6)
Median	116.0	-10.0
Min - Max	104 - 186	-31 - 51
PRE PAC INFUSION		
n	49	49
Mean (SD)	120.6 (12.9)	-10.0 (21.8)
Median	122.0	-9.0
Min - Max	98 - 146	-100 - 32
AFTER PAC INFUSION		
n	58	58
Mean (SD)	123.6 (15.0)	-7.0 (19.2)
Median	122.0	-7.5
Min - Max	99 - 191	-62 - 56
Cycle 6 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	52	52
Mean (SD)	120.8 (15.0)	-10.6 (23.0)
Median	122.0	-9.0
Min - Max	90 - 172	-110 - 37
PRE PAC INFUSION		
n	49	49
Mean (SD)	121.4 (17.0)	-8.4 (23.0)
Median	121.0	-6.0
Min - Max	90 - 188	-110 - 53
AFTER PAC INFUSION		
n	49	49
Mean (SD)	124.7 (15.9)	-6.0 (20.0)
Median	124.0	-4.0
Min - Max	99 - 173	-90 - 38
Cycle 7 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	53	53
Mean (SD)	122.8 (14.8)	-9.2 (17.7)
Median	127.0	-8.0
Min - Max	90 - 150	-61 - 26

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	46	46
Mean (SD)	123.5 (15.2)	-7.8 (17.1)
Median	124.0	-6.0
Min - Max	94 - 158	-57 - 27
AFTER PAC INFUSION		
n	50	50
Mean (SD)	125.6 (13.3)	-5.0 (17.2)
Median	125.0	-1.0
Min - Max	100 - 161	-80 - 27
Cycle 7 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	121.3 (14.2)	-8.5 (14.2)
Median	117.5	-7.0
Min - Max	104 - 150	-35 - 12
PRE PAC INFUSION		
n	43	43
Mean (SD)	119.3 (12.6)	-12.6 (17.8)
Median	120.0	-10.0
Min - Max	90 - 148	-80 - 15
AFTER PAC INFUSION		
n	50	50
Mean (SD)	123.2 (13.2)	-7.7 (16.1)
Median	120.0	-8.5
Min - Max	100 - 155	-70 - 23
Cycle 7 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	49	49
Mean (SD)	121.7 (16.9)	-9.1 (16.5)
Median	120.0	-7.0
Min - Max	100 - 200	-68 - 18
PRE PAC INFUSION		
n	44	44
Mean (SD)	121.0 (13.5)	-8.0 (16.8)
Median	120.0	-5.0
Min - Max	97 - 163	-72 - 17
AFTER PAC INFUSION		
n	45	45
Mean (SD)	120.0 (11.8)	-8.0 (14.0)
Median	120.0	-10.0
Min - Max	99 - 145	-46 - 19

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 8 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	46	46
Mean (SD)	122.3 (14.5)	-6.2 (15.8)
Median	121.5	-7.5
Min - Max	97 - 164	-37 - 30
PRE PAC INFUSION		
n	42	42
Mean (SD)	122.3 (12.6)	-5.9 (13.9)
Median	120.5	-6.5
Min - Max	100 - 160	-41 - 17
AFTER PAC INFUSION		
n	45	45
Mean (SD)	123.7 (13.6)	-4.9 (14.8)
Median	124.0	-4.0
Min - Max	98 - 159	-41 - 24
Cycle 8 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	10	10
Mean (SD)	126.8 (16.8)	-2.8 (16.2)
Median	124.5	-1.0
Min - Max	104 - 154	-30 - 22
PRE PAC INFUSION		
n	34	34
Mean (SD)	118.6 (10.4)	-11.2 (18.4)
Median	120.0	-10.0
Min - Max	100 - 137	-64 - 25
AFTER PAC INFUSION		
n	42	42
Mean (SD)	120.4 (13.6)	-9.0 (15.2)
Median	120.0	-9.0
Min - Max	95 - 154	-54 - 23
Cycle 8 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	44	44
Mean (SD)	122.3 (15.3)	-7.8 (17.2)
Median	120.5	-5.0
Min - Max	100 - 162	-53 - 28
PRE PAC INFUSION		
n	33	33
Mean (SD)	120.0 (11.0)	-7.9 (14.7)
Median	121.0	-10.0
Min - Max	100 - 148	-32 - 29

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	39	39
Mean (SD)	122.0 (11.7)	-7.8 (14.1)
Median	120.0	-9.0
Min - Max	100 - 161	-36 - 26
Cycle 9 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	35	35
Mean (SD)	123.1 (13.3)	-5.0 (16.1)
Median	123.0	-2.0
Min - Max	100 - 154	-42 - 26
PRE PAC INFUSION		
n	30	30
Mean (SD)	122.1 (12.7)	-3.6 (16.7)
Median	123.5	-0.5
Min - Max	100 - 163	-50 - 27
AFTER PAC INFUSION		
n	32	32
Mean (SD)	126.7 (12.9)	-1.7 (13.9)
Median	127.5	-1.5
Min - Max	103 - 170	-27 - 35
Cycle 9 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	7	7
Mean (SD)	120.1 (19.6)	-7.7 (24.5)
Median	112.0	-6.0
Min - Max	103 - 157	-42 - 22
PRE PAC INFUSION		
n	23	23
Mean (SD)	122.5 (10.1)	-8.3 (16.7)
Median	122.0	-3.0
Min - Max	100 - 151	-52 - 20
AFTER PAC INFUSION		
n	27	27
Mean (SD)	123.6 (12.1)	-6.2 (12.7)
Median	126.0	-6.0
Min - Max	101 - 149	-36 - 16
Cycle 9 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	33	33
Mean (SD)	121.0 (11.8)	-8.0 (14.8)
Median	121.0	-4.0
Min - Max	95 - 142	-54 - 13

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	29	29
Mean (SD)	120.8 (10.6)	-6.8 (12.8)
Median	120.0	-3.0
Min - Max	98 - 147	-30 - 19
AFTER PAC INFUSION		
n	26	26
Mean (SD)	122.9 (11.1)	-5.8 (15.0)
Median	123.0	1.0
Min - Max	94 - 140	-51 - 12
Cycle 10 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	32	32
Mean (SD)	122.3 (12.0)	-6.5 (15.5)
Median	126.0	-3.0
Min - Max	100 - 149	-50 - 18
PRE PAC INFUSION		
n	31	31
Mean (SD)	122.1 (12.0)	-5.2 (13.1)
Median	124.0	-2.0
Min - Max	99 - 151	-35 - 14
AFTER PAC INFUSION		
n	28	28
Mean (SD)	124.3 (11.1)	-5.4 (16.5)
Median	125.0	-2.0
Min - Max	97 - 151	-41 - 30
Cycle 10 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	119.3 (11.2)	-11.0 (18.2)
Median	119.0	-17.0
Min - Max	103 - 133	-28 - 20
PRE PAC INFUSION		
n	21	21
Mean (SD)	123.9 (14.1)	-7.5 (20.0)
Median	124.0	-5.0
Min - Max	104 - 165	-57 - 34
AFTER PAC INFUSION		
n	23	23
Mean (SD)	125.4 (13.1)	-5.6 (15.9)
Median	127.0	-7.0
Min - Max	101 - 163	-38 - 32

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 10 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	31	31
Mean (SD)	122.6 (14.5)	-6.6 (15.1)
Median	120.0	-6.0
Min - Max	99 - 156	-46 - 18
PRE PAC INFUSION		
n	28	28
Mean (SD)	120.7 (12.6)	-6.2 (13.5)
Median	120.0	-6.5
Min - Max	91 - 149	-35 - 21
AFTER PAC INFUSION		
n	24	24
Mean (SD)	119.9 (12.0)	-7.1 (14.9)
Median	118.5	-8.0
Min - Max	102 - 153	-51 - 22
Cycle 11 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	25	25
Mean (SD)	123.4 (14.4)	-5.6 (20.3)
Median	124.0	0.0
Min - Max	90 - 168	-45 - 27
PRE PAC INFUSION		
n	22	22
Mean (SD)	124.1 (14.4)	-3.9 (13.9)
Median	125.0	-0.5
Min - Max	100 - 158	-30 - 21
AFTER PAC INFUSION		
n	21	21
Mean (SD)	121.9 (12.0)	-7.3 (17.5)
Median	119.0	-7.0
Min - Max	104 - 161	-34 - 30
Cycle 11 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	116.3 (13.9)	1.5 (25.1)
Median	112.5	9.5
Min - Max	104 - 136	-35 - 22
PRE PAC INFUSION		
n	16	16
Mean (SD)	120.8 (10.1)	-10.6 (15.4)
Median	123.0	-4.0
Min - Max	100 - 139	-49 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	18	18
Mean (SD)	120.7 (10.2)	-7.5 (15.6)
Median	124.0	-7.0
Min - Max	100 - 139	-35 - 19
Cycle 11 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	21	21
Mean (SD)	122.6 (14.4)	-6.1 (13.5)
Median	122.0	-1.0
Min - Max	100 - 156	-30 - 13
PRE PAC INFUSION		
n	21	21
Mean (SD)	123.6 (14.9)	-4.8 (14.1)
Median	124.0	-1.0
Min - Max	99 - 154	-30 - 23
AFTER PAC INFUSION		
n	17	17
Mean (SD)	122.1 (9.9)	-3.9 (17.1)
Median	122.0	0.0
Min - Max	102 - 139	-49 - 19
Cycle 12 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	24	24
Mean (SD)	120.4 (14.4)	-9.6 (16.7)
Median	122.0	-8.0
Min - Max	98 - 144	-50 - 16
PRE PAC INFUSION		
n	21	21
Mean (SD)	127.2 (16.1)	-1.4 (15.8)
Median	127.0	0.0
Min - Max	105 - 167	-27 - 27
AFTER PAC INFUSION		
n	18	18
Mean (SD)	126.7 (18.0)	-0.6 (18.5)
Median	124.0	0.0
Min - Max	101 - 176	-31 - 34
Cycle 12 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	117.0 (15.0)	-13.3 (11.6)
Median	120.0	-18.5
Min - Max	98 - 130	-20 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	15	15
Mean (SD)	123.9 (11.5)	-5.1 (20.8)
Median	121.0	0.0
Min - Max	109 - 152	-61 - 21
AFTER PAC INFUSION		
n	16	16
Mean (SD)	125.8 (11.5)	-0.9 (11.4)
Median	127.0	0.0
Min - Max	104 - 151	-30 - 20
Cycle 12 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	23	23
Mean (SD)	121.0 (14.6)	-8.1 (15.3)
Median	119.0	-7.0
Min - Max	94 - 146	-34 - 22
PRE PAC INFUSION		
n	21	21
Mean (SD)	121.9 (13.1)	-6.7 (16.0)
Median	125.0	-4.0
Min - Max	91 - 152	-45 - 21
AFTER PAC INFUSION		
n	17	17
Mean (SD)	121.5 (12.5)	-3.8 (13.9)
Median	120.0	-2.0
Min - Max	102 - 147	-34 - 16
Cycle 13 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	21	21
Mean (SD)	124.0 (18.5)	-3.8 (19.2)
Median	127.0	1.0
Min - Max	90 - 158	-49 - 30
PRE PAC INFUSION		
n	20	20
Mean (SD)	124.0 (14.1)	-2.8 (15.3)
Median	126.5	-2.0
Min - Max	104 - 146	-41 - 31
AFTER PAC INFUSION		
n	13	13
Mean (SD)	120.5 (12.1)	-2.7 (16.5)
Median	124.0	0.0
Min - Max	100 - 138	-31 - 24

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 13 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	110.5 (13.4)	10.5 (2.1)
Median	110.5	10.5
Min - Max	101 - 120	9 - 12
PRE PAC INFUSION		
n	14	14
Mean (SD)	125.1 (9.5)	-5.6 (20.7)
Median	124.0	0.5
Min - Max	109 - 141	-51 - 26
AFTER PAC INFUSION		
n	15	15
Mean (SD)	119.7 (9.2)	-8.5 (16.8)
Median	120.0	-6.0
Min - Max	101 - 132	-53 - 9
Cycle 13 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	19	19
Mean (SD)	121.0 (13.0)	-5.4 (17.7)
Median	121.0	-3.0
Min - Max	102 - 145	-45 - 17
PRE PAC INFUSION		
n	19	19
Mean (SD)	118.8 (12.4)	-7.6 (15.1)
Median	120.0	-5.0
Min - Max	96 - 142	-35 - 16
AFTER PAC INFUSION		
n	15	15
Mean (SD)	119.7 (11.8)	-8.4 (15.2)
Median	123.0	-4.0
Min - Max	95 - 137	-43 - 9
Cycle 14 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	20	20
Mean (SD)	124.6 (13.7)	-4.7 (19.9)
Median	128.0	-3.5
Min - Max	101 - 148	-40 - 39
PRE PAC INFUSION		
n	18	18
Mean (SD)	120.8 (11.7)	-4.9 (13.9)
Median	121.5	-4.5
Min - Max	99 - 143	-32 - 29

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	14	14
Mean (SD)	121.6 (10.0)	-5.7 (14.9)
Median	120.0	-4.0
Min - Max	104 - 148	-35 - 20
Cycle 14 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	123.0 (28.6)	12.7 (13.1)
Median	107.0	14.0
Min - Max	106 - 156	-1 - 25
PRE PAC INFUSION		
n	10	10
Mean (SD)	123.7 (12.3)	-10.9 (19.5)
Median	125.5	-7.5
Min - Max	100 - 138	-34 - 23
AFTER PAC INFUSION		
n	12	12
Mean (SD)	119.8 (13.1)	-9.1 (15.9)
Median	119.0	-6.5
Min - Max	100 - 148	-31 - 18
Cycle 14 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	18	18
Mean (SD)	121.0 (11.5)	-9.9 (16.3)
Median	120.5	-5.5
Min - Max	95 - 140	-55 - 8
PRE PAC INFUSION		
n	16	16
Mean (SD)	122.3 (11.9)	-6.6 (11.9)
Median	121.5	-6.0
Min - Max	101 - 140	-28 - 16
AFTER PAC INFUSION		
n	12	12
Mean (SD)	122.3 (9.8)	-8.8 (13.6)
Median	121.5	-6.5
Min - Max	105 - 134	-38 - 7
Cycle 15 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	17	17
Mean (SD)	122.2 (11.3)	-7.3 (18.1)
Median	123.0	0.0
Min - Max	93 - 138	-44 - 24

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	16	16
Mean (SD)	122.9 (12.6)	-3.9 (14.2)
Median	125.0	-2.0
Min - Max	97 - 139	-30 - 25
AFTER PAC INFUSION		
n	10	10
Mean (SD)	126.2 (11.7)	-8.6 (19.6)
Median	129.0	-6.0
Min - Max	104 - 142	-41 - 28
Cycle 15 Day 8		
PRE PAC INFUSION		
n	10	10
Mean (SD)	119.5 (12.5)	-15.3 (21.4)
Median	120.0	-5.5
Min - Max	99 - 137	-52 - 6
AFTER PAC INFUSION		
n	10	10
Mean (SD)	119.4 (10.1)	-15.4 (16.1)
Median	121.5	-15.0
Min - Max	103 - 132	-43 - 2
Cycle 15 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	14	14
Mean (SD)	124.2 (10.9)	-4.9 (20.0)
Median	122.5	1.0
Min - Max	105 - 140	-55 - 26
PRE PAC INFUSION		
n	13	13
Mean (SD)	126.2 (11.8)	0.4 (13.3)
Median	130.0	0.0
Min - Max	105 - 139	-30 - 23
AFTER PAC INFUSION		
n	7	7
Mean (SD)	121.0 (11.0)	-9.0 (19.5)
Median	123.0	-7.0
Min - Max	100 - 135	-49 - 11
Cycle 16 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	118.3 (16.8)	-10.5 (23.7)
Median	117.5	-7.0
Min - Max	80 - 140	-65 - 26

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	12	12
Mean (SD)	123.3 (10.0)	-5.1 (16.3)
Median	123.0	-2.5
Min - Max	110 - 137	-28 - 22
AFTER PAC INFUSION		
n	7	7
Mean (SD)	129.6 (1.5)	-8.1 (15.0)
Median	130.0	-7.0
Min - Max	127 - 132	-31 - 16
Cycle 16 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	142.0 (NE)	3.0 (NE)
Median	142.0	3.0
Min - Max	142 - 142	3 - 3
PRE PAC INFUSION		
n	8	8
Mean (SD)	118.8 (17.1)	-19.4 (20.0)
Median	123.0	-11.0
Min - Max	90 - 139	-51 - 6
AFTER PAC INFUSION		
n	8	8
Mean (SD)	124.9 (15.0)	-13.3 (21.3)
Median	127.5	-12.5
Min - Max	100 - 150	-43 - 20
Cycle 16 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	14	14
Mean (SD)	122.6 (15.7)	-4.9 (20.9)
Median	123.5	-3.0
Min - Max	93 - 148	-35 - 29
PRE PAC INFUSION		
n	14	14
Mean (SD)	122.8 (12.2)	-5.4 (16.3)
Median	121.0	-4.0
Min - Max	107 - 145	-35 - 30
AFTER PAC INFUSION		
n	7	7
Mean (SD)	120.9 (11.6)	-13.7 (18.4)
Median	120.0	-16.0
Min - Max	103 - 138	-40 - 15

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 17 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	123.6 (13.7)	-5.7 (18.5)
Median	122.0	-3.0
Min - Max	101 - 145	-29 - 31
PRE PAC INFUSION		
n	11	11
Mean (SD)	124.2 (13.2)	-9.1 (14.3)
Median	126.0	-9.0
Min - Max	97 - 145	-30 - 12
AFTER PAC INFUSION		
n	7	7
Mean (SD)	130.1 (17.1)	-9.1 (17.9)
Median	129.0	-13.0
Min - Max	117 - 167	-30 - 15
Cycle 17 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	107.0 (NE)	-41.0 (NE)
Median	107.0	-41.0
Min - Max	107 - 107	-41 - -41
PRE PAC INFUSION		
n	7	7
Mean (SD)	126.0 (15.4)	-10.7 (14.1)
Median	130.0	-10.0
Min - Max	98 - 147	-27 - 16
AFTER PAC INFUSION		
n	8	8
Mean (SD)	125.5 (8.8)	-12.6 (14.3)
Median	124.5	-13.0
Min - Max	115 - 144	-30 - 7
Cycle 17 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	123.9 (14.3)	-9.2 (17.9)
Median	126.0	-9.5
Min - Max	100 - 143	-30 - 27
PRE PAC INFUSION		
n	12	12
Mean (SD)	119.6 (8.9)	-10.1 (14.0)
Median	121.5	-7.5
Min - Max	101 - 131	-35 - 11

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
AFTER PAC INFUSION		
n	8	8
Mean (SD)	121.8 (8.2)	-16.4 (17.3)
Median	122.0	-12.5
Min - Max	105 - 134	-48 - 7
Cycle 18 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	124.0 (12.5)	-5.5 (17.2)
Median	125.0	-4.0
Min - Max	104 - 140	-35 - 26
PRE PAC INFUSION		
n	13	13
Mean (SD)	120.9 (9.3)	-12.0 (17.3)
Median	123.0	-7.0
Min - Max	108 - 133	-46 - 15
AFTER PAC INFUSION		
n	8	8
Mean (SD)	125.3 (8.2)	-12.9 (24.9)
Median	124.0	-12.0
Min - Max	117 - 140	-55 - 26
Cycle 18 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	107.0 (NE)	-41.0 (NE)
Median	107.0	-41.0
Min - Max	107 - 107	-41 - -41
PRE PAC INFUSION		
n	6	6
Mean (SD)	126.0 (8.1)	-15.5 (20.6)
Median	129.0	-16.0
Min - Max	110 - 131	-41 - 17
AFTER PAC INFUSION		
n	7	7
Mean (SD)	126.0 (9.6)	-16.4 (23.4)
Median	128.0	-18.0
Min - Max	108 - 140	-43 - 15
Cycle 18 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	121.4 (8.7)	-11.8 (21.7)
Median	122.0	0.0
Min - Max	108 - 130	-60 - 16

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	11	11
Mean (SD)	121.2 (7.2)	-8.3 (15.7)
Median	122.0	0.0
Min - Max	112 - 131	-36 - 11
AFTER PAC INFUSION		
n	7	7
Mean (SD)	121.7 (8.8)	-15.0 (21.0)
Median	125.0	-13.0
Min - Max	104 - 130	-51 - 11
Cycle 19 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	124.4 (13.3)	-8.8 (17.0)
Median	123.0	-4.0
Min - Max	105 - 149	-37 - 16
PRE PAC INFUSION		
n	11	11
Mean (SD)	120.0 (9.7)	-9.5 (15.6)
Median	123.0	-10.0
Min - Max	100 - 133	-35 - 16
AFTER PAC INFUSION		
n	8	8
Mean (SD)	124.5 (7.9)	-13.6 (17.3)
Median	125.0	-14.5
Min - Max	110 - 135	-37 - 12
Cycle 19 Day 8		
PRE PAC INFUSION		
n	7	7
Mean (SD)	124.1 (12.0)	-12.6 (16.6)
Median	126.0	-8.0
Min - Max	106 - 139	-33 - 12
AFTER PAC INFUSION		
n	7	7
Mean (SD)	123.0 (10.9)	-13.7 (18.0)
Median	127.0	-16.0
Min - Max	105 - 133	-39 - 13
Cycle 19 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	120.4 (11.0)	-12.7 (18.9)
Median	121.0	-15.0
Min - Max	104 - 140	-43 - 26

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	11	11
Mean (SD)	122.6 (11.7)	-5.4 (12.7)
Median	122.0	-9.0
Min - Max	99 - 137	-25 - 21
AFTER PAC INFUSION		
n	7	7
Mean (SD)	119.0 (8.9)	-17.7 (19.0)
Median	119.0	-11.0
Min - Max	109 - 131	-53 - 1
Cycle 20 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	119.0 (16.4)	-14.1 (18.6)
Median	118.0	-17.0
Min - Max	94 - 144	-50 - 24
PRE PAC INFUSION		
n	10	10
Mean (SD)	117.8 (10.6)	-12.2 (16.5)
Median	120.0	-10.0
Min - Max	96 - 133	-49 - 6
AFTER PAC INFUSION		
n	7	7
Mean (SD)	124.0 (9.3)	-12.7 (17.1)
Median	121.0	-10.0
Min - Max	112 - 137	-35 - 8
Cycle 20 Day 8		
PRE PAC INFUSION		
n	7	7
Mean (SD)	120.1 (12.7)	-16.6 (25.7)
Median	120.0	-10.0
Min - Max	101 - 136	-62 - 22
AFTER PAC INFUSION		
n	7	7
Mean (SD)	129.3 (14.5)	-7.4 (22.4)
Median	130.0	-7.0
Min - Max	101 - 150	-39 - 20
Cycle 20 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	119.5 (14.0)	-13.6 (21.6)
Median	120.5	-14.5
Min - Max	93 - 145	-61 - 31

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	11	11
Mean (SD)	119.8 (11.9)	-8.2 (15.4)
Median	122.0	-7.0
Min - Max	103 - 139	-31 - 25
AFTER PAC INFUSION		
n	7	7
Mean (SD)	120.9 (12.1)	-15.9 (14.1)
Median	120.0	-15.0
Min - Max	100 - 134	-38 - 6
Cycle 21 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	123.8 (11.4)	-9.3 (15.4)
Median	127.0	-5.0
Min - Max	105 - 140	-38 - 10
PRE PAC INFUSION		
n	11	11
Mean (SD)	120.8 (11.7)	-7.2 (10.8)
Median	125.0	-7.0
Min - Max	95 - 131	-30 - 6
AFTER PAC INFUSION		
n	7	7
Mean (SD)	128.3 (16.6)	-8.4 (32.1)
Median	122.0	-11.0
Min - Max	114 - 163	-50 - 55
Cycle 21 Day 8		
PRE PAC INFUSION		
n	6	6
Mean (SD)	121.3 (17.9)	-16.5 (32.5)
Median	126.5	-13.5
Min - Max	95 - 143	-67 - 29
AFTER PAC INFUSION		
n	6	6
Mean (SD)	118.7 (10.5)	-19.2 (17.8)
Median	122.5	-11.0
Min - Max	102 - 129	-43 - -4
Cycle 21 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	114.0 (16.6)	-17.7 (26.6)
Median	118.0	-12.0
Min - Max	90 - 135	-68 - 21

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	9	9
Mean (SD)	116.7 (10.6)	-10.7 (19.3)
Median	120.0	-3.0
Min - Max	100 - 130	-45 - 13
AFTER PAC INFUSION		
n	6	6
Mean (SD)	118.3 (11.3)	-19.5 (25.8)
Median	117.5	-18.0
Min - Max	107 - 133	-64 - 11
Cycle 22 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	121.3 (12.8)	-11.8 (20.4)
Median	122.5	-11.5
Min - Max	97 - 144	-49 - 30
PRE PAC INFUSION		
n	10	10
Mean (SD)	119.4 (14.0)	-8.4 (19.7)
Median	122.0	-9.0
Min - Max	96 - 143	-44 - 29
AFTER PAC INFUSION		
n	6	6
Mean (SD)	127.3 (7.3)	-10.5 (29.1)
Median	128.0	-12.5
Min - Max	119 - 139	-52 - 25
Cycle 22 Day 8		
PRE PAC INFUSION		
n	4	4
Mean (SD)	126.8 (5.7)	-24.5 (21.9)
Median	128.0	-20.0
Min - Max	119 - 132	-53 - -5
AFTER PAC INFUSION		
n	4	4
Mean (SD)	128.3 (4.3)	-23.0 (15.3)
Median	128.5	-22.5
Min - Max	123 - 133	-39 - -8
Cycle 22 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	122.6 (11.6)	-10.7 (21.0)
Median	126.0	-4.0
Min - Max	101 - 141	-61 - 15

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	10	10
Mean (SD)	124.1 (11.6)	-3.7 (15.8)
Median	128.5	-5.0
Min - Max	100 - 140	-32 - 26
AFTER PAC INFUSION		
n	6	6
Mean (SD)	124.3 (17.5)	-13.5 (28.4)
Median	128.0	-10.5
Min - Max	95 - 145	-56 - 31
Cycle 23 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	116.2 (9.7)	-12.6 (19.7)
Median	116.0	-8.0
Min - Max	100 - 134	-58 - 5
PRE PAC INFUSION		
n	9	9
Mean (SD)	120.8 (7.9)	-5.1 (15.5)
Median	124.0	-1.0
Min - Max	107 - 128	-32 - 12
AFTER PAC INFUSION		
n	6	6
Mean (SD)	123.7 (7.0)	-14.2 (18.3)
Median	123.5	-13.0
Min - Max	116 - 133	-39 - 8
Cycle 23 Day 8		
PRE PAC INFUSION		
n	5	5
Mean (SD)	120.6 (14.5)	-22.0 (24.2)
Median	125.0	-10.0
Min - Max	102 - 135	-63 - -6
AFTER PAC INFUSION		
n	5	5
Mean (SD)	119.0 (11.6)	-23.6 (24.0)
Median	124.0	-18.0
Min - Max	105 - 133	-63 - -3
Cycle 23 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	115.8 (9.3)	-13.3 (20.7)
Median	114.0	-8.0
Min - Max	100 - 134	-59 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	9	9
Mean (SD)	122.3 (8.5)	-3.6 (16.2)
Median	123.0	0.0
Min - Max	109 - 132	-30 - 24
AFTER PAC INFUSION		
n	6	6
Mean (SD)	118.5 (9.8)	-19.3 (17.9)
Median	121.5	-13.5
Min - Max	102 - 128	-49 - -2
Cycle 24 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	10	10
Mean (SD)	122.6 (12.9)	-9.6 (18.9)
Median	123.0	-3.5
Min - Max	101 - 147	-39 - 15
PRE PAC INFUSION		
n	9	9
Mean (SD)	118.7 (8.6)	-7.2 (12.6)
Median	117.0	-2.0
Min - Max	104 - 130	-34 - 5
AFTER PAC INFUSION		
n	6	6
Mean (SD)	120.7 (13.6)	-17.2 (18.4)
Median	125.0	-17.0
Min - Max	103 - 134	-40 - 8
Cycle 24 Day 8		
PRE PAC INFUSION		
n	4	4
Mean (SD)	118.3 (21.8)	-20.0 (6.7)
Median	120.0	-19.0
Min - Max	90 - 143	-29 - -13
AFTER PAC INFUSION		
n	4	4
Mean (SD)	120.3 (12.0)	-18.0 (17.1)
Median	124.5	-12.0
Min - Max	103 - 129	-43 - -5
Cycle 24 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	10	10
Mean (SD)	116.6 (13.6)	-15.6 (20.1)
Median	121.0	-14.5
Min - Max	93 - 135	-45 - 11

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	9	9
Mean (SD)	119.1 (12.8)	-6.8 (11.7)
Median	124.0	-4.0
Min - Max	95 - 135	-25 - 13
AFTER PAC INFUSION		
n	6	6
Mean (SD)	122.7 (15.6)	-15.2 (11.8)
Median	124.5	-14.0
Min - Max	97 - 139	-33 - 0
Cycle 25 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	118.7 (13.0)	-16.1 (22.7)
Median	118.0	-4.0
Min - Max	100 - 138	-58 - 3
PRE PAC INFUSION		
n	10	10
Mean (SD)	119.3 (9.9)	-15.1 (18.0)
Median	121.5	-11.0
Min - Max	99 - 133	-49 - 5
AFTER PAC INFUSION		
n	4	4
Mean (SD)	115.0 (16.7)	-8.8 (1.9)
Median	114.5	-9.5
Min - Max	98 - 133	-10 - -6
Cycle 25 Day 8		
PRE PAC INFUSION		
n	3	3
Mean (SD)	124.7 (9.5)	-19.7 (11.2)
Median	128.0	-17.0
Min - Max	114 - 132	-32 - -10
AFTER PAC INFUSION		
n	3	3
Mean (SD)	129.7 (4.5)	-14.7 (13.3)
Median	130.0	-8.0
Min - Max	125 - 134	-30 - -6
Cycle 25 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	125.1 (14.7)	-12.1 (16.5)
Median	125.0	-6.5
Min - Max	101 - 148	-47 - 1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	8	8
Mean (SD)	120.8 (10.9)	-14.4 (15.4)
Median	123.0	-11.0
Min - Max	105 - 133	-39 - 2
AFTER PAC INFUSION		
n	5	5
Mean (SD)	122.8 (12.7)	-8.2 (18.1)
Median	128.0	-11.0
Min - Max	102 - 134	-30 - 20
Cycle 26 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	118.4 (11.0)	-19.8 (21.7)
Median	122.0	-10.0
Min - Max	98 - 132	-50 - 2
PRE PAC INFUSION		
n	8	8
Mean (SD)	122.1 (6.9)	-13.9 (21.1)
Median	124.5	-3.0
Min - Max	110 - 130	-55 - 3
AFTER PAC INFUSION		
n	4	4
Mean (SD)	122.3 (6.7)	-14.5 (14.3)
Median	122.5	-14.5
Min - Max	116 - 128	-32 - 3
Cycle 26 Day 8		
PRE PAC INFUSION		
n	5	5
Mean (SD)	123.0 (12.8)	-8.0 (18.7)
Median	128.0	-10.0
Min - Max	103 - 134	-32 - 20
AFTER PAC INFUSION		
n	5	5
Mean (SD)	123.8 (14.7)	-7.2 (23.9)
Median	128.0	-12.0
Min - Max	108 - 143	-32 - 29
Cycle 26 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	125.8 (8.9)	-12.4 (15.2)
Median	126.5	-10.0
Min - Max	108 - 136	-39 - 6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	8	8
Mean (SD)	122.5 (6.0)	-13.5 (21.2)
Median	121.0	-13.5
Min - Max	117 - 133	-55 - 11
AFTER PAC INFUSION		
n	4	4
Mean (SD)	119.8 (13.2)	-17.0 (17.1)
Median	124.0	-22.0
Min - Max	101 - 130	-30 - 6
Cycle 27 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	124.6 (10.3)	-13.5 (27.1)
Median	125.5	-4.0
Min - Max	108 - 138	-64 - 24
PRE PAC INFUSION		
n	8	8
Mean (SD)	120.1 (13.2)	-15.9 (27.1)
Median	122.0	-11.5
Min - Max	98 - 140	-64 - 26
AFTER PAC INFUSION		
n	4	4
Mean (SD)	130.8 (11.5)	-6.0 (25.3)
Median	131.5	-12.5
Min - Max	116 - 144	-29 - 30
Cycle 27 Day 8		
PRE PAC INFUSION		
n	3	3
Mean (SD)	127.3 (14.2)	-7.7 (26.7)
Median	134.0	-20.0
Min - Max	111 - 137	-26 - 23
AFTER PAC INFUSION		
n	3	3
Mean (SD)	134.3 (9.3)	-0.7 (26.1)
Median	137.0	-7.0
Min - Max	124 - 142	-23 - 28
Cycle 27 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	7	7
Mean (SD)	128.7 (6.0)	-4.6 (18.5)
Median	129.0	2.0
Min - Max	120 - 136	-34 - 22

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	7	7
Mean (SD)	123.9 (11.1)	-7.0 (20.6)
Median	126.0	-16.0
Min - Max	113 - 144	-32 - 30
AFTER PAC INFUSION		
n	4	4
Mean (SD)	127.0 (3.4)	-9.8 (21.0)
Median	127.0	-11.0
Min - Max	123 - 131	-34 - 17
Cycle 28 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	121.0 (9.1)	-12.5 (17.3)
Median	120.5	-7.0
Min - Max	109 - 133	-39 - 4
PRE PAC INFUSION		
n	4	4
Mean (SD)	124.0 (6.5)	-10.8 (14.9)
Median	125.5	-7.5
Min - Max	115 - 130	-30 - 2
AFTER PAC INFUSION		
n	2	2
Mean (SD)	128.0 (5.7)	-23.0 (7.1)
Median	128.0	-23.0
Min - Max	124 - 132	-28 - -18
Cycle 28 Day 8		
PRE PAC INFUSION		
n	2	2
Mean (SD)	132.0 (2.8)	-19.0 (15.6)
Median	132.0	-19.0
Min - Max	130 - 134	-30 - -8
AFTER PAC INFUSION		
n	2	2
Mean (SD)	131.5 (2.1)	-19.5 (10.6)
Median	131.5	-19.5
Min - Max	130 - 133	-27 - -12
Cycle 28 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	126.7 (6.7)	-6.8 (14.0)
Median	127.5	-6.5
Min - Max	115 - 135	-25 - 11

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	4	4
Mean (SD)	130.0 (6.5)	-4.8 (14.6)
Median	129.5	-4.5
Min - Max	123 - 138	-22 - 12
AFTER PAC INFUSION		
n	2	2
Mean (SD)	128.0 (2.8)	-23.0 (9.9)
Median	128.0	-23.0
Min - Max	126 - 130	-30 - -16
Cycle 29 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	7	7
Mean (SD)	125.4 (10.8)	-13.6 (24.3)
Median	127.0	-10.0
Min - Max	108 - 141	-45 - 27
PRE PAC INFUSION		
n	4	4
Mean (SD)	123.8 (9.6)	-11.0 (13.3)
Median	126.5	-9.5
Min - Max	110 - 132	-28 - 3
AFTER PAC INFUSION		
n	2	2
Mean (SD)	130.5 (3.5)	-20.5 (9.2)
Median	130.5	-20.5
Min - Max	128 - 133	-27 - -14
Cycle 29 Day 8		
PRE PAC INFUSION		
n	2	2
Mean (SD)	129.0 (1.4)	-22.0 (11.3)
Median	129.0	-22.0
Min - Max	128 - 130	-30 - -14
AFTER PAC INFUSION		
n	2	2
Mean (SD)	131.0 (1.4)	-20.0 (11.3)
Median	131.0	-20.0
Min - Max	130 - 132	-28 - -12
Cycle 29 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	119.5 (12.0)	-19.0 (29.6)
Median	124.0	-13.0
Min - Max	100 - 132	-72 - 10

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	123.7 (11.1)	-2.7 (5.5)
Median	125.0	-3.0
Min - Max	112 - 134	-8 - 3
AFTER PAC INFUSION		
n	1	1
Mean (SD)	130.0 (NE)	-12.0 (NE)
Median	130.0	-12.0
Min - Max	130 - 130	-12 - -12
Cycle 30 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	5	5
Mean (SD)	121.6 (11.5)	-6.6 (8.2)
Median	125.0	-10.0
Min - Max	105 - 132	-16 - 3
PRE PAC INFUSION		
n	3	3
Mean (SD)	122.7 (7.1)	-3.7 (8.1)
Median	124.0	0.0
Min - Max	115 - 129	-13 - 2
AFTER PAC INFUSION		
n	1	1
Mean (SD)	134.0 (NE)	-8.0 (NE)
Median	134.0	-8.0
Min - Max	134 - 134	-8 - -8
Cycle 30 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	126.0 (NE)	-16.0 (NE)
Median	126.0	-16.0
Min - Max	126 - 126	-16 - -16
AFTER PAC INFUSION		
n	1	1
Mean (SD)	130.0 (NE)	-12.0 (NE)
Median	130.0	-12.0
Min - Max	130 - 130	-12 - -12
Cycle 30 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	5	5
Mean (SD)	121.6 (9.9)	-6.6 (9.4)
Median	125.0	-8.0
Min - Max	106 - 130	-18 - 3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	124.3 (8.6)	-2.0 (7.2)
Median	126.0	0.0
Min - Max	115 - 132	-10 - 4
AFTER PAC INFUSION		
n	1	1
Mean (SD)	128.0 (NE)	-14.0 (NE)
Median	128.0	-14.0
Min - Max	128 - 128	-14 - -14
Cycle 31 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	127.8 (13.8)	4.5 (17.3)
Median	129.0	-0.5
Min - Max	110 - 143	-10 - 29
PRE PAC INFUSION		
n	3	3
Mean (SD)	122.3 (9.3)	-4.0 (7.5)
Median	125.0	-3.0
Min - Max	112 - 130	-12 - 3
AFTER PAC INFUSION		
n	1	1
Mean (SD)	126.0 (NE)	-16.0 (NE)
Median	126.0	-16.0
Min - Max	126 - 126	-16 - -16
Cycle 31 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	130.0 (NE)	-12.0 (NE)
Median	130.0	-12.0
Min - Max	130 - 130	-12 - -12
AFTER PAC INFUSION		
n	1	1
Mean (SD)	124.0 (NE)	-18.0 (NE)
Median	124.0	-18.0
Min - Max	124 - 124	-18 - -18
Cycle 31 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	124.0 (8.0)	0.8 (11.8)
Median	127.5	2.0
Min - Max	112 - 129	-14 - 13

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	119.3 (8.3)	-7.0 (8.2)
Median	122.0	-5.0
Min - Max	110 - 126	-16 - 0
AFTER PAC INFUSION		
n	1	1
Mean (SD)	124.0 (NE)	-18.0 (NE)
Median	124.0	-18.0
Min - Max	124 - 124	-18 - -18
Cycle 32 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	126.5 (11.3)	3.3 (15.8)
Median	127.5	0.0
Min - Max	112 - 139	-12 - 25
PRE PAC INFUSION		
n	3	3
Mean (SD)	122.3 (4.0)	-4.0 (10.4)
Median	123.0	1.0
Min - Max	118 - 126	-16 - 3
AFTER PAC INFUSION		
n	1	1
Mean (SD)	121.0 (NE)	-21.0 (NE)
Median	121.0	-21.0
Min - Max	121 - 121	-21 - -21
Cycle 32 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	130.0 (NE)	-12.0 (NE)
Median	130.0	-12.0
Min - Max	130 - 130	-12 - -12
AFTER PAC INFUSION		
n	1	1
Mean (SD)	126.0 (NE)	-16.0 (NE)
Median	126.0	-16.0
Min - Max	126 - 126	-16 - -16
Cycle 32 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	123.3 (5.0)	0.0 (11.2)
Median	125.0	1.5
Min - Max	116 - 127	-15 - 12

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	124.0 (0.0)	-2.3 (14.0)
Median	124.0	2.0
Min - Max	124 - 124	-18 - 9
AFTER PAC INFUSION		
n	1	1
Mean (SD)	122.0 (NE)	-20.0 (NE)
Median	122.0	-20.0
Min - Max	122 - 122	-20 - -20
Cycle 33 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	123.7 (8.0)	-2.7 (6.4)
Median	123.0	1.0
Min - Max	116 - 132	-10 - 1
PRE PAC INFUSION		
n	2	2
Mean (SD)	118.0 (4.2)	-0.5 (0.7)
Median	118.0	-0.5
Min - Max	115 - 121	-1 - 0
Cycle 33 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	130.0 (NE)	-12.0 (NE)
Median	130.0	-12.0
Min - Max	130 - 130	-12 - -12
Cycle 33 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	127.0 (5.7)	-5.0 (8.5)
Median	127.0	-5.0
Min - Max	123 - 131	-11 - 1
PRE PAC INFUSION		
n	1	1
Mean (SD)	119.0 (NE)	-3.0 (NE)
Median	119.0	-3.0
Min - Max	119 - 119	-3 - -3
Cycle 34 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	115.0 (8.5)	-3.5 (3.5)
Median	115.0	-3.5
Min - Max	109 - 121	-6 - -1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	2	2
Mean (SD)	127.0 (7.1)	8.5 (12.0)
Median	127.0	8.5
Min - Max	122 - 132	0 - 17
AFTER PAC INFUSION		
n	1	1
Mean (SD)	114.0 (NE)	-28.0 (NE)
Median	114.0	-28.0
Min - Max	114 - 114	-28 - -28
Cycle 34 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	133.0 (NE)	-9.0 (NE)
Median	133.0	-9.0
Min - Max	133 - 133	-9 - -9
Cycle 34 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	123.0 (2.8)	-9.0 (11.3)
Median	123.0	-9.0
Min - Max	121 - 125	-17 - -1
PRE PAC INFUSION		
n	1	1
Mean (SD)	122.0 (NE)	0.0 (NE)
Median	122.0	0.0
Min - Max	122 - 122	0 - 0
Cycle 35 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	122.7 (8.6)	-3.7 (5.5)
Median	121.0	-1.0
Min - Max	115 - 132	-10 - 0
PRE PAC INFUSION		
n	2	2
Mean (SD)	115.5 (4.9)	-3.0 (0.0)
Median	115.5	-3.0
Min - Max	112 - 119	-3 - -3
Cycle 35 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	126.0 (NE)	-16.0 (NE)
Median	126.0	-16.0
Min - Max	126 - 126	-16 - -16

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 35 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	116.0 (9.9)	-2.5 (4.9)
Median	116.0	-2.5
Min - Max	109 - 123	-6 - 1
PRE PAC INFUSION		
n	2	2
Mean (SD)	117.0 (7.1)	-1.5 (2.1)
Median	117.0	-1.5
Min - Max	112 - 122	-3 - 0
Cycle 36 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	118.5 (3.5)	0.0 (1.4)
Median	118.5	0.0
Min - Max	116 - 121	-1 - 1
PRE PAC INFUSION		
n	2	2
Mean (SD)	118.5 (0.7)	0.0 (4.2)
Median	118.5	0.0
Min - Max	118 - 119	-3 - 3
Cycle 36 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	124.5 (3.5)	6.0 (8.5)
Median	124.5	6.0
Min - Max	122 - 127	0 - 12
PRE PAC INFUSION		
n	2	2
Mean (SD)	119.5 (3.5)	1.0 (8.5)
Median	119.5	1.0
Min - Max	117 - 122	-5 - 7
Cycle 37 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	119.5 (0.7)	1.0 (5.7)
Median	119.5	1.0
Min - Max	119 - 120	-3 - 5
PRE PAC INFUSION		
n	2	2
Mean (SD)	117.5 (3.5)	-1.0 (1.4)
Median	117.5	-1.0
Min - Max	115 - 120	-2 - 0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 37 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	121.5 (0.7)	3.0 (5.7)
Median	121.5	3.0
Min - Max	121 - 122	-1 - 7
PRE PAC INFUSION		
n	2	2
Mean (SD)	123.5 (3.5)	5.0 (8.5)
Median	123.5	5.0
Min - Max	121 - 126	-1 - 11
Cycle 38 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	119.5 (2.1)	1.0 (2.8)
Median	119.5	1.0
Min - Max	118 - 121	-1 - 3
PRE PAC INFUSION		
n	2	2
Mean (SD)	115.5 (4.9)	-3.0 (0.0)
Median	115.5	-3.0
Min - Max	112 - 119	-3 - -3
Cycle 38 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	119.5 (0.7)	1.0 (5.7)
Median	119.5	1.0
Min - Max	119 - 120	-3 - 5
PRE PAC INFUSION		
n	2	2
Mean (SD)	117.0 (1.4)	-1.5 (3.5)
Median	117.0	-1.5
Min - Max	116 - 118	-4 - 1
Cycle 39 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	122.0 (1.4)	3.5 (6.4)
Median	122.0	3.5
Min - Max	121 - 123	-1 - 8
PRE PAC INFUSION		
n	2	2
Mean (SD)	117.0 (2.8)	-1.5 (2.1)
Median	117.0	-1.5
Min - Max	115 - 119	-3 - 0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 39 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	116.0 (5.7)	-2.5 (0.7)
Median	116.0	-2.5
Min - Max	112 - 120	-3 - -2
PRE PAC INFUSION		
n	2	2
Mean (SD)	114.5 (6.4)	-4.0 (1.4)
Median	114.5	-4.0
Min - Max	110 - 119	-5 - -3
Cycle 40 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	115.0 (NE)	0.0 (NE)
Median	115.0	0.0
Min - Max	115 - 115	0 - 0
PRE PAC INFUSION		
n	1	1
Mean (SD)	119.0 (NE)	4.0 (NE)
Median	119.0	4.0
Min - Max	119 - 119	4 - 4
Cycle 40 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	110.0 (NE)	-5.0 (NE)
Median	110.0	-5.0
Min - Max	110 - 110	-5 - -5
PRE PAC INFUSION		
n	1	1
Mean (SD)	109.0 (NE)	-6.0 (NE)
Median	109.0	-6.0
Min - Max	109 - 109	-6 - -6
Cycle 41 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	119.0 (NE)	4.0 (NE)
Median	119.0	4.0
Min - Max	119 - 119	4 - 4
PRE PAC INFUSION		
n	1	1
Mean (SD)	122.0 (NE)	7.0 (NE)
Median	122.0	7.0
Min - Max	122 - 122	7 - 7

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 41 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	109.0 (NE)	-6.0 (NE)
Median	109.0	-6.0
Min - Max	109 - 109	-6 - -6
PRE PAC INFUSION		
n	1	1
Mean (SD)	102.0 (NE)	-13.0 (NE)
Median	102.0	-13.0
Min - Max	102 - 102	-13 - -13
Cycle 42 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	113.0 (NE)	-2.0 (NE)
Median	113.0	-2.0
Min - Max	113 - 113	-2 - -2
PRE PAC INFUSION		
n	1	1
Mean (SD)	112.0 (NE)	-3.0 (NE)
Median	112.0	-3.0
Min - Max	112 - 112	-3 - -3
Cycle 42 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	114.0 (NE)	-1.0 (NE)
Median	114.0	-1.0
Min - Max	114 - 114	-1 - -1
PRE PAC INFUSION		
n	1	1
Mean (SD)	117.0 (NE)	2.0 (NE)
Median	117.0	2.0
Min - Max	117 - 117	2 - 2
Cycle 43 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	103.0 (NE)	-12.0 (NE)
Median	103.0	-12.0
Min - Max	103 - 103	-12 - -12
PRE PAC INFUSION		
n	1	1
Mean (SD)	109.0 (NE)	-6.0 (NE)
Median	109.0	-6.0
Min - Max	109 - 109	-6 - -6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 43 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	112.0 (NE)	-3.0 (NE)
Median	112.0	-3.0
Min - Max	112 - 112	-3 - -3
PRE PAC INFUSION		
n	1	1
Mean (SD)	110.0 (NE)	-5.0 (NE)
Median	110.0	-5.0
Min - Max	110 - 110	-5 - -5
Cycle 44 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	113.0 (NE)	-2.0 (NE)
Median	113.0	-2.0
Min - Max	113 - 113	-2 - -2
PRE PAC INFUSION		
n	1	1
Mean (SD)	118.0 (NE)	3.0 (NE)
Median	118.0	3.0
Min - Max	118 - 118	3 - 3
Cycle 44 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	106.0 (NE)	-9.0 (NE)
Median	106.0	-9.0
Min - Max	106 - 106	-9 - -9
PRE PAC INFUSION		
n	1	1
Mean (SD)	103.0 (NE)	-12.0 (NE)
Median	103.0	-12.0
Min - Max	103 - 103	-12 - -12
Study Drug Discontinuation		
n	89	89
Mean (SD)	123.4 (15.7)	-5.1 (16.7)
Median	122.0	-3.0
Min - Max	80 - 166	-70 - 31
Post-Baseline Last		
n	89	89
Mean (SD)	123.4 (15.7)	-5.1 (16.7)
Median	122.0	-3.0
Min - Max	80 - 166	-70 - 31

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	104.7 (9.0)	-28.3 (37.9)
Median	100.0	-9.0
Min - Max	99 - 115	-72 - -4
PRE PAC INFUSION		
n	3	3
Mean (SD)	107.7 (5.9)	-30.3 (36.5)
Median	110.0	-15.0
Min - Max	101 - 112	-72 - -4
AFTER PAC INFUSION		
n	7	7
Mean (SD)	120.4 (20.3)	-11.4 (25.0)
Median	119.0	-8.0
Min - Max	93 - 143	-62 - 10
Post-Baseline Minimum		
n	4	4
Mean (SD)	103.3 (15.9)	-35.8 (14.5)
Median	108.5	-34.0
Min - Max	80 - 116	-55 - -20
PRE ATEZO INFUSION (COHORT C)		
n	39	39
Mean (SD)	102.1 (12.3)	-30.4 (22.7)
Median	100.0	-25.0
Min - Max	60 - 121	-110 - 0
PRE PAC INFUSION		
n	36	36
Mean (SD)	100.6 (8.4)	-27.1 (16.2)
Median	100.0	-25.5
Min - Max	90 - 120	-79 - 0
AFTER PAC INFUSION		
n	23	23
Mean (SD)	101.8 (12.4)	-22.2 (16.7)
Median	100.0	-20.0
Min - Max	78 - 124	-65 - 4
Post-Baseline Maximum		
n	3	3
Mean (SD)	154.7 (9.2)	18.0 (11.3)
Median	160.0	24.0
Min - Max	144 - 160	5 - 25
PRE ATEZO INFUSION (COHORT C)		
n	31	31
Mean (SD)	145.3 (18.6)	10.1 (18.3)
Median	140.0	10.0
Min - Max	119 - 200	-31 - 45

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Systolic Blood Pressure (mmHg)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	23	23
Mean (SD)	140.4 (19.5)	21.0 (19.4)
Median	140.0	20.0
Min - Max	116 - 188	-25 - 71
AFTER PAC INFUSION		
n	45	45
Mean (SD)	149.0 (17.9)	19.5 (16.6)
Median	148.0	20.0
Min - Max	112 - 192	-25 - 57

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Baseline		
n	102	
Mean (SD)	78.1 (8.9)	
Median	79.0	
Min - Max	59 - 102	
Cycle 1 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	97	97
Mean (SD)	78.8 (10.9)	1.1 (10.4)
Median	78.0	1.0
Min - Max	54 - 117	-26 - 25
PRE PAC INFUSION		
n	78	78
Mean (SD)	76.1 (10.7)	-1.6 (10.9)
Median	74.5	-2.0
Min - Max	55 - 103	-24 - 28
AFTER PAC INFUSION		
n	95	95
Mean (SD)	76.2 (10.4)	-1.7 (8.9)
Median	77.0	-1.0
Min - Max	36 - 100	-42 - 17
Cycle 1 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	16	16
Mean (SD)	82.1 (14.0)	5.8 (14.8)
Median	78.0	4.0
Min - Max	64 - 112	-17 - 45
PRE PAC INFUSION		
n	85	85
Mean (SD)	80.0 (12.0)	2.0 (11.9)
Median	79.0	1.0
Min - Max	56 - 128	-29 - 43
AFTER PAC INFUSION		
n	92	92
Mean (SD)	79.8 (10.1)	2.0 (10.1)
Median	79.5	0.5
Min - Max	52 - 102	-19 - 35
Cycle 1 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	92	92
Mean (SD)	80.3 (11.1)	1.8 (10.7)
Median	80.0	1.0
Min - Max	53 - 113	-28 - 28

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	68	68
Mean (SD)	78.9 (9.3)	0.2 (10.4)
Median	78.0	0.0
Min - Max	60 - 102	-22 - 28
AFTER PAC INFUSION		
n	77	77
Mean (SD)	79.3 (10.4)	0.6 (10.6)
Median	79.0	-1.0
Min - Max	61 - 110	-20 - 37
Cycle 2 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	98	98
Mean (SD)	80.7 (12.0)	3.0 (11.3)
Median	79.0	2.0
Min - Max	61 - 135	-19 - 35
PRE PAC INFUSION		
n	79	79
Mean (SD)	78.2 (10.5)	0.2 (11.5)
Median	78.0	0.0
Min - Max	53 - 107	-25 - 35
AFTER PAC INFUSION		
n	89	89
Mean (SD)	78.3 (10.7)	1.0 (10.2)
Median	78.0	0.0
Min - Max	53 - 115	-25 - 27
Cycle 2 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	19	19
Mean (SD)	81.4 (15.0)	6.2 (13.7)
Median	82.0	4.0
Min - Max	54 - 120	-10 - 39
PRE PAC INFUSION		
n	79	79
Mean (SD)	83.1 (12.0)	4.9 (11.3)
Median	81.0	4.0
Min - Max	57 - 111	-21 - 33
AFTER PAC INFUSION		
n	87	87
Mean (SD)	82.1 (11.4)	4.0 (10.8)
Median	81.0	3.0
Min - Max	62 - 118	-20 - 33

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 2 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	88	88
Mean (SD)	82.1 (11.1)	4.5 (10.5)
Median	82.0	3.0
Min - Max	54 - 127	-16 - 37
PRE PAC INFUSION		
n	70	70
Mean (SD)	80.7 (9.8)	2.7 (10.2)
Median	79.5	-0.5
Min - Max	64 - 110	-16 - 35
AFTER PAC INFUSION		
n	83	83
Mean (SD)	80.7 (10.8)	2.8 (10.4)
Median	79.0	1.0
Min - Max	61 - 126	-25 - 35
Cycle 3 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	86	86
Mean (SD)	82.3 (12.0)	4.3 (11.3)
Median	82.0	2.5
Min - Max	60 - 118	-20 - 27
PRE PAC INFUSION		
n	70	70
Mean (SD)	79.9 (11.1)	2.5 (10.3)
Median	78.5	1.0
Min - Max	60 - 120	-24 - 22
AFTER PAC INFUSION		
n	82	82
Mean (SD)	81.3 (11.6)	3.4 (10.8)
Median	80.0	4.0
Min - Max	59 - 116	-20 - 26
Cycle 3 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	15	15
Mean (SD)	80.4 (15.2)	2.9 (14.4)
Median	80.0	2.0
Min - Max	60 - 106	-20 - 31
PRE PAC INFUSION		
n	74	74
Mean (SD)	83.0 (11.7)	5.1 (11.0)
Median	82.5	4.5
Min - Max	60 - 126	-16 - 35

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
AFTER PAC INFUSION		
n	80	80
Mean (SD)	81.2 (10.4)	3.0 (10.3)
Median	80.0	3.0
Min - Max	61 - 128	-20 - 30
Cycle 3 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	78	78
Mean (SD)	81.8 (11.5)	3.9 (11.7)
Median	80.0	2.0
Min - Max	61 - 127	-14 - 45
PRE PAC INFUSION		
n	62	62
Mean (SD)	80.3 (10.8)	2.1 (11.5)
Median	78.0	0.5
Min - Max	56 - 110	-20 - 42
AFTER PAC INFUSION		
n	77	77
Mean (SD)	81.5 (10.6)	3.5 (10.9)
Median	78.0	3.0
Min - Max	63 - 125	-17 - 33
Cycle 4 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	79	79
Mean (SD)	81.6 (11.1)	3.9 (10.4)
Median	81.0	2.0
Min - Max	57 - 116	-16 - 28
PRE PAC INFUSION		
n	69	69
Mean (SD)	79.3 (10.4)	1.4 (9.6)
Median	80.0	1.0
Min - Max	54 - 102	-15 - 34
AFTER PAC INFUSION		
n	78	78
Mean (SD)	80.0 (10.2)	1.7 (9.9)
Median	79.0	2.0
Min - Max	58 - 110	-18 - 27
Cycle 4 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	15	15
Mean (SD)	77.4 (12.4)	2.1 (9.7)
Median	78.0	1.0
Min - Max	54 - 100	-13 - 25

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	70	70
Mean (SD)	83.5 (11.6)	5.1 (11.4)
Median	82.0	5.0
Min - Max	60 - 120	-14 - 39
AFTER PAC INFUSION		
n	81	81
Mean (SD)	81.8 (10.6)	3.8 (10.0)
Median	82.0	4.0
Min - Max	62 - 121	-20 - 28
Cycle 4 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	79	79
Mean (SD)	81.9 (11.7)	3.5 (10.6)
Median	80.0	2.0
Min - Max	60 - 120	-20 - 45
PRE PAC INFUSION		
n	66	66
Mean (SD)	80.7 (10.1)	2.6 (10.7)
Median	80.0	2.0
Min - Max	58 - 105	-20 - 42
AFTER PAC INFUSION		
n	75	75
Mean (SD)	81.0 (10.7)	3.1 (12.0)
Median	78.0	2.0
Min - Max	60 - 108	-23 - 40
Cycle 5 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	65	65
Mean (SD)	78.5 (10.0)	1.0 (10.7)
Median	77.0	1.0
Min - Max	58 - 103	-26 - 25
PRE PAC INFUSION		
n	58	58
Mean (SD)	77.9 (10.4)	0.2 (10.8)
Median	77.5	0.0
Min - Max	53 - 107	-24 - 27
AFTER PAC INFUSION		
n	64	64
Mean (SD)	79.9 (10.7)	2.4 (11.9)
Median	78.0	0.0
Min - Max	54 - 107	-20 - 30

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 5 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	13	13
Mean (SD)	73.8 (10.0)	-2.5 (10.2)
Median	75.0	-3.0
Min - Max	61 - 91	-23 - 14
PRE PAC INFUSION		
n	55	55
Mean (SD)	80.4 (10.7)	2.6 (11.3)
Median	80.0	2.0
Min - Max	60 - 108	-17 - 43
AFTER PAC INFUSION		
n	59	59
Mean (SD)	79.2 (9.8)	1.7 (11.4)
Median	79.0	1.0
Min - Max	59 - 101	-21 - 30
Cycle 5 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	64	64
Mean (SD)	79.2 (11.0)	1.4 (11.7)
Median	78.0	0.0
Min - Max	40 - 105	-31 - 27
PRE PAC INFUSION		
n	56	56
Mean (SD)	78.8 (9.2)	1.0 (11.3)
Median	79.5	0.5
Min - Max	53 - 95	-28 - 29
AFTER PAC INFUSION		
n	58	58
Mean (SD)	80.0 (10.0)	2.4 (11.6)
Median	79.0	2.5
Min - Max	60 - 98	-19 - 25
Cycle 6 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	59	59
Mean (SD)	79.5 (9.0)	1.6 (11.5)
Median	80.0	2.0
Min - Max	58 - 100	-19 - 28
PRE PAC INFUSION		
n	57	57
Mean (SD)	81.0 (9.2)	3.4 (11.3)
Median	80.0	2.0
Min - Max	61 - 97	-20 - 26

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	58	58
Mean (SD)	81.4 (9.2)	3.7 (12.0)
Median	80.0	5.0
Min - Max	60 - 102	-21 - 30
Cycle 6 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	13	13
Mean (SD)	79.0 (10.9)	-2.1 (9.9)
Median	79.0	-2.0
Min - Max	64 - 101	-22 - 12
PRE PAC INFUSION		
n	49	49
Mean (SD)	79.3 (10.5)	1.8 (11.6)
Median	77.0	2.0
Min - Max	60 - 107	-21 - 29
AFTER PAC INFUSION		
n	58	58
Mean (SD)	79.3 (9.8)	1.2 (11.3)
Median	80.0	0.5
Min - Max	57 - 100	-24 - 28
Cycle 6 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	52	52
Mean (SD)	78.9 (9.0)	0.6 (11.2)
Median	79.0	0.5
Min - Max	59 - 100	-19 - 25
PRE PAC INFUSION		
n	49	49
Mean (SD)	78.9 (9.6)	1.1 (11.7)
Median	78.0	1.0
Min - Max	55 - 103	-26 - 22
AFTER PAC INFUSION		
n	48	48
Mean (SD)	80.6 (11.0)	2.3 (12.5)
Median	78.0	0.0
Min - Max	62 - 106	-15 - 35
Cycle 7 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	53	53
Mean (SD)	80.0 (9.5)	1.6 (11.8)
Median	80.0	1.0
Min - Max	56 - 100	-20 - 38

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	46	46
Mean (SD)	79.1 (9.4)	1.2 (11.8)
Median	77.5	0.5
Min - Max	63 - 105	-19 - 40
AFTER PAC INFUSION		
n	50	50
Mean (SD)	80.7 (9.8)	2.1 (12.6)
Median	78.0	-0.5
Min - Max	62 - 110	-20 - 41
Cycle 7 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	80.8 (12.5)	3.2 (17.3)
Median	80.0	-2.0
Min - Max	63 - 112	-17 - 50
PRE PAC INFUSION		
n	42	42
Mean (SD)	81.7 (10.4)	3.7 (11.3)
Median	80.0	2.5
Min - Max	59 - 101	-18 - 26
AFTER PAC INFUSION		
n	49	49
Mean (SD)	79.8 (8.3)	1.8 (11.2)
Median	78.0	1.0
Min - Max	61 - 96	-19 - 34
Cycle 7 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	49	49
Mean (SD)	81.2 (10.9)	2.6 (12.7)
Median	78.0	2.0
Min - Max	59 - 120	-18 - 44
PRE PAC INFUSION		
n	44	44
Mean (SD)	78.3 (9.3)	0.1 (12.1)
Median	78.0	-0.5
Min - Max	56 - 98	-25 - 20
AFTER PAC INFUSION		
n	45	45
Mean (SD)	82.2 (8.6)	4.1 (11.4)
Median	82.0	4.0
Min - Max	62 - 100	-16 - 31

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 8 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	46	46
Mean (SD)	80.8 (9.4)	2.6 (11.1)
Median	80.5	3.5
Min - Max	59 - 103	-19 - 30
PRE PAC INFUSION		
n	42	42
Mean (SD)	78.8 (9.0)	1.2 (11.3)
Median	78.0	0.0
Min - Max	53 - 106	-28 - 24
AFTER PAC INFUSION		
n	45	45
Mean (SD)	79.5 (8.5)	0.9 (10.5)
Median	78.0	-2.0
Min - Max	61 - 107	-15 - 25
Cycle 8 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	10	10
Mean (SD)	85.0 (10.2)	2.7 (12.7)
Median	83.5	1.5
Min - Max	72 - 110	-12 - 27
PRE PAC INFUSION		
n	34	34
Mean (SD)	79.6 (10.8)	1.8 (11.9)
Median	80.0	3.0
Min - Max	56 - 101	-14 - 25
AFTER PAC INFUSION		
n	42	42
Mean (SD)	80.0 (10.6)	1.6 (10.6)
Median	80.0	1.0
Min - Max	54 - 104	-18 - 26
Cycle 8 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	44	44
Mean (SD)	80.6 (10.2)	2.7 (11.8)
Median	79.0	1.5
Min - Max	59 - 104	-16 - 28
PRE PAC INFUSION		
n	33	33
Mean (SD)	78.5 (9.4)	0.8 (9.8)
Median	78.0	1.0
Min - Max	59 - 103	-18 - 21

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	39	39
Mean (SD)	79.2 (11.9)	0.7 (11.4)
Median	76.0	-3.0
Min - Max	60 - 110	-18 - 28
Cycle 9 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	35	35
Mean (SD)	79.7 (9.5)	2.0 (11.5)
Median	80.0	3.0
Min - Max	58 - 100	-23 - 36
PRE PAC INFUSION		
n	30	30
Mean (SD)	78.7 (11.2)	0.8 (11.4)
Median	78.0	-0.5
Min - Max	64 - 116	-17 - 34
AFTER PAC INFUSION		
n	32	32
Mean (SD)	76.3 (8.8)	-2.2 (10.6)
Median	77.0	-3.5
Min - Max	51 - 92	-30 - 14
Cycle 9 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	7	7
Mean (SD)	82.1 (12.6)	2.3 (10.7)
Median	88.0	0.0
Min - Max	64 - 100	-8 - 23
PRE PAC INFUSION		
n	23	23
Mean (SD)	79.7 (9.4)	1.3 (11.3)
Median	78.0	0.0
Min - Max	64 - 96	-16 - 24
AFTER PAC INFUSION		
n	27	27
Mean (SD)	81.3 (9.4)	3.2 (10.8)
Median	80.0	1.0
Min - Max	62 - 98	-20 - 28
Cycle 9 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	33	33
Mean (SD)	79.6 (9.7)	1.3 (11.4)
Median	81.0	2.0
Min - Max	54 - 97	-28 - 22

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	29	29
Mean (SD)	76.2 (10.6)	-2.6 (11.5)
Median	78.0	0.0
Min - Max	53 - 93	-25 - 16
AFTER PAC INFUSION		
n	26	26
Mean (SD)	82.0 (8.2)	3.2 (9.7)
Median	81.5	4.5
Min - Max	68 - 105	-12 - 25
Cycle 10 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	32	32
Mean (SD)	77.1 (9.6)	-0.3 (12.0)
Median	77.0	-1.0
Min - Max	60 - 99	-18 - 29
PRE PAC INFUSION		
n	31	31
Mean (SD)	77.0 (9.9)	-1.8 (11.4)
Median	75.0	-3.0
Min - Max	58 - 110	-22 - 22
AFTER PAC INFUSION		
n	28	28
Mean (SD)	79.4 (10.7)	0.9 (13.1)
Median	78.5	2.0
Min - Max	56 - 110	-25 - 24
Cycle 10 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	81.3 (8.8)	4.8 (10.3)
Median	78.5	9.0
Min - Max	71 - 94	-9 - 14
PRE PAC INFUSION		
n	21	21
Mean (SD)	80.0 (10.4)	0.3 (10.6)
Median	79.0	-2.0
Min - Max	64 - 104	-15 - 31
AFTER PAC INFUSION		
n	23	23
Mean (SD)	80.8 (8.3)	0.4 (9.3)
Median	81.0	0.0
Min - Max	64 - 98	-18 - 21

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 10 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	31	31
Mean (SD)	78.2 (9.7)	1.2 (10.5)
Median	77.0	0.0
Min - Max	61 - 109	-17 - 32
PRE PAC INFUSION		
n	28	28
Mean (SD)	75.4 (10.3)	-3.4 (10.6)
Median	76.0	-2.5
Min - Max	50 - 100	-29 - 12
AFTER PAC INFUSION		
n	24	24
Mean (SD)	79.1 (8.1)	0.5 (9.7)
Median	77.5	1.5
Min - Max	68 - 96	-21 - 19
Cycle 11 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	25	25
Mean (SD)	80.6 (9.2)	3.6 (10.0)
Median	80.0	4.0
Min - Max	65 - 105	-12 - 28
PRE PAC INFUSION		
n	22	22
Mean (SD)	78.6 (11.5)	0.1 (12.6)
Median	78.0	1.0
Min - Max	60 - 120	-21 - 34
AFTER PAC INFUSION		
n	21	21
Mean (SD)	76.1 (8.3)	-1.2 (10.7)
Median	75.0	-1.0
Min - Max	61 - 101	-20 - 24
Cycle 11 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	87.3 (8.3)	8.3 (13.8)
Median	89.5	7.0
Min - Max	76 - 94	-4 - 23
PRE PAC INFUSION		
n	16	16
Mean (SD)	75.7 (6.8)	-2.7 (10.2)
Median	77.0	-4.5
Min - Max	60 - 82	-21 - 12

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	18	18
Mean (SD)	78.9 (8.1)	0.9 (10.6)
Median	79.0	0.5
Min - Max	65 - 96	-21 - 18
Cycle 11 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	21	21
Mean (SD)	79.7 (9.8)	1.7 (11.9)
Median	80.0	1.0
Min - Max	61 - 100	-19 - 23
PRE PAC INFUSION		
n	21	21
Mean (SD)	77.6 (7.4)	-0.5 (10.5)
Median	77.0	-1.0
Min - Max	66 - 89	-22 - 19
AFTER PAC INFUSION		
n	17	17
Mean (SD)	79.6 (9.6)	1.8 (12.4)
Median	80.0	0.0
Min - Max	62 - 100	-19 - 22
Cycle 12 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	24	24
Mean (SD)	79.6 (10.2)	2.8 (11.8)
Median	78.5	0.5
Min - Max	64 - 99	-14 - 29
PRE PAC INFUSION		
n	21	21
Mean (SD)	77.1 (6.6)	0.0 (10.5)
Median	75.0	-2.0
Min - Max	67 - 89	-17 - 19
AFTER PAC INFUSION		
n	18	18
Mean (SD)	76.8 (10.9)	0.3 (11.4)
Median	78.0	0.0
Min - Max	54 - 101	-27 - 21
Cycle 12 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	75.5 (10.0)	-3.0 (7.6)
Median	74.0	-3.5
Min - Max	66 - 88	-10 - 5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	15	15
Mean (SD)	76.7 (7.8)	-0.5 (10.1)
Median	78.0	0.0
Min - Max	58 - 86	-23 - 16
AFTER PAC INFUSION		
n	16	16
Mean (SD)	75.6 (9.2)	-1.4 (12.4)
Median	76.5	-1.5
Min - Max	55 - 90	-20 - 18
Cycle 12 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	23	23
Mean (SD)	79.7 (10.1)	3.3 (12.5)
Median	80.0	4.0
Min - Max	67 - 108	-19 - 30
PRE PAC INFUSION		
n	21	21
Mean (SD)	76.1 (10.3)	-1.0 (12.4)
Median	76.0	1.0
Min - Max	55 - 102	-23 - 22
AFTER PAC INFUSION		
n	17	17
Mean (SD)	76.4 (11.5)	0.6 (12.0)
Median	75.0	-2.0
Min - Max	61 - 108	-20 - 28
Cycle 13 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	21	21
Mean (SD)	78.8 (9.1)	1.2 (10.0)
Median	76.0	0.0
Min - Max	67 - 99	-11 - 19
PRE PAC INFUSION		
n	20	20
Mean (SD)	78.6 (12.2)	0.7 (12.4)
Median	79.0	1.5
Min - Max	54 - 111	-20 - 32
AFTER PAC INFUSION		
n	13	13
Mean (SD)	79.0 (7.6)	1.2 (11.0)
Median	78.0	2.0
Min - Max	70 - 101	-14 - 21

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 13 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	77.5 (9.2)	-7.0 (2.8)
Median	77.5	-7.0
Min - Max	71 - 84	-9 - -5
PRE PAC INFUSION		
n	14	14
Mean (SD)	79.3 (6.9)	2.9 (9.6)
Median	79.5	4.5
Min - Max	67 - 90	-12 - 18
AFTER PAC INFUSION		
n	15	15
Mean (SD)	80.5 (7.5)	3.8 (9.2)
Median	82.0	2.0
Min - Max	64 - 90	-11 - 17
Cycle 13 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	19	19
Mean (SD)	79.5 (7.5)	2.1 (10.7)
Median	79.0	0.0
Min - Max	69 - 98	-16 - 19
PRE PAC INFUSION		
n	19	19
Mean (SD)	77.0 (10.7)	-0.1 (11.8)
Median	78.0	-2.0
Min - Max	57 - 94	-24 - 20
AFTER PAC INFUSION		
n	15	15
Mean (SD)	80.1 (10.2)	3.4 (11.3)
Median	80.0	2.0
Min - Max	65 - 109	-10 - 29
Cycle 14 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	20	20
Mean (SD)	79.4 (9.3)	2.8 (8.1)
Median	77.0	2.0
Min - Max	65 - 93	-10 - 15
PRE PAC INFUSION		
n	18	18
Mean (SD)	77.1 (9.6)	0.2 (11.5)
Median	77.5	0.0
Min - Max	56 - 93	-25 - 18

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	14	14
Mean (SD)	79.3 (7.1)	3.0 (7.8)
Median	78.0	2.5
Min - Max	72 - 95	-12 - 15
Cycle 14 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	85.7 (8.7)	0.0 (13.0)
Median	88.0	0.0
Min - Max	76 - 93	-13 - 13
PRE PAC INFUSION		
n	10	10
Mean (SD)	75.1 (7.5)	0.9 (8.7)
Median	76.5	1.5
Min - Max	60 - 86	-10 - 16
AFTER PAC INFUSION		
n	12	12
Mean (SD)	80.0 (12.4)	4.1 (13.3)
Median	78.5	4.0
Min - Max	67 - 114	-14 - 34
Cycle 14 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	18	18
Mean (SD)	78.9 (6.7)	2.7 (12.3)
Median	78.0	2.5
Min - Max	68 - 93	-17 - 23
PRE PAC INFUSION		
n	16	16
Mean (SD)	78.7 (6.1)	1.9 (10.8)
Median	79.5	2.0
Min - Max	63 - 88	-15 - 18
AFTER PAC INFUSION		
n	12	12
Mean (SD)	78.2 (4.4)	2.4 (11.0)
Median	79.0	2.0
Min - Max	68 - 83	-13 - 17
Cycle 15 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	17	17
Mean (SD)	80.2 (7.1)	4.0 (10.4)
Median	80.0	2.0
Min - Max	70 - 95	-18 - 23

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	16	16
Mean (SD)	77.6 (6.3)	1.1 (11.8)
Median	77.5	0.0
Min - Max	68 - 89	-17 - 28
AFTER PAC INFUSION		
n	10	10
Mean (SD)	79.0 (5.8)	1.5 (11.2)
Median	80.0	1.5
Min - Max	69 - 88	-17 - 17
Cycle 15 Day 8		
PRE PAC INFUSION		
n	10	10
Mean (SD)	79.5 (11.6)	2.0 (13.2)
Median	81.5	0.0
Min - Max	57 - 96	-24 - 26
AFTER PAC INFUSION		
n	10	10
Mean (SD)	76.6 (9.4)	-0.9 (12.4)
Median	78.5	-3.5
Min - Max	59 - 93	-22 - 23
Cycle 15 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	14	14
Mean (SD)	78.9 (7.3)	3.3 (8.1)
Median	79.5	5.0
Min - Max	68 - 90	-11 - 16
PRE PAC INFUSION		
n	13	13
Mean (SD)	76.6 (6.5)	0.6 (8.2)
Median	78.0	3.0
Min - Max	64 - 88	-12 - 12
AFTER PAC INFUSION		
n	7	7
Mean (SD)	77.3 (5.2)	-0.1 (8.4)
Median	78.0	-3.0
Min - Max	69 - 83	-12 - 11
Cycle 16 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	81.7 (6.8)	6.3 (11.6)
Median	81.0	4.0
Min - Max	73 - 97	-13 - 27

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	12	12
Mean (SD)	76.3 (8.4)	1.2 (7.9)
Median	76.0	1.0
Min - Max	64 - 89	-13 - 14
AFTER PAC INFUSION		
n	7	7
Mean (SD)	79.9 (8.8)	2.1 (11.7)
Median	81.0	7.0
Min - Max	61 - 88	-20 - 11
Cycle 16 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	80.0 (NE)	-2.0 (NE)
Median	80.0	-2.0
Min - Max	80 - 80	-2 - -2
PRE PAC INFUSION		
n	8	8
Mean (SD)	76.0 (11.0)	-0.9 (14.1)
Median	72.5	-2.5
Min - Max	65 - 97	-16 - 27
AFTER PAC INFUSION		
n	8	8
Mean (SD)	75.3 (12.7)	-1.6 (18.6)
Median	77.5	5.0
Min - Max	52 - 93	-29 - 23
Cycle 16 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	14	14
Mean (SD)	78.2 (9.8)	1.7 (10.4)
Median	75.5	3.5
Min - Max	67 - 97	-16 - 20
PRE PAC INFUSION		
n	14	14
Mean (SD)	78.1 (8.5)	1.3 (9.1)
Median	77.5	1.5
Min - Max	68 - 95	-15 - 13
AFTER PAC INFUSION		
n	7	7
Mean (SD)	75.6 (7.4)	-4.9 (10.4)
Median	78.0	-8.0
Min - Max	63 - 85	-16 - 15

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 17 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	78.4 (7.9)	2.3 (8.4)
Median	80.0	-1.0
Min - Max	67 - 90	-7 - 18
PRE PAC INFUSION		
n	11	11
Mean (SD)	75.3 (5.7)	-0.2 (7.9)
Median	77.0	0.0
Min - Max	63 - 84	-15 - 12
AFTER PAC INFUSION		
n	7	7
Mean (SD)	73.1 (10.1)	-4.7 (13.8)
Median	72.0	-3.0
Min - Max	55 - 88	-26 - 10
Cycle 17 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	80.0 (NE)	5.0 (NE)
Median	80.0	5.0
Min - Max	80 - 80	5 - 5
PRE PAC INFUSION		
n	7	7
Mean (SD)	82.6 (7.5)	5.4 (13.7)
Median	83.0	10.0
Min - Max	68 - 92	-13 - 22
AFTER PAC INFUSION		
n	8	8
Mean (SD)	79.6 (7.2)	2.8 (14.3)
Median	80.5	3.5
Min - Max	68 - 88	-21 - 24
Cycle 17 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	78.8 (6.3)	4.0 (9.3)
Median	78.5	3.0
Min - Max	67 - 92	-10 - 22
PRE PAC INFUSION		
n	12	12
Mean (SD)	77.0 (5.6)	0.8 (9.6)
Median	79.0	0.5
Min - Max	68 - 84	-21 - 16

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
AFTER PAC INFUSION		
n	8	8
Mean (SD)	76.8 (6.5)	-0.1 (10.9)
Median	79.0	3.5
Min - Max	64 - 83	-25 - 8
Cycle 18 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	79.6 (6.2)	3.9 (9.8)
Median	80.0	8.0
Min - Max	71 - 91	-16 - 16
PRE PAC INFUSION		
n	13	13
Mean (SD)	76.4 (11.2)	1.2 (14.7)
Median	78.0	0.0
Min - Max	56 - 98	-25 - 20
AFTER PAC INFUSION		
n	8	8
Mean (SD)	75.5 (8.6)	-1.4 (13.4)
Median	75.0	-2.0
Min - Max	64 - 90	-20 - 20
Cycle 18 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	73.0 (NE)	-2.0 (NE)
Median	73.0	-2.0
Min - Max	73 - 73	-2 - -2
PRE PAC INFUSION		
n	6	6
Mean (SD)	79.8 (6.8)	4.7 (11.1)
Median	78.0	4.0
Min - Max	70 - 89	-11 - 19
AFTER PAC INFUSION		
n	7	7
Mean (SD)	76.6 (6.9)	1.4 (12.0)
Median	79.0	-2.0
Min - Max	64 - 83	-17 - 17
Cycle 18 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	77.0 (7.0)	2.5 (6.8)
Median	78.0	1.0
Min - Max	63 - 89	-8 - 12

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	11	11
Mean (SD)	77.6 (6.6)	1.6 (6.7)
Median	78.0	0.0
Min - Max	68 - 88	-7 - 12
AFTER PAC INFUSION		
n	7	7
Mean (SD)	79.0 (7.7)	1.9 (11.1)
Median	79.0	2.0
Min - Max	69 - 90	-18 - 17
Cycle 19 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	76.5 (5.0)	2.1 (5.4)
Median	76.0	3.0
Min - Max	69 - 84	-6 - 12
PRE PAC INFUSION		
n	11	11
Mean (SD)	71.9 (7.7)	-4.1 (9.3)
Median	72.0	-4.0
Min - Max	59 - 84	-22 - 8
AFTER PAC INFUSION		
n	8	8
Mean (SD)	73.1 (6.6)	-3.8 (11.6)
Median	74.0	-4.0
Min - Max	63 - 80	-18 - 12
Cycle 19 Day 8		
PRE PAC INFUSION		
n	7	7
Mean (SD)	77.9 (6.6)	0.7 (8.3)
Median	80.0	-4.0
Min - Max	66 - 84	-8 - 12
AFTER PAC INFUSION		
n	7	7
Mean (SD)	77.1 (5.7)	0.0 (11.5)
Median	79.0	1.0
Min - Max	68 - 82	-19 - 15
Cycle 19 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	77.7 (7.6)	2.9 (10.8)
Median	77.0	3.5
Min - Max	66 - 90	-23 - 19

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	11	11
Mean (SD)	76.6 (8.2)	0.4 (11.3)
Median	76.0	2.0
Min - Max	61 - 90	-20 - 16
AFTER PAC INFUSION		
n	7	7
Mean (SD)	83.4 (9.0)	6.3 (15.7)
Median	84.0	4.0
Min - Max	67 - 97	-22 - 27
Cycle 20 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	76.4 (9.3)	1.7 (10.0)
Median	80.0	2.5
Min - Max	58 - 89	-15 - 15
PRE PAC INFUSION		
n	10	10
Mean (SD)	77.5 (8.2)	2.5 (10.6)
Median	78.0	0.5
Min - Max	64 - 89	-14 - 18
AFTER PAC INFUSION		
n	7	7
Mean (SD)	80.7 (9.0)	3.6 (13.5)
Median	81.0	2.0
Min - Max	66 - 89	-17 - 19
Cycle 20 Day 8		
PRE PAC INFUSION		
n	7	7
Mean (SD)	81.0 (7.1)	3.9 (10.7)
Median	82.0	4.0
Min - Max	70 - 89	-11 - 17
AFTER PAC INFUSION		
n	7	7
Mean (SD)	81.4 (7.1)	4.3 (12.6)
Median	82.0	4.0
Min - Max	68 - 90	-13 - 17
Cycle 20 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	80.0 (6.6)	5.3 (7.6)
Median	81.0	5.0
Min - Max	71 - 92	-7 - 22

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	11	11
Mean (SD)	77.3 (7.0)	1.0 (10.1)
Median	76.0	0.0
Min - Max	69 - 90	-15 - 20
AFTER PAC INFUSION		
n	7	7
Mean (SD)	77.9 (12.3)	0.7 (18.1)
Median	78.0	0.0
Min - Max	54 - 93	-35 - 23
Cycle 21 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	76.9 (8.5)	2.2 (9.1)
Median	74.0	0.5
Min - Max	66 - 88	-11 - 18
PRE PAC INFUSION		
n	11	11
Mean (SD)	74.5 (9.9)	-1.8 (13.3)
Median	77.0	0.0
Min - Max	55 - 91	-26 - 21
AFTER PAC INFUSION		
n	7	7
Mean (SD)	76.0 (8.1)	-1.1 (10.6)
Median	78.0	0.0
Min - Max	64 - 85	-23 - 10
Cycle 21 Day 8		
PRE PAC INFUSION		
n	6	6
Mean (SD)	74.0 (8.7)	-4.3 (14.0)
Median	75.0	-6.5
Min - Max	60 - 86	-21 - 16
AFTER PAC INFUSION		
n	6	6
Mean (SD)	76.0 (5.9)	-2.3 (14.6)
Median	77.0	-1.5
Min - Max	69 - 85	-20 - 15
Cycle 21 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	80.1 (10.4)	5.4 (11.1)
Median	78.0	6.0
Min - Max	71 - 107	-8 - 30

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	9	9
Mean (SD)	76.4 (5.5)	-0.3 (11.2)
Median	76.0	-2.0
Min - Max	67 - 83	-22 - 16
AFTER PAC INFUSION		
n	6	6
Mean (SD)	70.7 (10.0)	-7.7 (15.0)
Median	70.5	-4.5
Min - Max	58 - 83	-31 - 10
Cycle 22 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	79.9 (7.5)	5.2 (7.6)
Median	77.0	4.5
Min - Max	72 - 94	-6 - 16
PRE PAC INFUSION		
n	10	10
Mean (SD)	74.3 (7.6)	-2.6 (12.1)
Median	75.5	2.5
Min - Max	60 - 84	-23 - 14
AFTER PAC INFUSION		
n	6	6
Mean (SD)	75.2 (6.1)	-3.2 (9.2)
Median	73.5	-1.0
Min - Max	69 - 85	-20 - 7
Cycle 22 Day 8		
PRE PAC INFUSION		
n	4	4
Mean (SD)	73.0 (10.4)	-4.8 (10.9)
Median	73.5	-2.5
Min - Max	61 - 84	-20 - 6
AFTER PAC INFUSION		
n	4	4
Mean (SD)	72.5 (7.9)	-5.3 (12.3)
Median	71.0	-1.0
Min - Max	65 - 83	-23 - 4
Cycle 22 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	77.2 (7.1)	2.0 (9.6)
Median	76.0	1.0
Min - Max	67 - 89	-12 - 19

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	10	10
Mean (SD)	75.3 (5.0)	-1.6 (9.4)
Median	74.0	-2.5
Min - Max	70 - 85	-15 - 15
AFTER PAC INFUSION		
n	6	6
Mean (SD)	73.3 (8.1)	-5.0 (11.1)
Median	78.0	-2.5
Min - Max	62 - 80	-25 - 8
Cycle 23 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	79.7 (10.5)	5.9 (7.8)
Median	78.0	2.0
Min - Max	62 - 98	-2 - 21
PRE PAC INFUSION		
n	9	9
Mean (SD)	74.3 (5.3)	-2.6 (9.3)
Median	73.0	-1.0
Min - Max	66 - 82	-15 - 10
AFTER PAC INFUSION		
n	6	6
Mean (SD)	71.7 (6.3)	-6.7 (10.9)
Median	73.5	-4.5
Min - Max	63 - 78	-26 - 4
Cycle 23 Day 8		
PRE PAC INFUSION		
n	5	5
Mean (SD)	79.2 (6.7)	-0.8 (8.6)
Median	78.0	0.0
Min - Max	73 - 88	-11 - 9
AFTER PAC INFUSION		
n	5	5
Mean (SD)	78.4 (7.7)	-1.6 (9.1)
Median	78.0	0.0
Min - Max	71 - 90	-17 - 7
Cycle 23 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	75.9 (7.0)	2.3 (6.3)
Median	76.0	0.0
Min - Max	64 - 85	-4 - 14

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	9	9
Mean (SD)	75.2 (4.4)	-1.7 (9.3)
Median	76.0	-1.0
Min - Max	69 - 81	-14 - 14
AFTER PAC INFUSION		
n	6	6
Mean (SD)	75.2 (7.3)	-3.2 (13.0)
Median	79.0	0.5
Min - Max	62 - 80	-27 - 8
Cycle 24 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	10	10
Mean (SD)	74.7 (8.0)	-0.3 (11.8)
Median	76.0	1.5
Min - Max	59 - 83	-19 - 14
PRE PAC INFUSION		
n	9	9
Mean (SD)	74.6 (7.4)	-2.3 (12.3)
Median	76.0	2.0
Min - Max	58 - 84	-20 - 14
AFTER PAC INFUSION		
n	6	6
Mean (SD)	73.8 (5.5)	-4.5 (9.4)
Median	73.0	-2.5
Min - Max	68 - 80	-21 - 5
Cycle 24 Day 8		
PRE PAC INFUSION		
n	4	4
Mean (SD)	70.5 (9.3)	-7.5 (9.7)
Median	70.0	-6.5
Min - Max	62 - 80	-19 - 2
AFTER PAC INFUSION		
n	4	4
Mean (SD)	72.8 (5.9)	-5.3 (12.7)
Median	72.5	-2.5
Min - Max	66 - 80	-23 - 7
Cycle 24 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	10	10
Mean (SD)	77.2 (9.2)	2.2 (4.7)
Median	78.0	1.0
Min - Max	60 - 90	-4 - 9

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	9	9
Mean (SD)	77.4 (6.8)	0.6 (9.0)
Median	76.0	4.0
Min - Max	67 - 90	-14 - 14
AFTER PAC INFUSION		
n	6	6
Mean (SD)	76.3 (7.1)	-2.0 (9.6)
Median	74.5	0.0
Min - Max	69 - 89	-16 - 12
Cycle 25 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	76.1 (5.1)	-0.3 (8.0)
Median	76.0	1.0
Min - Max	68 - 82	-14 - 10
PRE PAC INFUSION		
n	10	10
Mean (SD)	73.4 (4.1)	-3.5 (7.9)
Median	72.5	-4.5
Min - Max	68 - 80	-16 - 8
AFTER PAC INFUSION		
n	4	4
Mean (SD)	77.3 (9.7)	-2.3 (16.7)
Median	76.5	-5.5
Min - Max	67 - 89	-17 - 19
Cycle 25 Day 8		
PRE PAC INFUSION		
n	3	3
Mean (SD)	70.7 (5.8)	-11.7 (6.8)
Median	74.0	-14.0
Min - Max	64 - 74	-17 - -4
AFTER PAC INFUSION		
n	3	3
Mean (SD)	70.7 (1.2)	-11.7 (6.0)
Median	70.0	-11.0
Min - Max	70 - 72	-18 - -6
Cycle 25 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	81.1 (10.4)	4.1 (8.2)
Median	80.5	1.5
Min - Max	64 - 94	-4 - 23

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	8	8
Mean (SD)	76.0 (6.6)	-1.8 (7.9)
Median	75.0	-1.0
Min - Max	68 - 88	-12 - 12
AFTER PAC INFUSION		
n	5	5
Mean (SD)	78.4 (8.6)	-2.8 (11.8)
Median	78.0	-3.0
Min - Max	68 - 91	-21 - 11
Cycle 26 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	79.6 (8.2)	4.8 (8.8)
Median	79.0	4.5
Min - Max	66 - 91	-10 - 21
PRE PAC INFUSION		
n	8	8
Mean (SD)	76.1 (9.0)	0.5 (11.9)
Median	75.5	1.5
Min - Max	64 - 90	-17 - 20
AFTER PAC INFUSION		
n	4	4
Mean (SD)	80.5 (9.5)	1.3 (15.2)
Median	79.5	-3.5
Min - Max	70 - 93	-11 - 23
Cycle 26 Day 8		
PRE PAC INFUSION		
n	5	5
Mean (SD)	80.4 (6.4)	-0.8 (13.0)
Median	79.0	-9.0
Min - Max	72 - 89	-10 - 19
AFTER PAC INFUSION		
n	5	5
Mean (SD)	76.0 (6.7)	-5.2 (12.8)
Median	76.0	-5.0
Min - Max	66 - 83	-23 - 13
Cycle 26 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	79.8 (5.8)	4.9 (5.7)
Median	79.5	4.5
Min - Max	73 - 86	-2 - 15

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	8	8
Mean (SD)	76.6 (9.5)	1.0 (6.3)
Median	77.5	0.0
Min - Max	60 - 87	-8 - 11
AFTER PAC INFUSION		
n	4	4
Mean (SD)	83.8 (7.3)	4.5 (7.9)
Median	81.5	4.5
Min - Max	78 - 94	-4 - 13
Cycle 27 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	74.5 (7.5)	-0.4 (6.2)
Median	72.0	0.0
Min - Max	65 - 84	-10 - 9
PRE PAC INFUSION		
n	8	8
Mean (SD)	71.3 (7.3)	-4.4 (6.4)
Median	71.0	-2.5
Min - Max	61 - 83	-14 - 2
AFTER PAC INFUSION		
n	4	4
Mean (SD)	73.8 (5.6)	-5.5 (5.4)
Median	71.5	-6.5
Min - Max	70 - 82	-11 - 2
Cycle 27 Day 8		
PRE PAC INFUSION		
n	3	3
Mean (SD)	84.0 (10.6)	4.3 (13.5)
Median	88.0	4.0
Min - Max	72 - 92	-9 - 18
AFTER PAC INFUSION		
n	3	3
Mean (SD)	85.0 (4.6)	5.3 (7.6)
Median	84.0	2.0
Min - Max	81 - 90	0 - 14
Cycle 27 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	7	7
Mean (SD)	74.4 (5.0)	-2.0 (7.9)
Median	74.0	-2.0
Min - Max	70 - 83	-12 - 13

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	7	7
Mean (SD)	73.4 (4.2)	-3.9 (6.6)
Median	74.0	-3.0
Min - Max	66 - 78	-12 - 5
AFTER PAC INFUSION		
n	4	4
Mean (SD)	79.0 (6.7)	-0.3 (13.3)
Median	78.0	-1.5
Min - Max	73 - 87	-15 - 17
Cycle 28 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	75.5 (7.8)	-0.7 (3.3)
Median	75.5	-1.0
Min - Max	66 - 86	-4 - 4
PRE PAC INFUSION		
n	4	4
Mean (SD)	80.5 (7.7)	2.5 (4.1)
Median	82.0	3.0
Min - Max	70 - 88	-2 - 6
AFTER PAC INFUSION		
n	2	2
Mean (SD)	84.0 (8.5)	1.0 (1.4)
Median	84.0	1.0
Min - Max	78 - 90	0 - 2
Cycle 28 Day 8		
PRE PAC INFUSION		
n	2	2
Mean (SD)	82.0 (2.8)	-1.0 (9.9)
Median	82.0	-1.0
Min - Max	80 - 84	-8 - 6
AFTER PAC INFUSION		
n	2	2
Mean (SD)	81.5 (3.5)	-1.5 (3.5)
Median	81.5	-1.5
Min - Max	79 - 84	-4 - 1
Cycle 28 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	79.5 (6.3)	3.3 (3.1)
Median	79.0	2.5
Min - Max	73 - 88	0 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	4	4
Mean (SD)	82.5 (7.0)	4.5 (3.0)
Median	83.0	4.0
Min - Max	74 - 90	2 - 8
AFTER PAC INFUSION		
n	2	2
Mean (SD)	83.5 (7.8)	0.5 (0.7)
Median	83.5	0.5
Min - Max	78 - 89	0 - 1
Cycle 29 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	7	7
Mean (SD)	78.0 (10.8)	3.6 (9.1)
Median	78.0	4.0
Min - Max	63 - 90	-7 - 15
PRE PAC INFUSION		
n	4	4
Mean (SD)	79.3 (8.2)	1.3 (3.4)
Median	79.5	0.5
Min - Max	70 - 88	-2 - 6
AFTER PAC INFUSION		
n	2	2
Mean (SD)	85.5 (4.9)	2.5 (2.1)
Median	85.5	2.5
Min - Max	82 - 89	1 - 4
Cycle 29 Day 8		
PRE PAC INFUSION		
n	2	2
Mean (SD)	83.0 (1.4)	0.0 (8.5)
Median	83.0	0.0
Min - Max	82 - 84	-6 - 6
AFTER PAC INFUSION		
n	2	2
Mean (SD)	82.0 (2.8)	-1.0 (9.9)
Median	82.0	-1.0
Min - Max	80 - 84	-8 - 6
Cycle 29 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	71.2 (7.1)	-2.7 (5.5)
Median	68.5	-5.0
Min - Max	64 - 80	-8 - 6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	75.3 (11.0)	0.7 (8.1)
Median	76.0	2.0
Min - Max	64 - 86	-8 - 8
AFTER PAC INFUSION		
n	1	1
Mean (SD)	86.0 (NE)	8.0 (NE)
Median	86.0	8.0
Min - Max	86 - 86	8 - 8
Cycle 30 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	5	5
Mean (SD)	75.4 (7.6)	1.6 (5.7)
Median	78.0	4.0
Min - Max	65 - 85	-5 - 7
PRE PAC INFUSION		
n	3	3
Mean (SD)	75.3 (5.5)	0.7 (2.5)
Median	75.0	1.0
Min - Max	70 - 81	-2 - 3
AFTER PAC INFUSION		
n	1	1
Mean (SD)	89.0 (NE)	11.0 (NE)
Median	89.0	11.0
Min - Max	89 - 89	11 - 11
Cycle 30 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	82.0 (NE)	4.0 (NE)
Median	82.0	4.0
Min - Max	82 - 82	4 - 4
AFTER PAC INFUSION		
n	1	1
Mean (SD)	84.0 (NE)	6.0 (NE)
Median	84.0	6.0
Min - Max	84 - 84	6 - 6
Cycle 30 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	5	5
Mean (SD)	78.6 (6.2)	4.8 (5.8)
Median	75.0	2.0
Min - Max	74 - 88	-1 - 12

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	80.7 (4.2)	6.0 (4.0)
Median	82.0	6.0
Min - Max	76 - 84	2 - 10
AFTER PAC INFUSION		
n	1	1
Mean (SD)	88.0 (NE)	10.0 (NE)
Median	88.0	10.0
Min - Max	88 - 88	10 - 10
Cycle 31 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	75.3 (8.3)	1.8 (5.3)
Median	76.5	3.5
Min - Max	64 - 84	-6 - 6
PRE PAC INFUSION		
n	3	3
Mean (SD)	79.3 (6.1)	4.7 (4.2)
Median	78.0	6.0
Min - Max	74 - 86	0 - 8
AFTER PAC INFUSION		
n	1	1
Mean (SD)	78.0 (NE)	0.0 (NE)
Median	78.0	0.0
Min - Max	78 - 78	0 - 0
Cycle 31 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	88.0 (NE)	10.0 (NE)
Median	88.0	10.0
Min - Max	88 - 88	10 - 10
AFTER PAC INFUSION		
n	1	1
Mean (SD)	84.0 (NE)	6.0 (NE)
Median	84.0	6.0
Min - Max	84 - 84	6 - 6
Cycle 31 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	72.8 (12.3)	-0.8 (9.1)
Median	73.5	0.5
Min - Max	58 - 86	-12 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	77.0 (8.2)	2.3 (5.5)
Median	79.0	5.0
Min - Max	68 - 84	-4 - 6
AFTER PAC INFUSION		
n	1	1
Mean (SD)	84.0 (NE)	6.0 (NE)
Median	84.0	6.0
Min - Max	84 - 84	6 - 6
Cycle 32 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	72.0 (11.0)	-1.5 (7.5)
Median	71.0	-2.0
Min - Max	60 - 86	-10 - 8
PRE PAC INFUSION		
n	3	3
Mean (SD)	76.0 (6.0)	1.3 (3.1)
Median	76.0	2.0
Min - Max	70 - 82	-2 - 4
AFTER PAC INFUSION		
n	1	1
Mean (SD)	84.0 (NE)	6.0 (NE)
Median	84.0	6.0
Min - Max	84 - 84	6 - 6
Cycle 32 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	84.0 (NE)	6.0 (NE)
Median	84.0	6.0
Min - Max	84 - 84	6 - 6
AFTER PAC INFUSION		
n	1	1
Mean (SD)	82.0 (NE)	4.0 (NE)
Median	82.0	4.0
Min - Max	82 - 82	4 - 4
Cycle 32 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	73.8 (9.3)	0.3 (5.9)
Median	72.5	-0.5
Min - Max	64 - 86	-6 - 8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	79.3 (4.2)	4.7 (2.3)
Median	78.0	6.0
Min - Max	76 - 84	2 - 6
AFTER PAC INFUSION		
n	1	1
Mean (SD)	80.0 (NE)	2.0 (NE)
Median	80.0	2.0
Min - Max	80 - 80	2 - 2
Cycle 33 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	72.7 (4.2)	-2.0 (2.0)
Median	74.0	-2.0
Min - Max	68 - 76	-4 - 0
PRE PAC INFUSION		
n	2	2
Mean (SD)	71.5 (7.8)	-1.5 (6.4)
Median	71.5	-1.5
Min - Max	66 - 77	-6 - 3
Cycle 33 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	79.0 (NE)	1.0 (NE)
Median	79.0	1.0
Min - Max	79 - 79	1 - 1
Cycle 33 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	74.0 (2.8)	-2.0 (5.7)
Median	74.0	-2.0
Min - Max	72 - 76	-6 - 2
PRE PAC INFUSION		
n	1	1
Mean (SD)	77.0 (NE)	3.0 (NE)
Median	77.0	3.0
Min - Max	77 - 77	3 - 3
Cycle 34 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	75.0 (4.2)	2.0 (2.8)
Median	75.0	2.0
Min - Max	72 - 78	0 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	2	2
Mean (SD)	75.5 (0.7)	2.5 (2.1)
Median	75.5	2.5
Min - Max	75 - 76	1 - 4
AFTER PAC INFUSION		
n	1	1
Mean (SD)	84.0 (NE)	6.0 (NE)
Median	84.0	6.0
Min - Max	84 - 84	6 - 6
Cycle 34 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	74.0 (NE)	-4.0 (NE)
Median	74.0	-4.0
Min - Max	74 - 74	-4 - -4
Cycle 34 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	77.5 (3.5)	1.5 (0.7)
Median	77.5	1.5
Min - Max	75 - 80	1 - 2
PRE PAC INFUSION		
n	1	1
Mean (SD)	74.0 (NE)	0.0 (NE)
Median	74.0	0.0
Min - Max	74 - 74	0 - 0
Cycle 35 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	76.7 (6.4)	2.0 (3.5)
Median	74.0	0.0
Min - Max	72 - 84	0 - 6
PRE PAC INFUSION		
n	2	2
Mean (SD)	73.0 (7.1)	0.0 (5.7)
Median	73.0	0.0
Min - Max	68 - 78	-4 - 4
Cycle 35 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	74.0 (NE)	-4.0 (NE)
Median	74.0	-4.0
Min - Max	74 - 74	-4 - -4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 35 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	73.0 (4.2)	0.0 (2.8)
Median	73.0	0.0
Min - Max	70 - 76	-2 - 2
PRE PAC INFUSION		
n	2	2
Mean (SD)	73.0 (7.1)	0.0 (5.7)
Median	73.0	0.0
Min - Max	68 - 78	-4 - 4
Cycle 36 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	73.0 (1.4)	0.0 (0.0)
Median	73.0	0.0
Min - Max	72 - 74	0 - 0
PRE PAC INFUSION		
n	2	2
Mean (SD)	73.0 (4.2)	0.0 (2.8)
Median	73.0	0.0
Min - Max	70 - 76	-2 - 2
Cycle 36 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	75.0 (1.4)	2.0 (0.0)
Median	75.0	2.0
Min - Max	74 - 76	2 - 2
PRE PAC INFUSION		
n	2	2
Mean (SD)	74.0 (5.7)	1.0 (4.2)
Median	74.0	1.0
Min - Max	70 - 78	-2 - 4
Cycle 37 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	71.0 (4.2)	-2.0 (2.8)
Median	71.0	-2.0
Min - Max	68 - 74	-4 - 0
PRE PAC INFUSION		
n	2	2
Mean (SD)	70.0 (7.1)	-3.0 (5.7)
Median	70.0	-3.0
Min - Max	65 - 75	-7 - 1

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 37 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	75.5 (0.7)	2.5 (2.1)
Median	75.5	2.5
Min - Max	75 - 76	1 - 4
PRE PAC INFUSION		
n	2	2
Mean (SD)	70.5 (0.7)	-2.5 (0.7)
Median	70.5	-2.5
Min - Max	70 - 71	-3 - -2
Cycle 38 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	74.0 (0.0)	1.0 (1.4)
Median	74.0	1.0
Min - Max	74 - 74	0 - 2
PRE PAC INFUSION		
n	2	2
Mean (SD)	74.0 (5.7)	1.0 (4.2)
Median	74.0	1.0
Min - Max	70 - 78	-2 - 4
Cycle 38 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	72.0 (2.8)	-1.0 (1.4)
Median	72.0	-1.0
Min - Max	70 - 74	-2 - 0
PRE PAC INFUSION		
n	2	2
Mean (SD)	73.0 (4.2)	0.0 (2.8)
Median	73.0	0.0
Min - Max	70 - 76	-2 - 2
Cycle 39 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	75.5 (7.8)	2.5 (6.4)
Median	75.5	2.5
Min - Max	70 - 81	-2 - 7
PRE PAC INFUSION		
n	2	2
Mean (SD)	71.0 (4.2)	-2.0 (2.8)
Median	71.0	-2.0
Min - Max	68 - 74	-4 - 0

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 39 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	75.5 (4.9)	2.5 (3.5)
Median	75.5	2.5
Min - Max	72 - 79	0 - 5
PRE PAC INFUSION		
n	2	2
Mean (SD)	77.0 (2.8)	4.0 (1.4)
Median	77.0	4.0
Min - Max	75 - 79	3 - 5
Cycle 40 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	68.0 (NE)	-4.0 (NE)
Median	68.0	-4.0
Min - Max	68 - 68	-4 - -4
PRE PAC INFUSION		
n	1	1
Mean (SD)	75.0 (NE)	3.0 (NE)
Median	75.0	3.0
Min - Max	75 - 75	3 - 3
Cycle 40 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	70.0 (NE)	-2.0 (NE)
Median	70.0	-2.0
Min - Max	70 - 70	-2 - -2
PRE PAC INFUSION		
n	1	1
Mean (SD)	64.0 (NE)	-8.0 (NE)
Median	64.0	-8.0
Min - Max	64 - 64	-8 - -8
Cycle 41 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	64.0 (NE)	-8.0 (NE)
Median	64.0	-8.0
Min - Max	64 - 64	-8 - -8
PRE PAC INFUSION		
n	1	1
Mean (SD)	70.0 (NE)	-2.0 (NE)
Median	70.0	-2.0
Min - Max	70 - 70	-2 - -2

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
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Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 41 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	67.0 (NE)	-5.0 (NE)
Median	67.0	-5.0
Min - Max	67 - 67	-5 - -5
PRE PAC INFUSION		
n	1	1
Mean (SD)	62.0 (NE)	-10.0 (NE)
Median	62.0	-10.0
Min - Max	62 - 62	-10 - -10
Cycle 42 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	68.0 (NE)	-4.0 (NE)
Median	68.0	-4.0
Min - Max	68 - 68	-4 - -4
PRE PAC INFUSION		
n	1	1
Mean (SD)	65.0 (NE)	-7.0 (NE)
Median	65.0	-7.0
Min - Max	65 - 65	-7 - -7
Cycle 42 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	63.0 (NE)	-9.0 (NE)
Median	63.0	-9.0
Min - Max	63 - 63	-9 - -9
PRE PAC INFUSION		
n	1	1
Mean (SD)	66.0 (NE)	-6.0 (NE)
Median	66.0	-6.0
Min - Max	66 - 66	-6 - -6
Cycle 43 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	78.0 (NE)	6.0 (NE)
Median	78.0	6.0
Min - Max	78 - 78	6 - 6
PRE PAC INFUSION		
n	1	1
Mean (SD)	74.0 (NE)	2.0 (NE)
Median	74.0	2.0
Min - Max	74 - 74	2 - 2

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
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Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 43 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	82.0 (NE)	10.0 (NE)
Median	82.0	10.0
Min - Max	82 - 82	10 - 10
PRE PAC INFUSION		
n	1	1
Mean (SD)	84.0 (NE)	12.0 (NE)
Median	84.0	12.0
Min - Max	84 - 84	12 - 12
Cycle 44 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	72.0 (NE)	0.0 (NE)
Median	72.0	0.0
Min - Max	72 - 72	0 - 0
PRE PAC INFUSION		
n	1	1
Mean (SD)	80.0 (NE)	8.0 (NE)
Median	80.0	8.0
Min - Max	80 - 80	8 - 8
Cycle 44 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	76.0 (NE)	4.0 (NE)
Median	76.0	4.0
Min - Max	76 - 76	4 - 4
PRE PAC INFUSION		
n	1	1
Mean (SD)	82.0 (NE)	10.0 (NE)
Median	82.0	10.0
Min - Max	82 - 82	10 - 10
Study Drug Discontinuation		
n	89	89
Mean (SD)	83.7 (14.8)	5.7 (13.4)
Median	82.0	4.0
Min - Max	57 - 135	-19 - 52
Post-Baseline Last		
n	89	89
Mean (SD)	83.7 (14.8)	5.7 (13.4)
Median	82.0	4.0
Min - Max	57 - 135	-19 - 52

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	85.0 (17.3)	11.7 (11.9)
Median	89.0	8.0
Min - Max	66 - 100	2 - 25
PRE PAC INFUSION		
n	3	3
Mean (SD)	82.0 (12.2)	-7.3 (16.0)
Median	88.0	-6.0
Min - Max	68 - 90	-24 - 8
AFTER PAC INFUSION		
n	7	7
Mean (SD)	83.6 (13.5)	6.4 (18.7)
Median	83.0	3.0
Min - Max	62 - 103	-19 - 40
Post-Baseline Minimum		
n	7	7
Mean (SD)	63.9 (3.1)	-14.3 (5.7)
Median	64.0	-16.0
Min - Max	60 - 70	-21 - -7
PRE ATEZO INFUSION (COHORT C)		
n	32	32
Mean (SD)	65.6 (9.7)	-13.3 (9.1)
Median	68.0	-14.5
Min - Max	40 - 96	-31 - 8
PRE PAC INFUSION		
n	33	33
Mean (SD)	63.7 (7.2)	-12.1 (8.1)
Median	64.0	-13.0
Min - Max	50 - 85	-29 - 4
AFTER PAC INFUSION		
n	30	30
Mean (SD)	64.6 (9.6)	-15.3 (9.8)
Median	64.5	-12.0
Min - Max	36 - 84	-42 - -1
Post-Baseline Maximum		
n	14	14
Mean (SD)	105.8 (14.6)	24.2 (17.9)
Median	102.0	21.0
Min - Max	88 - 130	5 - 63
PRE ATEZO INFUSION (COHORT C)		
n	31	31
Mean (SD)	102.3 (13.6)	23.3 (10.0)
Median	101.0	24.0
Min - Max	80 - 148	2 - 46

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Pulse Rate (beats/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	34	34
Mean (SD)	100.4 (9.8)	22.0 (11.3)
Median	98.5	22.5
Min - Max	86 - 120	4 - 43
AFTER PAC INFUSION		
n	23	23
Mean (SD)	95.0 (9.6)	20.6 (9.7)
Median	95.0	23.0
Min - Max	72 - 110	2 - 37

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Baseline		
n	101	
Mean (SD)	17.0 (2.1)	
Median	17.0	
Min - Max	12 - 25	
Cycle 1 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	96	95
Mean (SD)	17.7 (2.6)	0.7 (2.2)
Median	18.0	0.0
Min - Max	11 - 26	-6 - 8
PRE PAC INFUSION		
n	78	77
Mean (SD)	17.1 (2.0)	0.3 (1.8)
Median	17.0	0.0
Min - Max	12 - 24	-4 - 6
AFTER PAC INFUSION		
n	94	93
Mean (SD)	17.3 (2.4)	0.3 (2.0)
Median	17.0	0.0
Min - Max	11 - 24	-9 - 5
Cycle 1 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	16	16
Mean (SD)	17.8 (2.5)	0.9 (2.8)
Median	17.0	0.0
Min - Max	15 - 24	-3 - 8
PRE PAC INFUSION		
n	84	83
Mean (SD)	17.5 (1.9)	0.3 (2.0)
Median	18.0	0.0
Min - Max	12 - 22	-9 - 5
AFTER PAC INFUSION		
n	90	89
Mean (SD)	17.6 (2.1)	0.5 (2.3)
Median	18.0	0.0
Min - Max	11 - 23	-7 - 7
Cycle 1 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	92	92
Mean (SD)	17.3 (2.1)	0.2 (2.2)
Median	17.0	0.0
Min - Max	12 - 22	-9 - 5

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
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Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	66	66
Mean (SD)	17.1 (1.9)	0.2 (2.0)
Median	17.0	0.0
Min - Max	11 - 20	-5 - 5
AFTER PAC INFUSION		
n	75	75
Mean (SD)	17.6 (1.9)	0.6 (1.7)
Median	18.0	0.0
Min - Max	13 - 22	-3 - 5
Cycle 2 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	97	96
Mean (SD)	17.5 (2.0)	0.4 (1.9)
Median	18.0	0.0
Min - Max	12 - 23	-8 - 6
PRE PAC INFUSION		
n	78	77
Mean (SD)	17.1 (1.8)	0.2 (1.6)
Median	18.0	0.0
Min - Max	13 - 20	-5 - 4
AFTER PAC INFUSION		
n	90	89
Mean (SD)	17.6 (1.9)	0.4 (2.0)
Median	18.0	0.0
Min - Max	12 - 22	-6 - 6
Cycle 2 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	19	19
Mean (SD)	17.2 (2.2)	0.0 (2.0)
Median	17.0	0.0
Min - Max	12 - 22	-4 - 5
PRE PAC INFUSION		
n	79	79
Mean (SD)	17.3 (2.0)	0.2 (2.0)
Median	18.0	0.0
Min - Max	12 - 22	-6 - 5
AFTER PAC INFUSION		
n	86	86
Mean (SD)	17.7 (1.9)	0.5 (2.0)
Median	18.0	0.5
Min - Max	12 - 22	-4 - 6

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
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Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 2 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	86	85
Mean (SD)	17.4 (2.0)	0.5 (1.6)
Median	18.0	0.0
Min - Max	12 - 22	-5 - 4
PRE PAC INFUSION		
n	67	66
Mean (SD)	17.3 (1.8)	0.5 (1.5)
Median	17.0	0.0
Min - Max	14 - 20	-4 - 4
AFTER PAC INFUSION		
n	82	81
Mean (SD)	17.3 (1.9)	0.2 (1.8)
Median	18.0	0.0
Min - Max	12 - 22	-7 - 6
Cycle 3 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	86	85
Mean (SD)	17.4 (2.1)	0.3 (2.2)
Median	17.0	0.0
Min - Max	12 - 24	-5 - 8
PRE PAC INFUSION		
n	70	69
Mean (SD)	17.2 (1.7)	0.4 (1.9)
Median	17.5	0.0
Min - Max	13 - 22	-4 - 4
AFTER PAC INFUSION		
n	82	81
Mean (SD)	17.4 (1.8)	0.3 (1.8)
Median	18.0	0.0
Min - Max	12 - 22	-5 - 6
Cycle 3 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	15	15
Mean (SD)	18.3 (1.9)	0.5 (2.2)
Median	19.0	0.0
Min - Max	15 - 22	-5 - 4
PRE PAC INFUSION		
n	72	71
Mean (SD)	17.4 (2.0)	0.3 (2.2)
Median	17.0	0.0
Min - Max	12 - 22	-9 - 5

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
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Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	78	78
Mean (SD)	17.5 (1.9)	0.3 (2.2)
Median	18.0	0.0
Min - Max	12 - 22	-9 - 6
Cycle 3 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	78	77
Mean (SD)	17.5 (2.2)	0.4 (2.3)
Median	18.0	0.0
Min - Max	12 - 24	-6 - 8
PRE PAC INFUSION		
n	62	62
Mean (SD)	17.2 (1.7)	0.2 (1.7)
Median	17.0	0.0
Min - Max	13 - 20	-5 - 5
AFTER PAC INFUSION		
n	76	76
Mean (SD)	17.3 (1.8)	0.0 (1.7)
Median	17.5	0.0
Min - Max	14 - 22	-8 - 4
Cycle 4 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	79	79
Mean (SD)	17.4 (2.0)	0.3 (1.9)
Median	18.0	0.0
Min - Max	12 - 22	-8 - 5
PRE PAC INFUSION		
n	69	69
Mean (SD)	17.1 (1.9)	0.2 (1.7)
Median	17.0	0.0
Min - Max	12 - 21	-4 - 4
AFTER PAC INFUSION		
n	78	78
Mean (SD)	17.5 (1.9)	0.3 (1.9)
Median	18.0	0.0
Min - Max	13 - 22	-6 - 6
Cycle 4 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	15	15
Mean (SD)	17.3 (2.0)	0.3 (1.7)
Median	16.0	0.0
Min - Max	16 - 22	-4 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	70	70
Mean (SD)	17.3 (1.9)	0.2 (1.8)
Median	17.0	0.0
Min - Max	13 - 21	-4 - 5
AFTER PAC INFUSION		
n	81	81
Mean (SD)	17.5 (1.8)	0.3 (2.0)
Median	18.0	0.0
Min - Max	13 - 22	-6 - 6
Cycle 4 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	78	78
Mean (SD)	17.5 (2.1)	0.3 (2.4)
Median	18.0	0.0
Min - Max	12 - 22	-12 - 6
PRE PAC INFUSION		
n	66	66
Mean (SD)	17.2 (2.1)	0.2 (1.8)
Median	17.0	0.0
Min - Max	10 - 22	-6 - 4
AFTER PAC INFUSION		
n	74	74
Mean (SD)	17.5 (2.1)	0.2 (1.9)
Median	18.0	0.0
Min - Max	10 - 22	-6 - 5
Cycle 5 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	63	62
Mean (SD)	17.3 (2.1)	0.1 (2.2)
Median	17.0	0.0
Min - Max	12 - 22	-6 - 6
PRE PAC INFUSION		
n	59	58
Mean (SD)	17.0 (2.0)	0.0 (2.1)
Median	17.0	0.0
Min - Max	10 - 21	-6 - 6
AFTER PAC INFUSION		
n	63	62
Mean (SD)	16.9 (2.3)	-0.1 (2.3)
Median	18.0	0.0
Min - Max	8 - 21	-8 - 6

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
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Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 5 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	13	13
Mean (SD)	17.1 (2.2)	0.2 (3.1)
Median	17.0	0.0
Min - Max	12 - 20	-6 - 6
PRE PAC INFUSION		
n	55	54
Mean (SD)	17.3 (2.3)	0.1 (1.7)
Median	17.0	0.0
Min - Max	14 - 28	-4 - 4
AFTER PAC INFUSION		
n	59	58
Mean (SD)	17.2 (1.9)	0.0 (2.2)
Median	17.0	0.0
Min - Max	12 - 21	-7 - 6
Cycle 5 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	64	63
Mean (SD)	16.9 (2.1)	-0.3 (2.3)
Median	17.0	0.0
Min - Max	11 - 21	-8 - 6
PRE PAC INFUSION		
n	56	55
Mean (SD)	16.9 (1.8)	-0.1 (1.9)
Median	17.0	0.0
Min - Max	11 - 20	-5 - 5
AFTER PAC INFUSION		
n	58	57
Mean (SD)	17.1 (1.7)	0.2 (1.8)
Median	17.0	0.0
Min - Max	12 - 20	-4 - 6
Cycle 6 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	59	58
Mean (SD)	17.2 (2.0)	0.3 (2.2)
Median	17.0	0.0
Min - Max	13 - 24	-6 - 9
PRE PAC INFUSION		
n	57	56
Mean (SD)	17.1 (2.4)	0.1 (2.6)
Median	17.0	0.0
Min - Max	12 - 28	-4 - 14

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	58	57
Mean (SD)	17.2 (2.0)	0.3 (2.1)
Median	17.0	0.0
Min - Max	13 - 24	-4 - 10
Cycle 6 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	13	13
Mean (SD)	17.3 (2.8)	0.5 (3.6)
Median	17.0	0.0
Min - Max	13 - 24	-6 - 10
PRE PAC INFUSION		
n	49	49
Mean (SD)	16.8 (1.8)	-0.2 (2.0)
Median	17.0	0.0
Min - Max	12 - 20	-5 - 5
AFTER PAC INFUSION		
n	58	57
Mean (SD)	17.0 (2.0)	0.0 (1.9)
Median	17.0	0.0
Min - Max	12 - 21	-4 - 4
Cycle 6 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	52	51
Mean (SD)	17.1 (1.7)	0.1 (1.8)
Median	17.0	0.0
Min - Max	12 - 21	-5 - 5
PRE PAC INFUSION		
n	48	47
Mean (SD)	17.0 (1.5)	0.0 (1.9)
Median	17.0	0.0
Min - Max	14 - 21	-4 - 4
AFTER PAC INFUSION		
n	48	47
Mean (SD)	17.0 (1.5)	0.0 (1.7)
Median	17.0	0.0
Min - Max	15 - 20	-4 - 5
Cycle 7 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	53	52
Mean (SD)	17.3 (1.6)	0.4 (1.8)
Median	17.0	0.0
Min - Max	15 - 21	-4 - 6

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
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Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	46	46
Mean (SD)	17.0 (1.5)	0.3 (1.6)
Median	16.0	0.0
Min - Max	14 - 20	-3 - 4
AFTER PAC INFUSION		
n	50	50
Mean (SD)	17.0 (1.5)	0.2 (1.5)
Median	17.0	0.0
Min - Max	14 - 20	-3 - 3
Cycle 7 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	12	11
Mean (SD)	16.9 (2.8)	1.1 (2.9)
Median	18.0	2.0
Min - Max	12 - 20	-4 - 6
PRE PAC INFUSION		
n	42	42
Mean (SD)	17.0 (1.5)	0.1 (2.0)
Median	16.0	0.0
Min - Max	15 - 20	-5 - 5
AFTER PAC INFUSION		
n	49	49
Mean (SD)	17.3 (1.9)	0.6 (2.4)
Median	17.0	1.0
Min - Max	12 - 24	-4 - 10
Cycle 7 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	48	48
Mean (SD)	17.3 (1.7)	0.4 (1.8)
Median	17.0	0.5
Min - Max	14 - 22	-5 - 3
PRE PAC INFUSION		
n	44	43
Mean (SD)	17.2 (1.5)	0.3 (1.7)
Median	17.0	0.0
Min - Max	15 - 20	-3 - 5
AFTER PAC INFUSION		
n	45	44
Mean (SD)	17.2 (1.5)	0.5 (1.7)
Median	17.0	1.0
Min - Max	15 - 20	-3 - 4

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
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Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 8 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	46	46
Mean (SD)	17.5 (3.2)	0.8 (3.0)
Median	17.0	0.0
Min - Max	14 - 36	-3 - 18
PRE PAC INFUSION		
n	42	42
Mean (SD)	17.0 (1.6)	0.3 (1.5)
Median	16.5	1.0
Min - Max	14 - 21	-4 - 3
AFTER PAC INFUSION		
n	45	45
Mean (SD)	17.0 (1.7)	0.3 (1.4)
Median	17.0	0.0
Min - Max	12 - 20	-3 - 3
Cycle 8 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	10	10
Mean (SD)	16.8 (1.9)	0.7 (1.7)
Median	16.0	1.0
Min - Max	14 - 20	-2 - 3
PRE PAC INFUSION		
n	34	33
Mean (SD)	16.9 (1.2)	0.1 (1.5)
Median	17.0	0.0
Min - Max	14 - 19	-3 - 3
AFTER PAC INFUSION		
n	42	41
Mean (SD)	17.5 (2.1)	0.7 (2.3)
Median	17.0	1.0
Min - Max	12 - 24	-3 - 10
Cycle 8 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	44	43
Mean (SD)	17.1 (1.4)	0.5 (1.4)
Median	17.0	0.0
Min - Max	14 - 20	-2 - 4
PRE PAC INFUSION		
n	33	32
Mean (SD)	17.2 (1.7)	0.6 (1.8)
Median	17.0	0.0
Min - Max	12 - 20	-2 - 5

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
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Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	39	38
Mean (SD)	17.1 (1.4)	0.7 (1.6)
Median	17.0	0.0
Min - Max	14 - 20	-2 - 5
Cycle 9 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	35	34
Mean (SD)	17.2 (1.6)	0.6 (1.7)
Median	17.0	1.0
Min - Max	14 - 20	-4 - 3
PRE PAC INFUSION		
n	30	29
Mean (SD)	17.6 (3.8)	0.9 (3.7)
Median	17.0	1.0
Min - Max	15 - 36	-4 - 17
AFTER PAC INFUSION		
n	32	31
Mean (SD)	17.1 (1.6)	0.5 (2.0)
Median	16.0	0.0
Min - Max	15 - 20	-4 - 6
Cycle 9 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	7	7
Mean (SD)	17.4 (1.9)	1.0 (1.9)
Median	16.0	1.0
Min - Max	16 - 20	-2 - 4
PRE PAC INFUSION		
n	23	23
Mean (SD)	17.0 (1.4)	0.3 (1.9)
Median	17.0	0.0
Min - Max	15 - 20	-4 - 4
AFTER PAC INFUSION		
n	27	27
Mean (SD)	17.2 (1.4)	0.4 (2.0)
Median	18.0	0.0
Min - Max	15 - 20	-4 - 4
Cycle 9 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	33	32
Mean (SD)	17.0 (1.6)	0.4 (1.7)
Median	17.0	0.0
Min - Max	15 - 21	-4 - 5

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
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Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	29	28
Mean (SD)	17.1 (1.4)	0.4 (1.7)
Median	17.0	0.5
Min - Max	15 - 20	-3 - 4
AFTER PAC INFUSION		
n	26	26
Mean (SD)	17.2 (1.8)	0.7 (1.6)
Median	17.0	1.0
Min - Max	14 - 21	-2 - 5
Cycle 10 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	32	31
Mean (SD)	17.2 (1.7)	0.7 (1.7)
Median	17.0	1.0
Min - Max	15 - 20	-3 - 5
PRE PAC INFUSION		
n	31	30
Mean (SD)	16.5 (1.5)	0.1 (1.4)
Median	16.0	0.0
Min - Max	12 - 20	-3 - 2
AFTER PAC INFUSION		
n	28	28
Mean (SD)	16.8 (1.4)	0.1 (1.7)
Median	17.0	0.0
Min - Max	14 - 20	-4 - 3
Cycle 10 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	17.7 (2.0)	1.5 (2.0)
Median	17.0	2.0
Min - Max	16 - 20	-2 - 4
PRE PAC INFUSION		
n	21	21
Mean (SD)	16.8 (1.7)	0.0 (1.5)
Median	16.0	0.0
Min - Max	14 - 20	-3 - 4
AFTER PAC INFUSION		
n	23	23
Mean (SD)	16.9 (1.5)	0.0 (2.1)
Median	16.0	0.0
Min - Max	15 - 20	-3 - 6

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
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Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 10 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	31	30
Mean (SD)	16.5 (1.8)	0.1 (1.6)
Median	16.0	0.0
Min - Max	12 - 20	-3 - 4
PRE PAC INFUSION		
n	28	27
Mean (SD)	16.2 (1.7)	-0.3 (1.5)
Median	16.0	0.0
Min - Max	12 - 20	-3 - 2
AFTER PAC INFUSION		
n	24	24
Mean (SD)	16.7 (1.7)	0.0 (1.9)
Median	16.0	0.0
Min - Max	15 - 20	-3 - 6
Cycle 11 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	25	25
Mean (SD)	17.2 (1.6)	1.0 (1.6)
Median	17.0	1.0
Min - Max	15 - 20	-3 - 4
PRE PAC INFUSION		
n	22	22
Mean (SD)	16.5 (1.3)	0.4 (1.5)
Median	16.0	1.0
Min - Max	15 - 20	-3 - 2
AFTER PAC INFUSION		
n	21	21
Mean (SD)	16.9 (2.0)	0.7 (1.6)
Median	16.0	1.0
Min - Max	14 - 22	-3 - 3
Cycle 11 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	18.0 (1.8)	2.5 (1.7)
Median	18.0	2.0
Min - Max	16 - 20	1 - 5
PRE PAC INFUSION		
n	16	16
Mean (SD)	16.6 (1.4)	0.1 (1.3)
Median	16.5	0.0
Min - Max	14 - 20	-3 - 2

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
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Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	18	18
Mean (SD)	17.2 (1.9)	0.9 (1.7)
Median	16.5	1.0
Min - Max	15 - 22	-2 - 4
Cycle 11 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	21	21
Mean (SD)	16.6 (1.6)	0.4 (1.7)
Median	16.0	1.0
Min - Max	14 - 20	-4 - 3
PRE PAC INFUSION		
n	21	21
Mean (SD)	16.5 (1.1)	0.2 (1.3)
Median	16.0	0.0
Min - Max	15 - 18	-2 - 3
AFTER PAC INFUSION		
n	17	17
Mean (SD)	16.5 (1.1)	0.1 (1.9)
Median	16.0	0.0
Min - Max	15 - 19	-4 - 4
Cycle 12 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	24	23
Mean (SD)	17.2 (1.9)	1.0 (1.9)
Median	17.0	1.0
Min - Max	14 - 21	-2 - 6
PRE PAC INFUSION		
n	21	20
Mean (SD)	16.8 (1.6)	0.6 (1.8)
Median	16.0	0.0
Min - Max	14 - 20	-2 - 6
AFTER PAC INFUSION		
n	18	18
Mean (SD)	16.8 (1.7)	0.6 (1.9)
Median	16.0	0.0
Min - Max	14 - 20	-2 - 6
Cycle 12 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	17.8 (3.5)	1.5 (2.6)
Median	17.5	2.0
Min - Max	14 - 22	-2 - 4

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
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Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	15	15
Mean (SD)	16.5 (1.0)	0.1 (1.1)
Median	16.0	0.0
Min - Max	15 - 18	-2 - 2
AFTER PAC INFUSION		
n	16	16
Mean (SD)	16.7 (1.4)	0.4 (1.4)
Median	16.0	1.0
Min - Max	15 - 19	-2 - 3
Cycle 12 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	23	22
Mean (SD)	17.3 (1.8)	1.2 (2.0)
Median	18.0	1.0
Min - Max	14 - 20	-2 - 4
PRE PAC INFUSION		
n	21	20
Mean (SD)	17.1 (1.7)	0.7 (1.7)
Median	16.0	1.0
Min - Max	14 - 20	-2 - 4
AFTER PAC INFUSION		
n	17	17
Mean (SD)	16.8 (1.5)	0.6 (1.6)
Median	16.0	1.0
Min - Max	15 - 20	-3 - 4
Cycle 13 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	21	20
Mean (SD)	17.0 (1.7)	1.0 (1.7)
Median	16.0	1.0
Min - Max	15 - 21	-1 - 6
PRE PAC INFUSION		
n	20	20
Mean (SD)	16.8 (1.6)	0.5 (1.7)
Median	16.5	0.0
Min - Max	14 - 20	-2 - 4
AFTER PAC INFUSION		
n	13	13
Mean (SD)	16.5 (1.5)	0.5 (1.6)
Median	16.0	0.0
Min - Max	14 - 19	-2 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 13 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	18.5 (2.1)	3.5 (3.5)
Median	18.5	3.5
Min - Max	17 - 20	1 - 6
PRE PAC INFUSION		
n	14	14
Mean (SD)	16.2 (1.2)	0.1 (1.5)
Median	16.0	0.0
Min - Max	14 - 19	-3 - 2
AFTER PAC INFUSION		
n	15	15
Mean (SD)	16.3 (1.1)	0.3 (1.7)
Median	16.0	1.0
Min - Max	14 - 18	-3 - 4
Cycle 13 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	19	19
Mean (SD)	17.0 (2.3)	0.9 (1.7)
Median	17.0	1.0
Min - Max	12 - 20	-2 - 4
PRE PAC INFUSION		
n	19	19
Mean (SD)	16.9 (1.5)	0.8 (1.5)
Median	16.0	1.0
Min - Max	15 - 20	-2 - 4
AFTER PAC INFUSION		
n	15	15
Mean (SD)	16.8 (2.4)	0.8 (2.9)
Median	16.0	0.0
Min - Max	14 - 24	-2 - 10
Cycle 14 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	20	20
Mean (SD)	16.8 (1.9)	0.7 (1.9)
Median	16.0	0.0
Min - Max	14 - 20	-2 - 6
PRE PAC INFUSION		
n	18	18
Mean (SD)	16.8 (1.4)	0.7 (1.7)
Median	16.0	1.0
Min - Max	14 - 20	-2 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	14	14
Mean (SD)	16.7 (1.5)	0.7 (2.5)
Median	16.0	1.0
Min - Max	15 - 20	-3 - 6
Cycle 14 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	18.7 (3.2)	2.0 (3.6)
Median	20.0	1.0
Min - Max	15 - 21	-1 - 6
PRE PAC INFUSION		
n	10	10
Mean (SD)	16.4 (1.5)	0.3 (1.9)
Median	16.0	0.5
Min - Max	15 - 20	-3 - 4
AFTER PAC INFUSION		
n	12	12
Mean (SD)	16.6 (1.6)	0.7 (2.5)
Median	16.0	0.5
Min - Max	14 - 20	-3 - 6
Cycle 14 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	18	17
Mean (SD)	16.8 (1.4)	0.6 (1.5)
Median	16.0	1.0
Min - Max	15 - 20	-2 - 4
PRE PAC INFUSION		
n	16	15
Mean (SD)	16.9 (1.6)	0.8 (1.8)
Median	16.0	1.0
Min - Max	15 - 20	-3 - 4
AFTER PAC INFUSION		
n	12	12
Mean (SD)	16.3 (1.4)	0.3 (2.1)
Median	16.0	0.5
Min - Max	14 - 19	-3 - 4
Cycle 15 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	17	16
Mean (SD)	17.4 (1.9)	1.2 (1.8)
Median	17.0	1.5
Min - Max	14 - 22	-3 - 4

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	16	15
Mean (SD)	16.9 (1.5)	0.9 (1.8)
Median	16.5	1.0
Min - Max	15 - 20	-3 - 4
AFTER PAC INFUSION		
n	10	10
Mean (SD)	16.7 (1.6)	0.5 (2.3)
Median	17.0	0.5
Min - Max	14 - 19	-3 - 4
Cycle 15 Day 8		
PRE PAC INFUSION		
n	10	10
Mean (SD)	16.3 (1.3)	0.1 (1.9)
Median	16.0	1.0
Min - Max	14 - 18	-3 - 2
AFTER PAC INFUSION		
n	10	10
Mean (SD)	15.9 (1.3)	-0.3 (1.9)
Median	16.0	0.0
Min - Max	14 - 18	-3 - 2
Cycle 15 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	14	13
Mean (SD)	16.9 (1.7)	0.6 (1.6)
Median	16.0	1.0
Min - Max	14 - 20	-2 - 4
PRE PAC INFUSION		
n	13	12
Mean (SD)	16.7 (1.8)	0.6 (2.1)
Median	16.0	1.0
Min - Max	14 - 20	-3 - 4
AFTER PAC INFUSION		
n	7	7
Mean (SD)	16.7 (1.1)	0.3 (2.4)
Median	17.0	1.0
Min - Max	15 - 18	-3 - 4
Cycle 16 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	17.3 (2.1)	1.1 (1.6)
Median	17.5	1.0
Min - Max	14 - 20	-2 - 4

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	12	12
Mean (SD)	16.5 (1.1)	0.6 (1.6)
Median	16.5	1.0
Min - Max	14 - 18	-3 - 3
AFTER PAC INFUSION		
n	7	7
Mean (SD)	16.1 (1.6)	0.0 (2.6)
Median	16.0	0.0
Min - Max	14 - 19	-4 - 3
Cycle 16 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	17.0 (NE)	1.0 (NE)
Median	17.0	1.0
Min - Max	17 - 17	1 - 1
PRE PAC INFUSION		
n	8	8
Mean (SD)	16.5 (1.7)	0.4 (2.2)
Median	16.0	0.5
Min - Max	14 - 20	-3 - 4
AFTER PAC INFUSION		
n	8	8
Mean (SD)	15.9 (1.9)	-0.3 (2.6)
Median	16.0	0.0
Min - Max	14 - 20	-5 - 4
Cycle 16 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	14	13
Mean (SD)	16.8 (1.3)	0.7 (1.5)
Median	16.5	1.0
Min - Max	15 - 20	-2 - 4
PRE PAC INFUSION		
n	14	13
Mean (SD)	16.4 (1.6)	0.5 (2.2)
Median	16.0	1.0
Min - Max	14 - 20	-5 - 4
AFTER PAC INFUSION		
n	7	7
Mean (SD)	16.0 (1.3)	-0.1 (2.7)
Median	16.0	0.0
Min - Max	14 - 18	-5 - 4

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 17 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	16.7 (1.7)	1.0 (1.7)
Median	17.0	2.0
Min - Max	14 - 20	-2 - 3
PRE PAC INFUSION		
n	11	11
Mean (SD)	16.2 (1.5)	0.2 (1.8)
Median	16.0	0.0
Min - Max	14 - 20	-3 - 3
AFTER PAC INFUSION		
n	7	7
Mean (SD)	15.6 (1.1)	-0.6 (2.1)
Median	16.0	-1.0
Min - Max	14 - 17	-3 - 3
Cycle 17 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	16.0 (NE)	1.0 (NE)
Median	16.0	1.0
Min - Max	16 - 16	1 - 1
PRE PAC INFUSION		
n	7	7
Mean (SD)	16.0 (1.3)	-0.3 (1.5)
Median	16.0	0.0
Min - Max	14 - 18	-2 - 2
AFTER PAC INFUSION		
n	8	8
Mean (SD)	15.8 (1.2)	-0.4 (1.5)
Median	16.0	0.0
Min - Max	14 - 17	-3 - 1
Cycle 17 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	11
Mean (SD)	16.5 (1.6)	0.8 (1.7)
Median	16.0	1.0
Min - Max	14 - 20	-2 - 4
PRE PAC INFUSION		
n	12	11
Mean (SD)	16.7 (1.8)	0.8 (2.1)
Median	16.5	1.0
Min - Max	14 - 20	-3 - 4

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	8	8
Mean (SD)	15.9 (1.8)	-0.3 (2.7)
Median	16.0	-0.5
Min - Max	14 - 19	-5 - 3
Cycle 18 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	11	10
Mean (SD)	18.4 (6.0)	2.9 (6.2)
Median	17.0	1.0
Min - Max	14 - 36	-2 - 20
PRE PAC INFUSION		
n	13	12
Mean (SD)	16.9 (1.8)	1.0 (1.9)
Median	17.0	1.0
Min - Max	14 - 20	-2 - 4
AFTER PAC INFUSION		
n	8	8
Mean (SD)	16.5 (1.5)	0.4 (2.4)
Median	16.0	0.5
Min - Max	14 - 19	-3 - 4
Cycle 18 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	16.0 (NE)	1.0 (NE)
Median	16.0	1.0
Min - Max	16 - 16	1 - 1
PRE PAC INFUSION		
n	6	6
Mean (SD)	15.8 (1.2)	-0.5 (1.4)
Median	16.0	-0.5
Min - Max	14 - 17	-2 - 1
AFTER PAC INFUSION		
n	7	7
Mean (SD)	15.9 (1.2)	-0.3 (1.8)
Median	16.0	0.0
Min - Max	14 - 18	-3 - 2
Cycle 18 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	16.7 (1.6)	1.0 (1.5)
Median	16.0	1.0
Min - Max	15 - 20	-1 - 4

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	11	11
Mean (SD)	16.4 (2.2)	0.4 (2.5)
Median	16.0	1.0
Min - Max	14 - 21	-5 - 5
AFTER PAC INFUSION		
n	6	6
Mean (SD)	16.2 (1.5)	-0.2 (2.0)
Median	16.0	-0.5
Min - Max	15 - 19	-3 - 3
Cycle 19 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	16.7 (1.6)	1.0 (1.7)
Median	17.0	1.0
Min - Max	14 - 20	-2 - 4
PRE PAC INFUSION		
n	11	11
Mean (SD)	16.5 (1.9)	0.5 (1.8)
Median	16.0	1.0
Min - Max	14 - 20	-2 - 4
AFTER PAC INFUSION		
n	8	8
Mean (SD)	17.4 (2.7)	1.3 (2.6)
Median	16.0	0.5
Min - Max	14 - 22	-2 - 6
Cycle 19 Day 8		
PRE PAC INFUSION		
n	7	7
Mean (SD)	17.3 (2.8)	1.0 (2.2)
Median	17.0	0.0
Min - Max	14 - 23	-2 - 4
AFTER PAC INFUSION		
n	7	7
Mean (SD)	18.0 (3.4)	1.7 (2.7)
Median	17.0	1.0
Min - Max	15 - 25	-1 - 6
Cycle 19 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	11
Mean (SD)	16.8 (1.9)	0.7 (1.3)
Median	16.5	1.0
Min - Max	14 - 20	-2 - 2

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	10	10
Mean (SD)	16.8 (1.6)	0.7 (1.3)
Median	16.0	1.0
Min - Max	15 - 20	-1 - 2
AFTER PAC INFUSION		
n	7	7
Mean (SD)	16.7 (2.1)	0.4 (1.5)
Median	16.0	1.0
Min - Max	14 - 20	-2 - 2
Cycle 20 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	16.4 (1.4)	0.6 (1.3)
Median	16.0	1.0
Min - Max	14 - 19	-2 - 2
PRE PAC INFUSION		
n	9	9
Mean (SD)	16.2 (2.1)	0.1 (2.5)
Median	16.0	1.0
Min - Max	14 - 20	-5 - 3
AFTER PAC INFUSION		
n	7	7
Mean (SD)	16.6 (2.2)	0.3 (3.1)
Median	16.0	2.0
Min - Max	14 - 20	-5 - 4
Cycle 20 Day 8		
PRE PAC INFUSION		
n	7	7
Mean (SD)	17.0 (1.6)	0.7 (1.5)
Median	17.0	1.0
Min - Max	15 - 20	-1 - 3
AFTER PAC INFUSION		
n	7	7
Mean (SD)	16.4 (1.0)	0.1 (1.8)
Median	16.0	0.0
Min - Max	15 - 18	-2 - 3
Cycle 20 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	11
Mean (SD)	16.6 (1.5)	0.9 (1.4)
Median	16.5	1.0
Min - Max	14 - 19	-2 - 3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	11	10
Mean (SD)	16.5 (1.6)	0.4 (1.6)
Median	16.0	1.0
Min - Max	14 - 20	-2 - 2
AFTER PAC INFUSION		
n	7	7
Mean (SD)	16.3 (1.5)	0.0 (2.0)
Median	16.0	1.0
Min - Max	14 - 18	-3 - 2
Cycle 21 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	11
Mean (SD)	16.4 (1.2)	0.7 (1.4)
Median	16.0	1.0
Min - Max	15 - 19	-1 - 4
PRE PAC INFUSION		
n	11	10
Mean (SD)	16.5 (1.6)	0.6 (2.0)
Median	16.0	1.0
Min - Max	14 - 20	-3 - 4
AFTER PAC INFUSION		
n	7	7
Mean (SD)	16.6 (0.8)	0.3 (2.1)
Median	16.0	0.0
Min - Max	16 - 18	-3 - 4
Cycle 21 Day 8		
PRE PAC INFUSION		
n	6	6
Mean (SD)	17.0 (2.4)	0.7 (1.8)
Median	16.5	1.5
Min - Max	14 - 21	-2 - 2
AFTER PAC INFUSION		
n	6	6
Mean (SD)	16.5 (1.2)	0.2 (1.5)
Median	16.0	-0.5
Min - Max	15 - 18	-1 - 2
Cycle 21 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	10
Mean (SD)	16.4 (1.6)	0.8 (1.3)
Median	17.0	1.0
Min - Max	14 - 19	-2 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	9	9
Mean (SD)	16.6 (1.6)	0.4 (1.2)
Median	16.0	1.0
Min - Max	15 - 20	-1 - 2
AFTER PAC INFUSION		
n	6	6
Mean (SD)	16.3 (1.6)	0.0 (1.4)
Median	16.0	0.0
Min - Max	14 - 19	-2 - 2
Cycle 22 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	11
Mean (SD)	16.5 (1.3)	0.8 (1.5)
Median	16.0	1.0
Min - Max	14 - 19	-2 - 4
PRE PAC INFUSION		
n	10	9
Mean (SD)	16.5 (1.6)	0.3 (2.1)
Median	16.0	1.0
Min - Max	14 - 20	-3 - 4
AFTER PAC INFUSION		
n	6	6
Mean (SD)	16.3 (1.5)	0.0 (2.1)
Median	16.0	-0.5
Min - Max	14 - 18	-2 - 4
Cycle 22 Day 8		
PRE PAC INFUSION		
n	4	4
Mean (SD)	16.8 (2.5)	-0.3 (1.3)
Median	16.5	0.0
Min - Max	14 - 20	-2 - 1
AFTER PAC INFUSION		
n	4	4
Mean (SD)	17.0 (2.7)	0.0 (1.4)
Median	16.0	-0.5
Min - Max	15 - 21	-1 - 2
Cycle 22 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	10
Mean (SD)	16.4 (1.2)	0.7 (1.4)
Median	16.0	1.0
Min - Max	15 - 19	-1 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	10	9
Mean (SD)	16.2 (1.8)	0.1 (2.6)
Median	16.0	1.0
Min - Max	14 - 20	-5 - 4
AFTER PAC INFUSION		
n	6	6
Mean (SD)	16.2 (1.0)	-0.2 (2.6)
Median	16.0	0.0
Min - Max	15 - 18	-4 - 4
Cycle 23 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	8
Mean (SD)	16.6 (1.1)	0.9 (1.0)
Median	16.0	0.5
Min - Max	15 - 19	0 - 2
PRE PAC INFUSION		
n	9	8
Mean (SD)	16.1 (1.1)	0.3 (1.3)
Median	16.0	0.0
Min - Max	15 - 18	-1 - 2
AFTER PAC INFUSION		
n	6	6
Mean (SD)	15.7 (1.0)	-0.7 (1.6)
Median	16.0	-0.5
Min - Max	14 - 17	-3 - 1
Cycle 23 Day 8		
PRE PAC INFUSION		
n	5	5
Mean (SD)	16.2 (1.5)	-0.6 (2.6)
Median	16.0	0.0
Min - Max	14 - 18	-5 - 2
AFTER PAC INFUSION		
n	5	5
Mean (SD)	16.0 (0.7)	-0.8 (1.5)
Median	16.0	-1.0
Min - Max	15 - 17	-3 - 1
Cycle 23 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	9	8
Mean (SD)	16.2 (0.8)	0.9 (0.8)
Median	16.0	1.0
Min - Max	15 - 18	0 - 2

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	9	8
Mean (SD)	15.9 (0.8)	-0.1 (1.7)
Median	16.0	0.5
Min - Max	14 - 17	-3 - 2
AFTER PAC INFUSION		
n	6	6
Mean (SD)	16.3 (1.9)	0.0 (1.8)
Median	16.0	-0.5
Min - Max	14 - 19	-2 - 3
Cycle 24 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	10	9
Mean (SD)	15.8 (1.1)	0.1 (1.3)
Median	16.0	0.0
Min - Max	14 - 18	-2 - 2
PRE PAC INFUSION		
n	9	8
Mean (SD)	15.7 (1.1)	-0.3 (1.4)
Median	16.0	0.0
Min - Max	14 - 17	-2 - 2
AFTER PAC INFUSION		
n	6	6
Mean (SD)	15.8 (1.5)	-0.5 (1.0)
Median	15.5	-0.5
Min - Max	14 - 18	-2 - 1
Cycle 24 Day 8		
PRE PAC INFUSION		
n	4	4
Mean (SD)	17.3 (1.0)	0.3 (1.3)
Median	17.5	0.0
Min - Max	16 - 18	-1 - 2
AFTER PAC INFUSION		
n	4	4
Mean (SD)	16.8 (1.5)	-0.3 (2.5)
Median	16.0	-0.5
Min - Max	16 - 19	-3 - 3
Cycle 24 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	10	9
Mean (SD)	15.6 (0.7)	0.1 (1.3)
Median	16.0	0.0
Min - Max	14 - 16	-2 - 2

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	9	8
Mean (SD)	15.8 (1.3)	0.1 (1.4)
Median	16.0	0.5
Min - Max	14 - 18	-2 - 2
AFTER PAC INFUSION		
n	6	6
Mean (SD)	16.0 (0.0)	-0.3 (1.6)
Median	16.0	0.0
Min - Max	16 - 16	-3 - 2
Cycle 25 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	8
Mean (SD)	15.9 (0.9)	0.4 (1.4)
Median	16.0	0.5
Min - Max	14 - 17	-2 - 2
PRE PAC INFUSION		
n	10	9
Mean (SD)	15.8 (0.8)	-0.1 (1.3)
Median	16.0	0.0
Min - Max	14 - 17	-2 - 1
AFTER PAC INFUSION		
n	4	4
Mean (SD)	15.0 (0.8)	-1.5 (1.7)
Median	15.0	-1.0
Min - Max	14 - 16	-4 - 0
Cycle 25 Day 8		
PRE PAC INFUSION		
n	3	3
Mean (SD)	16.7 (3.1)	-0.7 (1.5)
Median	16.0	-1.0
Min - Max	14 - 20	-2 - 1
AFTER PAC INFUSION		
n	3	3
Mean (SD)	17.3 (4.2)	0.0 (2.6)
Median	16.0	-1.0
Min - Max	14 - 22	-2 - 3
Cycle 25 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	8	7
Mean (SD)	16.1 (0.6)	0.6 (1.0)
Median	16.0	1.0
Min - Max	15 - 17	-1 - 2

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	8	7
Mean (SD)	15.6 (0.7)	-0.6 (2.1)
Median	16.0	0.0
Min - Max	14 - 16	-5 - 2
AFTER PAC INFUSION		
n	5	5
Mean (SD)	16.2 (1.1)	-0.2 (1.3)
Median	16.0	-1.0
Min - Max	15 - 18	-1 - 2
Cycle 26 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	8	7
Mean (SD)	16.3 (1.8)	0.3 (1.5)
Median	16.0	0.0
Min - Max	14 - 20	-2 - 2
PRE PAC INFUSION		
n	8	7
Mean (SD)	15.5 (0.9)	-0.3 (1.8)
Median	16.0	0.0
Min - Max	14 - 16	-3 - 2
AFTER PAC INFUSION		
n	4	4
Mean (SD)	14.8 (1.0)	-1.8 (2.5)
Median	14.5	-1.5
Min - Max	14 - 16	-5 - 1
Cycle 26 Day 8		
PRE PAC INFUSION		
n	5	5
Mean (SD)	15.4 (1.9)	-1.0 (3.3)
Median	14.0	-2.0
Min - Max	14 - 18	-5 - 4
AFTER PAC INFUSION		
n	5	5
Mean (SD)	15.8 (1.8)	-0.6 (2.1)
Median	16.0	-1.0
Min - Max	14 - 18	-2 - 3
Cycle 26 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	8	7
Mean (SD)	16.0 (1.7)	0.0 (0.8)
Median	15.5	0.0
Min - Max	15 - 20	-1 - 1

Baseline is the patient's last observation prior to initiation of study drug.
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	8	7
Mean (SD)	16.1 (1.0)	-0.1 (1.1)
Median	16.0	0.0
Min - Max	15 - 18	-2 - 1
AFTER PAC INFUSION		
n	4	4
Mean (SD)	16.3 (1.9)	-0.3 (1.0)
Median	15.5	-0.5
Min - Max	15 - 19	-1 - 1
Cycle 27 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	8	7
Mean (SD)	16.0 (1.2)	0.3 (1.6)
Median	16.0	0.0
Min - Max	14 - 18	-2 - 3
PRE PAC INFUSION		
n	8	7
Mean (SD)	16.1 (1.4)	0.1 (2.0)
Median	16.0	0.0
Min - Max	14 - 18	-2 - 4
AFTER PAC INFUSION		
n	4	4
Mean (SD)	16.5 (1.9)	0.0 (2.7)
Median	17.0	-1.0
Min - Max	14 - 18	-2 - 4
Cycle 27 Day 8		
PRE PAC INFUSION		
n	3	3
Mean (SD)	17.7 (2.5)	1.3 (2.5)
Median	18.0	1.0
Min - Max	15 - 20	-1 - 4
AFTER PAC INFUSION		
n	3	3
Mean (SD)	18.7 (3.1)	2.3 (2.1)
Median	18.0	3.0
Min - Max	16 - 22	0 - 4
Cycle 27 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	7	6
Mean (SD)	15.7 (1.3)	0.3 (2.1)
Median	16.0	0.0
Min - Max	14 - 18	-2 - 4

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	7	6
Mean (SD)	16.3 (1.5)	0.2 (2.1)
Median	16.0	-0.5
Min - Max	14 - 18	-2 - 4
AFTER PAC INFUSION		
n	4	4
Mean (SD)	16.8 (2.5)	0.3 (2.2)
Median	16.5	0.0
Min - Max	14 - 20	-2 - 3
Cycle 28 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	15.5 (0.5)	0.2 (1.2)
Median	15.5	0.0
Min - Max	15 - 16	-1 - 2
PRE PAC INFUSION		
n	4	4
Mean (SD)	15.8 (0.5)	0.0 (0.8)
Median	16.0	0.0
Min - Max	15 - 16	-1 - 1
AFTER PAC INFUSION		
n	2	2
Mean (SD)	15.5 (0.7)	-1.0 (0.0)
Median	15.5	-1.0
Min - Max	15 - 16	-1 - -1
Cycle 28 Day 8		
PRE PAC INFUSION		
n	2	2
Mean (SD)	15.0 (1.4)	-1.5 (0.7)
Median	15.0	-1.5
Min - Max	14 - 16	-2 - -1
AFTER PAC INFUSION		
n	2	2
Mean (SD)	15.0 (1.4)	-1.5 (0.7)
Median	15.0	-1.5
Min - Max	14 - 16	-2 - -1
Cycle 28 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	16.0 (0.6)	0.7 (1.5)
Median	16.0	1.0
Min - Max	15 - 17	-1 - 3

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	4	4
Mean (SD)	15.3 (1.3)	-0.5 (1.0)
Median	15.0	0.0
Min - Max	14 - 17	-2 - 0
AFTER PAC INFUSION		
n	2	2
Mean (SD)	15.5 (0.7)	-1.0 (0.0)
Median	15.5	-1.0
Min - Max	15 - 16	-1 - -1
Cycle 29 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	7	7
Mean (SD)	16.0 (1.0)	0.6 (1.7)
Median	16.0	0.0
Min - Max	15 - 18	-1 - 4
PRE PAC INFUSION		
n	4	4
Mean (SD)	15.5 (0.6)	-0.3 (1.0)
Median	15.5	-0.5
Min - Max	15 - 16	-1 - 1
AFTER PAC INFUSION		
n	2	2
Mean (SD)	16.0 (0.0)	-0.5 (0.7)
Median	16.0	-0.5
Min - Max	16 - 16	-1 - 0
Cycle 29 Day 8		
PRE PAC INFUSION		
n	2	2
Mean (SD)	15.5 (0.7)	-1.0 (0.0)
Median	15.5	-1.0
Min - Max	15 - 16	-1 - -1
AFTER PAC INFUSION		
n	2	2
Mean (SD)	16.0 (0.0)	-0.5 (0.7)
Median	16.0	-0.5
Min - Max	16 - 16	-1 - 0
Cycle 29 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	16.0 (1.3)	0.8 (1.9)
Median	16.0	1.0
Min - Max	14 - 18	-2 - 4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	16.3 (0.6)	0.7 (0.6)
Median	16.0	1.0
Min - Max	16 - 17	0 - 1
AFTER PAC INFUSION		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1
Cycle 30 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	5	5
Mean (SD)	15.4 (0.9)	0.2 (1.3)
Median	16.0	0.0
Min - Max	14 - 16	-1 - 2
PRE PAC INFUSION		
n	3	3
Mean (SD)	15.3 (0.6)	-0.3 (0.6)
Median	15.0	0.0
Min - Max	15 - 16	-1 - 0
AFTER PAC INFUSION		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1
Cycle 30 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1
AFTER PAC INFUSION		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1
Cycle 30 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	5	5
Mean (SD)	16.2 (0.8)	1.0 (1.2)
Median	16.0	1.0
Min - Max	15 - 17	0 - 3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	16.0 (1.0)	0.3 (1.5)
Median	16.0	0.0
Min - Max	15 - 17	-1 - 2
AFTER PAC INFUSION		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1
Cycle 31 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	16.5 (1.3)	1.3 (1.9)
Median	16.5	0.5
Min - Max	15 - 18	0 - 4
PRE PAC INFUSION		
n	3	3
Mean (SD)	15.3 (0.6)	-0.3 (0.6)
Median	15.0	0.0
Min - Max	15 - 16	-1 - 0
AFTER PAC INFUSION		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1
Cycle 31 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	17.0 (NE)	0.0 (NE)
Median	17.0	0.0
Min - Max	17 - 17	0 - 0
AFTER PAC INFUSION		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1
Cycle 31 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	15.8 (0.5)	0.5 (1.3)
Median	16.0	0.5
Min - Max	15 - 16	-1 - 2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	15.3 (0.6)	-0.3 (0.6)
Median	15.0	0.0
Min - Max	15 - 16	-1 - 0
AFTER PAC INFUSION		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1
Cycle 32 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	16.5 (1.3)	1.3 (1.9)
Median	16.5	0.5
Min - Max	15 - 18	0 - 4
PRE PAC INFUSION		
n	3	3
Mean (SD)	15.7 (0.6)	0.0 (1.0)
Median	16.0	0.0
Min - Max	15 - 16	-1 - 1
AFTER PAC INFUSION		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1
Cycle 32 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1
AFTER PAC INFUSION		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1
Cycle 32 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	15.8 (1.0)	0.5 (1.7)
Median	15.5	0.0
Min - Max	15 - 17	-1 - 3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	15.7 (0.6)	0.0 (1.0)
Median	16.0	0.0
Min - Max	15 - 16	-1 - 1
AFTER PAC INFUSION		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1
Cycle 33 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	16.0 (1.0)	0.3 (0.6)
Median	16.0	0.0
Min - Max	15 - 17	0 - 1
PRE PAC INFUSION		
n	2	2
Mean (SD)	15.5 (0.7)	0.5 (0.7)
Median	15.5	0.5
Min - Max	15 - 16	0 - 1
Cycle 33 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	17.0 (NE)	0.0 (NE)
Median	17.0	0.0
Min - Max	17 - 17	0 - 0
Cycle 33 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	16.0 (0.0)	0.0 (1.4)
Median	16.0	0.0
Min - Max	16 - 16	-1 - 1
PRE PAC INFUSION		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
Cycle 34 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	15.5 (0.7)	0.5 (0.7)
Median	15.5	0.5
Min - Max	15 - 16	0 - 1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	2	2
Mean (SD)	15.5 (0.7)	0.5 (0.7)
Median	15.5	0.5
Min - Max	15 - 16	0 - 1
AFTER PAC INFUSION		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1
Cycle 34 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1
Cycle 34 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	16.5 (0.7)	0.5 (0.7)
Median	16.5	0.5
Min - Max	16 - 17	0 - 1
PRE PAC INFUSION		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
Cycle 35 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	15.7 (0.6)	0.0 (1.0)
Median	16.0	0.0
Min - Max	15 - 16	-1 - 1
PRE PAC INFUSION		
n	2	2
Mean (SD)	15.5 (0.7)	0.5 (0.7)
Median	15.5	0.5
Min - Max	15 - 16	0 - 1
Cycle 35 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	16.0 (NE)	-1.0 (NE)
Median	16.0	-1.0
Min - Max	16 - 16	-1 - -1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 35 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	15.5 (0.7)	0.5 (0.7)
Median	15.5	0.5
Min - Max	15 - 16	0 - 1
PRE PAC INFUSION		
n	2	2
Mean (SD)	16.0 (0.0)	1.0 (0.0)
Median	16.0	1.0
Min - Max	16 - 16	1 - 1
Cycle 36 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	15.0 (0.0)	0.0 (0.0)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
PRE PAC INFUSION		
n	2	2
Mean (SD)	15.0 (0.0)	0.0 (0.0)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
Cycle 36 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	15.5 (0.7)	0.5 (0.7)
Median	15.5	0.5
Min - Max	15 - 16	0 - 1
PRE PAC INFUSION		
n	2	2
Mean (SD)	15.0 (0.0)	0.0 (0.0)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
Cycle 37 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	15.0 (0.0)	0.0 (0.0)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
PRE PAC INFUSION		
n	2	2
Mean (SD)	14.5 (0.7)	-0.5 (0.7)
Median	14.5	-0.5
Min - Max	14 - 15	-1 - 0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 37 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	15.5 (0.7)	0.5 (0.7)
Median	15.5	0.5
Min - Max	15 - 16	0 - 1
PRE PAC INFUSION		
n	2	2
Mean (SD)	15.0 (0.0)	0.0 (0.0)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
Cycle 38 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	15.0 (0.0)	0.0 (0.0)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
PRE PAC INFUSION		
n	2	2
Mean (SD)	16.5 (2.1)	1.5 (2.1)
Median	16.5	1.5
Min - Max	15 - 18	0 - 3
Cycle 38 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	15.0 (0.0)	0.0 (0.0)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
PRE PAC INFUSION		
n	2	2
Mean (SD)	15.0 (0.0)	0.0 (0.0)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
Cycle 39 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	15.0 (0.0)	0.0 (0.0)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
PRE PAC INFUSION		
n	2	2
Mean (SD)	15.0 (0.0)	0.0 (0.0)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0

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Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 39 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	15.5 (0.7)	0.5 (0.7)
Median	15.5	0.5
Min - Max	15 - 16	0 - 1
PRE PAC INFUSION		
n	2	2
Mean (SD)	15.5 (0.7)	0.5 (0.7)
Median	15.5	0.5
Min - Max	15 - 16	0 - 1
Cycle 40 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
PRE PAC INFUSION		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
Cycle 40 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	16.0 (NE)	1.0 (NE)
Median	16.0	1.0
Min - Max	16 - 16	1 - 1
PRE PAC INFUSION		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
Cycle 41 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
PRE PAC INFUSION		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 41 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
PRE PAC INFUSION		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
Cycle 42 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
PRE PAC INFUSION		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
Cycle 42 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
PRE PAC INFUSION		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
Cycle 43 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
PRE PAC INFUSION		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 43 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
PRE PAC INFUSION		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
Cycle 44 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
PRE PAC INFUSION		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
Cycle 44 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
PRE PAC INFUSION		
n	1	1
Mean (SD)	15.0 (NE)	0.0 (NE)
Median	15.0	0.0
Min - Max	15 - 15	0 - 0
Study Drug Discontinuation		
n	85	84
Mean (SD)	16.8 (1.6)	-0.3 (2.0)
Median	16.0	0.0
Min - Max	12 - 22	-9 - 6
Post-Baseline Last		
n	84	84
Mean (SD)	16.8 (1.7)	-0.3 (2.0)
Median	16.0	0.0
Min - Max	12 - 22	-9 - 6

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	17.5 (3.0)	2.0 (2.7)
Median	16.0	1.0
Min - Max	16 - 22	0 - 6
PRE PAC INFUSION		
n	4	4
Mean (SD)	17.0 (1.2)	0.0 (0.8)
Median	17.0	0.0
Min - Max	16 - 18	-1 - 1
AFTER PAC INFUSION		
n	9	9
Mean (SD)	18.0 (2.1)	1.7 (2.8)
Median	18.0	1.0
Min - Max	16 - 21	-2 - 7
Post-Baseline Minimum		
n	2	2
Mean (SD)	15.0 (1.4)	-1.0 (1.4)
Median	15.0	-1.0
Min - Max	14 - 16	-2 - 0
PRE ATEZO INFUSION (COHORT C)		
n	39	39
Mean (SD)	15.6 (2.1)	-1.9 (2.8)
Median	16.0	-1.0
Min - Max	11 - 22	-12 - 2
PRE PAC INFUSION		
n	39	39
Mean (SD)	15.2 (1.5)	-1.9 (1.6)
Median	15.0	-1.0
Min - Max	11 - 18	-5 - 1
AFTER PAC INFUSION		
n	21	21
Mean (SD)	14.1 (2.4)	-2.0 (2.5)
Median	14.0	-2.0
Min - Max	8 - 18	-8 - 2
Post-Baseline Maximum		
n	2	2
Mean (SD)	26.0 (8.5)	8.0 (11.3)
Median	26.0	8.0
Min - Max	20 - 32	0 - 16
PRE ATEZO INFUSION (COHORT C)		
n	36	36
Mean (SD)	21.1 (4.3)	3.9 (4.3)
Median	20.0	3.0
Min - Max	16 - 36	-1 - 20

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Respiratory Rate (breaths/min)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	30	30
Mean (SD)	20.4 (3.9)	3.0 (3.7)
Median	20.0	2.0
Min - Max	17 - 36	-1 - 17
AFTER PAC INFUSION		
n	33	33
Mean (SD)	19.6 (1.9)	3.1 (1.9)
Median	20.0	3.0
Min - Max	17 - 25	0 - 7

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Baseline		
n	102	
Mean (SD)	36.45 (0.49)	
Median	36.50	
Min - Max	35.0 - 37.9	
Cycle 1 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	97	97
Mean (SD)	36.49 (0.41)	0.03 (0.46)
Median	36.50	0.00
Min - Max	35.0 - 37.7	-1.1 - 1.3
PRE PAC INFUSION		
n	78	78
Mean (SD)	36.54 (0.46)	0.04 (0.44)
Median	36.60	0.00
Min - Max	35.6 - 38.4	-1.1 - 1.3
AFTER PAC INFUSION		
n	94	94
Mean (SD)	36.49 (0.49)	0.05 (0.47)
Median	36.55	0.05
Min - Max	35.2 - 38.4	-1.7 - 1.4
Cycle 1 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	16	16
Mean (SD)	36.52 (0.70)	-0.04 (0.35)
Median	36.55	0.00
Min - Max	35.1 - 37.9	-0.7 - 0.7
PRE PAC INFUSION		
n	85	85
Mean (SD)	36.40 (0.52)	0.01 (0.52)
Median	36.50	0.00
Min - Max	35.2 - 38.2	-1.6 - 2.0
AFTER PAC INFUSION		
n	91	91
Mean (SD)	36.52 (0.56)	0.08 (0.56)
Median	36.60	0.00
Min - Max	35.0 - 38.9	-1.3 - 1.7
Cycle 1 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	92	92
Mean (SD)	36.57 (0.61)	0.09 (0.61)
Median	36.50	0.00
Min - Max	34.8 - 39.1	-1.2 - 3.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	66	66
Mean (SD)	36.59 (0.46)	0.09 (0.42)
Median	36.60	0.00
Min - Max	35.0 - 38.0	-0.9 - 1.3
AFTER PAC INFUSION		
n	77	77
Mean (SD)	36.52 (0.56)	0.06 (0.51)
Median	36.60	0.00
Min - Max	34.8 - 37.9	-1.3 - 1.3
Cycle 2 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	98	98
Mean (SD)	36.50 (0.46)	0.06 (0.51)
Median	36.50	0.00
Min - Max	35.4 - 38.2	-1.0 - 2.3
PRE PAC INFUSION		
n	77	77
Mean (SD)	36.44 (0.49)	-0.05 (0.47)
Median	36.50	-0.10
Min - Max	35.0 - 37.8	-1.8 - 1.1
AFTER PAC INFUSION		
n	89	89
Mean (SD)	36.41 (0.52)	-0.02 (0.47)
Median	36.50	0.00
Min - Max	34.5 - 37.9	-1.5 - 1.1
Cycle 2 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	19	19
Mean (SD)	36.31 (0.57)	-0.26 (0.61)
Median	36.30	-0.30
Min - Max	35.0 - 37.3	-1.3 - 1.4
PRE PAC INFUSION		
n	78	78
Mean (SD)	36.47 (0.54)	0.05 (0.51)
Median	36.50	0.00
Min - Max	34.3 - 37.8	-1.2 - 1.3
AFTER PAC INFUSION		
n	86	86
Mean (SD)	36.44 (0.49)	0.01 (0.47)
Median	36.40	0.00
Min - Max	34.7 - 37.9	-1.0 - 1.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 2 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	88	88
Mean (SD)	36.49 (0.51)	0.02 (0.48)
Median	36.50	0.00
Min - Max	34.7 - 37.7	-1.3 - 1.3
PRE PAC INFUSION		
n	70	70
Mean (SD)	36.54 (0.50)	0.05 (0.37)
Median	36.60	0.00
Min - Max	34.6 - 37.8	-0.7 - 1.1
AFTER PAC INFUSION		
n	83	83
Mean (SD)	36.56 (0.47)	0.09 (0.41)
Median	36.50	0.00
Min - Max	35.4 - 38.8	-0.9 - 1.3
Cycle 3 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	86	86
Mean (SD)	36.55 (0.55)	0.05 (0.52)
Median	36.50	0.00
Min - Max	35.1 - 38.3	-1.1 - 1.6
PRE PAC INFUSION		
n	70	70
Mean (SD)	36.52 (0.50)	-0.02 (0.43)
Median	36.50	-0.10
Min - Max	35.4 - 38.6	-1.4 - 1.1
AFTER PAC INFUSION		
n	82	82
Mean (SD)	36.52 (0.53)	0.05 (0.42)
Median	36.50	0.00
Min - Max	35.5 - 38.7	-0.8 - 1.7
Cycle 3 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	15	15
Mean (SD)	36.39 (0.47)	-0.03 (0.48)
Median	36.40	0.00
Min - Max	35.0 - 37.0	-0.8 - 0.8
PRE PAC INFUSION		
n	74	74
Mean (SD)	36.46 (0.44)	0.03 (0.41)
Median	36.50	0.00
Min - Max	35.1 - 37.4	-0.8 - 1.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
AFTER PAC INFUSION		
n	79	79
Mean (SD)	36.48 (0.47)	0.04 (0.48)
Median	36.50	0.00
Min - Max	35.3 - 38.0	-1.3 - 1.8
Cycle 3 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	78	78
Mean (SD)	36.38 (0.49)	-0.05 (0.52)
Median	36.40	0.00
Min - Max	35.0 - 37.5	-1.5 - 1.3
PRE PAC INFUSION		
n	62	62
Mean (SD)	36.48 (0.45)	0.02 (0.46)
Median	36.50	0.00
Min - Max	35.0 - 37.3	-1.3 - 1.1
AFTER PAC INFUSION		
n	77	77
Mean (SD)	36.44 (0.47)	-0.01 (0.49)
Median	36.50	0.00
Min - Max	35.1 - 37.5	-1.4 - 1.3
Cycle 4 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	79	79
Mean (SD)	36.46 (0.40)	-0.02 (0.47)
Median	36.50	0.00
Min - Max	35.0 - 37.8	-1.8 - 1.1
PRE PAC INFUSION		
n	68	68
Mean (SD)	36.53 (0.51)	0.04 (0.41)
Median	36.55	0.00
Min - Max	35.4 - 38.3	-1.0 - 1.2
AFTER PAC INFUSION		
n	77	77
Mean (SD)	36.45 (0.58)	0.00 (0.52)
Median	36.50	0.00
Min - Max	35.0 - 38.2	-1.5 - 1.6
Cycle 4 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	15	15
Mean (SD)	36.47 (0.53)	-0.23 (0.49)
Median	36.60	-0.10
Min - Max	35.3 - 37.3	-1.2 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	70	70
Mean (SD)	36.42 (0.48)	-0.01 (0.48)
Median	36.50	0.00
Min - Max	35.0 - 37.5	-1.0 - 1.8
AFTER PAC INFUSION		
n	80	80
Mean (SD)	36.39 (0.47)	-0.06 (0.53)
Median	36.40	0.00
Min - Max	35.0 - 37.8	-2.0 - 1.6
Cycle 4 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	79	79
Mean (SD)	36.46 (0.41)	0.00 (0.49)
Median	36.50	0.10
Min - Max	35.5 - 37.8	-1.3 - 1.6
PRE PAC INFUSION		
n	66	66
Mean (SD)	36.49 (0.42)	0.03 (0.46)
Median	36.55	0.00
Min - Max	35.6 - 37.7	-0.9 - 1.4
AFTER PAC INFUSION		
n	74	74
Mean (SD)	36.48 (0.51)	0.00 (0.59)
Median	36.50	0.00
Min - Max	35.0 - 37.9	-1.9 - 1.7
Cycle 5 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	65	65
Mean (SD)	36.41 (0.55)	-0.08 (0.47)
Median	36.50	0.00
Min - Max	35.1 - 37.9	-1.1 - 1.0
PRE PAC INFUSION		
n	57	57
Mean (SD)	36.46 (0.51)	-0.03 (0.41)
Median	36.50	0.00
Min - Max	35.0 - 37.9	-0.9 - 1.5
AFTER PAC INFUSION		
n	64	64
Mean (SD)	36.48 (0.54)	-0.01 (0.49)
Median	36.50	0.00
Min - Max	35.3 - 38.0	-1.2 - 1.8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 5 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	13	13
Mean (SD)	36.58 (0.47)	-0.06 (0.40)
Median	36.60	-0.10
Min - Max	35.5 - 37.2	-0.6 - 0.7
PRE PAC INFUSION		
n	55	55
Mean (SD)	36.32 (0.58)	-0.09 (0.49)
Median	36.50	-0.10
Min - Max	34.4 - 37.5	-1.0 - 1.4
AFTER PAC INFUSION		
n	59	59
Mean (SD)	36.44 (0.46)	0.01 (0.55)
Median	36.50	-0.10
Min - Max	35.0 - 37.7	-1.1 - 1.6
Cycle 5 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	64	64
Mean (SD)	36.40 (0.46)	-0.07 (0.44)
Median	36.40	-0.10
Min - Max	35.0 - 37.4	-1.3 - 0.8
PRE PAC INFUSION		
n	56	56
Mean (SD)	36.36 (0.55)	-0.11 (0.47)
Median	36.40	-0.10
Min - Max	35.0 - 37.8	-1.7 - 0.9
AFTER PAC INFUSION		
n	57	57
Mean (SD)	36.43 (0.45)	-0.03 (0.48)
Median	36.50	0.00
Min - Max	35.3 - 37.6	-1.0 - 1.3
Cycle 6 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	59	59
Mean (SD)	36.43 (0.47)	-0.09 (0.47)
Median	36.50	-0.10
Min - Max	35.2 - 37.5	-1.1 - 1.1
PRE PAC INFUSION		
n	57	57
Mean (SD)	36.46 (0.50)	-0.02 (0.48)
Median	36.50	0.10
Min - Max	35.2 - 37.7	-1.9 - 1.0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	58	58
Mean (SD)	36.39 (0.52)	-0.08 (0.50)
Median	36.50	-0.10
Min - Max	35.0 - 37.7	-1.9 - 1.1
Cycle 6 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	13	13
Mean (SD)	36.53 (0.38)	-0.18 (0.36)
Median	36.60	-0.10
Min - Max	35.7 - 37.0	-0.8 - 0.4
PRE PAC INFUSION		
n	49	49
Mean (SD)	36.36 (0.49)	-0.02 (0.41)
Median	36.50	0.00
Min - Max	35.0 - 37.2	-0.8 - 0.9
AFTER PAC INFUSION		
n	57	57
Mean (SD)	36.51 (0.46)	0.06 (0.45)
Median	36.60	0.00
Min - Max	35.0 - 37.6	-0.8 - 1.3
Cycle 6 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	52	52
Mean (SD)	36.39 (0.41)	-0.13 (0.44)
Median	36.50	-0.10
Min - Max	35.2 - 37.3	-1.3 - 0.8
PRE PAC INFUSION		
n	49	49
Mean (SD)	36.49 (0.46)	0.03 (0.48)
Median	36.50	0.00
Min - Max	35.1 - 37.6	-1.0 - 1.5
AFTER PAC INFUSION		
n	49	49
Mean (SD)	36.46 (0.38)	-0.03 (0.47)
Median	36.50	0.00
Min - Max	35.8 - 37.7	-1.1 - 1.1
Cycle 7 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	53	53
Mean (SD)	36.46 (0.43)	-0.03 (0.40)
Median	36.50	0.00
Min - Max	35.5 - 37.6	-1.6 - 0.7

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	46	46
Mean (SD)	36.46 (0.47)	-0.01 (0.46)
Median	36.50	0.00
Min - Max	35.1 - 37.6	-1.3 - 1.0
AFTER PAC INFUSION		
n	50	50
Mean (SD)	36.46 (0.48)	0.00 (0.47)
Median	36.40	0.00
Min - Max	35.1 - 37.6	-1.1 - 1.1
Cycle 7 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	36.64 (0.50)	-0.03 (0.53)
Median	36.65	-0.05
Min - Max	35.9 - 37.6	-1.2 - 0.8
PRE PAC INFUSION		
n	42	42
Mean (SD)	36.31 (0.45)	-0.10 (0.50)
Median	36.40	-0.10
Min - Max	35.1 - 37.2	-1.7 - 1.0
AFTER PAC INFUSION		
n	49	49
Mean (SD)	36.45 (0.50)	-0.03 (0.46)
Median	36.50	0.00
Min - Max	35.2 - 38.5	-1.3 - 1.0
Cycle 7 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	49	49
Mean (SD)	36.36 (0.55)	-0.13 (0.45)
Median	36.50	-0.10
Min - Max	35.0 - 37.8	-1.0 - 0.8
PRE PAC INFUSION		
n	44	44
Mean (SD)	36.44 (0.47)	0.02 (0.41)
Median	36.50	0.05
Min - Max	35.4 - 37.7	-1.2 - 0.8
AFTER PAC INFUSION		
n	44	44
Mean (SD)	36.51 (0.61)	0.03 (0.52)
Median	36.60	0.05
Min - Max	35.0 - 37.8	-1.3 - 0.9

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 8 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	46	46
Mean (SD)	36.38 (0.38)	-0.10 (0.38)
Median	36.40	-0.10
Min - Max	35.5 - 37.1	-0.8 - 0.7
PRE PAC INFUSION		
n	42	42
Mean (SD)	36.36 (0.43)	-0.05 (0.39)
Median	36.30	0.00
Min - Max	35.6 - 37.8	-0.8 - 0.9
AFTER PAC INFUSION		
n	45	45
Mean (SD)	36.40 (0.43)	-0.06 (0.38)
Median	36.50	-0.10
Min - Max	35.0 - 37.2	-1.2 - 0.8
Cycle 8 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	10	10
Mean (SD)	36.52 (0.38)	-0.30 (0.42)
Median	36.40	-0.25
Min - Max	36.0 - 37.1	-1.2 - 0.2
PRE PAC INFUSION		
n	34	34
Mean (SD)	36.48 (0.36)	0.06 (0.38)
Median	36.50	0.10
Min - Max	35.7 - 37.2	-1.0 - 0.9
AFTER PAC INFUSION		
n	42	42
Mean (SD)	36.52 (0.40)	0.04 (0.50)
Median	36.50	0.10
Min - Max	35.3 - 37.5	-1.3 - 1.2
Cycle 8 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	44	44
Mean (SD)	36.36 (0.52)	-0.12 (0.45)
Median	36.45	0.00
Min - Max	35.0 - 37.3	-1.3 - 0.9
PRE PAC INFUSION		
n	33	33
Mean (SD)	36.48 (0.46)	-0.06 (0.42)
Median	36.50	-0.10
Min - Max	35.8 - 37.9	-0.9 - 1.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	39	39
Mean (SD)	36.54 (0.43)	-0.04 (0.42)
Median	36.50	0.00
Min - Max	35.8 - 37.8	-1.0 - 0.9
Cycle 9 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	35	35
Mean (SD)	36.45 (0.43)	-0.06 (0.42)
Median	36.50	0.00
Min - Max	35.1 - 37.1	-0.8 - 0.9
PRE PAC INFUSION		
n	30	30
Mean (SD)	36.37 (0.48)	-0.06 (0.49)
Median	36.45	0.00
Min - Max	35.4 - 37.8	-1.0 - 1.2
AFTER PAC INFUSION		
n	32	32
Mean (SD)	36.49 (0.47)	0.01 (0.48)
Median	36.60	0.00
Min - Max	35.0 - 37.3	-0.9 - 1.1
Cycle 9 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	7	7
Mean (SD)	36.39 (0.49)	-0.46 (0.66)
Median	36.20	-0.80
Min - Max	35.9 - 37.2	-1.1 - 0.7
PRE PAC INFUSION		
n	23	23
Mean (SD)	36.40 (0.40)	-0.02 (0.43)
Median	36.40	0.00
Min - Max	35.8 - 37.2	-0.7 - 1.0
AFTER PAC INFUSION		
n	27	27
Mean (SD)	36.49 (0.38)	0.04 (0.45)
Median	36.40	0.00
Min - Max	36.0 - 37.6	-0.7 - 1.2
Cycle 9 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	33	33
Mean (SD)	36.42 (0.38)	-0.11 (0.46)
Median	36.50	-0.20
Min - Max	35.5 - 37.5	-0.7 - 1.2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE PAC INFUSION		
n	28	28
Mean (SD)	36.45 (0.51)	0.03 (0.48)
Median	36.50	-0.05
Min - Max	35.0 - 37.6	-0.7 - 1.0
AFTER PAC INFUSION		
n	25	25
Mean (SD)	36.48 (0.47)	0.00 (0.44)
Median	36.60	0.10
Min - Max	35.2 - 37.3	-0.7 - 1.0
Cycle 10 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	32	32
Mean (SD)	36.48 (0.36)	-0.06 (0.38)
Median	36.45	-0.05
Min - Max	35.6 - 37.2	-0.8 - 0.7
PRE PAC INFUSION		
n	31	31
Mean (SD)	36.44 (0.26)	-0.05 (0.39)
Median	36.40	-0.10
Min - Max	36.0 - 37.0	-0.8 - 1.1
AFTER PAC INFUSION		
n	28	28
Mean (SD)	36.46 (0.43)	-0.03 (0.47)
Median	36.40	-0.10
Min - Max	35.7 - 37.5	-0.9 - 1.1
Cycle 10 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	36.42 (0.21)	-0.33 (0.36)
Median	36.40	-0.35
Min - Max	36.1 - 36.7	-0.8 - 0.2
PRE PAC INFUSION		
n	21	21
Mean (SD)	36.51 (0.31)	0.04 (0.54)
Median	36.50	0.00
Min - Max	36.0 - 37.4	-0.7 - 1.4
AFTER PAC INFUSION		
n	23	23
Mean (SD)	36.48 (0.35)	-0.02 (0.49)
Median	36.40	-0.10
Min - Max	36.0 - 37.3	-1.1 - 1.3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 10 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	31	31
Mean (SD)	36.45 (0.36)	-0.11 (0.43)
Median	36.50	-0.10
Min - Max	35.5 - 37.3	-1.1 - 1.0
PRE PAC INFUSION		
n	28	28
Mean (SD)	36.44 (0.33)	-0.07 (0.49)
Median	36.40	-0.10
Min - Max	35.8 - 37.2	-0.9 - 1.3
AFTER PAC INFUSION		
n	24	24
Mean (SD)	36.48 (0.41)	-0.03 (0.51)
Median	36.45	-0.10
Min - Max	35.8 - 37.5	-1.0 - 1.2
Cycle 11 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	25	25
Mean (SD)	36.48 (0.35)	-0.04 (0.30)
Median	36.60	0.00
Min - Max	35.9 - 37.2	-0.8 - 0.6
PRE PAC INFUSION		
n	22	22
Mean (SD)	36.50 (0.28)	0.05 (0.46)
Median	36.50	0.00
Min - Max	36.0 - 37.1	-1.0 - 1.5
AFTER PAC INFUSION		
n	21	21
Mean (SD)	36.51 (0.35)	0.05 (0.40)
Median	36.50	-0.10
Min - Max	36.0 - 37.4	-0.7 - 1.0
Cycle 11 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	36.53 (0.30)	-0.13 (0.61)
Median	36.60	0.10
Min - Max	36.1 - 36.8	-1.0 - 0.3
PRE PAC INFUSION		
n	16	16
Mean (SD)	36.31 (0.38)	-0.11 (0.53)
Median	36.35	-0.10
Min - Max	35.5 - 37.1	-1.0 - 1.4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
AFTER PAC INFUSION		
n	18	18
Mean (SD)	36.42 (0.47)	0.01 (0.57)
Median	36.45	0.05
Min - Max	35.7 - 37.4	-0.9 - 1.6
Cycle 11 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	21	21
Mean (SD)	36.39 (0.46)	-0.15 (0.39)
Median	36.40	-0.10
Min - Max	35.4 - 37.2	-1.0 - 0.7
PRE PAC INFUSION		
n	20	20
Mean (SD)	36.43 (0.32)	-0.05 (0.40)
Median	36.55	-0.10
Min - Max	35.8 - 36.9	-0.7 - 1.0
AFTER PAC INFUSION		
n	17	17
Mean (SD)	36.51 (0.29)	0.06 (0.43)
Median	36.50	0.00
Min - Max	36.0 - 37.0	-0.6 - 1.3
Cycle 12 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	24	24
Mean (SD)	36.45 (0.28)	-0.09 (0.31)
Median	36.50	0.00
Min - Max	35.6 - 36.9	-0.9 - 0.3
PRE PAC INFUSION		
n	21	21
Mean (SD)	36.50 (0.32)	0.00 (0.45)
Median	36.60	0.00
Min - Max	35.6 - 37.0	-0.9 - 1.3
AFTER PAC INFUSION		
n	18	18
Mean (SD)	36.43 (0.41)	-0.04 (0.48)
Median	36.40	-0.05
Min - Max	35.6 - 37.2	-0.9 - 1.2
Cycle 12 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	36.05 (0.24)	-0.55 (0.60)
Median	35.95	-0.70
Min - Max	35.9 - 36.4	-1.1 - 0.3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	15	15
Mean (SD)	36.44 (0.32)	-0.01 (0.40)
Median	36.40	0.00
Min - Max	35.6 - 36.9	-0.7 - 1.1
AFTER PAC INFUSION		
n	16	16
Mean (SD)	36.36 (0.34)	-0.10 (0.48)
Median	36.40	-0.15
Min - Max	35.7 - 36.8	-0.8 - 1.1
Cycle 12 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	23	23
Mean (SD)	36.57 (0.32)	0.01 (0.28)
Median	36.60	0.00
Min - Max	36.0 - 37.3	-0.7 - 0.4
PRE PAC INFUSION		
n	21	21
Mean (SD)	36.51 (0.48)	0.01 (0.32)
Median	36.60	0.00
Min - Max	35.0 - 37.1	-0.9 - 0.7
AFTER PAC INFUSION		
n	17	17
Mean (SD)	36.53 (0.38)	0.05 (0.37)
Median	36.50	0.00
Min - Max	35.9 - 37.4	-0.4 - 1.2
Cycle 13 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	21	21
Mean (SD)	36.61 (0.27)	0.05 (0.29)
Median	36.60	0.10
Min - Max	36.1 - 37.0	-0.4 - 0.7
PRE PAC INFUSION		
n	20	20
Mean (SD)	36.48 (0.26)	-0.01 (0.38)
Median	36.50	0.00
Min - Max	35.8 - 37.0	-0.7 - 0.8
AFTER PAC INFUSION		
n	13	13
Mean (SD)	36.45 (0.44)	0.05 (0.48)
Median	36.50	0.00
Min - Max	35.4 - 37.3	-0.6 - 1.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 13 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	36.55 (0.21)	-0.25 (0.64)
Median	36.55	-0.25
Min - Max	36.4 - 36.7	-0.7 - 0.2
PRE PAC INFUSION		
n	14	14
Mean (SD)	36.49 (0.28)	0.09 (0.33)
Median	36.50	0.00
Min - Max	35.8 - 36.9	-0.3 - 0.8
AFTER PAC INFUSION		
n	15	15
Mean (SD)	36.42 (0.27)	0.01 (0.51)
Median	36.40	0.00
Min - Max	36.0 - 37.0	-1.0 - 1.4
Cycle 13 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	19	19
Mean (SD)	36.52 (0.35)	-0.04 (0.28)
Median	36.60	0.00
Min - Max	35.9 - 37.3	-0.6 - 0.5
PRE PAC INFUSION		
n	19	19
Mean (SD)	36.44 (0.37)	-0.02 (0.29)
Median	36.40	-0.10
Min - Max	35.4 - 37.0	-0.6 - 0.5
AFTER PAC INFUSION		
n	15	15
Mean (SD)	36.38 (0.32)	-0.03 (0.27)
Median	36.40	-0.10
Min - Max	35.4 - 36.7	-0.4 - 0.4
Cycle 14 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	20	20
Mean (SD)	36.50 (0.36)	-0.05 (0.32)
Median	36.45	0.00
Min - Max	35.7 - 37.2	-0.7 - 0.8
PRE PAC INFUSION		
n	18	18
Mean (SD)	36.44 (0.37)	0.00 (0.37)
Median	36.50	-0.05
Min - Max	35.4 - 36.9	-0.8 - 0.7

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
AFTER PAC INFUSION		
n	14	14
Mean (SD)	36.49 (0.29)	0.10 (0.44)
Median	36.45	0.05
Min - Max	36.1 - 37.2	-0.5 - 1.3
Cycle 14 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	36.73 (0.35)	-0.10 (0.66)
Median	36.70	-0.20
Min - Max	36.4 - 37.1	-0.7 - 0.6
PRE PAC INFUSION		
n	10	10
Mean (SD)	36.29 (0.32)	0.06 (0.46)
Median	36.35	0.00
Min - Max	35.6 - 36.6	-0.4 - 1.2
AFTER PAC INFUSION		
n	12	12
Mean (SD)	36.52 (0.37)	0.19 (0.51)
Median	36.55	0.15
Min - Max	35.9 - 37.1	-0.4 - 1.3
Cycle 14 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	18	18
Mean (SD)	36.53 (0.25)	0.01 (0.40)
Median	36.50	0.10
Min - Max	36.0 - 37.0	-1.1 - 0.5
PRE PAC INFUSION		
n	16	16
Mean (SD)	36.46 (0.28)	0.06 (0.44)
Median	36.50	0.10
Min - Max	36.0 - 36.9	-1.1 - 1.0
AFTER PAC INFUSION		
n	12	12
Mean (SD)	36.39 (0.43)	0.07 (0.49)
Median	36.55	0.10
Min - Max	35.2 - 36.8	-0.8 - 1.3
Cycle 15 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	17	17
Mean (SD)	36.44 (0.24)	-0.05 (0.24)
Median	36.50	0.00
Min - Max	35.9 - 36.8	-0.7 - 0.3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	16	16
Mean (SD)	36.46 (0.27)	0.10 (0.47)
Median	36.50	0.10
Min - Max	36.0 - 37.0	-1.1 - 1.3
AFTER PAC INFUSION		
n	10	10
Mean (SD)	36.23 (0.31)	-0.06 (0.66)
Median	36.20	0.00
Min - Max	35.7 - 36.8	-1.1 - 1.3
Cycle 15 Day 8		
PRE PAC INFUSION		
n	10	10
Mean (SD)	36.35 (0.30)	0.06 (0.43)
Median	36.40	0.00
Min - Max	36.0 - 36.9	-0.5 - 1.1
AFTER PAC INFUSION		
n	10	10
Mean (SD)	36.30 (0.23)	0.01 (0.62)
Median	36.30	-0.10
Min - Max	36.0 - 36.7	-1.1 - 1.2
Cycle 15 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	14	14
Mean (SD)	36.54 (0.24)	0.01 (0.21)
Median	36.60	0.05
Min - Max	36.0 - 36.9	-0.5 - 0.3
PRE PAC INFUSION		
n	13	13
Mean (SD)	36.47 (0.26)	0.08 (0.49)
Median	36.50	0.10
Min - Max	36.1 - 37.0	-1.0 - 1.3
AFTER PAC INFUSION		
n	7	7
Mean (SD)	36.34 (0.18)	0.03 (0.56)
Median	36.40	0.00
Min - Max	36.1 - 36.5	-0.7 - 1.1
Cycle 16 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	36.53 (0.20)	0.10 (0.29)
Median	36.55	0.10
Min - Max	36.1 - 36.7	-0.3 - 0.7

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE PAC INFUSION		
n	12	12
Mean (SD)	36.34 (0.22)	0.07 (0.33)
Median	36.40	0.10
Min - Max	35.9 - 36.6	-0.3 - 0.9
AFTER PAC INFUSION		
n	7	7
Mean (SD)	36.29 (0.32)	0.11 (0.29)
Median	36.30	0.10
Min - Max	35.7 - 36.6	-0.2 - 0.7
Cycle 16 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	36.80 (NE)	0.00 (NE)
Median	36.80	0.00
Min - Max	36.8 - 36.8	0.0 - 0.0
PRE PAC INFUSION		
n	8	8
Mean (SD)	36.30 (0.29)	0.05 (0.52)
Median	36.35	0.00
Min - Max	35.8 - 36.7	-0.5 - 1.2
AFTER PAC INFUSION		
n	8	8
Mean (SD)	36.28 (0.29)	0.03 (0.81)
Median	36.20	-0.10
Min - Max	35.9 - 36.7	-1.1 - 1.7
Cycle 16 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	14	14
Mean (SD)	36.64 (0.19)	0.16 (0.30)
Median	36.60	0.15
Min - Max	36.3 - 37.0	-0.2 - 0.9
PRE PAC INFUSION		
n	14	14
Mean (SD)	36.53 (0.30)	0.13 (0.44)
Median	36.55	0.10
Min - Max	36.1 - 37.3	-0.5 - 1.2
AFTER PAC INFUSION		
n	7	7
Mean (SD)	36.40 (0.17)	0.07 (0.58)
Median	36.40	0.00
Min - Max	36.2 - 36.6	-0.5 - 1.2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 17 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	36.46 (0.32)	-0.08 (0.37)
Median	36.50	0.00
Min - Max	35.8 - 36.9	-0.7 - 0.3
PRE PAC INFUSION		
n	10	10
Mean (SD)	36.42 (0.26)	0.10 (0.43)
Median	36.44	0.10
Min - Max	36.0 - 36.8	-0.3 - 1.2
AFTER PAC INFUSION		
n	6	6
Mean (SD)	36.32 (0.17)	0.17 (0.57)
Median	36.35	0.00
Min - Max	36.0 - 36.5	-0.3 - 1.3
Cycle 17 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	35.90 (NE)	-0.60 (NE)
Median	35.90	-0.60
Min - Max	35.9 - 35.9	-0.6 - -0.6
PRE PAC INFUSION		
n	7	7
Mean (SD)	36.34 (0.36)	0.13 (0.66)
Median	36.20	0.00
Min - Max	35.9 - 37.0	-0.9 - 1.0
AFTER PAC INFUSION		
n	8	8
Mean (SD)	36.29 (0.23)	0.04 (0.61)
Median	36.25	0.00
Min - Max	36.0 - 36.6	-1.0 - 1.0
Cycle 17 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	36.48 (0.35)	-0.01 (0.38)
Median	36.60	0.05
Min - Max	35.6 - 37.1	-0.9 - 0.5
PRE PAC INFUSION		
n	12	12
Mean (SD)	36.41 (0.46)	0.04 (0.62)
Median	36.50	0.15
Min - Max	35.3 - 37.0	-1.1 - 1.4

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
AFTER PAC INFUSION		
n	8	8
Mean (SD)	36.15 (0.39)	-0.10 (0.83)
Median	36.25	-0.15
Min - Max	35.6 - 36.6	-1.1 - 1.6
Cycle 18 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	36.46 (0.39)	-0.03 (0.38)
Median	36.50	0.00
Min - Max	35.9 - 37.3	-0.6 - 0.7
PRE PAC INFUSION		
n	13	13
Mean (SD)	36.43 (0.44)	0.05 (0.59)
Median	36.40	0.10
Min - Max	35.6 - 37.1	-0.9 - 1.4
AFTER PAC INFUSION		
n	8	8
Mean (SD)	36.00 (0.49)	-0.25 (0.76)
Median	36.15	-0.25
Min - Max	35.0 - 36.4	-1.3 - 1.0
Cycle 18 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	35.60 (NE)	-0.90 (NE)
Median	35.60	-0.90
Min - Max	35.6 - 35.6	-0.9 - -0.9
PRE PAC INFUSION		
n	6	6
Mean (SD)	36.42 (0.18)	0.35 (0.48)
Median	36.50	0.20
Min - Max	36.1 - 36.6	0.0 - 1.3
AFTER PAC INFUSION		
n	7	7
Mean (SD)	36.21 (0.34)	0.09 (0.71)
Median	36.30	-0.10
Min - Max	35.7 - 36.5	-0.8 - 1.5
Cycle 18 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	36.52 (0.47)	0.04 (0.42)
Median	36.60	0.10
Min - Max	35.2 - 37.0	-1.1 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE PAC INFUSION		
n	11	11
Mean (SD)	36.47 (0.37)	0.13 (0.74)
Median	36.60	0.10
Min - Max	35.8 - 36.9	-1.3 - 1.9
AFTER PAC INFUSION		
n	7	7
Mean (SD)	36.40 (0.20)	0.19 (0.68)
Median	36.40	0.00
Min - Max	36.1 - 36.7	-0.8 - 1.3
Cycle 19 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	36.48 (0.30)	0.00 (0.29)
Median	36.50	0.00
Min - Max	35.9 - 37.0	-0.4 - 0.5
PRE PAC INFUSION		
n	11	11
Mean (SD)	36.45 (0.37)	0.10 (0.43)
Median	36.40	0.00
Min - Max	36.0 - 37.1	-0.4 - 1.2
AFTER PAC INFUSION		
n	8	8
Mean (SD)	36.18 (0.17)	-0.08 (0.63)
Median	36.15	-0.15
Min - Max	36.0 - 36.5	-1.0 - 1.2
Cycle 19 Day 8		
PRE PAC INFUSION		
n	7	7
Mean (SD)	36.41 (0.24)	0.20 (0.68)
Median	36.40	0.10
Min - Max	36.0 - 36.8	-0.7 - 1.3
AFTER PAC INFUSION		
n	7	7
Mean (SD)	36.40 (0.19)	0.19 (0.70)
Median	36.30	0.20
Min - Max	36.2 - 36.6	-0.9 - 1.3
Cycle 19 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	36.38 (0.43)	-0.12 (0.40)
Median	36.50	-0.05
Min - Max	35.5 - 37.2	-0.8 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	11	11
Mean (SD)	36.48 (0.44)	0.13 (0.45)
Median	36.60	0.20
Min - Max	35.8 - 37.3	-0.7 - 0.9
AFTER PAC INFUSION		
n	7	7
Mean (SD)	36.20 (0.31)	-0.01 (0.67)
Median	36.20	0.00
Min - Max	35.8 - 36.6	-0.7 - 1.2
Cycle 20 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	36.43 (0.54)	-0.06 (0.39)
Median	36.55	0.05
Min - Max	35.0 - 37.1	-1.0 - 0.5
PRE PAC INFUSION		
n	9	9
Mean (SD)	36.28 (0.63)	0.03 (0.60)
Median	36.50	0.10
Min - Max	35.0 - 37.2	-1.0 - 1.1
AFTER PAC INFUSION		
n	7	7
Mean (SD)	36.19 (0.29)	-0.03 (0.60)
Median	36.10	0.00
Min - Max	35.9 - 36.6	-0.6 - 1.1
Cycle 20 Day 8		
PRE PAC INFUSION		
n	7	7
Mean (SD)	36.23 (0.35)	0.02 (0.37)
Median	36.21	0.00
Min - Max	35.6 - 36.6	-0.5 - 0.6
AFTER PAC INFUSION		
n	7	7
Mean (SD)	36.31 (0.23)	0.10 (0.56)
Median	36.30	0.00
Min - Max	36.0 - 36.6	-0.7 - 1.1
Cycle 20 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	36.41 (0.36)	-0.08 (0.39)
Median	36.50	0.00
Min - Max	35.7 - 36.9	-0.8 - 0.3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	11	11
Mean (SD)	36.48 (0.39)	0.13 (0.36)
Median	36.60	0.10
Min - Max	35.8 - 37.0	-0.5 - 0.9
AFTER PAC INFUSION		
n	7	7
Mean (SD)	36.26 (0.42)	0.04 (0.52)
Median	36.30	0.10
Min - Max	35.6 - 36.8	-0.7 - 1.0
Cycle 21 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	36.41 (0.36)	-0.08 (0.33)
Median	36.50	-0.05
Min - Max	35.7 - 36.9	-0.8 - 0.3
PRE PAC INFUSION		
n	11	11
Mean (SD)	36.49 (0.36)	0.14 (0.69)
Median	36.60	0.10
Min - Max	36.0 - 37.1	-1.1 - 1.8
AFTER PAC INFUSION		
n	7	7
Mean (SD)	36.21 (0.62)	0.00 (0.98)
Median	36.40	0.00
Min - Max	35.0 - 36.8	-1.1 - 1.8
Cycle 21 Day 8		
PRE PAC INFUSION		
n	6	6
Mean (SD)	36.43 (0.29)	0.18 (0.50)
Median	36.50	0.20
Min - Max	36.0 - 36.8	-0.5 - 1.0
AFTER PAC INFUSION		
n	6	6
Mean (SD)	36.47 (0.27)	0.22 (0.65)
Median	36.50	0.10
Min - Max	36.0 - 36.7	-0.4 - 1.4
Cycle 21 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	36.41 (0.44)	-0.08 (0.35)
Median	36.60	0.00
Min - Max	35.6 - 36.9	-0.7 - 0.3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	9	9
Mean (SD)	36.54 (0.35)	0.18 (0.71)
Median	36.50	0.10
Min - Max	35.8 - 37.1	-0.7 - 1.8
AFTER PAC INFUSION		
n	6	6
Mean (SD)	36.23 (0.32)	-0.02 (0.72)
Median	36.30	-0.20
Min - Max	35.8 - 36.6	-0.6 - 1.3
Cycle 22 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	12	12
Mean (SD)	36.52 (0.29)	0.03 (0.27)
Median	36.50	0.05
Min - Max	36.0 - 37.2	-0.5 - 0.6
PRE PAC INFUSION		
n	10	10
Mean (SD)	36.59 (0.27)	0.20 (0.61)
Median	36.50	0.10
Min - Max	36.3 - 37.1	-0.7 - 1.7
AFTER PAC INFUSION		
n	6	6
Mean (SD)	36.40 (0.17)	0.15 (0.78)
Median	36.35	0.00
Min - Max	36.2 - 36.6	-0.7 - 1.6
Cycle 22 Day 8		
PRE PAC INFUSION		
n	4	4
Mean (SD)	36.53 (0.13)	0.50 (0.69)
Median	36.50	0.30
Min - Max	36.4 - 36.7	-0.1 - 1.5
AFTER PAC INFUSION		
n	4	4
Mean (SD)	36.48 (0.26)	0.45 (0.45)
Median	36.55	0.30
Min - Max	36.1 - 36.7	0.1 - 1.1
Cycle 22 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	11	11
Mean (SD)	36.67 (0.34)	0.14 (0.35)
Median	36.60	0.10
Min - Max	36.3 - 37.6	-0.3 - 1.0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	10	10
Mean (SD)	36.50 (0.35)	0.11 (0.74)
Median	36.50	0.10
Min - Max	36.0 - 37.3	-1.0 - 1.7
AFTER PAC INFUSION		
n	6	6
Mean (SD)	36.48 (0.15)	0.23 (0.66)
Median	36.45	0.10
Min - Max	36.3 - 36.7	-0.6 - 1.4
Cycle 23 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	36.53 (0.52)	-0.04 (0.45)
Median	36.50	0.00
Min - Max	35.8 - 37.5	-0.7 - 0.9
PRE PAC INFUSION		
n	9	9
Mean (SD)	36.48 (0.44)	0.12 (0.69)
Median	36.50	0.10
Min - Max	35.7 - 37.4	-0.8 - 1.5
AFTER PAC INFUSION		
n	6	6
Mean (SD)	36.23 (0.16)	-0.02 (0.72)
Median	36.25	-0.10
Min - Max	36.0 - 36.4	-1.0 - 1.2
Cycle 23 Day 8		
PRE PAC INFUSION		
n	5	5
Mean (SD)	36.18 (0.33)	-0.06 (0.77)
Median	36.30	0.00
Min - Max	35.7 - 36.5	-0.8 - 1.0
AFTER PAC INFUSION		
n	4	4
Mean (SD)	36.38 (0.26)	0.35 (0.79)
Median	36.45	0.25
Min - Max	36.0 - 36.6	-0.5 - 1.4
Cycle 23 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	36.56 (0.32)	0.00 (0.26)
Median	36.50	0.10
Min - Max	35.9 - 37.1	-0.4 - 0.5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	9	9
Mean (SD)	36.39 (0.40)	0.03 (0.66)
Median	36.60	0.20
Min - Max	35.6 - 36.9	-1.1 - 1.2
AFTER PAC INFUSION		
n	5	5
Mean (SD)	36.28 (0.36)	0.20 (0.53)
Median	36.40	0.20
Min - Max	35.8 - 36.6	-0.5 - 1.0
Cycle 24 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	10	10
Mean (SD)	36.30 (0.39)	-0.22 (0.48)
Median	36.40	-0.05
Min - Max	35.6 - 36.9	-1.1 - 0.3
PRE PAC INFUSION		
n	9	9
Mean (SD)	36.50 (0.19)	0.14 (0.59)
Median	36.60	0.10
Min - Max	36.1 - 36.7	-0.5 - 1.6
AFTER PAC INFUSION		
n	6	6
Mean (SD)	36.28 (0.33)	0.03 (0.86)
Median	36.35	-0.10
Min - Max	35.8 - 36.6	-0.7 - 1.6
Cycle 24 Day 8		
PRE PAC INFUSION		
n	4	4
Mean (SD)	36.50 (0.18)	0.25 (0.90)
Median	36.50	0.20
Min - Max	36.3 - 36.7	-0.8 - 1.4
AFTER PAC INFUSION		
n	3	3
Mean (SD)	36.53 (0.06)	0.57 (0.81)
Median	36.50	0.20
Min - Max	36.5 - 36.6	0.0 - 1.5
Cycle 24 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	10	10
Mean (SD)	36.60 (0.37)	0.08 (0.30)
Median	36.55	0.15
Min - Max	36.0 - 37.2	-0.5 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE PAC INFUSION		
n	9	9
Mean (SD)	36.51 (0.23)	0.16 (0.63)
Median	36.60	0.00
Min - Max	36.0 - 36.8	-0.7 - 1.6
AFTER PAC INFUSION		
n	6	6
Mean (SD)	36.53 (0.22)	0.28 (0.71)
Median	36.60	0.15
Min - Max	36.1 - 36.7	-0.4 - 1.6
Cycle 25 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	9	9
Mean (SD)	36.35 (0.43)	-0.19 (0.48)
Median	36.40	-0.20
Min - Max	35.6 - 37.2	-0.9 - 0.6
PRE PAC INFUSION		
n	10	10
Mean (SD)	36.25 (0.44)	-0.13 (0.71)
Median	36.30	0.05
Min - Max	35.6 - 36.9	-1.1 - 1.3
AFTER PAC INFUSION		
n	3	3
Mean (SD)	36.37 (0.32)	0.47 (0.93)
Median	36.50	0.20
Min - Max	36.0 - 36.6	-0.3 - 1.5
Cycle 25 Day 8		
PRE PAC INFUSION		
n	3	3
Mean (SD)	36.40 (0.26)	0.53 (0.49)
Median	36.50	0.30
Min - Max	36.1 - 36.6	0.2 - 1.1
AFTER PAC INFUSION		
n	3	3
Mean (SD)	36.43 (0.15)	0.57 (0.72)
Median	36.40	0.20
Min - Max	36.3 - 36.6	0.1 - 1.4
Cycle 25 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	36.46 (0.41)	-0.06 (0.34)
Median	36.45	-0.15
Min - Max	35.9 - 37.1	-0.5 - 0.5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	8	8
Mean (SD)	36.53 (0.39)	0.19 (0.69)
Median	36.50	0.10
Min - Max	35.9 - 37.3	-0.8 - 1.5
AFTER PAC INFUSION		
n	5	5
Mean (SD)	36.36 (0.34)	0.16 (0.97)
Median	36.50	0.10
Min - Max	35.8 - 36.7	-0.8 - 1.7
Cycle 26 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	36.47 (0.38)	0.01 (0.33)
Median	36.40	-0.05
Min - Max	36.1 - 37.3	-0.4 - 0.7
PRE PAC INFUSION		
n	8	8
Mean (SD)	36.43 (0.36)	0.15 (0.59)
Median	36.40	0.05
Min - Max	36.0 - 37.1	-0.5 - 1.4
AFTER PAC INFUSION		
n	4	4
Mean (SD)	36.40 (0.42)	0.43 (1.01)
Median	36.40	0.10
Min - Max	35.9 - 36.9	-0.4 - 1.9
Cycle 26 Day 8		
PRE PAC INFUSION		
n	5	5
Mean (SD)	36.42 (0.29)	0.22 (1.03)
Median	36.40	0.10
Min - Max	36.0 - 36.8	-1.1 - 1.8
AFTER PAC INFUSION		
n	5	5
Mean (SD)	36.34 (0.28)	0.14 (1.02)
Median	36.20	0.00
Min - Max	36.1 - 36.8	-1.0 - 1.8
Cycle 26 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	36.51 (0.33)	0.05 (0.29)
Median	36.50	0.00
Min - Max	36.1 - 37.2	-0.4 - 0.6

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	8	8
Mean (SD)	36.40 (0.26)	0.13 (0.53)
Median	36.50	0.00
Min - Max	36.0 - 36.8	-0.4 - 1.3
AFTER PAC INFUSION		
n	4	4
Mean (SD)	36.45 (0.24)	0.48 (0.73)
Median	36.55	0.30
Min - Max	36.1 - 36.6	-0.2 - 1.5
Cycle 27 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	8	8
Mean (SD)	36.45 (0.34)	-0.01 (0.34)
Median	36.45	0.00
Min - Max	35.8 - 37.0	-0.7 - 0.4
PRE PAC INFUSION		
n	8	8
Mean (SD)	36.36 (0.33)	0.09 (0.66)
Median	36.45	0.05
Min - Max	35.6 - 36.7	-0.9 - 1.5
AFTER PAC INFUSION		
n	4	4
Mean (SD)	36.40 (0.18)	0.43 (0.73)
Median	36.40	0.15
Min - Max	36.2 - 36.6	-0.1 - 1.5
Cycle 27 Day 8		
PRE PAC INFUSION		
n	3	3
Mean (SD)	36.37 (0.25)	0.53 (0.49)
Median	36.40	0.30
Min - Max	36.1 - 36.6	0.2 - 1.1
AFTER PAC INFUSION		
n	3	3
Mean (SD)	36.30 (0.17)	0.47 (0.67)
Median	36.20	0.30
Min - Max	36.2 - 36.5	-0.1 - 1.2
Cycle 27 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	7	7
Mean (SD)	36.47 (0.44)	0.01 (0.41)
Median	36.50	0.10
Min - Max	35.7 - 37.1	-0.8 - 0.5

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE PAC INFUSION		
n	7	7
Mean (SD)	36.59 (0.36)	0.34 (0.44)
Median	36.60	0.10
Min - Max	36.2 - 37.3	0.0 - 1.2
AFTER PAC INFUSION		
n	4	4
Mean (SD)	36.16 (0.13)	0.19 (0.56)
Median	36.17	0.00
Min - Max	36.0 - 36.3	-0.3 - 1.0
Cycle 28 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	36.37 (0.29)	-0.07 (0.30)
Median	36.50	-0.05
Min - Max	36.0 - 36.6	-0.5 - 0.3
PRE PAC INFUSION		
n	4	4
Mean (SD)	36.58 (0.10)	0.13 (0.13)
Median	36.55	0.10
Min - Max	36.5 - 36.7	0.0 - 0.3
AFTER PAC INFUSION		
n	2	2
Mean (SD)	36.60 (0.00)	0.30 (0.14)
Median	36.60	0.30
Min - Max	36.6 - 36.6	0.2 - 0.4
Cycle 28 Day 8		
PRE PAC INFUSION		
n	2	2
Mean (SD)	36.50 (0.00)	0.20 (0.14)
Median	36.50	0.20
Min - Max	36.5 - 36.5	0.1 - 0.3
AFTER PAC INFUSION		
n	2	2
Mean (SD)	36.40 (0.14)	0.10 (0.00)
Median	36.40	0.10
Min - Max	36.3 - 36.5	0.1 - 0.1
Cycle 28 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	36.43 (0.24)	0.00 (0.31)
Median	36.45	0.05
Min - Max	36.0 - 36.7	-0.5 - 0.3

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE PAC INFUSION		
n	4	4
Mean (SD)	36.60 (0.08)	0.15 (0.13)
Median	36.60	0.15
Min - Max	36.5 - 36.7	0.0 - 0.3
AFTER PAC INFUSION		
n	2	2
Mean (SD)	36.65 (0.07)	0.35 (0.07)
Median	36.65	0.35
Min - Max	36.6 - 36.7	0.3 - 0.4
Cycle 29 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	7	7
Mean (SD)	36.47 (0.14)	0.03 (0.23)
Median	36.50	0.00
Min - Max	36.2 - 36.6	-0.3 - 0.4
PRE PAC INFUSION		
n	4	4
Mean (SD)	36.60 (0.08)	0.15 (0.17)
Median	36.60	0.10
Min - Max	36.5 - 36.7	0.0 - 0.4
AFTER PAC INFUSION		
n	2	2
Mean (SD)	36.60 (0.00)	0.30 (0.14)
Median	36.60	0.30
Min - Max	36.6 - 36.6	0.2 - 0.4
Cycle 29 Day 8		
PRE PAC INFUSION		
n	2	2
Mean (SD)	36.50 (0.00)	0.20 (0.14)
Median	36.50	0.20
Min - Max	36.5 - 36.5	0.1 - 0.3
AFTER PAC INFUSION		
n	2	2
Mean (SD)	36.45 (0.07)	0.15 (0.21)
Median	36.45	0.15
Min - Max	36.4 - 36.5	0.0 - 0.3
Cycle 29 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	6	6
Mean (SD)	36.43 (0.26)	-0.02 (0.25)
Median	36.50	0.05
Min - Max	36.0 - 36.7	-0.5 - 0.2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	36.53 (0.12)	0.00 (0.00)
Median	36.60	0.00
Min - Max	36.4 - 36.6	0.0 - 0.0
AFTER PAC INFUSION		
n	1	1
Mean (SD)	36.60 (NE)	0.20 (NE)
Median	36.60	0.20
Min - Max	36.6 - 36.6	0.2 - 0.2
Cycle 30 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	5	5
Mean (SD)	36.66 (0.09)	0.18 (0.08)
Median	36.70	0.20
Min - Max	36.5 - 36.7	0.1 - 0.3
PRE PAC INFUSION		
n	3	3
Mean (SD)	36.60 (0.10)	0.07 (0.06)
Median	36.60	0.10
Min - Max	36.5 - 36.7	0.0 - 0.1
AFTER PAC INFUSION		
n	1	1
Mean (SD)	36.50 (NE)	0.10 (NE)
Median	36.50	0.10
Min - Max	36.5 - 36.5	0.1 - 0.1
Cycle 30 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.40 (NE)	0.00 (NE)
Median	36.40	0.00
Min - Max	36.4 - 36.4	0.0 - 0.0
AFTER PAC INFUSION		
n	1	1
Mean (SD)	36.70 (NE)	0.30 (NE)
Median	36.70	0.30
Min - Max	36.7 - 36.7	0.3 - 0.3
Cycle 30 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	5	5
Mean (SD)	36.52 (0.18)	0.04 (0.09)
Median	36.50	0.10
Min - Max	36.3 - 36.7	-0.1 - 0.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	36.63 (0.06)	0.10 (0.10)
Median	36.60	0.10
Min - Max	36.6 - 36.7	0.0 - 0.2
AFTER PAC INFUSION		
n	1	1
Mean (SD)	36.70 (NE)	0.30 (NE)
Median	36.70	0.30
Min - Max	36.7 - 36.7	0.3 - 0.3
Cycle 31 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	36.48 (0.13)	0.00 (0.08)
Median	36.50	0.00
Min - Max	36.3 - 36.6	-0.1 - 0.1
PRE PAC INFUSION		
n	3	3
Mean (SD)	36.57 (0.15)	0.03 (0.06)
Median	36.60	0.00
Min - Max	36.4 - 36.7	0.0 - 0.1
AFTER PAC INFUSION		
n	1	1
Mean (SD)	36.40 (NE)	0.00 (NE)
Median	36.40	0.00
Min - Max	36.4 - 36.4	0.0 - 0.0
Cycle 31 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.60 (NE)	0.20 (NE)
Median	36.60	0.20
Min - Max	36.6 - 36.6	0.2 - 0.2
AFTER PAC INFUSION		
n	1	1
Mean (SD)	36.60 (NE)	0.20 (NE)
Median	36.60	0.20
Min - Max	36.6 - 36.6	0.2 - 0.2
Cycle 31 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	36.55 (0.13)	0.08 (0.05)
Median	36.55	0.10
Min - Max	36.4 - 36.7	0.0 - 0.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	36.50 (0.10)	-0.03 (0.06)
Median	36.50	0.00
Min - Max	36.4 - 36.6	-0.1 - 0.0
AFTER PAC INFUSION		
n	1	1
Mean (SD)	36.40 (NE)	0.00 (NE)
Median	36.40	0.00
Min - Max	36.4 - 36.4	0.0 - 0.0
Cycle 32 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	36.55 (0.06)	0.08 (0.15)
Median	36.55	0.10
Min - Max	36.5 - 36.6	-0.1 - 0.2
PRE PAC INFUSION		
n	3	3
Mean (SD)	36.60 (0.10)	0.07 (0.06)
Median	36.60	0.10
Min - Max	36.5 - 36.7	0.0 - 0.1
AFTER PAC INFUSION		
n	1	1
Mean (SD)	36.50 (NE)	0.10 (NE)
Median	36.50	0.10
Min - Max	36.5 - 36.5	0.1 - 0.1
Cycle 32 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.60 (NE)	0.20 (NE)
Median	36.60	0.20
Min - Max	36.6 - 36.6	0.2 - 0.2
AFTER PAC INFUSION		
n	1	1
Mean (SD)	36.40 (NE)	0.00 (NE)
Median	36.40	0.00
Min - Max	36.4 - 36.4	0.0 - 0.0
Cycle 32 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	4	4
Mean (SD)	36.53 (0.05)	0.05 (0.13)
Median	36.50	0.05
Min - Max	36.5 - 36.6	-0.1 - 0.2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
PRE PAC INFUSION		
n	3	3
Mean (SD)	36.50 (0.10)	-0.03 (0.06)
Median	36.50	0.00
Min - Max	36.4 - 36.6	-0.1 - 0.0
AFTER PAC INFUSION		
n	1	1
Mean (SD)	36.60 (NE)	0.20 (NE)
Median	36.60	0.20
Min - Max	36.6 - 36.6	0.2 - 0.2
Cycle 33 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	36.53 (0.15)	0.00 (0.10)
Median	36.50	0.00
Min - Max	36.4 - 36.7	-0.1 - 0.1
PRE PAC INFUSION		
n	2	2
Mean (SD)	36.55 (0.07)	-0.05 (0.07)
Median	36.55	-0.05
Min - Max	36.5 - 36.6	-0.1 - 0.0
Cycle 33 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	36.60 (NE)	0.20 (NE)
Median	36.60	0.20
Min - Max	36.6 - 36.6	0.2 - 0.2
Cycle 33 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	36.55 (0.21)	0.05 (0.07)
Median	36.55	0.05
Min - Max	36.4 - 36.7	0.0 - 0.1
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.60 (NE)	0.00 (NE)
Median	36.60	0.00
Min - Max	36.6 - 36.6	0.0 - 0.0
Cycle 34 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	36.60 (0.14)	0.00 (0.14)
Median	36.60	0.00
Min - Max	36.5 - 36.7	-0.1 - 0.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE PAC INFUSION		
n	2	2
Mean (SD)	36.60 (0.14)	0.00 (0.14)
Median	36.60	0.00
Min - Max	36.5 - 36.7	-0.1 - 0.1
AFTER PAC INFUSION		
n	1	1
Mean (SD)	36.50 (NE)	0.10 (NE)
Median	36.50	0.10
Min - Max	36.5 - 36.5	0.1 - 0.1
Cycle 34 Day 8		
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.50 (NE)	0.10 (NE)
Median	36.50	0.10
Min - Max	36.5 - 36.5	0.1 - 0.1
Cycle 34 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	36.65 (0.07)	0.15 (0.07)
Median	36.65	0.15
Min - Max	36.6 - 36.7	0.1 - 0.2
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.70 (NE)	0.10 (NE)
Median	36.70	0.10
Min - Max	36.7 - 36.7	0.1 - 0.1
Cycle 35 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	36.63 (0.06)	0.10 (0.10)
Median	36.60	0.10
Min - Max	36.6 - 36.7	0.0 - 0.2
PRE PAC INFUSION		
n	2	2
Mean (SD)	36.65 (0.07)	0.05 (0.07)
Median	36.65	0.05
Min - Max	36.6 - 36.7	0.0 - 0.1
Cycle 35 Day 8		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	36.60 (NE)	0.20 (NE)
Median	36.60	0.20
Min - Max	36.6 - 36.6	0.2 - 0.2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 35 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	36.50 (0.00)	-0.10 (0.00)
Median	36.50	-0.10
Min - Max	36.5 - 36.5	-0.1 - -0.1
PRE PAC INFUSION		
n	2	2
Mean (SD)	36.65 (0.07)	0.05 (0.07)
Median	36.65	0.05
Min - Max	36.6 - 36.7	0.0 - 0.1
Cycle 36 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	36.65 (0.07)	0.05 (0.07)
Median	36.65	0.05
Min - Max	36.6 - 36.7	0.0 - 0.1
PRE PAC INFUSION		
n	2	2
Mean (SD)	36.65 (0.07)	0.05 (0.07)
Median	36.65	0.05
Min - Max	36.6 - 36.7	0.0 - 0.1
Cycle 36 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	36.55 (0.07)	-0.05 (0.07)
Median	36.55	-0.05
Min - Max	36.5 - 36.6	-0.1 - 0.0
PRE PAC INFUSION		
n	2	2
Mean (SD)	36.55 (0.21)	-0.05 (0.21)
Median	36.55	-0.05
Min - Max	36.4 - 36.7	-0.2 - 0.1
Cycle 37 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	36.60 (0.14)	0.00 (0.14)
Median	36.60	0.00
Min - Max	36.5 - 36.7	-0.1 - 0.1
PRE PAC INFUSION		
n	2	2
Mean (SD)	36.60 (0.00)	0.00 (0.00)
Median	36.60	0.00
Min - Max	36.6 - 36.6	0.0 - 0.0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 37 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	36.65 (0.07)	0.05 (0.07)
Median	36.65	0.05
Min - Max	36.6 - 36.7	0.0 - 0.1
PRE PAC INFUSION		
n	2	2
Mean (SD)	36.45 (0.07)	-0.15 (0.07)
Median	36.45	-0.15
Min - Max	36.4 - 36.5	-0.2 - -0.1
Cycle 38 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	36.50 (0.00)	-0.10 (0.00)
Median	36.50	-0.10
Min - Max	36.5 - 36.5	-0.1 - -0.1
PRE PAC INFUSION		
n	2	2
Mean (SD)	36.65 (0.07)	0.05 (0.07)
Median	36.65	0.05
Min - Max	36.6 - 36.7	0.0 - 0.1
Cycle 38 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	36.65 (0.07)	0.05 (0.07)
Median	36.65	0.05
Min - Max	36.6 - 36.7	0.0 - 0.1
PRE PAC INFUSION		
n	2	2
Mean (SD)	36.60 (0.14)	0.00 (0.14)
Median	36.60	0.00
Min - Max	36.5 - 36.7	-0.1 - 0.1
Cycle 39 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	36.65 (0.07)	0.05 (0.07)
Median	36.65	0.05
Min - Max	36.6 - 36.7	0.0 - 0.1
PRE PAC INFUSION		
n	2	2
Mean (SD)	36.55 (0.07)	-0.05 (0.07)
Median	36.55	-0.05
Min - Max	36.5 - 36.6	-0.1 - 0.0

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 39 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	2	2
Mean (SD)	36.65 (0.07)	0.05 (0.07)
Median	36.65	0.05
Min - Max	36.6 - 36.7	0.0 - 0.1
PRE PAC INFUSION		
n	2	2
Mean (SD)	36.60 (0.00)	0.00 (0.00)
Median	36.60	0.00
Min - Max	36.6 - 36.6	0.0 - 0.0
Cycle 40 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	36.60 (NE)	0.00 (NE)
Median	36.60	0.00
Min - Max	36.6 - 36.6	0.0 - 0.0
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.60 (NE)	0.00 (NE)
Median	36.60	0.00
Min - Max	36.6 - 36.6	0.0 - 0.0
Cycle 40 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	36.60 (NE)	0.00 (NE)
Median	36.60	0.00
Min - Max	36.6 - 36.6	0.0 - 0.0
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.50 (NE)	-0.10 (NE)
Median	36.50	-0.10
Min - Max	36.5 - 36.5	-0.1 - -0.1
Cycle 41 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	36.60 (NE)	0.00 (NE)
Median	36.60	0.00
Min - Max	36.6 - 36.6	0.0 - 0.0
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.50 (NE)	-0.10 (NE)
Median	36.50	-0.10
Min - Max	36.5 - 36.5	-0.1 - -0.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	Change from Baseline
Cycle 41 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	36.40 (NE)	-0.20 (NE)
Median	36.40	-0.20
Min - Max	36.4 - 36.4	-0.2 - -0.2
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.40 (NE)	-0.20 (NE)
Median	36.40	-0.20
Min - Max	36.4 - 36.4	-0.2 - -0.2
Cycle 42 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	36.60 (NE)	0.00 (NE)
Median	36.60	0.00
Min - Max	36.6 - 36.6	0.0 - 0.0
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.60 (NE)	0.00 (NE)
Median	36.60	0.00
Min - Max	36.6 - 36.6	0.0 - 0.0
Cycle 42 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	36.40 (NE)	-0.20 (NE)
Median	36.40	-0.20
Min - Max	36.4 - 36.4	-0.2 - -0.2
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.50 (NE)	-0.10 (NE)
Median	36.50	-0.10
Min - Max	36.5 - 36.5	-0.1 - -0.1
Cycle 43 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	36.50 (NE)	-0.10 (NE)
Median	36.50	-0.10
Min - Max	36.5 - 36.5	-0.1 - -0.1
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.40 (NE)	-0.20 (NE)
Median	36.40	-0.20
Min - Max	36.4 - 36.4	-0.2 - -0.2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
Cycle 43 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	36.50 (NE)	-0.10 (NE)
Median	36.50	-0.10
Min - Max	36.5 - 36.5	-0.1 - -0.1
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.40 (NE)	-0.20 (NE)
Median	36.40	-0.20
Min - Max	36.4 - 36.4	-0.2 - -0.2
Cycle 44 Day 1		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	36.40 (NE)	-0.20 (NE)
Median	36.40	-0.20
Min - Max	36.4 - 36.4	-0.2 - -0.2
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.60 (NE)	0.00 (NE)
Median	36.60	0.00
Min - Max	36.6 - 36.6	0.0 - 0.0
Cycle 44 Day 15		
PRE ATEZO INFUSION (COHORT C)		
n	1	1
Mean (SD)	36.60 (NE)	0.00 (NE)
Median	36.60	0.00
Min - Max	36.6 - 36.6	0.0 - 0.0
PRE PAC INFUSION		
n	1	1
Mean (SD)	36.50 (NE)	-0.10 (NE)
Median	36.50	-0.10
Min - Max	36.5 - 36.5	-0.1 - -0.1
Study Drug Discontinuation		
n	88	88
Mean (SD)	36.44 (0.43)	0.00 (0.46)
Median	36.40	0.00
Min - Max	35.3 - 37.5	-1.3 - 1.2
Post-Baseline Last		
n	88	88
Mean (SD)	36.44 (0.43)	0.00 (0.46)
Median	36.40	0.00
Min - Max	35.3 - 37.5	-1.3 - 1.2

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out
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Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE ATEZO INFUSION (COHORT C)		
n	3	3
Mean (SD)	36.87 (0.31)	0.40 (0.52)
Median	36.80	0.10
Min - Max	36.6 - 37.2	0.1 - 1.0
PRE PAC INFUSION		
n	3	3
Mean (SD)	36.60 (0.26)	0.13 (0.61)
Median	36.70	0.00
Min - Max	36.3 - 36.8	-0.4 - 0.8
AFTER PAC INFUSION		
n	8	8
Mean (SD)	36.49 (0.66)	-0.15 (0.67)
Median	36.50	-0.05
Min - Max	35.4 - 37.7	-1.0 - 1.0
Post-Baseline Minimum		
n	3	3
Mean (SD)	36.30 (0.26)	-0.77 (0.50)
Median	36.20	-0.70
Min - Max	36.1 - 36.6	-1.3 - -0.3
PRE ATEZO INFUSION (COHORT C)		
n	35	35
Mean (SD)	35.76 (0.48)	-0.62 (0.40)
Median	35.90	-0.70
Min - Max	34.8 - 36.9	-1.3 - 0.3
PRE PAC INFUSION		
n	30	30
Mean (SD)	35.71 (0.59)	-0.73 (0.57)
Median	35.95	-0.75
Min - Max	34.3 - 36.6	-2.0 - 0.4
AFTER PAC INFUSION		
n	34	34
Mean (SD)	35.80 (0.55)	-0.68 (0.47)
Median	36.00	-0.65
Min - Max	34.5 - 36.7	-2.0 - 0.0
Post-Baseline Maximum		
n	8	8
Mean (SD)	36.95 (0.35)	0.79 (0.67)
Median	36.85	0.50
Min - Max	36.4 - 37.4	0.3 - 2.3
PRE ATEZO INFUSION (COHORT C)		
n	32	32
Mean (SD)	37.29 (0.62)	0.68 (0.72)
Median	37.15	0.45
Min - Max	36.4 - 39.1	-0.4 - 3.1

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

Vital Sign Results and Change from Baseline by Visit, Cohort C: TNBC, Safety Evaluable Population
Protocol: CO40016

Temperature (C)

Visit Analysis Timepoint	Ipatasertib + Atezolizumab + Paclitaxel (N=102) Value at Visit	 Change from Baseline
PRE PAC INFUSION		
n	30	30
Mean (SD)	37.12 (0.49)	0.64 (0.53)
Median	37.00	0.60
Min - Max	36.4 - 38.2	-0.2 - 2.0
AFTER PAC INFUSION		
n	32	32
Mean (SD)	37.13 (0.38)	0.79 (0.54)
Median	37.00	0.80
Min - Max	36.5 - 38.0	-0.1 - 1.8

Baseline is the patient's last observation prior to initiation of study drug.
Data Cutoff Date - 21MAR2023; Data Extraction Date - 21MAR2023

Program: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/program/t_vs_cb.sas
Output: root/clinical_studies/RO5532961/CDPT7890/CO40016/data_analysis/CSRFinal_Safety/prod/output/t_vs_cb_C_SE.out

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1. NARRATIVES

1.1 NARRATIVES FOR PATIENTS WHO DIED DUE TO ADVERSE EVENT(S)

Study Number/CRTN:	CO40016/304194	Patient number	1022
Demographics:	61-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Pulmonary embolism Death due to adverse event, SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER 2 negative right breast cancer (T2N2M0) approximately 5 years prior to study entry.

On Study Day −31, the patient was diagnosed with metastatic disease with ER/PR status unknown and HER 2 status not assessed in metastatic tissue. At screening, sites of disease involvement included lymph nodes (right sub clavicular and parasternal, left axillary and mediastinal), liver (segment II and VII), right lung cachexia, bone and pleural effusion.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right radical mastectomy	Approximately 5 years prior to study entry	NA
Cancer therapy	Adjuvant	Doxorubicin, cyclophosphamide, and fluorouracil (6 cycles each)	Approximately 5 years prior to study entry	Approximately 4 years and 9 months prior to study entry
Radiotherapy	Adjuvant	Chest wall (dose: 50 cGy, 25 fractions), supraclavicular lymph node (dose: 46 cGy, 25 fractions)	Approximately 4 years and 6 months prior to study entry	Approximately 4 years and 5 months prior to study entry

No medical or surgical history was reported. Concurrent conditions included obesity, hypertension, peripheral venous disease, osteoarthritis, gastritis, cholelithiasis, asthenia, pain in extremity (right arm) and peripheral swelling.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included diclofenac and moxonidine.

Event: Pulmonary embolism (thrombembolia of lung arteria)

Prior to the event of pulmonary embolism, the most recent dose of paclitaxel was administered on Study Day 15 and ipatasertib (400 mg) on Study Day 21.

On Study Day 25, at 13:45 hours, the patient died at home and the cause of death was reported as pulmonary embolism. No diagnostic tests were performed. She did not have any history of thrombotic events and any signs of clinical progression. No autopsy was performed.

The patient received last dose of paclitaxel on Study Day 15 and ipatasertib on Study Day 21.

The Investigator considered pulmonary embolism to be unrelated to ipatasertib and paclitaxel and related to concurrent illness.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Asthenia	3	Non-serious	8	Unresolved	Related	Related
Bone pain	3	Non-serious	8	Unresolved	Related	Related
Nausea	2	Non-serious	8	Unresolved	Related	Related
Eastern cooperative oncology group performance status worsened	2	Non-serious	8	15	Related	Related
Decreased appetite	2	Non-serious	8	Unresolved	Related	Related
Diarrhea	1	Non-serious	8	Unresolved	Related	Related
Anemia	1	Non-serious	14	Unresolved	Related	Related

Study Number/CRTN:	CO40016/304232	Patient number	1216
Demographics:	64-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Cardiopulmonary failure Death due to adverse event, SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with poorly differentiated, ER/PR and HER2 negative left breast cancer (T2N3MX; histological subtype ″other″), on Study Day –632, following left radical mastectomy.

On Study Day –48, the patient was diagnosed with metastatic disease with ER/PR status unknown and HER2 receptor not assessed in metastatic tissue. At screening, sites of disease involvement included bilateral ovary, left breast thoracic wall, left adrenal gland and bilateral bone (ribs, vertebral column, pelvis, and right acetabulum).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	–541	–477
Cancer therapy	Adjuvant	Paclitaxel (3 cycles)	–456	–414
Radiotherapy	Adjuvant	Chest wall and loco-regional lymph nodes (dose: 5000 cGy; 25 fractions)	–368	–336

The patient′s medical history included cerebrovascular accident. Concurrent conditions included type 2 diabetes mellitus, hypertension and hyperlipidemia.

At screening, the patient′s ECOG Performance Status was 1. Vitals showed blood pressure 137/71 mmHg, pulse rate 68 beats/min and respiratory rate 18 breaths/min. ECG was normal.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included metformin, lisinopril, lercanidipine, pentoxifylline and atorvastatin.

Event: Cardiopulmonary failure (cardiorespiratory failure)

Prior to the event of cardiopulmonary failure, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 7.

On Study Day 8, the patient was noted with Grade 2 hyperglycemia (non-serious, related to ipatasertib; glucose 10.03 mmol/L; normal range: 3.3-5.6 mmol/L) and Grade 2 neutropenia (non-serious, related to paclitaxel; neutropenia 1.3×10^9/L; normal range: 1.7-8.7 $\times 10^9$/L). She received treatment with filgrastim.

On Study Day 12, the patient died at home due to cardiopulmonary failure (details not reported). It was reported that there was no change in general health status since her last site visit on Study Day 8. No medical examination and treatment were given. An autopsy was not performed. The events of hyperglycemia and neutropenia remained unresolved at the time of patient′s death.

The last dose of paclitaxel was administered on Study Day 1 and ipatasertib on Study Day 7.

The Investigator considered cardiopulmonary failure, to be unrelated to ipatasertib and paclitaxel and related to disease under study and concurrent illness (hypertension). It was reported that the baseline conditions diabetes mellitus type 2, history of stroke 4 years ago and tobacco use could also be the suspected causes for this event.

No other events were experienced by the patient during the study.

1.2 NARRATIVES FOR PATIENTS WHO DIED DUE TO DISEASE PROGRESSION

Study Number/CRTN:	CO40016/305173	Patient number	1032
Demographics:	56-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Category:	Death due to disease progression		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR negative and HER 2 negative left breast cancer (T2N0M0), approximately 3 years prior to study entry.

The patient was diagnosed with metastatic disease on Study Day −66 with ER/PR status unknown and HER2 receptor not assessed in metastatic tissue. At screening, sites of disease involvement included lung (left upper lobe and right lower lobe) and sternum.

Past cancer treatment is listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left lumpectomy	Approximately 2 years and 11 months prior to study entry	NA

No medical or surgical history was reported. Concurrent conditions included ischemic stroke, aortic valve incompetence and seasonal allergy.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included bisoprolol and bemiparin.

On Study Day 445, a radiographic response assessment showed disease progression.

On Study Day 468, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 455 and ipatasertib given on Study Day 466. The patient entered into the long-term follow-up.

On Study Day 478, the patient died due to disease progression. An autopsy was not performed.

AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Dysgeusia	1	Non-serious	8	15	Unrelated	Related
Urinary tract infection	2	Non-serious	9	9	Unrelated	Unrelated
Alanine aminotransferase increased	1	Non-serious	29	Unresolved	Unrelated	Unrelated
Aspartate aminotransferase increased	1	Non-serious	29	Unresolved	Unrelated	Unrelated
Diarrhea	2	Non-serious	35	307	Related	Unrelated
Extrasystoles	2	Non-serious	57	Unresolved	Unrelated	Unrelated
Asthenia	3	Non-serious	70	Unresolved	Related	Related
Dyspepsia	1	Non-serious	70	Unresolved	Related	Related
Neuropathy peripheral	2	Non-serious	197	308	Unrelated	Related
Dermatitis	2	Non-serious	239	Unresolved	Related	Related
Diarrhea	2	Non-serious	337	339	Related	Unrelated
Neuropathy peripheral	3	Non-serious	337	Unresolved	Unrelated	Related
Oropharyngeal pain	1	Non-serious	375	393	Unrelated	Unrelated
Diarrhea	2	Non-serious	375	478	Related	Unrelated
Dizziness	1	Non-serious	428	448	Unrelated	Unrelated

Study Number/CRTN:	CO40016/320127	Patient number	1122
Demographics:	37-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Category:	Death due to disease progression		

The patient was randomized on Study Day 1.

The patient was diagnosed with moderately differentiated, ER/PR and HER 2 negative metastatic left breast cancer (T4N3M1; histological grade not otherwise specified) on Study Day −53. At screening, sites of disease involvement included right breast tumor, lymph nodes (bilateral axillary and bilateral sub-supraclavicular) and multiple lesions in lung.

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent conditions included anemia, gallbladder obstruction, left breast pain, asthenia, lymphostasis (left upper extremity) and pain in extremity (left arm).

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included ascorbic acid/ferrous sulfate, omeprazole, and ketorolac.

On Study Day 72, the patient showed symptomatic deterioration (pain in right breast).

On the same day (Study Day 72), study treatment with ipatasertib and paclitaxel was permanently discontinued due to symptomatic deterioration with the last dose of paclitaxel given on Study Day 64 and ipatasertib on Study Day 71. The patient entered into the long-term follow-up.

On Study Day 81, the patient died due to disease progression. It was unknown whether an autopsy was performed.

AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	7	9	Related	Unrelated
Alanine aminotransferase increased	1	Non-serious	29	Unresolved	Related	Related
Aspartate aminotransferase increased	1	Non-serious	29	Unresolved	Related	Related
Hypoalbuminemia	1	Non-serious	29	Unresolved	Unrelated	Unrelated
Erysipelas	2	Non-serious	53	72	Unrelated	Unrelated
Leukocytosis	1	Non-serious	57	71	Related	Related

Study Number/CRTN:	CO40016/318262	Patient number	1146
Demographics:	28-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Category:	Death due to disease progression		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER 2 negative right breast cancer (T2N3M1), on Study Day −35.

On Study Day −28, metastatic disease was confirmed with ER/PR unknown and HER2 receptor not assessed in metastatic tissue. At screening, sites of disease involvement included lymph node (mediastinal and right axillary), liver (segment VII), right breast and multiple bone metastasis.

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent conditions included back pain and breast pain.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included magnesium oxide, paracetamol/tramadol, and oxycodone.

On Study Day 46, the patient showed symptomatic deterioration (back pain).

On Study Day 54, study treatment with ipatasertib and paclitaxel was permanently discontinued due to symptomatic deterioration with the last dose of paclitaxel given on Study Day 43 and ipatasertib on Study Day 49. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in the table below:

Treatments	**Start Day**	**Stop Day**
Gemcitabine and cisplatin (1 cycle each)	54	54

On Study Day 55, the patient died due to disease progression. An autopsy was not performed.

AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious/ Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Diarrhea	1	Non-serious	2	49	Related	Unrelated
Peripheral sensory neuropathy	1	Non-serious	6	Unresolved	Unrelated	Related
Insomnia	1	Non-serious	14	Unresolved	Unrelated	Unrelated
Stomatitis	2	Non-serious	25	43	Unrelated	Related
Alopecia	1	Non-serious	25	Unresolved	Unrelated	Related
Decreased appetite	2	Non-serious	30	Unresolved	Related	Related
Nausea	3	Non-serious	30	Resolving	Related	Related
Vomiting	3	Non-serious	30	36	Related	Related
Fatigue	2	Non-serious	30	Unresolved	Related	Related
Constipation	1	Non-serious	50	Unresolved	Unrelated	Unrelated
Hypocalcemia	1	Non-serious	52	52	Unrelated	Unrelated

Study Number/CRTN:	CO40016/318135	Patient number	1215
Demographics:	47-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1(PT) Category:	Diarrhea SAE		
Event 2 (PT) Category:	Pleural effusion SAE		
Event 3 (PT) Category:	Diarrhea SAE		
Additional category:	Death due to disease progression		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER positive, PR and HER 2 negative left breast cancer (T1N2M0) on Study Day −706.

On Study Day −32, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative disease. At screening, sites of disease involvement included right ventricular outflow and mid ventricular lymph node.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Docetaxel and doxorubicin (4 cycles each)	−639	−492
Surgery	Curative	Left simple mastectomy	−310	NA
Radiotherapy	Other	Left breast (dose unknown; 15 fractions)	−273	−262

No medical or surgical history was reported. Concurrent conditions included hypothyroidism and diabetes mellitus.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. The same day, she also started loperamide prophylactically (total daily dose: 2 mg) for diarrhea.

Concomitant medications ongoing at Study Day 1 included metformin and levothyroxine.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 9 and ipatasertib (400 mg) on Study Day 10.

On Study Day 11, the patient experienced general weakness, Grade 1 dry cough (non-serious, related) and Grade 1 (initial intensity) diarrhea. On Study Day 15, event of diarrhea worsened to Grade 2, and she was hospitalized for further evaluation. Chest X-ray and stool test was done (results not reported). She received treatment with racecadotril, loperamide, cefoperazone/sulbactam, amikacin, pantoprazole, ondansetron, *Saccharomyces boulardii*, megestrol, cefixime/ornidazole, esomeprazole, lactulose for diarrhea and acetylcysteine for dry cough. On Study Day 19, the events of diarrhea and dry cough were considered resolved and she was discharged from the hospital.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of Diarrhea	6	PO	1	8
Diarrhea	2	PO	9	11
Diarrhea	6	PO	12	15
Prophylaxis of Diarrhea	2	PO	19	24
Prophylaxis of Diarrhea	2	PO	31	38
Prophylaxis of Diarrhea	2	PO	59	80

Due to this event, there was no change in study treatment with paclitaxel; however, study treatment with ipatasertib was interrupted on Study Day 16 and the next dose was given at a reduced dose of 300 mg on Study Day 19.

The Investigator considered diarrhea to be unrelated to paclitaxel and related to ipatasertib and other causes (unspecified).

Event 2: Pleural effusion

Prior to the event of pleural effusion, the most recent dose of paclitaxel was administered on Study Day 73 and ipatasertib (300 mg) on Study Day 80.

On Study Day 87, the patient experienced shortness of breath. Chest X-ray was performed, and she was diagnosed with Grade 3 pleural effusion, leading to hospitalization. Pleural tapping was performed. She received treatment with pheniramine. On Study Day 89, a radiographic

response assessment (CT) showed partial response. On Study Day 94, the event of pleural effusion was considered resolved and she was discharged from the hospital.

Due to this event, Cycle 4 Day 1 dose of paclitaxel was not administered and study treatment with ipatasertib was interrupted on Study Day 87. The next dose of paclitaxel and ipatasertib was administered on Study Day 94.

The Investigator considered pleural effusion to be unrelated to ipatasertib and paclitaxel and related to other causes unspecified.

Event 3: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 101 and ipatasertib (300 mg) on Study Day 105.

On Study Day 106, the patient experienced vomiting, second episode of Grade 1 (initial intensity) diarrhea. On Study Day 108, the event of diarrhea worsened to Grade 2 (diffuse loose stools), leading to hospitalization. Upon admission, her ECOG performance status was 2. She also complained of pain in chest wall. Study treatment with ipatasertib and paclitaxel was interrupted, and supportive care was started. She received prophylactic treatment with megestrol, ursodeoxycholic acid, paracetamol/tramadol, *Saccharomyces boulardii,* buprenorphine, ascorbic acid/cyanocobalamin/folic acid/nicotinic acid/pantothenic acid/pyridoxine/riboflavin/thiamine/zinc sulfate, pantoprazole, cefoperazone/sulbactam, ipratropium/levosalbutamol, diclofenac, gabapentin/nortriptyline, paracetamol, tramadol, ofloxacin, paracetamol, budesonide/formoterol and fusidic acid. She also received palliative radiation therapy for the pain in the chest (details in the table below) which was well tolerated. Later, during hospitalization, she was shifted to the HDU unit due to anxiety and tachycardia (heart rate not reported). It was reported that she was conscious, oriented and afebrile. Breast ultrasound was performed (results not reported). On Study Day 112, the event of diarrhea was considered resolved; however, hospitalization was continued. On Study Day 121, she was discharged from the hospital.

The patient received on-study anti-cancer therapy as listed in table below:

Treatment	Start Day	Stop Day
Radiotherapy to skin (left chest wall skin; dose: 102 cGy; 3 fractions)	110	112

Due to the event of diarrhea, study treatment with paclitaxel was interrupted after Study Day 101 and ipatasertib after Study Day 107.

The Investigator considered diarrhea to be unrelated to paclitaxel and related to ipatasertib and other causes unspecified.

On Study Day 114, a radiographic assessment showed disease progression with new lesions in bone (multiple sclerotic lesions), liver (hepatomegaly with multiple focal lesions in liver), brain (mild linear continuous pachymeningeal enhancement seen along cerebral convexities on both sides) and right breast (multiple enlarged right axillary nodes with increased soft tissue thickening).

On Study Day 114, study treatment with paclitaxel and ipatasertib was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 101 and ipatasertib on Study Day 107. The patient entered into the long-term follow-up.

On Study Day 121, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Neutropenia	2	Non-serious	16	17	Unrelated	Unrelated
Anemia	3	Non-serious	17	30	Unrelated	Unrelated
Pain	1	Non-serious	57	59	Unrelated	Unrelated

1.3 NARRATIVES FOR PATIENTS WHO EXPERIENCED SERIOUS ADVERSE EVENT(S)

Study Number/CRTN:	CO40016/304778	Patient number	1003
Demographics:	76-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Categories:	Pneumonia SAE, AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Hyperglycemia Grade ≥ 3 Hyperglycemia		
Event 3 (PT) Category:	Glucose tolerance impaired Grade ≥ 3 Hyperglycemia		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER negative, PR positive and HER 2 negative left breast cancer (T2N0M0), on Study Day −782, followed by simple mastectomy.

On Study Day −51, the patient was diagnosed with metastatic disease with ER/PR negative, HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included segment 8 of liver.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Cyclophosphamide, methotrexate, and fluorouracil (8 cycles each)	−740	−566
Radiotherapy	Adjuvant	Left chest wall (dose: 4600 cGy, 23 fraction)	−685	−652
Radiotherapy	Adjuvant	Left internal mammary (dose: 5600 cGy, 28 fraction)	−685	−645
Cancer therapy	Adjuvant	Letrozole	−545	−26

The patient's medical history included lower limb fracture (right knee) and cough. Surgical history included medical device implantation (nail fixation). Concurrent conditions included insomnia, hypertension, endometrial thickening, hepatic steatosis, osteoporosis, and *Helicobacter* gastritis.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included atenolol, losartan, amlodipine, and lansoprazole.

Event 1: Pneumonia
Event 2: Hyperglycemia (Hyperglycemia after S/P steroid)
Event 3: Glucose tolerance impaired (Glucose intolerance)

Prior to the events of pneumonia, hyperglycemia, and glucose tolerance impaired, the most recent dose of ipatasertib (400 mg) was administered on Study Day 48 and paclitaxel on Study Day 49.

On Study Day 56, the patient experienced Grade 1 fever (body temperature: 38.9°C) without chills. A laboratory work-showed WBC count 3.21 $\times$ $10^3/\mu L$ (normal range: 3.2-9 $\times$ $10^3/\mu L$),

neutrophil count 2.340 $\times$ $10^3/\mu L$ (normal range: 1.28-6.75 $\times$ $10^3/\mu L$), C-reactive protein 11.98 mg/dL (normal range: $<$ 0.5 mg/dL) and glucose 163 mg/dL (normal range: 70-100 mg/dL). She was diagnosed with Grade 2 hyperglycemia (non-serious, related to ipatasertib). On the same day (Study Day 56), she was hospitalized. On Study Day 57, a chest CT-scan showed bilateral lung inflammation and suspected pulmonary embolism. The results were also suggestive of infection (suspected by *Pneumocystis jirovecii* and Cytomegalovirus). Subsequently, she was diagnosed with serious Grade 3 pneumonia.

On Study Day 58, she was noted with non-serious Grade 3 glucose tolerance impaired. On Study Day 59, she was reported with non-serious Grade 3 hyperglycemia which was assessed as unrelated to ipatasertib. She received treatment with ceftazidime, amoxicillin/clavulanic acid, paracetamol, azithromycin, methylprednisolone, and sulfamethoxazole/trimethoprim for the event of pneumonia, insulin, metformin and pioglitazone for glucose tolerance impaired and hyperglycemia. On Study Day 79, the event of pneumonia was considered resolved. On Study Day 80, the events of glucose tolerance impaired and hyperglycemia (Grade 2 and Grade 3) were considered resolved. No information regarding discharge was reported.

Relevant lab values are listed in the table below:

Study Day	**Glucose** (normal range: 70-100 mg/dL)	**HbA1c** (normal range: 4-6%)
Screening	126	6.4
56	163	9.3
59	305	–
80	116	7

Due to the event of pneumonia, study treatment with ipatasertib and paclitaxel was permanently discontinued on Study Day 79 with the last dose of ipatasertib given on Study Day 48 and paclitaxel on Study Day 49. The patient entered into the long-term follow-up.

Action taken with study treatment due to the events of hyperglycemia and glucose tolerance impaired was reported as not applicable.

The Investigator considered pneumonia to be unrelated to ipatasertib and paclitaxel and related to other unspecified causes.

The Investigator considered hyperglycemia (Grade 3) and glucose tolerance impaired to be unrelated to ipatasertib and paclitaxel and related to concomitant medication (steroid treatment given for pneumonia).

On Study Day 162, a radiographic response assessment showed disease progression.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Paclitaxel (12 cycles)	185	262
Paclitaxel (12 cycles)	441	521
Doxorubicin (4 cycles)	731	794
Capecitabine (15 cycles)	815	1039
Vinorelbine (unknown cycles)	1102	Ongoing

On Study Day 1356, the patient was permanently discontinued from the study as the study was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Decreased appetite	2	Non-serious	4	97	Unrelated	Related
Constipation	1	Non-serious	6	8	Unrelated	Unrelated
Diarrhea	1	Non-serious	10	14	Related	Unrelated
Vomiting	1	Non-serious	12	13	Related	Unrelated
Neutrophil count decreased	2	Non-serious	14	21	Unrelated	Related
Alopecia	1	Non-serious	16	171	Unrelated	Related
Vomiting	1	Non-serious	21	21	Related	Unrelated
Influenza like illness	1	Non-serious	24	42	Unrelated	Unrelated
Anemia	2	Non-serious	28	63	Unrelated	Related
Vomiting	1	Non-serious	29	30	Unrelated	Related
Neuropathy peripheral	1	Non-serious	31	171	Unrelated	Related
Mucosal inflammation	1	Non-serious	31	58	Unrelated	Related
Neutrophil count decreased	2	Non-serious	35	42	Unrelated	Related
Conjunctival edema	1	Non-serious	59	72	Unrelated	Unrelated

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Periorbital edema	1	Non-serious	59	72	Unrelated	Unrelated
Nausea	1	Non-serious	62	80	Unrelated	Unrelated
Vomiting	1	Non-serious	65	80	Unrelated	Unrelated
Oral herpes	2	Non-serious	66	88	Unrelated	Unrelated
Rash	1	Non-serious	67	73	Unrelated	Unrelated
Hemorrhoids	2	Non-serious	69	73	NA	NA
Tongue ulceration	2	Non-serious	76	88	NA	NA

Study Number/CRTN:	CO40016/304878	Patient number	1005
Demographics:	59-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Alanine aminotransferase increased Grade $\geq$ 3 hepatotoxicity		
Event 2 (PT) Category:	Aspartate aminotransferase increased Grade $\geq$ 3 hepatotoxicity		
Event 3 (PT) Category:	Fracture SAE		

The patient was randomized on Study Day 1.

The patient was diagnosed with ductal, moderately differentiated, ER/PR negative, HER 2 negative left breast cancer (T2N3cM1) on Study Day −37. At screening, sites of disease involvement included left breast and left paraaortic lymph node.

No past cancer treatments were reported.

The patient′s medical history included left breast inflammation and headache. No surgical history was reported. Concurrent condition included osteoporosis.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medication ongoing at Study Day 1 was reported.

Event 1: Alanine aminotransferase increased (ALT increased)
Event 2: Aspartate aminotransferase increased (AST increased)

Prior to the events of alanine aminotransferase increased and aspartate aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 379 and ipatasertib (400 mg) on Study Day 385.

On Study Day 393, a scheduled laboratory work-up showed ALT 318 U/L (normal range: 0-40 U/L) and AST 254 U/L (normal range: 0-40 U/L). The patient was diagnosed with non-serious Grade 3 **alanine aminotransferase increased,** and **aspartate aminotransferase increased**. She received treatment with *Silybin marianum* and adenine hydrochloride/bifendate/carnitine orotate/cyanocobalamin/liver extract/pyridoxine/riboflavin. On Study Day 399, the event of alanine aminotransferase increased was considered resolved. On Study Day 400, the event of aspartate aminotransferase increased improved to Grade 2. On Study Day 406, the event of aspartate aminotransferase increased was considered resolved.

Relevant lab values are listed in the table below:

Study Day	**AST** (normal range: 0-40 U/L)	**ALT** (normal range: 0-40 U/L)	**Total bilirubin** (normal range: 0.2-1.2 mg/dL)	**ALP** (normal range: 40-120 U/L)
Screening	22	22	0.2	97
365	21	18	0.3	69
393	254	318	0.6	258
400	137	71	1.5	402
407	62	30	0.6	226

Due to the events of alanine aminotransferase increased and aspartate aminotransferase increased, Cycle 15 Day 1 and Cycle 15 Day 8 of paclitaxel were not administered and study treatment with ipatasertib was interrupted on Study Day 393. The next dose of paclitaxel (at a reduced dose of 65 mg/m^2) and ipatasertib (at a reduced dose of 300 mg) was given on Study Day 407.

The Investigator considered alanine aminotransferase increased and aspartate aminotransferase increased to be related to ipatasertib and paclitaxel.

Event 3: Fracture

Prior to the event of fracture, the most recent dose of paclitaxel was administered on Study Day 645 and ipatasertib (300 mg) on Study Day 646.

On Study Day 645, the patient experienced Grade 2 back pain (non-serious, unrelated) and visited the local hospital. An X-ray was performed, and fracture was suspected. On Study Day 647, she presented to the emergency room due to ongoing back pain. An MRI of whole spine revealed acute benign Grade 3 compression **fracture** at T8, leading to hospitalization for supportive care. The bone densitometry showed spine anteroposterior bone mass density (L1-L2) 0.605 g/cm^2 (55% of young normal; T-score -4.1), femur (neck) bone mass density 0.632 g/cm^2 (67% of young normal; T-score -2.6), femur (troch) bone mass density 0.513 g/cm^2 (70% of young normal; T-score -2.0) and femur (total) bone mass density 0.672 g/cm^2 (69% of young normal; T-score -2.5). She received treatment with denosumab and tramadol. She was on bed-rest and her condition was observed. She further received treatment with calcium carbonate/cholecalciferol. On Study Day 659, a repeat X-ray showed more collapsed compression fracture at T8, along with osteopenia. On Study Day 668, the event of back pain improved to Grade 1, and fracture improved to Grade 2. On Study Day 674, digital X-ray radiogrammetry (T-spine; anteroposterior lateral view) results were consistent with pervious X-ray (done on Study Day 659). It was reported that the pain was improving and repeated X-rays did not show worsening. On Study Day 687, the event of fracture was considered resolved and she was discharged from the hospital. The event of back pain remained unresolved at the time of study discontinuation.

Due to the event of fracture, there was no change in the study treatment with ipatasertib; however, Cycle 24 Day 8 was interrupted, and Cycle 24 Day 15 of paclitaxel was delayed and was given on Study Day 668.

The Investigator considered fracture to be unrelated to ipatasertib and paclitaxel and related to concurrent illness (osteoporosis).

On Study Day 841, the patient was discontinued from the study treatment as per physician's decision with the last dose of ipatasertib given on Study Day 833 and paclitaxel on Study Day 827. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Left breast surgery	855	NA
Radiotherapy to left breast + supraclavicular lymph node (dose: 5290 cGy, 23 fractions)	903	932

On Study Day 1342, the patient was permanently discontinued from the study as the study was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Myalgia	1	Non-serious	3	5	Unrelated	Related
Diarrhea	1	Non-serious	5	5	Related	Unrelated
Nausea	1	Non-serious	9	21	Related	Unrelated
Pruritus	2	Non-serious	9	24	Related	Unrelated
Diarrhea	1	Non-serious	11	14	Related	Unrelated
Myalgia	1	Non-serious	11	11	Unrelated	Related
Stomatitis	1	Non-serious	16	66	Related	Related
Alopecia	2	Non-serious	17	Unresolved	NA	Related
Myalgia	1	Non-serious	18	20	NA	Related
Peripheral sensory neuropathy	1	Non-serious	19	24	Unrelated	Related
Peripheral sensory neuropathy	2	Non-serious	30	Unresolved	Unrelated	Related
Myalgia	1	Non-serious	30	252	Unrelated	Related
Nausea	1	Non-serious	32	47	Related	Unrelated
Diarrhea	1	Non-serious	39	39	Related	Unrelated
Insomnia	1	Non-serious	67	122	Unrelated	Unrelated
Aspartate aminotransferase increased	1	Non-serious	71	126	Related	Related
Alanine aminotransferase increased	1	Non-serious	71	100	Related	Related
Stomatitis	1	Non-serious	73	97	Related	Related
Diarrhea	1	Non-serious	102	103	Related	Related
Fatigue	2	Non-serious	103	Unresolved	Related	Related
Productive cough	1	Non-serious	124	140	Unrelated	Unrelated

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	131	132	Related	Unrelated
Diarrhea	1	Non-serious	153	163	Related	Unrelated
Diarrhea	1	Non-serious	186	187	Related	Unrelated
Diarrhea	1	Non-serious	192	192	Related	NA
Dyspepsia	1	Non-serious	192	195	Related	Unrelated
Dyspepsia	1	Non-serious	198	329	Related	Related
Diarrhea	1	Non-serious	210	211	Related	Unrelated
Diarrhea	1	Non-serious	215	221	Related	Unrelated
Nail discoloration	1	Non-serious	216	Unresolved	Unrelated	Related
Diarrhea	1	Non-serious	233	237	Related	Unrelated
Edema	1	Non-serious	241	Unresolved	Unrelated	Related
Diarrhea	1	Non-serious	241	244	Related	Unrelated
Diarrhea	1	Non-serious	253	254	Related	Unrelated
Diarrhea	1	Non-serious	269	271	Related	Unrelated
Nausea	1	Non-serious	272	520	Related	Unrelated
Diarrhea	1	Non-serious	296	299	Related	Related
Diarrhea	1	Non-serious	330	330	Related	Unrelated
Oropharyngeal pain	1	Non-serious	357	360	Related	Related
Decreased appetite	1	Non-serious	358	385	Related	Related
Diarrhea	1	Non-serious	362	363	Unrelated	Related
Diarrhea	1	Non-serious	374	377	Related	Related
Pruritus	2	Non-serious	384	415	Related	Related
Diarrhea	1	Non-serious	416	417	Related	Related
Tooth fracture	1	Non-serious	436	444	Unrelated	Unrelated

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Dermatitis acneiform	1	Non-serious	465	483	Related	Related
Diarrhea	1	Non-serious	478	479	Related	Related
Aspartate aminotransferase increased	2	Non-serious	505	511	Unrelated	Unrelated
Alanine aminotransferase increased	2	Non-serious	505	511	Unrelated	Unrelated
Pruritus	1	Non-serious	520	552	Related	Related
Diarrhea	1	Non-serious	521	522	Related	Related
Diarrhea	1	Non-serious	636	638	Related	Related
Constipation	1	Non-serious	647	682	Related	Related
Diarrhea	1	Non-serious	686	687	Related	Related
Dyspepsia	1	Non-serious	692	707	Related	Related
Diarrhea	1	Non-serious	748	749	Related	Related
Hyperlipidemia	2	Non-serious	785	Unresolved	Unrelated	Unrelated
Diarrhea	1	Non-serious	800	801	Related	Related
Pruritis	1	Non-serious	803	Unresolved	Related	Related

Study Number/CRTN:	CO40016/304878	Patient number	1015
Demographics:	55-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Neutropenia SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER/PR negative and HER 2 negative (histological grade unknown) left breast cancer (T2N1M0), on Study Day –635.

The patient was diagnosed with metastatic disease on Study Day −72 with ER/PR status unknown and HER 2 status not assessed in metastatic tissue. At screening, sites of disease involvement included left axillary and supraclavicular lymph node

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Date
Cancer therapy	Neoadjuvant	Cyclophosphamide, doxorubicin and unknown taxane (4 cycles each)	−631	−485
Surgery	Curative	Left simple mastectomy and sentinel lymph node biopsy	−450	NA
Radiotherapy	Adjuvant	Left breast (dose unknown)	−399	−368

No medical or surgical history and concurrent conditions were reported.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

On Study Day 15, the patient was noted with Grade 3 neutropenia (non-serious, related; WBC count $1.9 \times 10^3/\mu L$; normal range: 4-10 $\times 10^3/\mu L$ and neutrophils 39.8%; normal range: 50-75%). She received treatment with filgrastim. On Study Day 21, the event of neutropenia was considered resolved.

On Study Day 29, the patient was noted with second episode of Grade 3 neutropenia (non-serious, related; WBC count $2.1 \times 10^3/\mu L$; normal range: 4-10 $\times 10^3/\mu L$ and neutrophils 39.8%, normal range: 50-75%). She received treatment with lenograstim. On the same day (On Study Day 29), the event of neutropenia was considered resolved. Due to this event study treatment with paclitaxel was reduced to 65 mg/m^2 and ipatasertib to 300 mg on Study Day 30.

Event Neutropenia

Prior to the event of neutropenia, the most recent dose of paclitaxel was administered on Study Day 30 and ipatasertib (300 mg) on Study Day 36.

On Study Day 37, the patient was noted with medically significant Grade 4 neutropenia (WBC count $1.3 \times 10^3/\mu L$; normal range: 4-10 $\times 10^3/\mu L$ and neutrophils 13.4%; normal range: 50-75%). She received treatment with filgrastim. On Study Day 42, the event of neutropenia was considered resolved.

Relevant lab values are listed in the table below:

Study Day	**WBC count** (normal range: 4-10 $\times$ $10^3/\mu L$)	**Neutrophils** (normal range: 50-75 %)
Screening	4.2	63.7
8	3.9	54
15	1.9	39.8
21	2.4	34
22	10.2	72
29	2.1	39.8
30	3.5	54
37	1.3	13.4
43	5.1	58.8

Due to this event, study treatment with ipatasertib was interrupted on Study Day 37 and the next dose was given at a reduced dose of 200 mg on Study Day 43; however, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 30.

The Investigator considered neutropenia to be related to ipatasertib and paclitaxel.

On Study Day 106, a radiographic response assessment showed disease progression with new nodule in right lung.

On Study Day 111, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose given on Study Day 105. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Methotrexate, fluorouracil and cyclophosphamide (5 cycles each)	114	239
Eribulin (2 cycles)	262	288
Doxorubicin and cyclophosphamide (2 cycles each)	345	366
Vinorelbine and gemcitabine (1 cycle each)	407	407
Radiotherapy (breast and supraclavicular lymph node, dose: 1560 cGy, 3 fractions)	420	422
Methotrexate (1 cycle)	423	423

On Study Day 436, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	3	4	Related	Unrelated
Dyspepsia	1	Non-serious	9	Unresolved	Related	Related
Alopecia	2	Non-serious	17	98	Unrelated	Related
Rash pustular	1	Non-serious	27	51	Related	Related
Peripheral sensory neuropathy	1	Non-serious	33	Unresolved	Unrelated	Related
Asthenia	1	Non-serious	45	167	Related	NA
Lymph node pain	1	Non-serious	89	Unresolved	Unrelated	Unrelated
Diarrhea	1	Non-serious	104	105	Related	Unrelated

Study Number/CRTN:	CO40016/304194	Patient number	1022
Demographics:	61-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Pulmonary embolism Death due to adverse event, SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.1; Narratives for patients who died due to adverse event(s).

Study Number/CRTN:	CO40016/304787	Patient number	1028
Demographics:	65-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Hyperglycemia Grade $\geq$ 3 hyperglycemia		
Event 2 (PT) Categories:	Hyperglycemia SAE, Grade $\geq$ 3 hyperglycemia		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, ER/PR and HER 2 negative, locally advanced unresectable, metastatic left breast cancer (T4bN2M1; histological grade unknown) on Study Day −73.

At screening, sites of disease involvement included left breast, lung (bilateral parenchyma, right pleura and right lung base), liver (segments VIII and III and hepatic parenchyma), left axillary lymph node, bone (skull and sternum) and left adrenal gland.

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent conditions included diabetes mellitus and hypertension.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included glibenclamide.

Event 1: Hyperglycemia (Asymptomatic fasting hyperglycemia)

Prior to the event of hyperglycemia, the most recent dose of paclitaxel was administered on Study Day 29 and ipatasertib (400 mg) on Study Day 33.

On Study Day 34, the patient was noted with asymptomatic non-serious Grade 3 fasting hyperglycemia (glucose 259 mg/dL; normal range: 70-99 mg/dL). No additional treatment was given for the event; however, from Study Day 37, glibenclamide 5 mg QD was increased to 5 mg BID. On Study Day 39, the event of hyperglycemia was considered resolved.

Due to this event, there was no change in the study treatment with paclitaxel; however, ipatasertib was interrupted on Study Day 36 and the next dose was given on Study Day 40.

The Investigator considered hyperglycemia to be related to paclitaxel and ipatasertib.

On Study Day 66, the patient was noted with Grade 2 hyperglycemia (non-serious; related, glucose on Study Day 69: 215 mg/dL; normal range: 70-99 mg/dL). No treatment was given for the event; however, on the same day (Study Day 66), dose of ipatasertib was reduced to 300 mg. Further, study treatment with ipatasertib was interrupted from Study Day 70 to Study Day 83 due to this event. On Study Day 77, the event of hyperglycemia was considered resolved.

Event 2: Hyperglycemia

Prior to the event of hyperglycemia, the most recent dose of paclitaxel was administered on Study Day 78 and ipatasertib (300 mg) on Study Day 91.

On Study Day 92, at 12:30 hours, during a scheduled visit, the patient was noted with Grade 4 hyperglycemia (non-fasting glucose: 558 mg/dL, normal range not reported), leading to hospitalization. She received treatment with insulin for hyperglycemia. It was reported that she was also referred to the nutritionist for dietary advice since she had a history of associated diabetes mellitus. She responded well to the insulin treatment and on Study Day 93, the event of hyperglycemia was considered resolved. On the same day (Study Day 93), she was discharged from the hospital.

Hyperglycemia treatment details:

Treatment	Indication	Dose (Units: mg)	Route	Frequency	Start day	Stop day
Insulin	Hyperglycemia	—	SC	Unknown	92	93

Relevant lab values are listed in the table below:

Study Day	Glucose (normal range: 70-99 mg/dL)
Screening	128
34	259
41	92
69	215
77	151
83	140
92	558*
93	85*
98	177

*Normal range: not reported

Due to this event, study treatment with paclitaxel was interrupted after Study Day 78 and ipatasertib after Study Day 92.

On Study Day 120, symptomatic response assessment showed clinical progression with a decline in performance status (ECOG status 3) and study treatment with ipatasertib and paclitaxel was permanently discontinued with the last dose of paclitaxel administered on Study Day 78 and ipatasertib on Study Day 92. The patient entered into the long-term follow-up.

On the same day (Study Day 120), the patient withdrew consent from the study.

The Investigator considered hyperglycemia to be unrelated to paclitaxel and related to ipatasertib and other causes (unspecified).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	9	9	Related	Related
Constipation	1	Non-serious	28	33	Unrelated	Unrelated
Diarrhea	1	Non-serious	47	72	Related	Related
Weight decreased	2	Non-serious	57	Resolving	Unrelated	Unrelated
Asthenia	2	Non-serious	66	79	Related	Related
Hypertensive crisis	2	Non-serious	71	77	Unrelated	Unrelated
Hypertensive urgency	3	Non-serious	84	92	Unrelated	Unrelated
Asthenia	3	Non-serious	91	Resolving	Related	Related
Hypertension	2	Non-serious	92	Resolving	Unrelated	Unrelated
Infusion related reaction	1	Non-serious	99	99	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304878	Patient number	1040
Demographics:	31-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Febrile neutropenia SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR negative and HER 2 negative left breast cancer (T2N0M0), approximately 3 years and 10 months prior to study entry.

The patient was diagnosed with metastatic disease on Study Day –47 with ER/PR negative and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included left chest wall, lymph nodes (right hilar and left interlobar) and sternum.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left lumpectomy and sentinel lymph node biopsy	Approximately 3 years and 9 months prior to study entry	NA
Cancer therapy	Adjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	Approximately 3 years and 8 months prior to study entry	Approximately 3 years and 6 months prior to study entry
Radiotherapy	Adjuvant	Left breast (dose: 5000 cGy, 25 fractions)	Approximately 3 years and 5 months prior to study entry	Approximately 3 years and 4 months prior to study entry
Radiotherapy	Adjuvant	Tumor bed boost (dose: 1600 cGy, 8 fractions)	Approximately 3 years and 4 months prior to study entry	Approximately 3 years and 4 months prior to study entry

No medical or surgical history was reported. Concurrent conditions included hyperthyroidism and cough.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included ranitidine and thiamazole.

On Study Day 199, the patient was noted with Grade 3 neutrophil count decreased (non-serious, related) with neutrophils 21.2% (normal range: 50-75%). She received treatment with filgrastim. On Study Day 200, the event of neutrophil count decreased was considered resolved.

Event: Febrile neutropenia

Prior to the event of febrile neutropenia, the most recent dose of paclitaxel was administered on Study Day 206 and ipatasertib (400 mg) on Study Day 208.

On Study Day 209, the patient′s body temperature was above 38°C. A laboratory work-up showed WBC count 1.8×10^3/L (normal range: 4-10 $\times 10^3/\mu$L), absolute neutrophil count 800 /μL and C-reactive protein 16.75 mg/dL (normal range not reported for both). She was diagnosed with Grade 3 febrile neutropenia, leading to hospitalization. She received treatment with filgrastim and piperacillin. On Study Day 210, test for influenza A and B virus and nasopharyngeal swab was negative. On Study Day 211, the event of febrile neutropenia was considered resolved and she was discharged from the hospital.

Relevant lab values are listed in the table below:

Study Day	**WBC count** (normal range: 4-10 $\times 10^3/\mu L$)	**Neutrophils** (normal range: 50-75%)
Screening	4.5	56.6
200	13	78.3
209	1.8	800*
210	4.2	2740*
211	10.1	7500*

*Units: /μL, normal range not reported

Due to this event, study treatment with paclitaxel was reduced to 65 mg/m^2 on Study Day 214 and ipatasertib was initially interrupted on Study Day 210 and resumed at a reduced dose of 300 mg on Study Day 214.

The Investigator considered febrile neutropenia to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 392, a radiographic response assessment showed disease progression with multiple new lesions in brain.

On Study Day 396, study treatment with paclitaxel and ipatasertib was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 382 and ipatasertib on Study Day 386. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Radiotherapy (Whole brain; dose: 4000 cGy, 10 fractions)	400	413
Capecitabine (3 cycles)	445	500
Gemcitabine and cisplatin (2 cycles each)	511	533
Eribulin (4 cycles)	563	682
Brain surgery	570	NA
Brain surgery	648	NA
Brain (tumor related orthopedic surgical intervention)	728	NA
Brain surgery	743	NA

On Study Day 761, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Vasculitis	1	Non-serious	2	30	Unrelated	Unrelated
Nausea	1	Non-serious	3	355	Related	Unrelated
Rash maculo-papular	1	Non-serious	3	92	Related	Related
Diarrhea	1	Non-serious	5	6	Related	Unrelated
Diarrhea	1	Non-serious	13	15	Related	Unrelated
Alopecia	2	Non-serious	14	Unresolved	Unrelated	Related
Peripheral sensory neuropathy	1	Non-serious	19	26	Unrelated	Related
Peripheral sensory neuropathy	1	Non-serious	40	Unresolved	Unrelated	Related
Diarrhea	1	Non-serious	42	43	Related	Unrelated
Dyspepsia	1	Non-serious	42	137	Related	Unrelated
Diarrhea	1	Non-serious	52	54	Unrelated	Related
Productive cough	1	Non-serious	52	87	Related	Related
Diarrhea	1	Non-serious	74	76	Related	Unrelated
Influenza like illness	2	Non-serious	76	81	Related	Related
Diarrhea	1	Non-serious	101	106	Related	Unrelated
Rash Maculo-Papular	1	Non-serious	101	137	Related	Related
Oropharyngeal pain	1	Non-serious	120	123	Related	Related
Diarrhea	1	Non-serious	136	137	Related	Unrelated
Diarrhea	1	Non-serious	159	160	Related	Related
Decreased appetite	1	Non-serious	159	163	Related	Related
Dermatitis acneiform	1	Non-serious	187	386	Related	Related
Diarrhea	1	Non-serious	187	189	Related	Related
Face edema	1	Non-serious	191	Unresolved	Related	Unrelated
Dyspepsia	1	Non-serious	207	Unresolved	Related	Related
Abdominal pain	1	Non-serious	208	209	Related	Unrelated
Diarrhea	1	Non-serious	208	209	Related	Related
Diarrhea	1	Non-serious	217	218	Related	Related
Diarrhea	1	Non-serious	242	243	Related	Related
Diarrhea	1	Non-serious	249	250	Related	Related
Skin hyperpigmentation	1	Non-serious	262	Unresolved	Unrelated	Related
Diarrhea	1	Non-serious	271	272	Related	Related
Diarrhea	1	Non-serious	329	330	Related	Related
Diarrhea	1	Non-serious	333	334	Related	Related
Diarrhea	1	Non-serious	357	358	Related	Related

Study Number/CRTN:	CO40016/306203	Patient number	1047
Demographics:	70-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Category:	Abscess jaw SAE		

The patient was randomized on Study Day −2.

The patient was initially diagnosed with lobular, ER/PR positive and HER 2 negative left breast cancer (T2N3aM0; histological grade unknown), approximately 10 years prior to study entry.

On Study Day −54, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included bone (right anterior 5th rib, midline vertebral body L2 and L4 and posterior left iliac bone).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left radical mastectomy	Approximately 10 years prior to study entry	NA
Radiotherapy	Adjuvant	Left breast (reconstructed chest wall, axillary bed and left supraclavicular fossa) (dose: 5280 cGy, 36 fractions)	Approximately 9 years prior to study entry	Approximately 9 years prior to study entry
Cancer therapy	Adjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	Approximately 9 years prior to study entry	Approximately 9 years prior to study entry
Cancer therapy	Adjuvant	Paclitaxel (12 cycles)	Approximately 9 years prior to study entry	Approximately 9 years prior to study entry
Cancer therapy	Adjuvant	Anastrozole (96 cycles)	Approximately 9 years prior to study entry	−33

No medical/surgical history was reported. Concurrent conditions included sinus tachycardia, hyperlipidemia, osteoporosis, and hypothyroidism.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included atenolol, simvastatin, levothyroxine, acetylsalicylic acid, calcium carbonate and cholecalciferol.

On Study Day 8, study treatment with ipatasertib was interrupted and the patient was started on metformin for Grade 2 hyperglycemia (non-serious, related to ipatasertib, onset day: Study Day 7 and resolution day: Study Day 11).

Event 1: Alanine aminotransferase increased (ALT increased)
Event 2: Aspartate aminotransferase increased (AST increased)

Prior to the events of alanine aminotransferase increased and aspartate aminotransferase increased, the most recent dose of ipatasertib (400 mg) was administered on Study Day 7 and paclitaxel on Study Day 8.

On Study Day 14, a laboratory work-up showed ALT 313 U/L (normal range: 13-56 U/L), AST 279 U/L (normal range: 13-35 U/L) and ALP 315 U/L (normal range: 45-117 U/L) and the patient was diagnosed with Grade 3 alanine aminotransferase increased, Grade 3 aspartate aminotransferase increased and Grade 2 blood alkaline phosphatase increased (non-serious, related to paclitaxel). She had no other symptoms, and skin was normal. Ongoing treatment with metformin stopped. No treatment was reported these events. On Study Day 20, the event of aspartate aminotransferase increased was considered resolved. On Study Day 28, the events of alanine aminotransferase increased, and blood alkaline phosphatase increased were considered resolved.

Relevant lab values are listed in the table below:

Study Day	**AST** (normal range: 13-35 U/L)	**ALT** (normal range: 13-56 U/L)	**ALP** (normal range: 45-117 U/L)	**Bilirubin** (normal range: 0.2-1.3 mg/dL)
Screening	20	22	71	0.4
7	16	31	60	0.7
14	279	313	315	0.4
27	22	40	104	0.5
34	18	32	96	0.5

Due to the events of alanine aminotransferase increased and aspartate aminotransferase increased, study treatment with paclitaxel (Cycle 1 Day 15) was interrupted and ipatasertib interruption was prolonged. The next dose of paclitaxel and ipatasertib (at a reduced dose of 300 mg) was given on Study Day 28.

The Investigator considered alanine aminotransferase increased to be unrelated to ipatasertib and paclitaxel and related to concomitant medication (metformin).

The Investigator considered aspartate aminotransferase increased to be unrelated to ipatasertib and related to paclitaxel and concomitant medication (metformin).

Event 3: Abscess jaw (Right mandibula abscess)

Prior to the event of abscess jaw, the most recent dose of ipatasertib (300 mg) was administered on Study Day 1126 and paclitaxel on Study Day 1148.

On Study Day 1161, the patient presented to hospital with redness on right cheek and spontaneous purulent discharge. A superficial wound culture and a CT scan of mandible was performed, and the patient was diagnosed with Grade 3 right mandibular abscess (preferred term: abscess jaw), leading to hospitalization**.** She was treated with levofloxacin. On Study Day 1166, the event of abscess jaw was considered resolved with sequelae (unspecified) and the patient was discharged from the hospital.

Due to the event of abscess jaw, study treatment with paclitaxel and ipatasertib was interrupted and later on Study Day 1161, study treatment with paclitaxel and ipatasertib and study was permanently discontinued as she enters post-trial access program with the last dose of ipatasertib administered on Study Day 1126 and paclitaxel given on Study Day 1148.

The Investigator considered abscess jaw to be unrelated to ipatasertib and paclitaxel and related to disease under study.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	2	Non-serious	4	11	Related	Unrelated
Decreased appetite	1	Non-serious	4	168	Related	Unrelated
Neutrophil count decreased	2	Non-serious	14	20	Related	Related
Hypophosphatasemia	2	Non-serious	14	28	Unrelated	Unrelated
Urinary tract infection	2	Non-serious	34	42	Unrelated	Unrelated
Diarrhea	2	Non-serious	37	85	Related	Unrelated
Hyperkaliemia	1	Non-serious	41	42	Unrelated	Related
Blood creatinine increased	1	Non-serious	41	55	Unrelated	Related

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Rash	1	Non-serious	64	91	Unrelated	Unrelated
Vascular access site infection	1	Non-serious	70	85	Unrelated	Unrelated
Diarrhea	1	Non-serious	85	Unresolved	Related	Unrelated
Tooth fracture	1	Non-serious	94	140	Unrelated	Unrelated
Blood cholesterol increased	1	Non-serious	139	Unresolved	Related	Unrelated
Blood triglycerides increased	1	Non-serious	139	223	Related	Unrelated
Blood lactate dehydrogenase increased	1	Non-serious	167	195	Unrelated	Unrelated
Anemia	1	Non-serious	181	335	Related	Related
Blood lactate dehydrogenase increased	1	Non-serious	223	363	Unrelated	Unrelated
Blood phosphorus increased	1	Non-serious	223	279	Related	Unrelated
Neuropathy peripheral	1	Non-serious	267	308	Unrelated	Related
Fatigue	1	Non-serious	267	Unresolved	Related	Related
Hypophosphatasemia	1	Non-serious	307	363	Related	Related
Anemia	2	Non-serious	335	342	Related	Unrelated
Anemia	1	Non-serious	342	503	Related	Related
Alanine aminotransferase increased	1	Non-serious	342	391	Related	Related
Rib Fracture	1	Non-serious	440	Unresolved	Unrelated	Unrelated
Fall	1	Non-serious	474	474	Unrelated	Unrelated
Skin abrasion	1	Non-serious	474	483	Unrelated	Unrelated
Anemia	2	Non-serious	503	Unresolved	Related	Related
Hypoalbuminemia	1	Non-serious	531	538	Unrelated	Unrelated
Blood triglycerides increased	1	Non-serious	559	Unresolved	Related	Unrelated
Hypoalbuminemia	2	Non-serious	559	Unresolved	Unrelated	Unrelated

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Swelling face	3	Non-serious	1064	1074	Unrelated	Unrelated
Lymphoedema	3	Non-serious	1064	Resolving	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304776	Patient number	1070
Demographics:	66-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Febrile neutropenia SAE		
Event 2 (PT) Categories:	Rash AE leading to study treatment discontinuation, Grade $\geq$ 3 rash		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER/PR negative and HER 2 negative right breast cancer (T2N0M0; histological grade unknown) on Study Day -982.

On Study Day -51, the patient was diagnosed with metastatic disease with ER/PR status unknown and HER2 status not assessed in metastatic tissue. At screening, sites of disease involvement included liver, left kidney (adrenal nodule), bilateral lung (numerous varying-sized nodules in bilateral lungs) and bone (sternoclavicular joint).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Afatinib (cycles unknown) and paclitaxel (3 cycles)	-962	-889
Surgery	Curative	Right partial mastectomy	-863	NA
Cancer therapy	Adjuvant	Cyclophosphamide and epirubicin (4 cycles each)	-850	-787
Radiotherapy	Adjuvant	Right breast (dose: 5000 cGy, 25 fractions)	-632	-596

Radiotherapy	Adjuvant	Breast tumor bed (1000 cGy, 5 fractions)	-595	-589

The patient′s medical history included hypoesthesia, pain in extremity and chronic lymphocytic leukemia. Surgical history included central venous catheterization. Concurrent conditions included hypertension, viral hepatitis carrier, hyperlipidemia, functional gastrointestinal disorder, myofascial pain syndrome and palpitations.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included atorvastatin, olmesartan and amlodipine.

Event 1: Febrile neutropenia

Prior to the event of febrile neutropenia, the most recent dose of paclitaxel was administered on Study Day 15 and ipatasertib (400 mg) on Study Day 17.

On Study Day 9, the patient experienced Grade 2 mucosal inflammation (non-serious, related to paclitaxel). On Study Day 15, she was noted with Grade 2 white blood cell count decreased (non-serious, related to paclitaxel) with WBC count at 2.63 x $10^3/\mu L$ (normal range: 3.54-9.06 $\times$ $10^3/\mu L$).

On Study Day 18, she experienced fever (body temperature 37.8°C), chills and was noted to have Grade 3 hypotension (non-serious, unrelated; blood pressure 63/35 mmHg). A laboratory work-up showed WBC count 0.59 x $10^3/\mu L$ (normal range: 3.54-9.06 x $10^3/\mu L$), neutrophils 31.0 % (normal range: 38.3-71.1 %) and CRP 16.07 mg/dL (normal range not reported). She was diagnosed with Grade 3 febrile neutropenia. Blood culture was performed (returned positive on Study Day 21 for *Clostridium sordellii*). Urine culture was also performed (result not reported) and urine tests revealed albumin/creatinine 80 mg/g (1+). She received treatment with paracetamol for fever, norepinephrine for hypotension, nystatin, triamcinolone and benzydamine for mucosal inflammation and cefepime, filgrastim, metronidazole, oseltamivir for febrile neutropenia. On the same day (Study Day 18), her body temperature returned to normal (body temperature 36.5°C) and also the event of hypotension was considered resolved (blood pressure 107/67 mmHg). On Study Day 19, she was hospitalized for further evaluation. Relevant laboratory values are reported in the table below. On Study Day 20, the event of white blood cell count decreased was considered resolved. She further received treatment with amoxicillin/clavulanic acid for febrile neutropenia and paracetamol for mucosal inflammation. On Study Day 24, the event of febrile neutropenia was considered resolved and the patient was discharged from the hospital. On Study Day 79, the event of mucosal inflammation was considered resolved.

Relevant lab values are listed in the table below:

Study Day	**WBC count** (normal range: 3.54-9.06 $\times$ $10^3/\mu L$)	**Neutrophils** (normal range: 38.3-71.1 %)
Screening	6.58	71.3
15	2.63	64
18	0.59	31.0
21	3.89	53.3
29	7.78	73.3

There was no change in study treatment due to this event.

The Investigator considered febrile neutropenia to be related to paclitaxel and unrelated to ipatasertib.

Event 2: Rash (skin rash)

Prior to the event of rash, the most recent dose of paclitaxel was administered on Study Day 15 and ipatasertib (400 mg) on Study Day 21.

On Study Day 24, the patient experienced non-serious Grade 1 (initial intensity) rash (site unspecified). On Study Day 26, the event of rash worsened to Grade 3. She received treatment with levocetirizine, betamethasone, buclizine, clobetasol, prednisolone and tetracycline for the event. On Study Day 44, the event improved to Grade 1. On Study Day 169, the event of rash was considered resolved.

Due to this event, study treatment with ipatasertib and paclitaxel was permanently discontinued on Study Day 42 with the last dose of paclitaxel administered on Study Day 30 and ipatasertib administered on Study Day 36. The patient entered into the long-term follow-up.

The Investigator considered rash to be unrelated to paclitaxel and related to ipatasertib and concomitant medication (unspecified).

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Vinorelbine and capecitabine (1 cycle)	58	149
Eribulin	169	Ongoing

On Study Day 1047, the patient was permanently discontinued from the study as per physician's decision (long term follow-up terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	9	24	Related	Unrelated
Abdominal pain	1	Non-serious	19	19	Related	Unrelated
Anxiety	2	Non-serious	19	23	Unrelated	Unrelated
Decreased appetite	2	Non-serious	19	24	Unrelated	Unrelated
Electrolyte imbalance	2	Non-serious	21	23	Unrelated	Unrelated
Anemia	2	Non-serious	21	28	Unrelated	Unrelated
Arthralgia	2	Non-serious	21	24	Unrelated	Unrelated
Fatigue	1	Non-serious	22	24	Related	Related
Cough	2	Non-serious	23	30	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304332	Patient number	1072
Demographics:	58-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Schwannoma SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with pathological, ER/PR negative and HER2 negative right breast cancer (T3N1M0), approximately 17 years prior to study entry.

The patient was diagnosed with metastatic disease approximately 12 years prior to study entry with ER /PR negative and HER2 negative disease with soft tissue, breast mussel in metastatic tissue. At screening, sites of disease involvement included right soft tissue (tumor in the thickness of the thoracic muscles), bone (L1-2), right pectoral soft tissue, lymph node broncho pulmonal, bilateral lung and bone (Th2, left caput humeral, left ilium).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Cyclophosphamide, methotrexate and fluorouracil (dose: 3 cycles each)	Approximately 17 years prior to study entry	Approximately 17 years prior to study entry
Surgery	Curative	Right radical mastectomy	Approximately 17 years prior to study entry	–
Cancer therapy	Adjuvant	Doxorubicin (dose: 3 cycles)	Approximately 17 years prior to study entry	Approximately 16 years prior to study entry
Radiotherapy	Adjuvant	Mediastinum (dose: 38 cGy)	Approximately 16 years prior to study entry	Approximately 16 years s prior to study entry
Cancer therapy	Adjuvant	Tamoxifen	Approximately 16 years prior to study entry	Approximately 12 years prior to study entry
Radiotherapy	Metastatic	Mediastinum (dose: 40 cGy)	Approximately 12 years prior to study entry	Approximately 11 years prior to study entry

No medical/surgical history was reported. The patient′s concurrent conditions included hypertension, osteochondrosis, pain in extremity (right arm), hypoesthesia, hepatic cyst, and hemangioma of liver.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included bisoprolol/perindopril, famotidine, ondansetron, diphenhydramine, and tramadol.

Event: Schwannoma (Schwannoma of the spinal canal C5-C6)

Prior to the event of schwannoma, the most recent dose of paclitaxel was administered on Study Day 596 and ipatasertib (300 mg) on Study Day 609.

On Study Day 604, the patient was suspected with schwannoma of the spinal canal at C5-C6. On Study Day 621, the patient was hospitalized. Study Day 623, the patient underwent removal of subtotal intracapsular lesion and extradural cystic neoplasm in right spinal canal and root canal at level of C5-C6, thus lateral stenosis of spinal canal was eliminated. On Study Day 629, the histology confirmed the diagnosis of Grade 3 schwannoma. She received treatment with thioctic acid, serrapeptase, pregabalin and diclofenac/lidocaine for schwannoma. On Study Day 632, the patient was discharged from the hospital. The event of schwannoma remained unresolved at the time of patient′s death (see narrative below).

Due to this event, study treatment with ipatasertib and paclitaxel was interrupted on Study Day 609 and Study Day 708, respectively and was never resumed (see narrative below).

The Investigator considered schwannoma to be unrelated to paclitaxel and ipatasertib and related to concurrent illness (unspecified).

Study treatment with ipatasertib was permanently discontinued due to other reason with the last dose given on Study Day 609.

The patient received on study anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Other collar area on the right (dose: 36 cGy) and bone (lower thoracic spine) (dose: 32 cGy)	651	696

On Study Day 723, a radiographic response assessment showed disease progression with new lesion in left lung (segment 5 and 8).

On Study Day 729, study treatment with paclitaxel was permanently discontinued due to disease progression with the last dose given on Study Day 708. The patient entered into the long-term follow-up.

On Study Day 1080, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Dermatitis allergic	1	Non-serious	2	3	Unrelated	Unrelated
Drug hypersensitivity	1	Non-serious	2	3	Unrelated	Unrelated
Constipation	1	Non-serious	3	6	Unrelated	Unrelated
Alopecia	2	Non-serious	6	175	Unrelated	Related
Diarrhea	2	Non-serious	7	7	Related	Unrelated
Hypersensitivity	1	Non-serious	9	9	Unrelated	Related
Diarrhea	1	Non-serious	11	11	Related	Unrelated
Dermatitis allergic	1	Non-serious	16	16	Unrelated	Related
Diarrhea	1	Non-serious	16	16	Related	Unrelated
Diarrhea	2	Non-serious	17	17	Related	Unrelated
Diarrhea	2	Non-serious	20	20	Related	Unrelated
Hypersensitivity	1	Non-serious	30	30	Unrelated	Related
Hypersensitivity	1	Non-serious	44	44	Unrelated	Related
Hypersensitivity	1	Non-serious	57	58	Unrelated	Related
Fatigue	2	Non-serious	66	68	Unrelated	Unrelated
Neutropenia	2	Non-serious	128	139	Unrelated	Yes
Lipase increased	2	Non-serious	139	167	Related	Unrelated
Neutropenia	2	Non-serious	183	197	Unrelated	Related
Neutropenia	2	Non-serious	211	223	Unrelated	Related
Diarrhea	1	Non-serious	227	227	Yes	Unrelated
Laryngitis	2	Non-serious	284	289	Unrelated	Unrelated
Neutropenia	2	Non-serious	323	337	Unrelated	Related
Neutropenia	2	Non-serious	603	617	Unrelated	Related
Pathological fracture	1	Non-serious	641	Unresolved	Unrelated	Unrelated
Neutropenia	1	Non-serious	715	727	NA	Related

Study Number/CRTN:	CO40016/304878	Patient number	1074
Demographics:	40-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Spinal fracture SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR negative and HER 2 negative right breast cancer (T3N0M0) approximately 7 years prior to study entry.

On Study Day -430, the patient was diagnosed with locally recurrent disease. On Study Day –48, she was diagnosed with metastatic disease with ER/PR negative and HER 2 negative disease in metastatic tissue. At screening, sites of disease involvement included (right adrenal gland and bone (spine C6, L2, L3 and right femur).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neo-adjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	Approximately 7 years prior to study entry	Approximately 7 years prior to study entry
Surgery	Curative	Right lumpectomy	Approximately 7 years prior to study entry	NA
Radiotherapy	Adjuvant	Breast (right chest wall) (dose: 1000 cGy, 4 fractions)	Approximately 7 years prior to study entry	Approximately 7 years prior to study entry
Radiotherapy	Adjuvant	Breast (right chest wall) (dose: 5000 cGy, 25 fractions)	Approximately 7 years prior to study entry	Approximately 6 years prior to study entry
Surgery	Curative	Right simple mastectomy	-379	NA
Surgery	Curative	Right breast (re-excision of surgical margins)	-184	NA
Radiotherapy	Metastatic	Bone (C-6) (dose: 3000 cGy, 10 fractions)	-29	-15

No medical or surgical history was reported. Concurrent condition included bone pain.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included paracetamol/tramadol.

Event: Spinal fracture

Prior to the event of spinal fracture, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 2.

On Study Day 2, the patient experienced Grade 2 back pain (non-serious, unrelated). Treatment with paracetamol/tramadol was maintained and she was receiving pamidronate prophylactically from Study Day 1 for bone metastasis.

On Study Day 3, the patient presented to the emergency room with ongoing bone pain. A spine MRI with enhancement revealed osteolytic bony destruction with soft tissue mass at L 2 and L 3 vertebral bodies with pathological fracture, L 3 with posterior cortical bulging with thickening and contrast enhancement along the posterior longitudinal ligament causing L 3 spinal canal stenosis. There was no involvement in L 2-5 level. She was hospitalized with the diagnosis of Grade 3 spinal fracture. She was started on treatment with morphine, pethidine, codeine/ibuprofen/paracetamol, and pelubiprofen. On Study Day 5, posterior spinal fusion surgery was performed. It was reported that her pain improved and there was no sensory abnormality. She further received treatment with ketorolac, hydromorphone, tapentadol and dexketoprofen for bone/back pain. On Study Day 5, the event of spinal fracture was considered resolved. On Study Day 7, she experienced Grade 1 (initial intensity) left leg paresthesia (non-serious, unrelated). She was started on treatment with gabapentin. On Study Day 8, she was discharged from the hospital. On Study Day 10, the event of back pain improved to Grade 1. On Study Day 81, the events of back pain and paresthesia worsened to Grade 2 and remained unresolved at the time of patient′s death.

The patient received on-study radiotherapy as listed in the table below:

Treatments	Start Day	Stop Day
Radiotherapy to bone (L2-3), dose: 2800 cGy, 4 fractions	29	34

Due to this event, study treatment with ipatasertib was interrupted on Study Day 3 and Cycle 1 Day 8 and Day 15 dose of paclitaxel was interrupted. The next dose of ipatasertib and paclitaxel was given on Study Day 42.

The Investigator considered spinal fracture to be unrelated to ipatasertib and paclitaxel and related to disease under study.

On Study Day 97, a radiographic assessment showed disease progression.

On Study Day 99, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel and ipatasertib given on Study Day 85 and Study Day 89, respectively. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Radiotherapy to bone (hip): 3000 cGy, 10 fractions	110	125
Capecitabine (1 cycle)	145	158
Radiotherapy to whole brain: 2100 cGy, 7 fractions	162	170

On Study Day 183, the patient died due to disease progression. No autopsy was performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Fatigue	1	Non-serious	4	Unresolved	Related	Related
Alopecia	2	Non-serious	11	Unresolved	Unrelated	Related
Pruritus	1	Non-serious	32	37	Unrelated	Unrelated
Decreased appetite	1	Non-serious	44	Unresolved	Related	Related
Diarrhea	1	Non-serious	53	55	Related	Related
Myalgia	1	Non-serious	57	59	Unrelated	Related
Diarrhea	1	Non-serious	58	62	Related	Related
Dysuria	1	Non-serious	59	Unresolved	Unrelated	Unrelated
Constipation	1	Non-serious	77	78	Unrelated	Unrelated
Constipation	1	Non-serious	90	Unresolved	Unrelated	Unrelated
Nausea	1	Non-serious	90	Unresolved	Unrelated	Unrelated

Study Number/CRTN:	CO40016/314283	Patient number	1087
Demographics:	60-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Hyperthermia SAE		
Event 3 (PT) Category:	Hypotension AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER 2 negative, right breast cancer (T3N3M0) on Study Day −698.

On Study Day −27, the patient was diagnosed with metastatic disease with ER/PR status unknown and HER 2 status not assessed in metastatic tissue. At screening, sites of disease involvement included lung (right upper lobe and multiple lung tissue metastases on both sides) and lymph node (retrocaval, preaortic, aortic window and bifurcation node).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	-556	-493
Surgery	Curative	Right radical mastectomy	-447	NA
Cancer therapy	Adjuvant	Doxorubicin and docetaxel (2 cycles each)	-424	-393
Radiotherapy	Adjuvant	Postoperative scar area of the right breast and lymph outflow area (dose: 42 cGy, 16 fractions)	-258	-238

No medical or surgical history was reported. Concurrent conditions included hypertension, pyelonephritis chronic, obesity, angina pectoris, endometrial hyperplasia, uterine leiomyoma, goitre and thrombocytopenia.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medication ongoing at Study Day 1 was reported.

On Study Day 8, the patient experienced Grade 1 diarrhea (non-serious, related) for which she received treatment with loperamide (total daily dose: 12 mg). On Study Day 10, diarrhea was considered resolved.

Event 1: Diarrhea
Event 2: Hyperthermia
Event 3: Hypotension

Prior to the events of diarrhea, hyperthermia and hypotension, the most recent dose of paclitaxel was administered on Study Day 15 and ipatasertib (400 mg) on Study Day 21.

On Study Day 24, the patient experienced non-serious Grade 2 diarrhea. Treatment with loperamide was maintained. On Study Day 27, she presented with diarrhea up to 6-7 times per day and Grade 2 hyperthermia (body temperature 39 C) with severe weakness and was hospitalized on the following day (Study Day 28). On the same day (Study Day 28), she was noted with non-serious Grade 3 hypotension (blood pressure value not reported). She received unspecified IV fluids, paracetamol for hyperthermia and unspecified medication for hypotension. On Study Day 29, the events of hyperthermia and hypotension were considered resolved. On Study Day 51, she was discharged from the hospital. On Study Day 57, the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of diarrhea	4	PO	1	8
Diarrhea	12	PO	8	10
Prophylaxis of diarrhea	4	PO	10	81

There was no change in the study treatment due to the event of hyperthermia.

Due to the event of diarrhea, there was no change in study treatment with paclitaxel; however, due to the event of hypotension, Cycle 2 of paclitaxel was interrupted, and the next dose was given on Study Day 67 (Cycle 3 Day 1) at a reduced dose of 65 mg/m^2.

Due to the events of diarrhea and hypotension, study treatment with ipatasertib was permanently discontinued with the last dose of ipatasertib administered on Study Day 21.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

The Investigator considered hyperthermia and hypotension to be related to ipatasertib and paclitaxel.

On Study Day 112, a radiographic response assessment showed disease progression with new lesions in bilateral paracaval and paraaortic lymph nodes.

On Study Day 115, study treatment with paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 106. The patient entered into the long-term follow-up.

On Study Day 205, the patient died due to disease progression. No autopsy was performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nausea	2	Non-serious	2	3	Related	Related
Arthralgia	2	Non-serious	2	Unresolved	Related	Related
Hyperglycemia	1	Non-serious	7	10	Related	Unrelated
Thrombocytopenia	2	Non-serious	7	8	Related	Related
Bone pain	2	Non-serious	10	Unresolved	Related	Related
Asthenia	3	Non-serious	17	Unresolved	Related	Related
Oliguria	1	Non-serious	17	42	Related	Unrelated
Peripheral sensory neuropathy	1	Non-serious	28	Unresolved	Unrelated	Related
Cough	1	Non-serious	28	71	Unrelated	Unrelated
Dyspnea	1	Non-serious	28	Unresolved	Unrelated	Unrelated
Bone pain	2	Non-serious	69	83	Unrelated	Related
Cystitis	2	Non-serious	85	91	Unrelated	Unrelated
Nausea	2	Non-serious	101	119	Not Applicable	Related
Bone pain	2	Non-serious	101	112	Not Applicable	Related
Vomiting	1	Non-serious	112	113	Not Applicable	Related

Study Number/CRTN:	CO40016/318263	Patient number	1093
Demographics:	45-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Abdominal pain SAE		
Event 2 (PT) Category:	Nausea SAE		
Event 3 (PT) Category:	Vomiting SAE		
Event 4 (PT) Category:	Fatigue SAE		
Event 5 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		
Event 6 (PT) Categories:	Peritonitis SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR negative and HER 2 equivocal left breast cancer (T1N0M0), approximately 4 years and 3 months prior to study entry.

On Study Day −78, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included bilateral upper lung.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left partial mastectomy	Approximately 4 years and 2 months prior to study entry	NA
Cancer therapy	Adjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	Approximately 4 years and 2 months prior to study entry	Approximately 3 years and 11 months prior to study entry

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Adjuvant	Whole breast (dose: 5040 cGy, 28 fractions)	Approximately 3 years and 11 months prior to study entry	Approximately 3 years and 10 months prior to study entry
Radiotherapy	Adjuvant	Breast (dose: 900 cGy, 5 fractions)	Approximately 3 years and 10 months prior to study entry	Approximately 3 years and 9 months prior to study entry

The patient′s medical history included cholelithiasis. Surgical history included cholecystectomy. Concurrent conditions included major depression, insomnia and anxiety.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included escitalopram, zolpidem and alprazolam. She started receiving loperamide (total daily dose: 4 mg) for diarrhea from Study Day 1.

Event 1: Abdominal pain
Event 2: Nausea
Event 3: Vomiting

Prior to the event of abdominal pain, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 4.

On Study Day 5, the patient experienced Grade 1 diarrhea (non-serious, related to ipatasertib) and Grade 3 abdominal pain. Treatment with loperamide was maintained for diarrhea and she was started on tiropramide for abdominal pain. On Study Day 12, she experienced Grade 2 nausea and vomiting (both non-serious, related to paclitaxel). She received treatment with lorazepam.

Prior to the serious events of nausea and vomiting, the most recent dose of paclitaxel was administered on Study Day 8 and ipatasertib (400 mg) on Study Day 13.

On Study Day 14, the event of diarrhea was considered resolved; however, the events of nausea and vomiting worsened to Grade 3.

On Study Day 15, the patient was hospitalized due to abdominal pain, nausea and vomiting. Her abdominal X-ray was reported to be normal on Study Days 15-16. It was further reported that she had diarrhea only on the day of hospitalization. She received treatment with granisetron, tramadol and tiropramide and was kept NPO until Study Day 16. She also received prophylactic treatment with pantoprazole for abdomen discomfort and nutritional support. On Study Day 18, she resumed oral intake. On Study Day 19, a repeat abdominal X-ray was normal. The events

of abdominal pain, nausea and vomiting gradually improved and on Study Day 20, the event of abdominal pain was reported to have improved to Grade 1. On the same day (Study Day 20), the events of abdominal pain, vomiting and nausea were considered resolved and the patient was discharged from the hospital.

Due to the events of nausea and vomiting, there was no change in study treatment with ipatasertib; however; due to the event of abdominal pain, ipatasertib was interrupted from Study Day 13 and the next dose was given on Study Day 20 at a reduced dose of 300 mg.

Due to the events of abdominal pain, nausea and vomiting, Cycle 1 Day 15 of paclitaxel was delayed and was given on Study Day 20.

The Investigator considered abdominal pain to be unrelated to paclitaxel and related to ipatasertib and other causes (unspecified).

The Investigator considered nausea and vomiting to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 62, the patient experienced Grade 1 diarrhea (non-serious, related to ipatasertib). On Study Day 71, she was noted with Grade 1 weight decreased (non-serious, unrelated) and Grade 1 anemia (non-serious, related to paclitaxel; hemoglobin: 8.5 mg/dL; normal range: 12-15.3 mg/dL). She received packed red blood cells transfusion for anemia and loperamide for diarrhea. No treatment was reported for the event of weight decreased.

Event 4: Fatigue

Prior to the event of fatigue, the most recent dose of paclitaxel was administered on Study Day 71 and ipatasertib (300 mg) on Study Day 78.

On Study Day 85, the patient was hospitalized with Grade 3 fatigue. A laboratory work-up showed WBC count 19440, absolute neutrophil count 15660, sodium 124, potassium 3.61, chloride 84, lactate dehydrogenase 294, erythrocyte sedimentation rate 58 and C-reactive protein 6.26 (units and normal ranges not reported). An influenza virus A and B antigen test was negative. She received nutritional support, hydration with normal saline and cefepime prophylactically for fever. On Study Day 86, a repeat laboratory work-up showed, sodium 129 and potassium 4.09 and chloride 94 (units and normal ranges not reported). She further received intravenous fluids (dextrose/sodium chloride/potassium chloride). On Study Day 85, anemia was considered resolved. On Study Day 89, the event of fatigue improved to Grade 1 and was considered resolved. On the same day (Study Day 89), the patient was discharged from the hospital. On Study Day 144, the event of diarrhea was considered resolved. The event of weight decreased was considered as resolving at the time of last report.

Due to the event of fatigue, Cycle 4 of study treatment with paclitaxel and ipatasertib was delayed and was given on Study Day 89.

The Investigator considered fatigue to be related to ipatasertib and paclitaxel.

On Study Day 12, the patient was diagnosed with Grade 1 neuropathy peripheral (signs/symptoms and diagnostic details not reported; non-serious, related to paclitaxel). She received treatment with tapentadol and pregabalin for neuropathy peripheral.

Event 5: Neuropathy peripheral
Event 6: Peritonitis

Prior to the event of Grade 3 neuropathy peripheral, the most recent dose of paclitaxel was administered on Study Day 120 and ipatasertib (300 mg) on Study Day 126.

On Study Day 127, the ongoing event of neuropathy peripheral worsened to Grade 3 (symptoms not reported). Treatment with tapentadol and pregabalin was maintained.

Prior to the event of peritonitis, the most recent dose of paclitaxel was administered on Study Day 120 and ipatasertib (300 mg) on Study Day 143.

On Study Day 144, the patient presented to the hospital with abdominal pain. An abdomen-pelvis CT scan showed Grade 3 peritonitis leading to hospitalization. On the following day (Study Day 145), small bowel resection and segmental biopsy were performed. Pathological results revealed ulcer and perforation with diffuse acute serositis, marked submucosal and sub-serosal edema and transmural ischemic changes. She received treatment with cefepime, piperacillin/tazobactam and ciprofloxacin and also received calcium chloride/gluconate sodium/magnesium chloride/sodium acetate/sodium chloride, norepinephrine, albumin human, chlorphenamine, calcium chloride dihydrate/potassium chloride/sodium chloride/sodium lactate, glucose/potassium chloride/sodium chloride, pethidine, acetylcysteine and pantoprazole prophylactically. On Study Day 155, the event of peritonitis was considered resolved and she was discharged from the hospital. On Study Day 168, the event of neuropathy peripheral was considered resolved.

Due to the event of neuropathy peripheral, there was no change in study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 120.

Due to the event of peritonitis, study treatment with ipatasertib was permanently discontinued with the last dose given on Study Day 144. The patient entered into the long-term follow-up.

The Investigator considered neuropathy peripheral to be related to paclitaxel and unrelated to ipatasertib.

The Investigator considered peritonitis to be unrelated to ipatasertib and paclitaxel and related to other unspecified causes.

On Study Day 972, the patient was permanently discontinued from the study as long term follow up was suspended due to final clinical cut-off date.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Decreased appetite	1	Non-serious	29	120	Unrelated	Related
Nausea	2	Non-serious	44	55	Unrelated	Related
Asthenia	2	Non-serious	50	55	Unrelated	Unrelated
Pyrexia	1	Non-serious	53	54	Unrelated	Unrelated
Headache	1	Non-serious	53	54	Unrelated	Unrelated
Nausea	2	Non-serious	57	144	Unrelated	Related
Abdominal pain	1	Non-serious	87	87	Related	Unrelated
Anemia	2	Non-serious	89	120	Unrelated	Related
Asthenia	2	Non-serious	168	Unresolved	Related	NA

Study Number/CRTN:	CO40016/ 305247	Patient number	1095
Demographics:	59-year-old female (Race unknown)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Diarrhea Grade $\geq$ 3 diarrhea		
Event 3 (PT) Category:	Glaucoma SAE		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER 2 negative right breast cancer (T1cN0M0), approximately 6 years prior to study entry.

On Study Day −63 the patient was diagnosed with metastatic disease with ER/PR and HER 2 negative in metastatic tissue. following right lymph node biopsy. At screening, sites of disease involvement included lymph node (right retro pectoral adenopathy), mediastinum and bone (multiple).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Epirubicin, fluorouracil and cyclophosphamide (3 cycles each)	Approximately 6 years prior to study entry.	Approximately 6 years prior to study entry.
Cancer therapy	Adjuvant	Docetaxel (3 cycles each)	Approximately 6 years prior to study entry	Approximately 6 years prior to study entry
Cancer therapy	Adjuvant	Letrozole	Approximately 5 years 9 months prior to study entry	−262

The patient′s medical history included rash papular. Surgical history included appendicectomy and cataract operation. Concurrent conditions included hypothyroidism, dyslipidemia, Arnold-Chiari malformation, hypoacusis, deafness, glaucoma, atopy, arthralgia, axillary pain and vision blurred.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included levothyroxine, ezetimibe, hypromellose and dorzolamide/timolol.

Event 1: Peripheral sensory neuropathy (lower limbs peripheral sensory neuropathy)

Prior to the event of peripheral sensory neuropathy, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 29.

On Study Day 30, the patient was diagnosed with non-serious Grade 1 (initial intensity) lower limbs peripheral sensory neuropathy (presenting signs and symptoms and diagnostic details not reported). On Study Day 80, she experienced Grade 1 peripheral sensory neuropathy of fingers (non-serious, related). On Study Day 156, the event of lower limbs peripheral sensory neuropathy worsened to Grade 2 and to Grade 3 on Study Day 167. She received treatment with pregabalin. The event of peripheral sensory neuropathy (lower limbs and fingers) remained unresolved at the time of study discontinuation.

Due to the event of peripheral sensory neuropathy (lower limbs), there was no change in study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose administered on Study Day 154.

The Investigator considered peripheral sensory neuropathy to be related to paclitaxel and unrelated to ipatasertib.

Prior to the event of Grade 3 diarrhea, the patient experienced multiple episodes of diarrhea as listed in the table below. Treatment for the events included loperamide.

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	6	6	Related	Related
Diarrhea	1	Non-serious	9	30	Related	Related
Diarrhea	1	Non-serious	73	76	Related	Related

Event 2: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 91.

On Study Day 88, the patient experienced Grade 2 right upper abdominal pain (non-serious, unrelated). No treatment was reported for this event. On Study Day 92, she experienced non-serious Grade 1 (initial intensity) diarrhea. On Study Day 121, the event of diarrhea worsened to Grade 3 (6-8 stools per day). She received treatment with loperamide and racecadotril for the event. On Study Day 120, the event of upper abdominal pain was considered resolved. On Study Day 127, the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of diarrhea	2	PO	1	1
Diarrhea	2	PO	6	6
Diarrhea	2	PO	15	15
Diarrhea	2	PO	29	29
Diarrhea	2	PO	57	57
Prophylaxis of diarrhea	2	PO	64	64
Prophylaxis of diarrhea	2	PO	67	67
Prophylaxis of diarrhea	2	PO	70	71
Diarrhea	2	PO	73	74

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of diarrhea	2	PO	78	78
Prophylaxis of diarrhea	2	PO	84	84
Prophylaxis of diarrhea	2	PO	88	88
Prophylaxis of diarrhea	4	PO	91	91
Diarrhea	6	PO	94	94
Diarrhea	4	PO	95	95
Diarrhea	6	PO	96	96
Diarrhea	2	PO	97	97
Diarrhea	6	PO	98	98
Diarrhea	4	PO	101	102
Diarrhea	2	PO	103	104
Diarrhea	4	PO	105	105
Diarrhea	2	PO	112	112
Diarrhea	4	PO	117	117
Diarrhea	6	PO	118	119
Diarrhea	10	PO	120	120
Diarrhea	12	PO	121	125
Diarrhea	8	PO	126	126
Diarrhea	4	PO	127	127
Prophylaxis of diarrhea	2	PO	133	133
Diarrhea	2	PO	140	140
Diarrhea	4	PO	144	144
Diarrhea	2	PO	147	147
Diarrhea	4	PO	150	150
Diarrhea	2	PO	152	152
Diarrhea	2	PO	154	154
Prophylaxis of diarrhea	2	PO	156	158
Prophylaxis of diarrhea	6	PO	159	159
Prophylaxis of diarrhea	2	PO	160	160
Diarrhea	2	PO	213	283
Diarrhea	2	PO	220	221
Diarrhea	2	PO	235	236
Diarrhea	2	PO	238	240
Diarrhea	2	PO	242	244
Diarrhea	4	PO	245	245
Diarrhea	2	PO	246	246
Diarrhea	2	PO	253	253

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	257	257
Diarrhea	4	PO	258	258
Diarrhea	2	PO	260	261
Diarrhea	2	PO	264	264
Diarrhea	2	PO	269	270
Diarrhea	2	PO	273	274
Diarrhea	2	PO	328	328
Diarrhea	2	PO	331	332
Diarrhea	2	PO	382	382
Diarrhea	2	PO	386	387
Diarrhea	2	PO	400	400

Due to the event of diarrhea, study treatment with ipatasertib was interrupted on Study Day 126 and Cycle 5 Day 15 dose of paclitaxel was delayed. The next dose of paclitaxel and ipatasertib (at a reduced dose of 300 mg) was given on Study Day 133.

The Investigator considered diarrhea to be related to ipatasertib and paclitaxel.

Event 3: Glaucoma (Worsening of glaucoma)

Prior to the event of glaucoma, the most recent dose of ipatasertib (400 mg) was administered on Study Day 189.

On Study Day 198, the patient′s pre-existing condition of glaucoma worsened to Grade 3 (considered serious as causing persistent or significant disability). Treatment with hypromellose and dorzolamide/timolol was maintained and she additionally received treatment with acetazolamide, bimatoprost, flurbiprofen, fluorometholone and hyaluronate. The event of glaucoma remained unresolved at the time of study discontinuation.

Due to this event, study treatment with ipatasertib was interrupted on Study Day 198 and the next dose was given on Study Day 210.

The Investigator considered glaucoma to be unrelated to ipatasertib and paclitaxel and related to concurrent illness.

On Study Day 404, a radiographic response assessment showed disease progression with new lesions in unspecified bilateral bone. On the same day (Study Day 404), study treatment with ipatasertib was permanently discontinued due to disease progression with last dose of ipatasertib administered on Study Day 404. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine (unknown cycles)	415	816
Radiotherapy to left iliac wing and left hip cup (dose: 2000 cGy, 5 fractions)	463	469
Radiotherapy to whole brain (dose: 3000 cGy, 10 fractions)	889	902

On Study Day 972, the patient was permanently discontinued from the study as per the physician's decision (long term follow-up terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nausea	1	Non-serious	2	37	Related	Related
Rhinitis allergic	1	Non-serious	3	126	Unrelated	Unrelated
Spinal pain	1	Non-serious	9	15	Unrelated	Unrelated
Alopecia	1	Non-serious	12	Unresolved	Unrelated	Related
Loss of consciousness	3	Non-serious	20	20	Unrelated	Unrelated
Fatigue	1	Non-serious	26	97	Unrelated	Related
Axillary pain	1	Non-serious	30	155	Unrelated	Unrelated
Vertigo	1	Non-serious	34	34	Unrelated	Related
Epistaxis	1	Non-serious	45	45	Related	Related
Hematoma	1	Non-serious	61	88	Unrelated	Unrelated
Nausea	1	Non-serious	84	87	Related	Related
Epistaxis	1	Non-serious	86	120	Related	Related
Weight decreased	1	Non-serious	91	Unresolved	Unrelated	Unrelated
Gastroesophageal reflux disease	1	Non-serious	95	134	Unrelated	Unrelated
Fatigue	3	Non-serious	98	101	Unrelated	Related
Pneumonia	1	Non-serious	117	133	Unrelated	Unrelated
Stomatitis	1	Non-serious	120	134	Unrelated	Related
Vomiting	1	Non-serious	124	134	Related	Related
Dermatitis diaper	1	Non-serious	127	132	Unrelated	Unrelated
Tongue edema	1	Non-serious	127	139	Unrelated	Unrelated
Diarrhea	1	Non-serious	140	155	Related	Related
Myalgia	1	Non-serious	140	281	Related	Related
Edema peripheral	1	Non-serious	169	281	Unrelated	Unrelated
Headache	1	Non-serious	208	281	Unrelated	Unrelated
Diarrhea	1	Non-serious	211	283	Related	Related
Sciatica (left T3)	2	Non-serious	231	Unresolved	Unrelated	Unrelated
Headache	1	Non-serious	350	392	Unrelated	Unrelated
Sciatica (right)	1	Non-serious	388	Unresolved	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304777	Patient number	1106
Demographics:	63-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Macular edema SAE		
Event 2 (PT) Category:	Epiretinal membrane SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with lobular, moderately differentiated, ER/PR and HER 2 negative right breast cancer (T3N1MX), on Study Day –817.

On Study Day –243, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included right chest wall and left lung.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Epirubicin and cyclophosphamide (4 cycles each)	–798	–735
Cancer therapy	Neoadjuvant	Docetaxel (4 cycles)	–714	–651
Surgery	Curative	Right simple mastectomy, bilateral sentinel lymph node biopsy and unspecified surgery of left breast	–629	NA
Radiotherapy	Adjuvant	Right chest wall, 60X and right supraclavicular region, 6X (dose: 5000 cGy, 25 fractions)	–587	–551
Radiotherapy	Adjuvant	Right breast tumor bed, 6X (dose: 1000 cGy, 5 fractions)	–550	–544
Radiotherapy	Adjuvant	Left breast, 6X (dose: 5000 cGy, 25 fractions)	–528	–493
Radiotherapy	Adjuvant	Left breast tumor bed, 6X (dose: 1000 cGy, 5 fractions)	–490	–486

No medical or surgical history was reported. Concurrent conditions included macular edema and epiretinal membrane (both in right eye) and senile cataract (both eyes).

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications were ongoing at Study Day 1.

Event 1: Macular edema (Epiretinal membrane and macula edema OD)
Event 2: Epiretinal membrane (Epiretinal membrane and macula edema OD)

Prior to the events of macular edema and epiretinal membrane, the most recent dose of paclitaxel was administered on Study Day 99 and ipatasertib (400 mg) on Study Day 100.

On Study Day 101, the patient presented with blurred vision in the right eye. Her visual acuity in right eye was 6/10 cc and in left eye was 6/6 cc. Slit lamp exam revealed mild bilateral conjunctivitis and worsening of pre-existing condition of macular edema and epiretinal membrane to Grade 3, leading to hospitalization. She received treatment with dexamethasone, acetazolamide, diazepam, and triamcinolone; however, she was still experiencing blurry vision from her right eye. She was explained the risk and benefits of vitrectomy, membrane peeling and intravitreal administration of dexamethasone following which she underwent pars plana vitrectomy and was injected with dexamethasone intravitreal implant in the right eye. On Study Day 103, the events of macular edema and epiretinal membrane were considered resolved and she was discharged from the hospital on atropine, chloramphenicol, fluorometholone, gentamicin, timolol maleate and paracetamol.

There was no change in study treatment due to these events.

The Investigator considered macular edema and epiretinal membrane to be unrelated to paclitaxel and ipatasertib and related to concurrent illness.

On Study Day 275, an overall response assessment showed disease progression.

On Study Day 281, study treatment with paclitaxel and ipatasertib was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 267 and ipatasertib on Study Day 273. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine	337	Ongoing

On Study Day 931, the patient was permanently discontinued from the study as per physician's decision (long term follow-up terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Neutropenia	2	Non-serious	8	10	Unrelated	Related
Neutropenia	2	Non-serious	43	44	Unrelated	Related
Neutropenia	3	Non-serious	59	64	Unrelated	Related
Diarrhea	1	Non-serious	120	281	Related	Unrelated
Constipation	1	Non-serious	120	295	Unrelated	Unrelated
Thermal burn	1	Non-serious	131	141	Unrelated	Unrelated
Urinary tract infection	1	Non-serious	143	155	Unrelated	Unrelated
Neutropenia	2	Non-serious	155	157	Unrelated	Related
Neutropenia	2	Non-serious	239	246	Unrelated	Related

Study Number/CRTN:	CO40016/318099	Patient number	1113
Demographics:	80-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Pulmonary embolism SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER/PR and HER 2 negative left breast cancer (TXNXM0; histological grade unknown) on Study Day −664 following left modified radical mastectomy performed on the same day.

On Study Day −35, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included right mediastinum, pretracheal, precranial and subcarinal lymph nodes.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Paclitaxel (12 cycles)	−641	−564
Cancer therapy	Adjuvant	Cyclophosphamide and doxorubicin (4 cycles each)	−543	−480
Radiotherapy	Adjuvant	Left breast (dose: 50 cGy, 12 fractions)	−455	−423

No medical or surgical history was reported. Concurrent condition included hypertension.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included lansoprazole and perindopril.

Event: Pulmonary embolism

Prior to the event of pulmonary embolism, the most recent dose of paclitaxel was administered on Study Day 79 and ipatasertib (400 mg) on Study Day 84.

On Study Day 90, the patient was hospitalized with pain, dyspnea, edema and cough. A pulmonary CT-angiography was performed which showed hypodense filling defects in bilateral pulmonary artery and segmented branches. Subsequently, she was diagnosed with Grade 3 pulmonary embolism. She started receiving hydration and treatment with bemiparin, paracetamol and enoxaparin. On the following day (on Study Day 91), her laboratory work-up showed hemoglobin 10.5 g/dL (normal range: 11.2-15.7 g/dL) and she was diagnosed with Grade 2 anemia (initial intensity: Grade 1), (non-serious, related). She received red blood cells transfusion for anemia. On Study Day 93, venous doppler ultrasound of upper and lower extremity was normal except 34 x 13 mm cyst in left popliteal fossa. She further received treatment with methylprednisolone, furosemide and butamirate. On Study Day 96, she was discharged from the hospital. On Study Day 132, the event of pulmonary embolism was considered resolved. The event of anemia remained unresolved at the time of patient's death.

Due to the event of pulmonary embolism, study treatment with ipatasertib and paclitaxel was permanently discontinued on Study Day 123 with the last dose of paclitaxel administered on Study Day 79 and ipatasertib on Study Day 84. The patient entered into the long-term follow-up.

The Investigator considered pulmonary embolism, to be related to ipatasertib and paclitaxel.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine (2 cycles)	124	Ongoing

On Study Day 249, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Hyponatremia	3	Non-serious	1	8	NA	NA
Constipation	1	Non-serious	3	5	Unrelated	Unrelated
Hyponatremia	1	Non-serious	8	36	Unrelated	Unrelated
Diarrhea	1	Non-serious	9	16	Related	Related
Vomiting	1	Non-serious	12	12	Related	Related
Hyponatremia	1	Non-serious	43	91	Unrelated	Unrelated
Dyspepsia	1	Non-serious	44	123	Related	Related
Hypokalemia	1	Non-serious	50	64	Unrelated	Unrelated
Alopecia	1	Non-serious	51	79	Unrelated	Related
Diarrhea	2	Non-serious	84	86	Related	Related
Vomiting	2	Non-serious	84	86	Related	Related
Hyperglycemia	1	Non-serious	91	101	Unrelated	Unrelated
Hyponatremia	3	Non-serious	91	102	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304776	Patient number	1123
Demographics:	55-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Large intestine perforation SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER 2 negative, metastatic left breast cancer (TXNXM1) on Study Day –22.

At screening, sites of disease involvement included left breast, hypodense lesion in segment IV of liver, multiple bone metastases, mild bilateral pleural effusion and left axillary lymphadenopathy.

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent conditions included peripheral swelling, tumor ulceration, cancer pain and decreased appetite.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included diclofenac, morphine, paracetamol, metronidazole, tranexamic acid, and metoclopramide.

On Study Day 11, the patient experienced Grade 3 nausea (initial intensity: Grade 2), Grade 2 vomiting (both non-serious, related) and was also noted with Grade 1 weight decreased to 44.5 kg (screening body weight: 48 kg; non-serious, related). She received treatment with granisetron for nausea and vomiting. No treatment was given for the event of weight decreased.

Event: Large intestine perforation (perforation of the colon, splenic flexure)

Prior to the event of large intestine perforation, the most recent dose of paclitaxel was administered on Study Day 21 and ipatasertib (400 mg) on Study Day 26.

On Study Day 27, the patient experienced Grade 2 diarrhea (non-serious, related to ipatasertib) and pain in right lower abdomen. She received treatment with loperamide (total daily dose: 8 mg) for this event. After few hours, the pain was cramping and distended.

On Study Day 28, she presented to the emergency room with mild abdominal distension and pain. Her vital signs were noted to be normal. Physical examination revealed hard abdomen with rebound pain and diffuse tenderness. A laboratory work-up also showed Grade 2 electrolyte imbalance (non-serious, related) with sodium 126 mmol/L (normal range: 136-145 mmol/L) and potassium 3.4 mmol/L (normal range: 3.5-5.1 mmol/L). It also showed WBC 17.09 K/μL (normal range: 3.54-9.06 x 10^3/μL), lactic acid 5.78 mmol/L, HSCRP (high-sensitivity C-reactive protein) 20.36 mg/dL (normal ranges not reported). It was reported that she had poor appetite recently.

On the same day (Study Day 28), her vital signs progressed with heart rate 108 bpm, respiratory rate 20 breaths/min and blood pressure 115/65 mmHg. A CT-scan showed colon perforation and pneumoperitoneum and she was diagnosed with Grade 4 large intestine perforation (initial intensity: Grade 3). Emergency surgery was suggested with high risk of complication. Surgical findings revealed necrotic changes of transverse colon at splenic flexure with large perforation, multiple perforations along transverse colon and proximal distal colon.

She underwent loop ileostomy and further received treatment with tramadol, fentanyl citrate, alprazolam, cefalexin, diosmectite, pantoprazole, imipenem, piperacillin, anidulafungin, dexmedetomidine, vitamins (unspecified), norepinephrine, sodium bicarbonate, albumin and thiamine. On Study Day 74, the event of electrolyte imbalance was considered resolved. On Study Day 79, the events of nausea, vomiting, large intestine perforation and diarrhea were considered resolved and she was discharged from the hospital. The event of weight decreased remained unresolved at the time of study discontinuation.

Due to this event, study treatment with ipatasertib and paclitaxel was permanently discontinued on Study Day 41 with the last dose of paclitaxel given on Study Day 21 and ipatasertib on Study Day 27. On the same day (Study Day 41), the patient was also discontinued from the study due to this event.

The Investigator considered large intestine perforation to be related to ipatasertib, paclitaxel, concurrent illness, and disease under study.

Other AE experienced by the patient during the study:

Event	**Most extreme grade**	**Serious/ Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Depression	1	Non-serious	20	Unresolved	Unrelated	Unrelated

Study Number/CRTN:	CO40016/307254	Patient number	1134
Demographics:	55-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Nausea SAE		

The patient was randomized on Study Day -3.

The patient was diagnosed with ductal, poorly differentiated, ER/PR and HER2 negative, metastatic left breast cancer (T3N3bM1), on Study Day -48. At screening, sites of disease involvement included left breast, liver, left axillary lymph node and bone (multiple).

No past cancer treatment was reported.

No medical or surgical history was reported. Concurrent condition included pain.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medication ongoing at Study Day 1 was reported.

Event: Nausea

Prior to the event of nausea, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 1.

On Study Day 1, the patient experienced Grade 1 (initial intensity) nausea and Grade 2 decreased appetite (non-serious, related). On Study Day 7, she experienced Grade 1 (initial intensity) diarrhea (once per day) (non-serious, related to ipatasertib). On Study Day 8, she received Cycle 1 Day 8 dose of paclitaxel as scheduled. The same day (Study Day 8), she experienced Grade 2 vomiting (non-serious, related) and the event of diarrhea worsened to Grade 2. On Study Day 10, she visited the emergency department due to persistent diarrhea, nausea and vomiting. On Study Day 11, nausea worsened to Grade 3, and she was hospitalized. She was diagnosed with Grade 2 enteritis infectious (non-serious, unrelated; diagnostic details not reported). She received treatment with loperamide, metoclopramide, potassium chloride/sodium chloride/sodium lactate, calcium chloride dihydrate/potassium chloride/sodium chloride/sodium lactate, vitamin B1/vitamin B6/vitamin B12, piperacillin sodium/tazobactam and domperidone. On Study Day 12, the event of vomiting was considered resolved. On Study Day 15, the event of diarrhea improved to Grade 1. On Study Day 16, the event of nausea improved to Grade 1 and the event of enteritis infectious was considered resolved. On Study Day 18, the events of nausea, decreased appetite and diarrhea were considered resolved and she was discharged from the hospital.

Due to the event of nausea, Cycle 1 Day 15 of paclitaxel was delayed and was given on Study Day 22; study treatment with ipatasertib was initially interrupted on Study Day 11 and was resumed at reduced dose of 300 mg on Study Day 22.

The Investigator considered nausea to be related to ipatasertib and paclitaxel.

On Study Day 107, a radiographic response assessment showed disease progression. Subsequently, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel and ipatasertib administered on Study Day 92 and Study Day 106, respectively. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Eribulin	120	198
Cyclophosphamide and doxorubicin (3 cycles each)	218	267
Radiotherapy to left breast (45 cGy, 15 fractions)	285	306
Gimeracil/oteracil/tegafur (1 cycle)	312	343

On Study Day 356, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Fatigue	1	Non-serious	1	113	Related	Related
Constipation	1	Non-serious	3	5	Unrelated	Unrelated
White blood cell count decreased	2	Non-serious	11	22	Unrelated	Related
Neutrophil count decreased	3	Non-serious	11	22	Unrelated	Related
Headache	1	Non-serious	11	11	Unrelated	Unrelated
Alopecia	1	Non-serious	22	Unresolved	Unrelated	Related
Abdominal pain upper	1	Non-serious	29	113	Related	Unrelated
Pruritus	1	Non-serious	29	44	Unrelated	Unrelated
White blood cell count decreased	2	Non-serious	29	44	Unrelated	Related
Weight decreased	1	Non-serious	29	120	Related	Related
Nausea	2	Non-serious	30	64	Related	Related
Decreased appetite	2	Non-serious	32	64	Related	Related
Vomiting	1	Non-serious	32	34	Related	Related
Product dose omission issue	—	Non-serious	32	32	—	—
Diarrhea	1	Non-serious	33	44	Related	Unrelated
Neutrophil count decreased	2	Non-serious	36	44	Unrelated	Related
Product dose omission issue	—	Non-serious	36	36	—	—
Vomiting	1	Non-serious	44	45	Related	Related
Product dose omission issue	—	Non-serious	46	46	—	—
Abdominal pain	3	Non-serious	53	55	Unrelated	Unrelated
Headache	1	Non-serious	54	64	Unrelated	Unrelated

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Aspartate aminotransferase increased	1	Non-serious	58	72	Unrelated	Related
Alanine aminotransferase increased	2	Non-serious	58	120	Unrelated	Related
White blood cell count decreased	2	Non-serious	58	64	Unrelated	Related
Neutrophil count decreased	2	Non-serious	58	64	Unrelated	Related
Diarrhea	1	Non-serious	69	70	Related	Unrelated
Pruritus	1	Non-serious	79	113	Unrelated	Related
Aspartate aminotransferase increased	1	Non-serious	92	99	Unrelated	Related
Neutrophil count decreased	3	Non-serious	99	113	Unrelated	Related
White blood cell count decreased	2	Non-serious	99	113	Unrelated	Related
Aspartate aminotransferase increased	1	Non-serious	113	Unresolved	Unrelated	Related
Pyrexia	1	Non-serious	128	134	Unrelated	Unrelated
Neutrophil count decreased	4	Non-serious	128	155	Unrelated	Unrelated
Alanine aminotransferase increased	1	Non-serious	128	Unresolved	Unrelated	Unrelated
White blood cell count decreased	3	Non-serious	128	141	Unrelated	Unrelated

Study Number/CRTN:	CO40016/306641	Patient number	1139
Demographics:	37-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Pulmonary embolism SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER 2 negative right breast cancer (T1aN0MX) on Study Day –427.

On Study Day −60, the patient was diagnosed with locally recurrent, metastatic disease with ER/PR and HER2 negative disease in recurrent/metastatic tissue. At screening, sites of disease involvement included right lobe of liver, upper right lobe of lung and mediastinum lymph node.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neo-adjuvant	Doxorubicin	−426	−365
Surgery	Curative	Right radical mastectomy	−325	NA

No medical/surgical history or concurrent conditions were reported.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included methylprednisolone.

Event: Pulmonary embolism

Prior to the event of pulmonary embolism, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 43.

On Study Day 57, the patient presented with severe dyspnea, cough, and chest pain. Arterial blood gas analysis showed low peripheral capillary oxygen saturation (value not reported). A thorax CT-scan showed Grade 4 pulmonary embolism**,** leading to hospitalization. She received treatment with tinzaparin, dexamethasone, hydrocortisone, sulfamethoxazole/trimethoprim, alprazolam, theophylline, furosemide, metoclopramide, fentanyl, and morphine. No information regarding discharge was reported. The event remained unresolved at the time of patient′s death (see narrative below).

There was no change in study treatment due to this event.

The Investigator considered pulmonary embolism to be unrelated to ipatasertib and paclitaxel and related to disease under study.

On Study Day 57, an overall response assessment showed disease progression with multiple new lesions in brain, bilateral liver (section II, III, V, VII), upper lobe of left adrenal gland and bilateral lung.

On Study Day 57, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of ipatasertib and paclitaxel given on Study Day 43. The patient entered into the long-term follow-up.

On Study Day 76, the patient died due to disease progression. An autopsy was not performed.

No other AEs were experienced by the patient during the study.

Study Number/CRTN:	CO40016/304623	Patient number	1142
Demographics:	72-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea Grade $\geq$ 3 diarrhea		
Event 2 (PT) Categories:	Diarrhea SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER 2 negative right breast cancer (T1cN1aMx), approximately 5 years prior to study entry.

On Study Day −62, the patient was diagnosed with locally recurrent unresectable disease with ER/PR and HER 2-negative disease in recurrent tissue. At screening, sites of disease involvement included right supraclavicular lymph node and right breast.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right partial mastectomy	Approximately 5 years prior to study entry	NA
Cancer therapy	Adjuvant	Doxorubicin (4 cycles), cyclophosphamide (4 cycles) and paclitaxel (11 cycles)	Approximately 5 years prior to study entry	Approximately 4 years and 9 months prior to study entry
Radiotherapy	Adjuvant	Right breast tumor bed (dose: 90 cGy, 20 fractions)	Approximately 4 years and 7 months prior to study entry	Approximately 4 years and 6 months prior to study entry

The patient′s medical history included borrelia infection. Concurrent conditions included chronic obstructive pulmonary disease, cataract, hypertension, hypothyroidism, hypercholesterolemia, rheumatoid arthritis, stress urinary incontinence, osteoporosis, peripheral sensory neuropathy, and procedural pain of right axilla.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. The same day, she also started loperamide prophylactically (total daily dose: 4 mg) for diarrhea.

Concomitant medications ongoing at Study Day 1 included curcumin/lecithin/*Mangifera indica*/*Piper nigrum*/pyridoxine/resveratrol/riboflavin, magnesium aspartate/potassium aspartate, aclidinium/formoterol, fenoterol/ipratropium, theophylline, levothyroxine, telmisartan, rosuvastatin, amlodipine, hydroxychloroquine, nebivolol, erdosteine, calcium carbonate, ibandronic acid, magnesium lactate, potassium chloride and gabapentin.

Event 1: Diarrhea (Grade 3)
Event 2: Diarrhea (Grade 2)

Prior to the first episode of diarrhea, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 3.

On Study Day 4, the patient experienced non-serious Grade 1 (initial intensity) diarrhea which on the same day, worsened to Grade 2. On the following day, (Study Day 5), the event of diarrhea worsened to Grade 3 (9 stools in a day). Treatment with loperamide was maintained and she received treatment with *Lactobacillus* helveticus. On Study Day 6, the patient experienced Grade 1 vomiting (non-serious, related to ipatasertib). She received treatment with thiethylperazine for vomiting. On Study Day 37, she experienced Grade 2 pyrexia (non-serious, related, body temperature not reported). On Study Day 41, the first episode of diarrhea was considered resolved.

Prior to the second episode of diarrhea, the most recent dose of paclitaxel was administered on Study Day 35 and ipatasertib (300 mg) on Study Day 41.

On Study Day 42, the patient experienced fever (body temperature not reported) and second episode of Grade 2 diarrhea. Laboratory work-up showed hyponatremia with sodium 129 mmol/L (normal range: 137-145 mmol/L), hypokalemia with potassium 3 mmol/L (normal range: 3.5-5.1 mmol/L), and hypomagnesemia with magnesium 0.65 mmol/L (normal range: 0.76-1.12 mmol/L). She was diagnosed with gastrointestinal toxicity. Subsequently, she was hospitalized. During hospitalization, her body temperature spiked to 38.3°C and she was also noted with tachycardia (heart rate not reported), hypotension 90/60 mmHg and oxygen saturation of 56%. She received treatment with paracetamol for fever, calcium chloride dihydrate/magnesium chloride hexahydrate/malic acid/potassium chloride/sodium acetate trihydrate/sodium chloride, potassium chloride, sodium chloride, magnesium sulfate and codeine for diarrhea. Grade changes for the event of diarrhea are mentioned in the table below. On Study Day 46, blood and urine cultures were positive for *Klebsiella pneumoniae* and she was diagnosed with Grade 2 pneumonia klebsiella (non-serious, unrelated). She received treatment with trimethoprim/sulfamethoxazole. On Study Day 48, the event of pneumonia klebsiella was considered resolved. On Study Day 49, the event of pyrexia was considered resolved. On the same day (Study Day 49), she was noted with Grade 3 hyperkalemia (initial intensity Grade 1; non-serious, unrelated). On Study Day 55, the event of hyperkalemia

resolved without any treatment. On Study Day 59, the patient was discharged from the hospital. The events vomiting and second episode of diarrhea remained unresolved at the time of patient's death (see narrative below).

Diarrhea grade changes:

Study Day	Diarrhea grade changes
4	2
5	3
6	2
10	1
20	2
22	2
23	1
30	1

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of Diarrhea	4	PO	1	3
Diarrhea	6	PO	4	4
Diarrhea	12	PO	5	5
Diarrhea	10	PO	6	9
Diarrhea	6	PO	9	41
Diarrhea	6	PO	10	11
Diarrhea	4	PO	12	12
Diarrhea	2	PO	13	13
Diarrhea	4	PO	16	16
Diarrhea	2	PO	17	17
Diarrhea	6	PO	18	18
Diarrhea	8	PO	19	20
Diarrhea	10	PO	21	21
Diarrhea	12	PO	22	22
Diarrhea	8	PO	23	23
Diarrhea	4	PO	24	24
Diarrhea	2	PO	25	27
Diarrhea	4	PO	28	28
Diarrhea	2	PO	29	31
Diarrhea	4	PO	32	33
Diarrhea	2	PO	34	34
Diarrhea	8	PO	35	35
Diarrhea	2	PO	36	36
Diarrhea	8	PO	37	37
Diarrhea	10	PO	38	38
Diarrhea	8	PO	39	39
Diarrhea	6	PO	40	41
Diarrhea	4	PO	42	42
Diarrhea	10	PO	43	43
Diarrhea	4	PO	44	44

Study Day	Sodium (normal range: 137-145 mmol/L)	Potassium (normal range: 3.5-5.1 mmol/L)	Magnesium (normal range: 0.76-1.12 mmol/L)
Screening	141	4.1	0.85
42	129	3	0.65
44	137	3.8	–
49	139	5.4	–
51	139	6.1	–
53	132	6.3	–
55	130	5.1	0.98
56	131	4.9	0.92

Due to the non-serious event of diarrhea (Grade 3), Cycle 1 Day 8 dose of paclitaxel was not administered and study treatment with ipatasertib was interrupted on Study Day 8. The next dose of paclitaxel (at a reduced of 65 mg/m^2) and ipatasertib (at a reduced of 300 mg) was given on Study Day 16.

Due to the second episode of diarrhea, study treatment with ipatasertib and paclitaxel was permanently discontinued with the last dose of paclitaxel given on Study Day 35 and ipatasertib on Study Day 41. The patient entered into the long-term follow-up.

The Investigator considered first episode of diarrhea (Grade 3) to be related to ipatasertib and unrelated to paclitaxel.

The Investigator considered second episode of diarrhea (Grade 2) to be related to ipatasertib and paclitaxel.

On Study Day 176, a radiographic response assessment showed disease progression.

The patient received follow-up anti-cancer therapy as listed in the table below:

Treatments	Start Day	Stop Day
Radiotherapy to right supraclavicular (dose: 2 cGy, 1 fraction)	217	217

On Study Day 221, the patient died due to pulmonary embolism (further details not reported). Underlying cancer was the contributing factor. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nausea	1	Non-serious	2	184	Related	Related
Vomiting	1	Non-serious	2	2	Related	Unrelated
Renal failure	2	Non-serious	8	15	Related	Related
Dyspnea	2	Non-serious	13	Unresolved	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Oropharyngeal pain	1	Non-serious	21	184	Related	Related
Lipase increased	3	Non-serious	56	72	Related	Unrelated

Study Number/CRTN:	CO40016/305120	Patient number	1154
Demographics:	65-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Diarrhea SAE, AE leading to study treatment discontinuation, Grade $\geq$ 3 diarrhea		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER 2 negative left breast cancer (T2N3aM1) on Study Day −89.

On Study Day −70, metastatic disease was confirmed with ER/PR and HER 2-negative disease in metastatic tissue. At screening, sites of disease involvement included left breast, lymph nodes (left axillary and midline mediastinal), right upper lobe of lung, segment VII of liver and L1 vertebral bone.

No past cancer treatments were reported.

The patient′s medical history included hemolytic uremic syndrome, anxiety, and acute kidney injury. Concurrent conditions included irritable bowel syndrome, hypertension, gastroesophageal reflux disease, asthma, hypersensitivity, and blood pressure measurement.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included amitriptyline, perindopril, mebeverine, esomeprazole, loratadine, atenolol, antacids and beclometasone.

On Study Day 2, the patient experienced Grade 1 intermittent abdominal pain upper (non-serious, related). Treatment with mebeverine was maintained.

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 2.

On Study Day 3, the patient experienced Grade 1 (initial intensity) diarrhea. Treatment with loperamide and codeine was started. On Study Day 25, she experienced Grade 1 abdominal pain (non-serious, unrelated). She received treatment with trimethoprim. On Study Day 31, the event of abdominal pain was considered resolved.

On Study Day 38, the event of diarrhea worsened to Grade 3. The dose of loperamide was increased to 8 mg. Grade changes for diarrhea and loperamide dosing details are listed in the table below. The patient experienced 6 episodes of watery diarrhea on Study Day 65, for which she had taken codeine (4 doses) and loperamide (3 doses) On Study Day 66, she complained of 3 more episodes of diarrhea. She was advised to stop ipatasertib the same day. On the following day, (Study Day 67), the patient presented to the emergency room and reported 4 episodes of diarrhea. She was hospitalized. A laboratory work-up showed sodium 132 mmol/L, and urea 4.9 mmol/L (normal range not reported). Treatment with loperamide and codeine was maintained and was given single dose of IV antibiotic (unspecified) and 2 liters of IV hydration following which diarrhea improved. On Study Day 68, frequency of diarrhea decreased to 2 episodes. The same day (Study Day 68), the patient was discharged from the hospital. Diarrhea frequency further reduced to one on the following day (Study Day 69). On Study Day 70, the event of diarrhea was considered resolved with sequelae. At the time of patient′s death, the event of abdominal pain upper remained unresolved.

Diarrhea grade changes:

Study Day	Diarrhea grade changes
12	2
16	1
38	3
42	1
65	2
66	3
70	1

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	3	37
Diarrhea	8	PO	38	38
Diarrhea	2	PO	39	Ongoing

Due to this event, there was no change in study treatment with paclitaxel; however, study treatment with ipatasertib was initially interrupted on Study Day 14 and was resumed on Study Day 17 at a reduced dose of 300 mg. Ipatasertib was further interrupted from

Study Days 38-49 and Study Days 66-77. Later, ipatasertib was permanently discontinued with the last dose given on Study Day 65.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 282, an overall response assessment showed disease progression with new lesion in right superior hilar lymph node.

On Study Day 307, study treatment with paclitaxel was permanently discontinued due to disease progression with the last dose given on Study Day 295. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Vinorelbine (6 cycles)	406	456
Epirubicin and cyclophosphamide (1 cycle each)	491	491

On Study Day 526, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious/ Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Neutropenia	3	Non-serious	7	519	Unrelated	Related
Blood creatinine increased	1	Non-serious	28	Unresolved	Unrelated	Related
Oropharyngeal pain	1	Non-serious	36	38	Unrelated	Related
Nail infection	1	Non-serious	118	Unresolved	Unrelated	Unrelated
Hemorrhoids	1	Non-serious	141	Unresolved	Unrelated	Related
Upper-airway cough syndrome	1	Non-serious	164	175	Unrelated	Unrelated
Non-cardiac chest pain	2	Non-serious	203	Resolving	Unrelated	Unrelated
Oropharyngeal pain	1	Non-serious	231	237	Unrelated	Unrelated
Hyponatremia	1	Non-serious	238	239	Unrelated	Unrelated
Periodontal disease	1	Non-serious	246	Unresolved	Unrelated	Unrelated
Chest pain	2	Non-serious	253	261	Unrelated	Unrelated
Peripheral neuropathy	2	Non-serious	279	Unresolved	Unrelated	Related
Hordeolum	1	Non-serious	288	Unresolved	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304638	Patient number	1160
Demographics:	69-year-old White male		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Vomiting SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with poorly differentiated, ER/PR and HER 2-negative, locally advanced unresectable left breast cancer (T2N0M1; histological subtype not otherwise specified), on Study Day −139 following left breast biopsy performed on the same day.

On Study Day −86, metastatic disease was confirmed with ER/PR and HER 2-negative disease in metastatic tissue. At screening, sites of disease involvement included in left breast and right lung.

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent conditions included hypertonia, type 2 diabetes mellitus, benign prostatic hyperplasia, and anemia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received his first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included metformin, linagliptin, enalapril/hydrochlorothiazide, enalaprilat, amlodipine, nebivolol, doxazosin and tamsulosin.

Event: Vomiting

Prior to the event of vomiting, the most recent dose of paclitaxel and ipatasertib (400 mg) on Study Day 99.

On Study Day 100, the patient experienced Grade 4 vomiting (more than 10 episodes within 24 hours; considered medically significant) and Grade 2 anuria (non-serious, unrelated). Due to profuse vomiting, he received parenteral fluid supplementation and symptomatic therapy. He also received treatment with ondansetron and electrolytes (unspecified). On the following day (Study Day 101), the events of vomiting and anuria were considered resolved.

Due to this event, there was no change in study treatment with paclitaxel; however, study treatment with ipatasertib was interrupted on Study Day 101 and the next dose was given on Study Day 102.

The Investigator considered vomiting to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 113, the patient withdrew consent from the study with the last dose of paclitaxel given on Study Day 99 and ipatasertib on Study Day 103.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious/ Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Back pain	1	Non-serious	9	13	Unrelated	Unrelated
Anemia	3	Non-serious	84	98	Unrelated	Related

Study Number/CRTN:	CO40016/304336	Patient number	1178
Demographics:	61-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Tumor hemorrhage SAE		
Event 2 (PT) Category:	Tumor hemorrhage SAE		

The patient was randomized on Study Day 1.

The patient was diagnosed with ductal, moderately differentiated, ER/PR and HER 2-negative metastatic right breast cancer (T4N1M1) on Study Day –48. At screening, sites of disease involvement included right breast, right superior lobe of the lung, liver segment IV and lymph nodes (bilateral axillary, right subclavian and jugular).

No past cancer treatments were reported.

No medical or surgical history were reported. Concurrent conditions included tumor pain, hypertension, hyperthyroidism, anxiety, and anemia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included gabapentin, thiamazole, ramipril, sertraline, alprazolam, folic acid, and ferrous sulfate.

On Study Day 92, the patient was noted with worsening of her pre-existing condition of anemia to Grade 3 (non-serious, unrelated; hemoglobin value not reported). The cause of anemia was unknown. Treatment with folic acid and ferrous sulfate was maintained and she further received blood transfusion therapy for the event anemia. On Study Day 101, the event of anemia (hemoglobin 9.7 g/dL; normal range: 12-16 g/dL) was considered resolved.

Event 1: Tumor hemorrhage (Tumor bleeding)

Prior to the event of tumor hemorrhage, the most recent dose of paclitaxel was administered on Study Day 169 and ipatasertib (400 mg) on Study Day 173.

On Study Day 174, the patient was noted with anemia (hemoglobin 7.7 g/dL, normal range not reported) and was diagnosed with Grade 3 tumor hemorrhage (diagnostic details and relevant laboratory work-up not reported), leading to hospitalization. It was reported that the anemia was caused by tumor bleeding. She received blood transfusion therapy. On Study Day 176, the event of tumor hemorrhage was considered resolved. On Study Day 177, she was discharged from the hospital.

There was no change in study treatment due to this event.

The Investigator considered tumor hemorrhage to be unrelated to ipatasertib and paclitaxel and related to concurrent illness.

Event 2: Tumor hemorrhage (Tumor bleeding)

Prior to the event of tumor hemorrhage, the most recent dose of paclitaxel was administered on Study Day 309 and ipatasertib (400 mg) on Study Day 312.

On Study Day 313, the patient was noted with anemia (hemoglobin 8.4 g/dL, normal range not reported) and was diagnosed with Grade 2 tumor hemorrhage (diagnostic details and relevant laboratory work-up not reported), leading to hospitalization on Study Day 314. It was reported that the anemia was caused by tumor bleeding. She received blood transfusion therapy.

The patient received on-study anti-cancer therapy as listed in table below:

Treatment	Start Day	Stop Day
Radiotherapy to breast (primitive tumor, dose: unknown cGy, 14 fractions)	317	336

Due to the event of tumor hemorrhage, study treatment with paclitaxel was interrupted after Study Day 309 and ipatasertib after Study Day 312 and later permanently discontinued.

On Study Day 336, the patient was discontinued from the study treatment as the patient had to receive the radiotherapy treatment with the last dose of paclitaxel was administered on Study Day 309 and ipatasertib on Study Day 312. The patient entered into the long-term follow-up.

On Study Day 355, the event of tumor hemorrhage was considered resolved and she was discharged from the hospital.

The Investigator considered tumor hemorrhage to be unrelated to ipatasertib and paclitaxel and related to disease under study.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Cisplatin (4 cycles) and fluorouracil (5 cycles)	492	NA
Pegylated liposomal doxorubicin hydrochloride	667	NA

On Study Day 778, the patient was permanently discontinued from the study as per the physician's decision (LTFU terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	13	13	Related	Unrelated
Accidental overdose	1	Non-serious	22	22	Unrelated	Unrelated
Fall	2	Non-serious	36	36	Unrelated	Unrelated
Alopecia	1	Non-serious	65	Unresolved	Unrelated	Related
Thrombocytosis	1	Non-serious	92	127	Unrelated	Unrelated
Pyrexia	2	Non-serious	93	94	Unrelated	Unrelated
Diarrhea	1	Non-serious	104	183	Related	Unrelated
Diarrhea	1	Non-serious	239	336	Related	Unrelated
Hypercholesterolemia	3	Non-serious	308	Unresolved	Unrelated	Unrelated

Study Number/CRTN:	CO40016/318136	Patient number	1180
Demographics:	65-year-old white female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Febrile neutropenia SAE		
Event 2 (PT) Category:	Anemia SAE		
Event 3 (PT) Category:	Urinary tract infection SAE		
Event 4 (PT) Category:	Pneumonia SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR negative, right breast cancer (T3N0M0; HER 2-receptor not assessed), approximately 4 years and 6 months prior to study entry.

On Study Day −88, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included bilateral liver (segment VII) and bilateral cranium bone.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Cyclophosphamide (6 cycles)	Approximately 4 years and 4 months prior to study entry	Approximately 4 years prior to study entry
Radiotherapy	Metastatic	Left femur bone (dose: 2000 cGy, 3 fractions)	−74	−70

No medical or surgical history was reported. Concurrent conditions included hypertension and pain.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included metoprolol.

Event 1: Febrile neutropenia
Event 2: Anemia
Event 3: Urinary tract infection

Prior to the event of febrile neutropenia, the most recent dose of paclitaxel was administered on Study Day 36 and ipatasertib (400 mg) on Study Day 40.

On Study Day 41, the patient experienced fatigue and her body was temperature 38°C. Laboratory work-up showed WBC count 1.19 $\times$ $10^3/\mu L$ (normal range: 4-10 $\times$ $10^3/\mu L$), neutrophil count 0.5, lymphocyte count 0.6 (units and normal range not reported) and increased CRP levels (value not reported). She was diagnosed with Grade 4 febrile neutropenia, leading to hospitalization. It was reported that the fatigue was secondary to febrile neutropenia. MRI of brain was performed since she was extremely prone to sleep; however, no metastasis was found. She received treatment with paracetamol, filgrastim and cefoperazone/sulbactam, following which her CRP level decreased. On Study Day 46, the event of febrile neutropenia was considered resolved and she was discharged from the hospital.

Due to the event of febrile neutropenia, Cycle 2 Day 15 dose of paclitaxel was not administered and ipatasertib was interrupted on Study Day 42.

Prior to the events of anemia and urinary tract infection, the most recent dose of paclitaxel was given on Study Day 36 and ipatasertib (400 mg) on Study Day 41.

On Study Day 59, the patient presented to the emergency room with fever (body temperature: 37.4°C) and excessive fatigue. Laboratory work-up showed hemoglobin 79 g/L (normal range: 115-155 g/L), WBC count 9.17 $\times$ $10^3/\mu L$, neutrophils 83.7% (normal range: 45-78%), lymphocytes 10.7% (normal range: 10-48%) and CRP 100 (units and normal range not reported). Urinalysis showed blood (+1). She was diagnosed with Grade 3 anemia and Grade 3 urinary tract infection, leading to hospitalization. She received blood transfusion treatment therapy for anemia and penicillin for urinary tract infection. On Study Day 61, the event of anemia was considered resolved. On Study Day 64, the event of urinary tract infection was considered resolved and she was discharged from the hospital.

Due to the events of anemia and urinary tract infection, study treatment with paclitaxel and ipatasertib remained interrupted. The next dose of paclitaxel at a reduced dose of 65 mg/m^2 and ipatasertib at a reduced dose of 300 mg due to the event of febrile neutropenia was given on Study Day 62.

Relevant lab values are listed in the table below:

Study Day	WBC count (normal range: 4-10 × $10^3/\mu L$)	Neutrophils (normal range: 45-78%)	Lymphocytes (normal range: 10-48%)	Hemoglobin (normal range: 130-175 g/L)	Body temperature (°C)
Screening	4.94	69.5	17.6	118	36.6
35	6.66	85.9	6.9	112	—
36	—	—	—	—	36.7
41	1.19	0.5[a]	0.6[a]	100	38
42	2.34	1.57[a]	0.59[a]	100	36.8
					36.8
					37.7
43	—	2.59[a]	—	—	36.7
					36.8
					36.9
44	12.82	85	14.4	103	—
45	15.22	88.2	11.4	95	—
46	18.24	87.3	12	104	—
59	9.17	83.7	10.7	79	37.4
61	10.9	9.06[a]	11.6	106	36.7
62	—	9.88[a]	—	109	36.8
					36.9
63	4.16	74.8	21.1	108	36.7
64	4.2	84.3	12.6	110	—

[a]units and normal range not reported

The Investigator considered febrile neutropenia to be unrelated to ipatasertib and related to paclitaxel.

The Investigator considered anemia to be unrelated to ipatasertib and related to paclitaxel and other unspecified causes.

The Investigator considered urinary tract infection to be unrelated to ipatasertib and paclitaxel and related to other unspecified causes.

Event 4: Pneumonia (lung infection)

Prior to the event of pneumonia, the most recent dose of paclitaxel was given on Study Day 62 and ipatasertib (300 mg) on Study Day 71.

On Study Day 72, the patient experienced fever (body temperature 38°C). Her C-reactive protein level was high (value not reported). She was diagnosed with Grade 3 pneumonia (diagnostic details not reported; cause unknown). On Study Day 74, she was hospitalized. She received treatment with ofloxacin. No information regarding discharge was reported. The event of pneumonia remained unresolved at the time of study discontinuation.

Due to the event of pneumonia, study treatment with paclitaxel was interrupted after Study Day 62 and ipatasertib after Study Day 73.

On Study Day 74, the patient withdrew consent from the study with the last of paclitaxel given on Study Day 62 and ipatasertib on Study Day 73.

The Investigator considered pneumonia to be unrelated to ipatasertib and paclitaxel related to other unspecified causes.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	2	Non-serious	5	73	Related	Related
Nausea	1	Non-serious	6	Unresolved	Unrelated	Related
Lipedema	1	Non-serious	42	42	Unrelated	Unrelated
Neuropathy peripheral	2	Non-serious	57	Unresolved	Unrelated	Related

Study Number/CRTN:	CO40016/304331	Patient number	1190
Demographics:	61-year-old white female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Tumor necrosis SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ER/PR and HER 2 negative right breast cancer (T3N1M0; histological confirmation not done), approximately 13 years prior to study entry following unspecified surgery of breast.

On Study Day −54, the patient was diagnosed with metastatic disease with ER/PR and HER 2-negative disease in recurrent/metastatic tissue. At screening, sites of disease involvement included lungs (right segment III and left segment II), lymph node (left axillary, left supraclavicular and multiple axillary), left adrenal gland and soft tissue (skin fold in left breast).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neo-adjuvant	Methotrexate, fluorouracil and cyclophosphamide (2 cycles each)	Approximately 13 years prior to study entry	Approximately 13 years prior to study entry
Surgery	Curative	Right radical mastectomy	Approximately 13 years prior to study entry	NA
Cancer therapy	Adjuvant	Cyclophosphamide, fluorouracil and doxorubicin (3 cycles each)	Approximately 13 years prior to study entry	Approximately 12 years prior to study entry
Radiotherapy	Adjuvant	Right side lymph efflux (dose: 4000 cGy)	Approximately 13 years prior to study entry	Approximately 12 years prior to study entry

No medical or surgical history was reported. Concurrent conditions included essential hypertension, obstructive pancreatitis, spinal disorder (thoracic-lumbar spine), type 2 diabetes mellitus, lipoma (right kidney) and Grade 2 obesity.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included amlodipine/valsartan and metformin.

Event: Tumor necrosis

Prior to the event of tumor necrosis, the most recent dose of paclitaxel was administered on Study Day 99 and ipatasertib (400 mg) on Study Day 105.

On Study Day 106, the patient experienced fever (body temperature upto 39°C) with shivering. Her laboratory work-up showed WBC count 15.88×10^9/L, and absolute neutrophil count 13.93×10^9/L (normal ranges not reported). An ultrasound of axillary area showed 5.5×4.5 cm formation with unclear contours with multiple hypo and echogenic elements probably caused by tumor lysis. She was diagnosed with Grade 2 (initial intensity) tumor necrosis. She received treatment with paracetamol, calcium chloride/magnesium chloride/potassium chloride/sodium chloride/sodium lactate, cefoperazone/sulbactam, metronidazole, calcium chloride/magnesium chloride/potassium chloride/sodium chloride/sodium lactate/sorbitol. On the following day (Study Day 107), her condition worsened with increasing fatigue, increase in body temperature and worsening of tumor necrosis to Grade 4. Subsequently, she was hospitalized. On Study Day 110, 100-120 mL of seropurulent fluid was drained. She further received treatment with levofloxacin, pantoprazole and ketoprofen. On Study Day 113, the event of tumor necrosis was considered resolved and she was discharged from the hospital.

The patient received on-study anti-cancer therapy as listed in table below:

Treatment	Start Day	Stop Day
Palliative surgery of left lymph node	113	NA

Due to this event, Cycle 4 Day 22 dose of paclitaxel was interrupted and ipatasertib was interrupted on Study Day 106. The next dose of ipatasertib and paclitaxel was given on Study Day 127.

The Investigator considered tumor necrosis to be related to ipatasertib and paclitaxel.

On Study Day 218, a radiographic response assessment showed disease progression.

On the same day (Study Day 218), study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel and ipatasertib given on Study Day 211 and Study Day 217 respectively. The patient entered into the long-term follow-up.

On Study Day 257, the patient died due to disease progression. An autopsy was performed (details not reported).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Dyslipidemia	1	Non-serious	57	Unresolved	Related	Unrelated
Blood alkaline phosphatase increased	1	Non-serious	64	71	Unrelated	Unrelated
Bronchitis	2	Non-serious	83	92	Unrelated	Unrelated
Anemia	2	Non-serious	85	Unresolved	Unrelated	Related
Hyperglycemia	2	Non-serious	106	Unresolved	Related	Unrelated
Postoperative wound complication	2	Non-serious	113	134	Unrelated	Unrelated
Respiratory tract infection viral	2	Non-serious	153	157	Unrelated	Unrelated
Pyrexia	2	Non-serious	201	205	Unrelated	Unrelated

Study Number/CRTN:	CO40016/318137	Patient number	1199
Demographics:	77-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Categories:	Diarrhea SAE, AE leading to study treatment discontinuation, Grade $\geq$ 3 diarrhea		
Event 2 (PT) Category:	Atrial fibrillation SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed locally advanced unresectable ductal, moderately differentiated, ER/PR and HER 2 negative left breast cancer (T3N3cM0), on Study Day −68. At screening, sites of disease involvement included right breast (upper posterior lobe), left breast and left axilla lymph node.

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent conditions included hypertension, obesity and cardiac valve disease.

At screening, the patient′s ECOG Performance Status was 1. ECG at screening was normal. ECHO showed LVEF 60%.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. The same day, she also started loperamide prophylactically (total daily dose: 4 mg) for diarrhea.

Concomitant medications ongoing at Study Day 1 included hydrochlorothiazide/losartan and metoprolol.

On Study Day 94, the patient experienced Grade 2 decreased appetite (non-serious, related to ipatasertib).

Event 1: Diarrhea
Event 2: Atrial fibrillation

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 92 and ipatasertib (400 mg) on Study Day 97.

On Study Day 98, the patient experienced Grade 3 diarrhea with poor oral intake.

Prior to the event of atrial fibrillation, the most recent dose of paclitaxel was administered on Study Day 92 and ipatasertib (400 mg) on Study Day 98.

On the following day (Study Day 99), a laboratory work-up showed sodium 134 mmol/L (normal range: 136-146 mmol/L), potassium 3.4 mmol/L (normal range: 3.5-5.1 mmol/L), calcium 8.2 mg/dL (normal range: 8.8-10.6 mg/dL), magnesium 1.1 mg/dL (normal range: 1.9-2.5 mg/dL), lactate dehydrogenase 258 U/L (normal range: 0-247 U/L) and serum creatinine 1.56 mg/dL (normal range: 0.51-0.95 mg/dL). Urine and stool test were also performed (results not reported). On the same day (Study Day 99), she was hospitalized. She received treatment with metoclopramide, ciprofloxacin, methylprednisolone, potassium bicarbonate/potassium citrate monohydrate and pantoprazole.

On Study Day 105, an ECG showed Grade 1 atrial fibrillation, leading to prolongation of hospitalization. An echocardiography showed left ventricular hypertrophy, left atrial enlargement with normal left ventricular ejection fraction. She was also noted with mild mitral regurgitation but no prolapses, moderate tricuspid valve regurgitation with pulmonary hypertension to be 45 mmHg. She received treatment with metoprolol and enoxaparin. On the same day (Study Day 105), the event of diarrhea was considered resolved. On Study Day 109, she was discharged from the hospital. On Study Day 125, the event of decreased appetite was considered resolved. The event of atrial fibrillation was considered resolving at the time of patient's death (see narrative below).

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of Diarrhea	4	PO	1	4
Diarrhea	4	PO	37	39
Diarrhea	6	PO	45	45
Diarrhea	2	PO	76	76
Diarrhea	4	PO	77	77

Study Day	Sodium (normal range: 136-146 mmol/L)	Potassium (normal range: 3.5-5.1 mmol/L)	Calcium (normal range: 8.8-10.6 mg/dL)	Magnesium (normal range: 1.9-2.5 mg/dL)	Creatinine (normal range: 0.51-0.95 mg/dL)	LDH (normal range: 0-247 U/L)
Screening	135	3.6	9.5	1.8	1	162
99	134	3.4	8.2	1.1	1.56	258
100	135	3	7.5	–	1.45	–
102	139	2.5	7.3	–	1	–
103	140	3.4	7.3	–	0.96	–
104	140	4.1	7.8	–	0.87	–
105	139	3.6	8.2	–	0.89	–

Due to the event of diarrhea and atrial fibrillation, study treatment with paclitaxel was interrupted after Study Day 92 and was later permanently discontinued due to the event of diarrhea with the last dose given on Study Day 92. Study treatment with ipatasertib was interrupted on Study Day 99 and the next dose was given on Study Day 128 at a reduced dose of 300 mg.

The Investigator considered diarrhea and atrial fibrillation to be unrelated to paclitaxel and related to ipatasertib and disease under study.

On Study Day 310, study treatment with ipatasertib was permanently discontinued as per the physician’s decision (the patient's blinded information was shared with the team and the decision to continue an alternative treatment method for the patient was made by PI) with the last dose of ipatasertib administered on Study Day 309. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine (unknown cycles)	317	Ongoing

On Study Day 343, an overall response assessment showed disease progression.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Left breast lymph node resection	443	NA

On Study Day 715, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	1	Non-serious	2	21	Unrelated	Unrelated
Diarrhea	1	Non-serious	37	39	Unrelated	Related
Asthenia	1	Non-serious	39	44	Unrelated	Related
Headache	1	Non-serious	39	44	Unrelated	Unrelated
Nausea	2	Non-serious	45	85	Related	Related
Renal impairment	2	Non-serious	45	48	Related	Unrelated
Blood creatinine increased	1	Non-serious	53	70	Related	Unrelated
Pyrexia	1	Non-serious	53	57	Unrelated	Unrelated
Cystitis	1	Non-serious	53	57	Unrelated	Unrelated
Cough	1	Non-serious	57	85	Unrelated	Unrelated
Blood magnesium decreased	1	Non-serious	57	268	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	57	Resolving	Unrelated	Related
Anemia	2	Non-serious	99	104	Unrelated	Related
Proteinuria	2	Non-serious	99	150	Unrelated	Unrelated
Neuropathy peripheral	3	Non-serious	99	128	Unrelated	Related
Neutropenia	2	Non-serious	102	106	Unrelated	Related
Hypokalemia	1	Non-serious	102	103	Unrelated	Related
Anemia	2	Non-serious	107	108	Unrelated	Related
Mucosal inflammation	1	Non-serious	109	113	Unrelated	Unrelated
Pneumonia	2	Non-serious	247	254	Unrelated	Unrelated

Study Number/CRTN:	CO40016/307262	Patient number	1201
Demographics:	45-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Categories:	Erythema multiforme SAE, AE leading to study treatment discontinuation		
Event 2 (PT) Categories:	Hypersensitivity SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER/PR and HER 2 negative left breast cancer, (T2N0M0; histological grade unknown), approximately 12 years prior to study entry.

The patient was diagnosed with metastatic disease with ER/PR and HER 2-negative approximately 10 years prior to study entry. At screening, sites of disease involvement included in lungs (right lower lobe, multiple lesions bilaterally), multiple lesions bilateral unspecified bone and right mediastinum lymph node.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant*	Goserelin	Approximately 12 years prior to study entry.	Approximately 11 years prior to study entry.
Cancer therapy	Neo-Adjuvant	Paclitaxel and capecitabine	Approximately 12 years prior to study entry.	Approximately 12 years prior to study entry.
Surgery	Curative	Left simple mastectomy and axillary dissection	Approximately 12 years prior to study entry.	NA
Cancer therapy	Adjuvant	Cyclophosphamide and pirarubicin	Approximately 12 years prior to study entry.	Approximately 11 years prior to study entry.
Radiotherapy	Adjuvant	Breast (dose: 5000 cGy, 25 fractions)	Approximately 11 years prior to study entry.	Approximately 11 years prior to study entry.
Cancer therapy	Metastatic	Goserelin	Approximately 10 years prior to study entry.	Approximately 9 years prior to study entry.
Cancer therapy	Metastatic	Tamoxifen	Approximately 10 years prior to study entry.	Approximately 9 years prior to study entry.
Cancer therapy	Metastatic	Medroxyprogesterone	Approximately 9 years prior to study entry	Approximately 9 years prior to study entry
Surgery	—	Resection of metastatic lesion in lung	Approximately 9 years prior to study entry	NA
Cancer therapy	Adjuvant^	Capecitabine	Approximately 9 years prior to study entry	Approximately 8 years prior to study entry

*Goserelin was initiated under neo-adjuvant setting and continued through to adjuvant setting

^Capecitabine was given under adjuvant setting relative to metastatic resection (major protocol deviation)

No medical or surgical history was reported. Concurrent conditions included insomnia and cancer pain.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included zolpidem.

Event 1: Erythema multiforme
Event 2: Hypersensitivity (allergic reaction)

Prior to the event of erythema multiforme, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 8.

On Study Day 9, the patient experienced rash on back and neck. On the following day (Study Day 10), she presented to the emergency department due to abdominal pain, Grade 1 pyrexia (body temperature: 39.8°C), Grade 1 diarrhea, Grade 1 vomiting (all non-serious, related to ipatasertib) and spread of rash to trunk and limbs. Subsequently, she was hospitalized. She received treatment with calcium chloride dihydrate/potassium chloride/sodium chloride/sodium lactate for diarrhea and fever, paracetamol for fever. On the same day (Study Day 10), the event of vomiting was considered resolved. She further received treatment with dexchlorpheniramine; however, her rash was spreading. On Study Day 11, dermatologist suspected drug induced rash due to investigational drug or precipitated calcium carbonate/cholecalciferol or magnesium carbonate. A skin biopsy was performed, and rash was judged to be Grade 3 erythema multiforme (not caused by infection). Treatment with difluprednate, prednisolone (40 mg, IV), rupatadine and gentamycin was started; following which her condition improved. On Study Day 17, the event of diarrhea was considered resolved. On Study Day 18, the event of pyrexia was considered resolved. It was reported that her skin rash was improving, fairly relieved and remained only on trunk. Treatment with prednisone was reduced to 25 mg PO. On Study Day 23, the event of erythema multiforme improved to Grade 1 and she was discharged from the hospital.

Due to the event of erythema multiforme, there was no change in the study treatment with paclitaxel; however, study treatment with ipatasertib was permanently discontinued with the last dose given on Study Day 10.

Prior to the event of hypersensitivity, the most recent dose of paclitaxel was administered on Study Day 36; ipatasertib had already been discontinued.

On Study Day 36, at 14:32 hours, infusion with paclitaxel was started. At 14:52 hours, paclitaxel infusion was slowed because of increased coughing. At 15:00 hours, the patient's body temperature was 36.6°C, blood pressure was 122/84 mmHg, heart rate was 89 beats/min and SpO_2 was 98% in room air. Infusion with paclitaxel was continued. At 15:22 hours, coughing improved; however, she developed hives on bilateral upper limbs and abdomino-thoracic part without itching and dyspnea. Vitals showed body temperature 36.1°C, blood pressure 114/75 mmHg, heart rate 70 beats/min and SpO_2 98% in room air. She was diagnosed with Grade 2 allergic reaction (preferred term: hypersensitivity), leading to hospitalization. On the following day (Study Day 37), she experienced rash (site unspecified) due to allergic reaction. The dermatologist diagnosed it to be erythematous rash. She received treatment with dexchlorpheniramine and prednisolone; following which her general status became well. On Study Day 38, she was discharged from the hospital. She had good general condition and on Study Day 64, the events of erythema multiforme and hypersensitivity were considered resolved.

Due to the event of hypersensitivity, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 36. The patient entered into the long-term follow-up.

The Investigator considered erythema multiforme to be related to ipatasertib and unrelated to paclitaxel.

The Investigator considered hypersensitivity to be related to paclitaxel and unrelated to ipatasertib.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatment	Start Day	Stop Day
Paclitaxel albumin (18 cycles)	64	451

On Study Day 469, a radiographic response assessment showed disease progression with new lesion in brain (right temporal lobe).

The patient received follow-up anti-cancer therapies as listed in table below:

Treatment	Start Day	Stop Day
Eribulin (8 cycles)	507	668
Vinorelbine (unknown cycles)	682	Ongoing

On Study Day 713, the patient was permanently discontinued from the study as per physician's decision (LTFU terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	2	Non-serious	6	10	Unrelated	Related
Neutropenia	2	Non-serious	8	10	Unrelated	Related

Study Number/CRTN:	CO40016/318135	Patient number	1215
Demographics:	47-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1(PT) Category:	Diarrhea SAE		
Event 2 (PT) Category:	Pleural effusion SAE		
Event 3 (PT) Category:	Diarrhea SAE		
Additional category:	Death due to disease progression		

A narrative for this patient is available under Section 1.2; Narratives for patients who died due to disease progression.

Study Number/CRTN:	CO40016/304232	Patient number	1216
Demographics:	64-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Cardiopulmonary failure Death due to adverse event, SAE		

A narrative for this patient is available under Section 1.1; Narratives for patients who died due to adverse event(s).

Study Number/CRTN:	CO40016/318101	Patient number	1231
Demographics:	81-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea SAE		
Event 2 (PT) Categories:	Diarrhea SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER 2-negative, left breast cancer (T2N3M1), on Study Day −63 following left partial mastectomy performed on the same day.

On Study Day −36, metastatic disease was confirmed with ER/PR and HER 2-negative disease in metastatic tissue. At screening, sites of disease involvement included lymph node (right upper paratracheal, midline preaortic in mediastinum region).

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent conditions included hypertension and pulmonary embolism.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. The same day, she also started loperamide prophylactically (total daily dose: 4 mg) for diarrhea.

Concomitant medications ongoing at Study Day 1 included irbesartan, troxerutin and edoxaban tosilate.

Event 1: Diarrhea
Event 2: Diarrhea

Prior to the first episode of diarrhea, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 8.

On Study Day 9, the patient experienced Grade 1 (initial intensity) diarrhea and nausea. On Study Day 12, diarrhea worsened to Grade 2. She received treatment with loperamide (details

in the table below) and cinchocaine/fluocortolone hexanoate/fluocortolone pivalate. On Study Day 14, she was hospitalized. Her ECOG performance status was reported to be 3. Stool culture was requested but the patient could not co-operate. Her WBC count was 3.19 x 10^9/L (normal range: 4-10 x 10^9/L) and neutrophil count was 1.43 x 10^9/L (normal range: 2-7 x 10^9/L), and infection was ruled out. On Study Day 18, the event of diarrhea was considered resolved and she was discharged from the hospital.

Due to the first episode of diarrhea, there was no change in study treatment with paclitaxel; however, study treatment with ipatasertib was interrupted on Study Day 13 and was resumed at a reduced dose of 200 mg on Study Day 29.

Prior to the second episode of diarrhea, the most recent dose of paclitaxel was administered on Study Day 36 and ipatasertib (200 mg) was administered on Study Day 42.

On Study Day 43, the patient experienced second episode of Grade 2 diarrhea leading to hospitalization. Her ECOG performance status was reported to be 3. Stool culture was requested but the patient could not co-operate. On Study Day 47, the second episode of diarrhea was considered resolved and she was discharged from the hospital.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of Diarrhea	4	PO	1	1
Prophylaxis of Diarrhea	2	PO	2	2
Prophylaxis of Diarrhea	4	PO	5	6
Prophylaxis of Diarrhea	2	PO	7	8
Diarrhea	4	PO	9	9
Diarrhea	8	PO	10	11
Diarrhea	12	PO	12	13
Diarrhea	14	PO	14	14
Diarrhea	16	PO	15	15
Diarrhea	14	PO	16	16
Diarrhea	8	PO	17	18
Prophylaxis of Diarrhea	12	PO	29	30
Prophylaxis of Diarrhea	6	PO	31	33
Prophylaxis of Diarrhea	12	PO	34	36
Prophylaxis of Diarrhea	16	PO	37	37
Prophylaxis of Diarrhea	12	PO	38	40
Prophylaxis of Diarrhea	16	PO	41	41
Prophylaxis of Diarrhea	12	PO	42	42
Diarrhea	10	PO	46	46
Prophylaxis of Diarrhea	6	PO	47	51
Prophylaxis of Diarrhea	4	PO	52	54
Prophylaxis of Diarrhea	2	PO	55	55
Diarrhea	16	PO	74	74
Diarrhea	12	PO	75	76

Due to the second episode of diarrhea, there was no change in study treatment with paclitaxel; however, study treatment with ipatasertib was permanently discontinued with the last dose given on Study Day 42.

The Investigator considered diarrhea (first episode) to be related to ipatasertib and unrelated to paclitaxel.

The Investigator considered diarrhea (second episode) to be unrelated to paclitaxel and related to ipatasertib and disease under study.

On Study Day 226, study treatment with paclitaxel was permanently discontinued due to possibility of neurotoxicity with the last dose given on Study Day 205. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	**Start Day**	**Stop Day**
Capecitabine (unknown cycle)	230	Ongoing

On Study Day 301, a radiographic response assessment showed disease progression with new lesion in brain (bilateral cerebral and right cerebellar).

On Study Day 422, the patient died due to disease progression. An autopsy was not performed.

Other events experienced by the patient during the study:

Event	**Most extreme grade**	**Serious/ Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Leukopenia	1	Non-serious	14	17	Related	Related
Neutropenia	2	Non-serious	14	17	Related	Related
Anemia	2	Non-serious	14	36	Related	Related
Asthenia	2	Non-serious	15	64	Related	Related
Decreased appetite	2	Non-serious	36	64	Related	Related
Anemia	2	Non-serious	71	321	NA	Related
Neutropenia	1	Non-serious	89	106	NA	Related
Tremor	1	Non-serious	106	106	NA	Unrelated
Constipation	1	Non-serious	123	124	NA	Unrelated
Neutropenia	2	Non-serious	134	145	NA	Related
Hyperemia	2	Non-serious	152	177	NA	Related
Neutropenia	2	Non-serious	159	170	NA	Related
Rash	1	Non-serious	170	177	NA	Related
Neuropathy peripheral	1	Non-serious	170	331	NA	Related
Neutropenia	2	Non-serious	188	198	NA	Related
Leukopenia	1	Non-serious	188	198	NA	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Neutropenia	2	Non-serious	205	226	NA	Related
Leukopenia	2	Non-serious	212	226	NA	Related

Study Number/CRTN:	CO40016/318146	Patient number	1237
Demographics:	54-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Categories:	COVID-19 pneumonia SAE, COVID-19 SAE		
Event 2 (PT) Category:	Hyperglycemia AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal poorly differentiated ER/PR and HER2 negative left breast cancer (T3N0M1), on Study Day −64

The patient was diagnosed with metastatic disease on Study Day −34 with ER /PR negative and HER 2 negative in metastatic tissue. At screening, sites of disease involvement included lung (nodule in apico-posterior segment and upper lobule), and lymph node (right axillary).

No past cancer treatment was reported.

No medical/surgical history was reported. The patient′s concurrent conditions included hyperglycemia, hypertension, dyslipidemia, spinal osteoarthritis, bronchitis, and hypertriglyceridemia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included salbutamol, losartan, and simvastatin.

Event 1: COVID-19 pneumonia

Prior to the event of COVID-19 pneumonia, the most recent dose of paclitaxel was administered on Study Day 121 and ipatasertib (400 mg) on Study Day 124.

On Study Day 124, the patient presented to the emergency room due to dyspnea, dry cough, and tiredness; however, denied fever. On Study Day 125, a CT scan showed glass opacities with congruent areas of consolidation, bilateral multifocal distribution predominantly in peripheral and posterior region with involvement of less than 25% of the pulmonary parenchyma. She was diagnosed with pneumonia and was hospitalized. She received treatment with ceftriaxone was started. On Study Day 126, a laboratory work-up showed WBC count 10900/mm^3 (normal range: 3500-10500/mm^3), neutrophil count 9047/mm^3 (normal range: 1700-7000/mm^3), and lymphocyte count 1526/mm^3 (normal range: 1000-5000/mm^3). A PCR test for COVID-19 was positive and the event was re-assessed as COVID-19 pneumonia. It was reported that she had no travel history in past 2 weeks. She then received treatment with azithromycin; following which her condition improved. On Study Day 127, she was discharged from the hospital. On Study Day 128, the event of COVID-19 improved to Grade 2. On Study Day 137, the event of COVID-19 was considered resolved.

Due to this event, Cycle 5 Day 15 dose of paclitaxel was not administered and treatment with ipatasertib was interrupted on Study Day 128. The next dose of study treatment was administered on Study Day 142.

The Investigator considered COVID-19 to be related to paclitaxel and unrelated to ipatasertib.

Event 2: Hyperglycemia

Prior to the event of hyperglycemia, the most recent dose of paclitaxel was administered on Study Day 212 and ipatasertib (400 mg) on Study Day 223.

On Study Day 224, the patient′s pre-existing condition of hyperglycemia worsened to non-serious Grade 2 (glucose 160.1 mg/dL; normal range: 70-99 mg/dL). She received treatment with metformin and gliclazide. On Study Day 238, the event of hyperglycemia was considered resolved.

Relevant lab values are listed in the table below:

Study Day	**Glucose** (normal range: 70-99 mg/dL)	**HbA1c** (normal range: 4.4-6.5 %)
Screening	123.9	6.4
224	160.1	7.8
232	179.8	7.9

Due to this event, there was no change in study treatment with paclitaxel; however, ipatasertib was permanently discontinued with the last dose administered on Study Day 232.

The Investigator considered hyperglycemia to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 933, the study treatment with paclitaxel and study was permanently discontinued as per physician decision (patient to enter a rollover study) with the last dose given on Study Day 919.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Vomiting	1	Non-serious	4	4	Related	Related
Dermatitis acneiform	1	Non-serious	7	86	Related	Unrelated
Dermatitis acneiform	1	Non-serious	10	86	Related	Unrelated
Influenza	2	Non-serious	22	32	Related	Related
Dizziness	2	Non-serious	82	88	Related	Related
Neutropenia	2	Non-serious	85	91	Unrelated	Related
Neutropenia	2	Non-serious	99	105	Unrelated	Related
Nasopharyngitis	2	Non-serious	100	104	Unrelated	Related
Fall	2	Non-serious	113	119	Unrelated	Unrelated
Hypertriglyceridemia	3	Non-serious	113	849	Related	Unrelated
Neutropenia	2	Non-serious	120	123	Unrelated	Related
Neutropenia	2	Non-serious	155	197	Unrelated	Related
Neuropathy peripheral	1	Non-serious	186	246	Unrelated	Related
Diarrhea	1	Non-serious	216	217	Related	Unrelated
Diarrhea	1	Non-serious	227	228	Related	Unrelated
Diarrhea	1	Non-serious	230	231	Related	Unrelated
Neutropenia	2	Non-serious	239	259	Not applicable	Related
Neuropathy in feet and hands	2	Non-serious	247	Resolving	Not applicable	Related
Hyperglycemia	2	Non-serious	309	Unresolved	Not applicable	Unrelated
Diarrhea	2	Non-serious	319	321	Not applicable	Related
Vomit	1	Non-serious	319	321	Not applicable	Related
Nausea	2	Non-serious	319	321	Not applicable	Related
Neutropenia	2	Non-serious	322	337	Unrelated	Related
Epigastric pain	2	Non-serious	347	373	Unrelated	Related

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Helicobacter pylori infection	2	Non-serious	367	Unresolved	Unrelated	Unrelated
Hot flushes	2	Non-serious	402	Resolving	Unrelated	Unrelated
Dysuria	2	Non-serious	421	427	Unrelated	Unrelated
Neutropenia	2	Non-serious	436	448	Unrelated	Related
Urinary tract infection	2	Non-serious	438	444	Not applicable	Unrelated
Venous thrombosis	2	Non-serious	443	Resolving	Not applicable	Unrelated
Headache	2	Non-serious	462	507	Unrelated	Unrelated
Pulmonary infiltrate	1	Non-serious	498	721	Unrelated	Unrelated
Headache	2	Non-serious	515	530	Unrelated	Unrelated
Sinusopathy (sinusitis)	2	Non-serious	527	536	Unrelated	Unrelated
Neutropenia	2	Non-serious	547	559	Unrelated	Related
Hemorrhoidary crisis	2	Non-serious	612	Resolving	Unrelated	Unrelated
Diarrhea	2	Non-serious	655	656	Unrelated	Related
Vomit	1	Non-serious	655	656	Unrelated	Related
Cramp	2	Non-serious	657	658	Unrelated	Unrelated
Anxiety	2	Non-serious	728	741	Not applicable	Unrelated
Neutropenia	2	Non-serious	743	756	Not applicable	Related
Dysuria	2	Non-serious	755	763	Not applicable	Unrelated
Lumbar pain	2	Non-serious	755	769	Not applicable	Unrelated
Neutropenia	3	Non-serious	848	861	Not applicable	Related
Hypercholesterolemia	2	Non-serious	875	Resolving	Not applicable	Unrelated

Study Number/CRTN:	CO40016/304460	Patient number	1239
Demographics:	44-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Lymphocyte count decreased SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, PR and HER 2 negative left breast cancer (T2N1M0; ER status unknown) on Study Day −693.

On Study Day −50, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included left lower lobe of lung and bilateral lung nodules.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Cyclophosphamide and doxorubicin (4 cycles each)	−682	−634
Cancer therapy	Neoadjuvant	Paclitaxel (4 cycles)	−620	−578
Surgery	Curative	Left breast lumpectomy	−560	NA
Radiotherapy	Adjuvant	Left breast (dose: 6000 cGy, 30 fractions)	−515	−476

No medical or surgical history was reported. Concurrent condition included joint dislocation.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitants medications were ongoing at Study Day 1.

Event: Lymphocyte count decreased

Prior to the event of lymphocyte count decreased, the most recent dose of paclitaxel was administered on Study Day 43 and ipatasertib (400 mg) on Study Day 70. Cycle 3 of paclitaxel was not given as the patient could not visit the site for treatment administration due to COVID-19.

On Study Day 71, a laboratory work-up showed $0.10\times10^3/\mu L$ (normal range: $1.32\text{-}3.57\times10^3/\mu L$) and the patient was diagnosed with Grade 4 lymphocyte count decreased (considered serious as life-threatening). No treatment was reported for this event. On Study Day 97, the event of lymphocyte count decreased was considered resolved.

Relevant lab values are listed in the table below:

Study Day	WBC count (normal range: 4.4-11.3×10^3/μL)	Neutrophil count (normal range: 1.8-7.7×10^3/μL	Lymphocyte count (normal range: 1-4.8×10^3/μL)
Screening	3.27	2.01	0.95
60	3.82^	2.43@	0.89*
71	3.41^	1.99@	0.10*

^normal range: 4-10×10^3/μL, @normal range: 1.78-5.38×10^3/μL *normal range: 1.32-3.57×10^3/μL,

There was no change in study treatment due to this event.

The Investigator considered lymphocyte count decreased to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 167, a radiographic response assessment showed disease progression. Subsequently, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 158 and ipatasertib on Study Day 164. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Gemcitabine and carboplatin (6 cycles each)	180	285
Carboplatin (2 cycles)	326	–

On Study Day 722, the patient was permanently discontinued from the study as per the physician's decision (LTFU terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	1	Non-serious	5	23	Unrelated	Related
Neutrophil count decreased	1	Non-serious	43	60	Unrelated	Related
White blood cell count decreased	2	Non-serious	97	116	Unrelated	Related
Neutrophil count decreased	2	Non-serious	97	116	Unrelated	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Lymphocyte count decreased	2	Non-serious	104	116	Unrelated	Related
Blood cholesterol increased	1	Non-serious	116	Unresolved	Related	Unrelated
White blood cell count decreased	2	Non-serious	123	130	Unrelated	Related
Neutrophil count decreased	2	Non-serious	123	130	Related	Unrelated
Lymphocyte count decreased	1	Non-serious	123	130	Unrelated	Related
White blood cell count decreased	2	Non-serious	144	151	Unrelated	Related
Neutrophil count decreased	1	Non-serious	144	151	Unrelated	Related
Lymphocyte count decreased	1	Non-serious	144	151	Unrelated	Related
White blood cell count decreased	2	Non-serious	158	Unresolved	Unrelated	Related
Neutrophil count decreased	2	Non-serious	158	Unresolved	Unrelated	Related
Lymphocyte count decreased	2	Non-serious	158	Unresolved	Unrelated	Related

Study Number/CRTN:	CO40016/305252	Patient number	1242
Demographics:	66-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Dyspnea SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with moderately differentiated, ER/PR and HER 2 negative, left breast cancer (T3N0M0; histological subtype not otherwise specified), on Study Day −883.

On Study Day −484, the patient was diagnosed with locally recurrent disease and on Study Day −35, she was diagnosed with metastatic disease with ER/PR and HER 2-negative disease in recurrent/metastatic tissue. At screening, sites of disease involvement included infiltration of the chest wall.

Past cancer treatments are listed in the table below:

Type of treatment	**Therapy Setting/Intent**	**Treatments details**	**Start Day**	**Stop Day**
Cancer therapy	Neoadjuvant	Docetaxel (4 cycles)	−849	−786
Cancer therapy	Neoadjuvant	Cyclophosphamide and epirubicin (3 cycles each)	−765	−723
Surgery	Curative	Left radical mastectomy	−694	NA
Cancer therapy	Adjuvant	Capecitabine	−675	−499
Radiotherapy	Adjuvant	Left thoracic wall of breast (dose: 50 cGy, 25 fractions)	−637	−603
Cancer therapy	Neoadjuvant	Carboplatin and docetaxel (3 cycles each)	−464	−415
Surgery	Curative	Right simple mastectomy	−373	NA
Radiotherapy	Adjuvant	Right breast chest wall (dose: 50 cGy, 25 fractions)	−308	−270

The patient′s medical history included skin cancer, hypertriglyceridemia, colon cancer, uterine cancer and ruptured cerebral aneurysm. Concurrent conditions included hypertension, hypercholesterolemia, factor V Leiden mutation, obesity, hereditary non-polyposis colorectal cancer syndrome and lymphopenia.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included fluindione and candesartan

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 5.

On Study Day 6, the patient experienced non-serious Grade 3 diarrhea. She received treatment with loperamide (details in table below), diosmectite and racecadotril. Grade changes for the event are reported in the table below. On Study Day 131, the event of diarrhea was considered resolved.

Diarrhea grade changes:

Study Day	Diarrhea grade changes
8	2
12	1
35	2
36	1
41	2
50	3
57	1

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of Diarrhea	4	PO	1	1
Diarrhea	4	PO	6	6
Diarrhea	24	PO	7	7
Diarrhea	4	PO	8	8
Diarrhea	6	PO	10	10
Diarrhea	4	PO	22	22
Diarrhea	2	PO	23	23
Diarrhea	2	PO	26	27
Diarrhea	8	PO	35	35
Diarrhea	4	PO	36	36
Diarrhea	8	PO	37	38
Diarrhea	2	PO	40	40
Diarrhea	6	PO	41	41
Diarrhea	8	PO	42	42
Diarrhea	4	PO	43	43
Diarrhea	4	PO	45	45
Diarrhea	8	PO	46	47

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	48	48
Diarrhea	8	PO	49	49
Diarrhea	6	PO	50	51
Diarrhea	8	PO	52	53
Diarrhea	6	PO	54	56
Diarrhea	4	PO	96	96
Diarrhea	8	PO	97	97

Due to this event, there was no change in study treatment with paclitaxel; however, study treatment with ipatasertib was initially interrupted on Study Day 8 and resumed at a reduced dose of 300 mg on Study Day 22.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

Event 2: Dyspnea

Prior to the event of dyspnea, the most recent dose of ipatasertib (300 mg) was administered on Study Day 49 and paclitaxel on Study Day 57. Ipatasertib was interrupted from Study Day 57 due an unspecified adverse event.

On Study Day 68, a chest CT scan showed images with band of frosted glass in lungs.

On Study Day 71, the patient experienced Grade 4 dyspnea without cough and fever leading to hospitalization. No cardiac insufficiency was noted and a COVID-19 PCR test was reported to be negative and No treatment was reported for this event. On Study Day 77, the event of dyspnea was considered resolved.

Due to this event, study treatment with ipatasertib and paclitaxel was interrupted.

The Investigator considered dyspnea to be unrelated to paclitaxel and ipatasertib and related to other causes (morphine given as treatment for non-cardiac chest pain was stopped).

On Study Day 155, a radiographic response assessment showed disease progression with new lesion in skin (bilateral rib cage). Subsequently, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 131 and ipatasertib on Study Day 140. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Eribulin (6 cycles)	148	188

On Study Day 412, the patient died due to disease progression. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Non-cardiac chest pain	3	Non-serious	1	8	Unrelated	Unrelated
Hypomagnesaemia	2	Non-serious	7	89	Unrelated	Unrelated
Pruritus	1	Non-serious	10	21	Unrelated	Unrelated
Urinary tract infection	2	Non-serious	11	21	Unrelated	Unrelated
Neutropenia	3	Non-serious	14	28	Unrelated	Related
Lymphopenia	3	Non-serious	14	Unresolved	Unrelated	Related
Anemia	2	Non-serious	14	Unresolved	Unrelated	Related
Cystitis	2	Non-serious	18	57	Unrelated	Unrelated
Hematuria	1	Non-serious	21	21	Unrelated	Unrelated
Hyperglycemia	1	Non-serious	43	56	Unrelated	Unrelated
Eczema	1	Non-serious	44	56	Unrelated	Unrelated
Asthenia	3	Non-serious	50	Unresolved	Related	Related
Neuropathy peripheral	2	Non-serious	71	Unresolved	Unrelated	Related
Neutropenia	1	Non-serious	103	Unresolved	Unrelated	Related

Study Number/CRTN:	CO40016/304786	Patient number	1245
Demographics:	45-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Alanine aminotransferase increased Grade $\geq$ 3 hepatotoxicity		
Event 2 (PT) Category:	Aspartate aminotransferase increased Grade $\geq$ 3 hepatotoxicity		
Event 3 (PT) Categories:	COVID-19 SAE, COVID-19 SAE		

The patient was randomized on Study Day −3.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER 2-negative left breast cancer (T4bN1M0) on Study Day −847.

On Study Day −34, the patient was diagnosed with metastatic disease with ER/PR unknown and HER2 receptor not assessed in metastatic tissue. At screening, sites of disease involvement included lungs including left superior and right inferior lobe and lymph nodes (mediastinum, paratracheal and infracarinal).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neo-adjuvant	Doxorubicin, cyclophosphamide, and docetaxel (4 cycles each)	−783	−586
Surgery	Curative	Left radical mastectomy	−472	NA

The patient's medical history included constipation and vomiting. Concurrent condition included arthralgia.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

Event 1: Alanine aminotransferase increased (ALT increased)
Event 2: Aspartate aminotransferase increased (AST increased)

Prior to the events of alanine aminotransferase increased and aspartate aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 7.

On Study Day 8, the patient was diagnosed with non-serious Grade 3 alanine aminotransferase increased (ALT 231.7 U/L; normal range: 4-36 U/L) and non-serious Grade 3 aspartate aminotransferase increased (AST 167.1 U/L; normal range: 8-33 U/L). No treatment was reported for these events. On Study Day 59, the events of alanine aminotransferase increased, and aspartate aminotransferase increased were considered resolved.

Relevant lab values are listed in the table below:

Study Day	AST (normal range: 8-33 U/L)	ALT (normal range: 4-36 U/L)	ALP (normal range: 35-104 U/L)	Total bilirubin (normal range: 2-21 μmol/L)
Screening	31.6	21.8	122	0.7*
1	30.8	30.8	107	0.27
8	167.1	231.7	120	0.8
15	31.4	48.4	110	0.4
22	64.9	85.4	137	0.26

Study Day	AST (normal range: 8-33 U/L)	ALT (normal range: 4-36 U/L)	ALP (normal range: 35-104 U/L)	Total bilirubin (normal range: 2-21 μmol/L)
31	33.1	56.1	Not done	Not done
38	47.3	58.7	119	6.7
45	33.7	40.7	117	0.6*
59	30.5	24.5	97	0.6*

*Normal range: 0-1.4 mg/dL

Due to this event, study treatment with ipatasertib and paclitaxel was interrupted on Study Day 8. The next dose of paclitaxel (at a reduced dose of 65 mg/m^2) and ipatasertib (at a reduced dose of 300 mg) was given on Study Day 15.

The Investigator considered alanine aminotransferase increased and aspartate aminotransferase increased to be related to ipatasertib and paclitaxel.

Event 3: COVID-19

Prior to the event of COVID-19, the most recent dose of paclitaxel was administered on Study Day 122 and ipatasertib (300 mg) on Study Day 128.

On Study Day 124, the patient experienced cough, fatigue and myalgia. On Study Day 129, she underwent a thorax CT, and the results were not clinically relevant. On Study Day 131, the patient a polymerase chain reaction (PCR) swab tested was positive and she was diagnosed with medically significant Grade 1 COVID-19. She had no travel/contact history prior to symptoms. On Study Day 150 and Study Day 164, her swab PCR test was again positive. She received treatment of codeine/paracetamol and budesonide/formoterol.

On Study Day 156, a radiographic response assessment showed disease progression.

Due to the event of COVID-19, study treatment with paclitaxel and ipatasertib was interrupted on Study Day 122 and Study Day 128, respectively and was never resumed due to disease progression (see narrative below).

On Study Day 165, the event of COVID-19 was considered resolved.

On Study Day 165, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 122 and ipatasertib on Study Day 128. The patient entered into the long-term follow-up.

The Investigator considered COVID-19 to be unrelated to ipatasertib and paclitaxel and related to concurrent illness.

The patient received follow-up anti-cancer therapy as listed in the table below:

Treatments	Start Day	Stop Day
Gemcitabine and cisplatin (unknown cycles)	165	530

On Study Day 620, the patient was permanently discontinued from the study as long term follow-up was terminated by Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Hyperglycemia	1	Non-serious	1	38	Unrelated	Unrelated
Fatigue	1	Non-serious	2	Resolving	Unrelated	Related
Vomiting	2	Non-serious	3	10	Related	Related
Nausea	1	Non-serious	3	10	Related	Related
Anemia	1	Non-serious	38	Resolving	Related	Related
Depression	1	Non-serious	61	85	Unrelated	Unrelated
Diarrhea	1	Non-serious	97	104	Related	Related

Study Number/CRTN:	CO40016/305649	Patient number	1247
Demographics:	53-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Diarrhea SAE, Grade $\geq$ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with poorly differentiated, ER/PR and HER 2-negative left breast cancer (T4bN1M0; histological subtype: other) on Study Day −126.

On Study Day −74, the patient was diagnosed with locally advanced unresectable disease with ER/PR and HER 2-negative disease in recurrent tissue. At screening, sites of disease involvement included upper quadrant of left breast and left axillary lymph node.

No past cancer treatments were reported.

The patient′s medical history included chronic gastritis and gastroesophageal reflux disease. Concurrent conditions included anemia, cancer pain and anxiety.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. The same day, she also started loperamide (total daily dose: 4 mg) for diarrhea.

Concomitant medication ongoing at Study Day 1 included tramadol.

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 3.

On Study Day 4, the patient experienced Grade 1 (initial intensity) diarrhea. On Study Day 7, she experienced Grade 1 vomiting, Grade 1 dyspepsia and Grade 2 dehydration (all non-serious, related to ipatasertib). She received treatment with sodium chloride for dehydration, ondansetron for vomiting and bismuth subsalicylate and hyoscine butylbromide for dyspepsia. On the same day, the events of dehydration and vomiting were considered resolved.

On Study Day 14, she was noted with Grade 1 hypomagnesemia (non-serious, unrelated; magnesium: 1.48 mg/dL; normal range: 1.6-2.6 mg/dL). On Study Day 21, she experienced Grade 1 (initial intensity) vomiting (non-serious, related to ipatasertib). On Study Day 25, she experienced 8 episodes of diarrhea associated with vomiting. The events of vomiting and diarrhea were assessed as worsened to Grade 3 leading to hospitalization. A laboratory work-up showed Grade 3 dehydration (non-serious, related to ipatasertib). A stool culture performed was negative. On the same day, the dose of ongoing loperamide was increased to 12 mg (total daily dose). She further received ondansetron, and dimenhydrinate for vomiting, sodium chloride and unspecified electrolytes for dehydration, magnesium sulfate for hypomagnesemia and omeprazole for dyspepsia. Grade changes for diarrhea and loperamide dosing details are listed in the table below.

On Study Day 26, the patient was diagnosed with Grade 1 parasitic gastroenteritis (non-serious, unrelated; diagnostic details not reported). On the same day (Study Day 26), diarrhea improved to Grade 1 and also the events of vomiting, and hypomagnesemia were considered resolved. On Study Day 27, dehydration was considered resolved. On Study Day 28, the patient was discharged from the hospital. She further received treatment with nitazoxanide for parasitic gastroenteritis and *Bacillus clausii* spores for diarrhea. On Study Day 33, the events of diarrhea and parasitic gastroenteritis was considered resolved. On Study Day 39, the event of dyspepsia was considered resolved.

Diarrhea grade changes:

Study Day	Diarrhea grade changes
9	2
12	1
20	2
22	1
23	2
25	3
26	1

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	1	6
Diarrhea	6	PO	7	10
Diarrhea	8	PO	11	12
Diarrhea	12	PO	13	14
Diarrhea	6	PO	15	22
Diarrhea	8	PO	23	24
Diarrhea	12	PO	25	25
Diarrhea	8	PO	26	27
Diarrhea	6	PO	28	33
Diarrhea	4	PO	43	56
Diarrhea	6	PO	57	59
Diarrhea	10	PO	60	60
Diarrhea	6	PO	61	66

Relevant lab values are listed in the table below:

Study Day	Sodium (normal range: 135-145 mEq/L)	Potassium (normal range: 3.3-5.4 mEq/L)	Magnesium (normal range: 1.6-2.6 mg/dL)
Screening	144	5	2.23
1	134	4.9	2.1
8	132	5.2	2.13
14	135	3.8	1.48
43	135	4.8	2.13
49	136	5	2.16
56	136	4.3	2.14

Due to the event of diarrhea, there was no change in study treatment with paclitaxel; however, study treatment with ipatasertib was interrupted on Study Day 11 and the next dose was given on Study Day 15. Ipatasertib was again interrupted on Study Day 26 and resumed at a reduced dose of 300 mg on Study Day 43.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 60, a radiographic response assessment showed disease progression.

On Study Day 79, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 57 and ipatasertib on Study Day 63. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Doxorubicin and cyclophosphamide (1 cycle each)	81	81
Radiotherapy to left breast and supraclavicular axillo region lymph node (dose: 4500 cGy, 18 fractions)	168	212

On Study Day 284, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Vomiting	1	Non-serious	1	1	Unrelated	Unrelated
Nausea	1	Non-serious	7	10	Related	Unrelated
Dyspnea	1	Non-serious	8	8	Unrelated	Related
Flushing	2	Non-serious	8	8	Unrelated	Related
Infected neoplasm	2	Non-serious	11	14	Unrelated	Unrelated
Pruritus	1	Non-serious	13	55	Unrelated	Related
Dyspnea	1	Non-serious	15	15	Related	Related
Flushing	1	Non-serious	15	15	Unrelated	Related
Eosinophilia	2	Non-serious	43	56	Unrelated	Related
Diarrhea	2	Non-serious	43	67	Related	Unrelated
Nausea	1	Non-serious	45	67	Related	Unrelated
Dyspepsia	1	Non-serious	45	67	Related	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Dyspnea	1	Non-serious	50	50	Unrelated	Related
Flushing	1	Non-serious	50	50	Unrelated	Related
Fatigue	1	Non-serious	60	61	Unrelated	Unrelated
Constipation	1	Non-serious	66	76	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	74	76	Unrelated	Related

1.4 NARRATIVES FOR PATIENTS WHO EXPERIENCED ADVERSE EVENTS LEADING TO STUDY TREATMENT DISCONTINUATION

Study Number/CRTN:	CO40016/304778	Patient number	1003
Demographics:	76-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Categories:	Pneumonia SAE, AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Hyperglycemia Grade ≥ 3 Hyperglycemia		
Event 3 (PT) Category:	Glucose tolerance impaired Grade ≥ 3 Hyperglycemia		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304753	Patient number	1007
Demographics:	69-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR positive and HER2 negative right breast cancer (T1cN0MX), approximately 10 years prior to study entry.

The patient was diagnosed with metastatic disease approximately 4 years and 9 months prior to study entry with ER /PR negative and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included lymph node (aortopulmonary and manubrium sternum) and lung (upper right pulmonary lobe).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right simple mastectomy	Approximately 10 years prior to study entry	NA
Cancer therapy	Adjuvant	Fluorouracil, doxorubicin, cyclophosphamide, and paclitaxel (3 cycles each)	Approximately 10 years prior to study entry	Approximately 10 years prior to study entry
Radiotherapy	Adjuvant	Right breast (dose: 5040 cGy, 28 fractions)	Approximately 10 years prior to study entry	Approximately 10 years prior to study entry
Radiotherapy	Metastatic	Right lymph node (dose: 7080 cGy, 29 fractions)	Approximately 4 years and 6 months prior to study entry	Approximately 4 years and 5 months prior to study entry

The patient′s medical history included lumbar spinal stenosis. Surgical history included spinal operation and central venous catheterization. Concurrent conditions included meningioma, pain, dizziness, osteoarthritis, and intervertebral disc protrusion.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

Event: Neuropathy peripheral (peripheral neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel was administered on Study Day 100 and ipatasertib (400 mg) on Study Day 106.

On Study Day 114, the patient was diagnosed with non-serious Grade 3 neuropathy peripheral (presenting signs and symptoms not reported). No treatment was given for this event. On Study Day 142, the event of neuropathy peripheral improved to Grade 2.

On Study Day 218, the patient experienced Grade 1 (initial intensity) sciatica (non-serious, unrelated). On Study Day 221, the event of sciatica worsened to Grade 2. She received treatment with diclofenac, ibuprofen, and metamizole for the event of sciatica. On Study Day 254, she developed non-serious Grade 1 paralysis of the recurrent laryngeal nerve (non-serious, causality with study treatment reported as not applicable). No treatment was given for this event. The event of paralysis of the recurrent laryngeal nerve was considered resolving and the events of sciatica and neuropathy peripheral remained unresolved at the time of patient′s death.

Due to this event, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 100.

The Investigator considered neuropathy peripheral to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 225, a radiographic response assessment showed disease progression with new lesion in bone (right ilium corpus).

On Study Day 240, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose given on Study Day 218. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Carboplatin (3 cycles)	261	338
Pegylated liposomal doxorubicin (3 cycles)	359	415
Radiotherapy to osteolysis of sacrum bone (dose: 3000 cGy, 12 fractions)	363	442
Radiotherapy to mediastinal and right hilar lymph node (dose: 4000 cGy, 12 fractions)	468	489

On Study Day 928, the patient died to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	12	Resolving	Related	Unrelated
Fatigue	1	Non-serious	15	Unresolved	Unrelated	Unrelated
Cough	2	Non-serious	32	114	Unrelated	Unrelated
Nasopharyngitis	1	Non-serious	40	64	Unrelated	Unrelated
Alopecia	2	Non-serious	40	40	Unrelated	Related
Asthenia	1	Non-serious	64	142	Related	Related
Breast pain	1	Non-serious	223	Resolving	Unrelated	N/A

Study Number/CRTN:	CO40016/304878	Patient number	1015
Demographics:	55-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Neutropenia SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304194	Patient number	1022
Demographics:	61-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Pulmonary embolism Death due to adverse event, SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.1; Narratives for patients who died due to adverse event(s).

Study Number/CRTN:	CO40016/304878	Patient number	1061

Demographics:	68-year-old Asian female
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)
Cohort	Cohort A
Event (PT) Category:	Neutrophil count decreased AE leading to study treatment discontinuation

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER/PR and HER 2 negative right breast cancer (T2N0M0; histological grade unknown), approximately 11 years prior to study entry.

On Study Day −68, the patient was diagnosed with metastatic disease with ER/PR status unknown and HER2 receptor not assessed in metastatic tissue. At screening, sites of disease involvement included right pleural effusion, right paratracheal lymph node, spine and bilateral lungs.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right breast modified radical mastectomy and sentinel right lymph node biopsy	Approximately 11 years prior to study entry.	NA
Cancer therapy	Adjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	Approximately 11 years prior to study entry	Approximately 11 years prior to study entry

The patient′s medical history included spinal stenosis. No surgical history was reported. Concurrent conditions included diabetes mellitus, hypertension, hyperlipidemia and dyspnea.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included amlodipine besilate/telmisartan, cilostazol, *Artemisia argyi*, gemfibrozil, pitavastatin, anagliptin/metformin, chlorphenamine, chlorhexidine and codeine/ibuprofen/paracetamol.

On Study Day 8, a laboratory work-up showed WBC count $1.3\times10^3/\mu L$ (normal range: $4\text{-}10\times10^3/\mu L$) and neutrophils 44.7% (normal range: 50-75%). The patient was diagnosed with Grade 3 neutrophil count decreased (non-serious, related). On Study Day 15, the event of

neutrophil count decreased worsened to Grade 4. She received treatment with lenograstim. On Study Day 21, the event of neutrophil count decreased was considered resolved.

Due to this event, study treatment with paclitaxel and ipatasertib was initially interrupted on Study Day 8 and the next dose of paclitaxel (at a reduced dose of 65 mg/m^2) and ipatasertib (at a reduced dose of 300 mg) was given on Study Day 22.

Event: Neutrophil count decreased

Prior to the event of neutrophil count decreased, the most recent dose of paclitaxel was administered on Study Day 29 and ipatasertib (300 mg) on Study Day 35.

On Study Day 36, a laboratory work-up showed WBC count $1.2\times10^3/\mu L$ (normal range: $4\text{-}10\times10^3/\mu L$) and neutrophils 20.9% (normal range: 50-75%). The patient was diagnosed with non-serious Grade 4 neutrophil count decreased. She received treatment with lenograstim. On Study Day 56, the event of neutrophil count decreased was considered resolved.

Relevant lab values are listed in the table below:

Study Day	**WBC count** (normal range: $4\text{-}10\times10^3/\mu L$)	**Neutrophils** (normal range: 50-75%)
Screening	4.7	56.2
1	5.2	62.0
8	1.3	44.7
15	2.2	12.5
22	4.2	55.0
29	3.3	51.0
36	1.2	20.9
57	4.1	62.6

Due to this event, study treatment with ipatasertib and paclitaxel was permanently discontinued on Study Day 57 with the last dose of paclitaxel given on Study Day 29 and ipatasertib on Study Day 35. The patient entered into the long-term follow-up.

The Investigator considered neutrophil count decreased to be related to ipatasertib and paclitaxel.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	**Start Day**	**Stop Day**
Paclitaxel	57	Ongoing

On Study Day 1076, the patient was permanently discontinued from the study as per physician's decision (LTFU terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Peripheral sensory neuropathy	1	Non-serious	2	Unresolved	Unrelated	Related
Myalgia	1	Non-serious	2	Unresolved	Related	Related
Nausea	1	Non-serious	2	15	Related	Related
Vomiting	1	Non-serious	2	3	Related	Related
Hyperglycemia	2	Non-serious	6	56	Related	Unrelated
Vomiting	1	Non-serious	8	9	Unrelated	Unrelated
Diarrhea	1	Non-serious	8	10	Related	Unrelated
Asthenia	2	Non-serious	8	Unresolved	Related	Related
Edema peripheral	1	Non-serious	12	Unresolved	Unrelated	Related
Alopecia	2	Non-serious	17	Unresolved	Unrelated	Related
Diarrhea	2	Non-serious	25	37	Related	Unrelated
Decreased appetite	2	Non-serious	25	51	Related	Related
Rash pustular	1	Non-serious	25	51	Related	Related
Dyspepsia	2	Non-serious	32	51	Related	Related

Study Number/CRTN:	CO40016/307260	Patient number	1069
Demographics:	68-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Peripheral motor neuropathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, moderately differentiated Grade 2, ER/PR negative and HER2 negative left breast cancer (T2N1M0) approximately 2 years and 10 months prior to study entry followed by left breast biopsy performed on the same day.

The patient was diagnosed with metastatic disease on Study Day −34 with ER /PR negative and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included lung (left upper lobular).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Paclitaxel (12 cycles) and trastuzumab (4 cycles)	Approximately 2 years 9 months prior to study entry	Approximately 2 years 7 months prior to study entry
Cancer therapy	Neoadjuvant	Epirubicin, fluorouracil and cyclophosphamide (4 cycles each)	Approximately 2 years 6 months prior to study entry	Approximately 2 years 4 months prior to study entry
Surgery	Curative	Left simple mastectomy	Approximately 2 years 3 months prior to study entry	NA
Cancer therapy	Adjuvant	Trastuzumab (18 cycles)	Approximately 2 years and 1 month prior to study entry	Approximately 1 year and 1 month prior to study entry

No medical/surgical history was reported. The patient′s concurrent conditions included hypertension, insomnia, constipation, vertigo positional, edema peripheral, peripheral sensory neuropathy, hyperplastic cholecystopathy and dry eye.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included hyaluronate, telmisartan, alisma plantago-aquatica subsp. Orientale tuber/artemisia capillaries flower/atractylodes lancea rhizome/ Cinnamomum cassia bark/polyporus umbellatus sclerotium/poria CoCos sclerotium, triazolam, betahistine, lactomin and dimeticone.

Due to the event of Grade 2 diarrhea (initial intensity Grade 1; non-serious, related), study treatment with paclitaxel was reduced from 80 mg/m^2 to 65 mg/m^2.

Event 1: Peripheral sensory neuropathy (Worsening of peripheral sensory neuropathy)

Event 2: Peripheral motor neuropathy

Prior to the event of peripheral sensory neuropathy, the most recent dose of paclitaxel was administered on Study Day 154 and ipatasertib (300 mg) on Study Day 161.

On Study Day 168, the ongoing event of peripheral sensory neuropathy worsened to Grade 2. She received treatment with duloxetine for peripheral sensory neuropathy. Relevant grade changes reported in the table below. The event of peripheral sensory neuropathy remained unresolved at the time of study discontinuation.

Prior to the event of peripheral motor neuropathy, the most recent dose of paclitaxel was administered on Study Day 203 and ipatasertib (300 mg) on Study Day 189.

On Study Day 210, the patient was noted with Grade 1 peripheral motor neuropathy. She received treatment with mecobalamin and duloxetine for peripheral motor neuropathy. Relevant grade changes reported in the table below. The events of peripheral sensory and motor neuropathy remained unresolved at the time of study discontinuation.

Relevant grade changes reported in the table below:

Event	Study Day	Grade change
Worsening of peripheral sensory neuropathy	294	1
Worsening of peripheral sensory neuropathy	483	2
Worsening of peripheral sensory neuropathy	490	1
Worsening of peripheral sensory neuropathy	518	2
Worsening of peripheral sensory neuropathy	791	3
Peripheral motor neuropathy	392	2
Peripheral motor neuropathy	419	1
Peripheral motor neuropathy	490	2
Peripheral motor neuropathy	791	3

Due to these events, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose given on Study Day 770 (Cycle 28 Day 15).

The Investigator considered peripheral sensory neuropathy and peripheral motor neuropathy to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 1283, a radiographic response assessment showed disease progression with progression in target lesions.

On Study Day 1312, study treatment with ipatasertib and study was permanently discontinued due to disease progression with the last dose given on Study Day 1287.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nasopharyngitis	1	Non-serious	4	9	Unrelated	Unrelated
Alopecia	2	Non-serious	28	1302	Unrelated	Related
Dysgeusia	1	Non-serious	35	224	Unrelated	Related
Stomatitis	1	Non-serious	60	70	Related	Related
Syncope	3	Non-serious	69	70	Unrelated	Unrelated
Neck pain	1	Non-serious	69	84	Unrelated	Unrelated
Pruritus	2	Non-serious	70	224	Unrelated	Related
Stomatitis	2	Non-serious	94	99	Related	Related
Neutrophil count decreased	2	Non-serious	140	252	Related	Related
Abdominal pain upper	1	Non-serious	168	224	Related	Related
Paronychia	1	Non-serious	252	280	Unrelated	Related
Vertigo	1	Non-serious	266	267	Unrelated	Unrelated
Rash maculo-papular	1	Non-serious	274	Unresolved	Related	Related
Neutrophil count decreased	2	Non-serious	336	728	Unrelated	Related
Constipation	1	Non-serious	337	1204	Unrelated	Related
Stomatitis	1	Non-serious	367	586	Unrelated	Related
White blood cell count decreased	1	Non-serious	419	448	Unrelated	Related
Spondylolysis	1	Non-serious	448	Unresolved	Unrelated	Unrelated
White blood cell count decreased	1	Non-serious	511	728	Unrelated	Related
Headache	1	Non-serious	531	546	Unrelated	Unrelated
Tinea pedis	1	Non-serious	567	573	Unrelated	Unrelated
Stomatitis	1	Non-serious	616	1288	Unrelated	Yes
Headache	1	Non-serious	618	664	Unrelated	Unrelated
Headache	1	Non-serious	728	756	Unrelated	Unrelated
White blood cell count decreased	2	Non-serious	784	812	Unrelated	Related
Neutrophil count decreased	2	Non-serious	784	812	Unrelated	Related
Oropharyngeal pain	1	Non-serious	834	840	Unrelated	Unrelated
Pyrexia	1	Non-serious	835	836	Unrelated	Unrelated
White blood cell count decreased	1	Non-serious	840	896	Unrelated	Related
Neutrophil count decreased	1	Non-serious	840	896	Unrelated	Related
White blood cell count decreased	1	Non-serious	924	1176	Unrelated	Related

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Neutrophil count decreased	2	Non-serious	924	1176	Unrelated	Related
Vertigo	1	Non-serious	1036	1092	Unrelated	Unrelated
White blood cell count decreased	1	Non-serious	1204	Unresolved	Unrelated	Related
Neutrophil count decreased	2	Non-serious	1204	Unresolved	Unrelated	Related
Vertigo	1	Non-serious	1208	1219	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304776	Patient number	1070
Demographics:	66-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Febrile neutropenia SAE		
Event 2 (PT) Categories:	Rash AE leading to study treatment discontinuation, Grade ≥ 3 rash		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304641	Patient number	1075
Demographics:	75-year old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Categories:	Alanine aminotransferase increased AE leading to study treatment discontinuation, Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Categories:	Alanine aminotransferase increased AE leading to study treatment discontinuation, Grade ≥ 3 hepatotoxicity		

The patient was randomized on Study Day 1.

The patient was diagnosed with ductal, poorly differentiated, ER/PR and HER 2 negative, metastatic right breast cancer (T1cN3cM1), on Study Day -77. At screening, sites of disease involvement included lymph nodes (right axilla level II and III and right infraclavicular) and lung (right hilus).

No past cancer treatment was reported.

The patient′s medical history included leiomyoma. Surgical history included cholecystectomy and appendicectomy. Concurrent conditions included hypertonia and hyperchlorhydria.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included metoprolol, pantoprazole, indapamide/perindopril, amlodipine, perindopril, furosemide, potassium chloride and clopidogrel.

Event 1: Alanine aminotransferase increased (Increase liver function; ALT)
Event 2: Aspartate aminotransferase increased (Increase liver function; AST)

Prior to the events of alanine aminotransferase increased and aspartate aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 6.

On Study Day 7, a laboratory work-up showed ALT 230 U/L (normal range: 0-31 U/L) and AST 255 U/L (normal range: 0-37 U/L). The patient was diagnosed with non-serious Grade 3 alanine aminotransferase increased**,** and aspartate aminotransferase increased. No treatment was administered for these events. The events of alanine aminotransferase and aspartate aminotransferase increased remained unresolved at the time of study discontinuation.

Relevant lab values are listed in the table below:

Study Day	**AST** (normal range: 0-37 U/L)	**ALT** (normal range: 0-31 U/L)	**Total bilirubin** (normal range: 0-20.6 μmol/L)	**ALP** (normal range: 30-270 U/L)
Screening	15	15	7.3	95
1	16	14	4.9	100
7	255	230	30.4	184

Due to the events of alanine aminotransferase increased and aspartate aminotransferase increased, there was no change in study treatment with paclitaxel, however, study treatment with ipatasertib was permanently discontinued with the last dose of ipatasertib administered on Study Day 6.

The Investigator considered alanine aminotransferase increased and aspartate aminotransferase increased to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 11, the patient withdrew consent from the study with the last dose of paclitaxel administered on Study Day 7.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	4	11	Unrelated	Related
Asthenia	1	Non-serious	4	Unresolved	Unrelated	Unrelated
Hyperglycemia	2	Non-serious	7	Unresolved	Related	Unrelated
Diarrhea	2	Non-serious	9	Unresolved	Unrelated	Related

Study Number/CRTN:	CO40016/304778	Patient number	1079
Demographics:	64-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Hyperglycemia AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR positive and HER 2 equivocal, left breast cancer (T1cN2MX), approximately 11 years prior to study entry.

On Study Day -352, the patient was diagnosed with ER/PR negative and HER 2 negative disease. At screening, sites of disease involvement included lymph node (lymphadenopathy in left side upper internal mammary chain), lung (right upper, lower, and middle lobe and nodule in posterior aspect of left lower lobe) and left pleural.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left modified radical mastectomy and left axillary lymph node dissection	Approximately 11 years prior to study entry	NA
Cancer therapy	Adjuvant	Doxorubicin (3 cycles), cyclophosphamide, methotrexate and fluorouracil (6 cycles each)	Approximately 11 years prior to study entry	Approximately 10 years prior to study entry
Radiotherapy	Adjuvant	Left chest wall and supraclavicular fossa (dose: 4600 cGy, 23 fractions)	Approximately 10 years prior to study entry	Approximately 10 years prior to study entry
Cancer therapy	Adjuvant	Tamoxifen and exemestane	Approximately 10 years prior to study entry	Approximately 4 years and 9 months prior to study entry
Cancer therapy	Adjuvant	Tamoxifen	Approximately 3 years and 8 months prior to study entry	–348

The patient′s medical history included ulcerative gastritis, hyperthyroidism, diabetes mellitus inadequate control, seborrheic keratosis, lipoma and pleural fibrosis. Surgical history included thyroid nodule removal, central venous catheterization and thoracic operation. Concurrent conditions included type 2 diabetes mellitus, hyperglycemia (Grade 2), hepatic steatosis, uterine leiomyoma, gastritis, osteopenia, urinary incontinence and insomnia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included glimepiride, linagliptin, metformin and lorazepam.

Event 1: Diarrhea
Event 2: Hyperglycemia (Fasting hyperglycemia)

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 8 and ipatasertib (400 mg) on Study Day 10.

On Study Day 11, the patient experienced non-serious Grade 2 (initial intensity) diarrhea. No test was performed to determine infectious etiology. On Study Day 12, the event of diarrhea

worsened to Grade 3. She received treatment with loperamide (details in table below). On Study Day 16, the event of diarrhea improved to Grade 1.

Prior to the event of hyperglycemia, the most recent dose of paclitaxel was administered on Study Day 8 and ipatasertib (400 mg) on Study Day 16.

On Study Day 17, the patient was noted with non-serious Grade 2 fasting hyperglycemia (glucose 195 mg/dL; normal range: 70-100 mg/dL). No treatment was given for the event. On Study Day 32, the event of diarrhea worsened to Grade 2 which improved to Grade 1 on Study Day 33. Relevant laboratory values are given in the table below. On Study Day 64, the event of diarrhea was considered resolved. On Study Day 85, the event of hyperglycemia was considered resolved.

Loperamide treatment details:

Indication	Total Daily Dose (Units: mg)	Route	Start day	Stop day
Diarrhea prophylaxis	4	PO	1	10
Diarrhea	4	PO	11	12
Diarrhea	6	PO	13	16
Diarrhea	4	PO	17	18
Diarrhea	4	PO	20	20
Diarrhea	2	PO	21	21
Diarrhea	2	PO	26	26
Diarrhea	4	PO	27	27
Diarrhea	2	PO	28	28
Diarrhea	4	PO	29	31
Diarrhea	6	PO	32	32
Diarrhea	4	PO	33	48
Diarrhea	6	PO	49	49
Diarrhea	4	PO	50	50
Diarrhea	6	PO	51	51
Diarrhea	4	PO	52	56

Relevant lab values are listed in the table below:

Study Day	Glucose (normal range: 70-100 mg/dL)	HbA1c (normal range: 4-6 %)
Screening	162	7.1
8	219	—
17	195	—
29	159	—
36	176	—
43	156	—
57	206	7.9
71	151	—
85	145	—

Due to the event of diarrhea, there was no change in study treatment with paclitaxel; however, study treatment with ipatasertib was interrupted on Study Day 18 and was resumed at a

reduced dose of 300 mg on Study Day 29. Ipatasertib was again interrupted on Study Day 36 and was resumed at a further reduced dose of 200 mg on Study Day 43.

Due to the event of hyperglycemia, there was no change in study treatment with paclitaxel, however, study treatment with ipatasertib was permanently discontinued with last dose of ipatasertib administered on Study Day 56

The Investigator considered diarrhea to be unrelated to paclitaxel and related to ipatasertib and other unspecified causes.

The Investigator considered hyperglycemia to be unrelated paclitaxel and related to ipatasertib and concurrent illness.

On Study Day 388, a radiographic response assessment showed disease progression with new lesions in mediastinum (left side of lateral aortic arch) and bone (sternum and left 6th rib).

On Study Day 409, study treatment with paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 381. She entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Vinorelbine	409	484
Radiotherapy to whole brain plus brain boost (dose: 4500 cGy; 15 fractions)	499	519

On Study Day 822, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious / non-serious**	**Onset Day**	**Resolution Day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Alopecia	2	Non-serious	24	Unresolved	Unrelated	Related
Hypomagnesemia	1	Non-serious	29	85	Unrelated	Unrelated
Neuropathy peripheral	2	Non-serious	29	Unresolved	Unrelated	Related
Influenza like illness	2	Non-serious	55	120	Unrelated	Unrelated
Diarrhea	1	Non-serious	160	262	NA	Unrelated
Toothache	1	Non-serious	169	173	NA	Unrelated
Edema peripheral	1	Non-serious	251	409	NA	Related

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Hypomagnesemia	1	Non-serious	283	Unresolved	NA	Related
Influenza like illness	1	Non-serious	321	325	NA	Unrelated
Tongue ulceration	1	Non-serious	328	339	NA	Unrelated
Diarrhea	1	Non-serious	338	338	NA	Unrelated
Influenza like illness	1	Non-serious	354	381	NA	Unrelated
Back pain	1	Non-serious	375	395	NA	Unrelated
Cough	2	Non-serious	388	409	NA	Unrelated

Study Number/CRTN:	CO40016/304879	Patient number	1084
Demographics:	62-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Hyperglycemia Grade $\geq$ 3 hyperglycemia		
Event 2 (PT) Category:	Edema AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER positive, PR and HER 2 negative, left breast cancer (T1micN0M0) on Study Day −357.

On Study Day −49, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included left breast nodule, bilateral skin and bilateral axillary lymph node.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	—	Left modified radical mastectomy	−344	N/A
Cancer therapy	Metastatic	Anastrozole	−323	−60

No medical or surgical history was reported. Concurrent condition included diabetes mellitus.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included alogliptin/metformin.

Event 1: Hyperglycemia

Prior to the event of hyperglycemia, the most recent dose of paclitaxel was administered on Study Day 29 and ipatasertib (400 mg) on Study Day 35.

On Study Day 36, the patient was noted with non-serious Grade 3 hyperglycemia (blood glucose 299 mg/dL; normal range: 70-110 mg/dL). Treatment with alogliptin/metformin was maintained for diabetes mellitus. No additional treatment was reported for hyperglycemia. Grade changes during the event course are reported in the table below. On Study Day 92, the event of hyperglycemia improved to Grade 1. On Study Day 142, the patient was started on gliclazide for hyperglycemia. On Study Day 238, the event of hyperglycemia was considered resolved.

Hyperglycemia grade changes:

Study Day	Grade changes
43	2
57	3
85	2
92	1

Relevant lab values are listed in the table below:

Study Day	Glucose (normal range: 70-110 mg/dL)	HbA1c (normal range: 2-6%)
Screening	131	7
36	299	—
43	182	—
57	286	8.6
73	256	—
85	170	—
92	119	—
99	112	—
106	108	—
113	96	—
120	101	—
134	85	—
141	100	6.9
160	87	6.9
169	95	—
197	94	—
225	86	6.9
253	107	—

Due to this event, Cycle 4 Day 1 of paclitaxel was not administered and ipatasertib was interrupted on Study Day 85. The next dose of paclitaxel (Cycle 4 Day 8) and ipatasertib (at a reduced dose of 300 mg) was given on Study Day 92.

The Investigator considered hyperglycemia to be related to ipatasertib and unrelated to paclitaxel.

Event 2: Edema

Prior to the event of edema, the most recent dose of paclitaxel was administered on Study Day 169 and ipatasertib (300 mg) on Study Day 174.

On Study Day 175, the patient developed non-serious Grade 2 edema (initial intensity: Grade 1). No treatment was reported for this event. The event of edema remained unresolved at the time of study discontinuation.

Due to the event of edema, there was no change in the study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose administered on Study Day 771.

The Investigator considered edema to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 836, a radiographic assessment showed disease progression.

On Study Day 841, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose of ipatasertib given on Study Day 833. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine, atezolizumab and tiragolumab	869	NA

On Study Day 992, the patient was permanently discontinued from the study treatment as per the physician’s decision (long term follow-up terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Alopecia	1	Non-serious	16	Unresolved	Related	Related
Diarrhea	1	Non-serious	38	238	Related	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nail discoloration	1	Non-serious	52	Unresolved	Unrelated	Related
Upper respiratory tract infection	1	Non-serious	77	106	Unrelated	Unrelated
Insomnia	1	Non-serious	85	Unresolved	Unrelated	Unrelated
Neutrophil count decreased	3	Non-serious	106	120	Unrelated	Related
Rash	1	Non-serious	109	176	Related	Related
Constipation	1	Non-serious	225	232	Related	Unrelated
Cystitis	1	Non-serious	276	280	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	309	Resolving	Unrelated	Related
Headache	1	Non-serious	666	687	Unrelated	Unrelated

Study Number/CRTN:	CO40016/314283	Patient number	1087
Demographics:	60-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Hyperthermia SAE		
Event 3 (PT) Category:	Hypotension AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/318263	Patient number	1093
Demographics:	45-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Abdominal pain SAE		
Event 2 (PT) Category:	Nausea SAE		
Event 3 (PT) Category:	Vomiting SAE		
Event 4 (PT) Category:	Fatigue SAE		
Event 5 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		
Event 6 (PT) Categories:	Peritonitis SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/ 305247	Patient number	1095
Demographics:	59-year-old female (Race unknown)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Diarrhea Grade $\geq$ 3 diarrhea		
Event 3 (PT) Category:	Glaucoma SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/305631	Patient number	1104
Demographics:	41-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Categories:	Diarrhea AE leading to study treatment discontinuation, Grade ≥ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal and not otherwise specified histological subtype, poorly differentiated, ER/PR and HER 2 negative, right breast cancer (T3N3M0), on Study Day -36.

On Study Day -33, the patient was diagnosed with locally advanced unresectable disease with ER/PR and HER 2 negative disease in recurrent/metastatic tissue. At screening, sites of disease involvement included lymph node (ganglion with fatty hilum in the right axilla) and right breast (external upper quadrant).

No past cancer treatment was reported.

No medical history was reported. Surgical history included carpal tunnel decompression. No concurrent condition was reported.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medication ongoing at Study Day 1 was reported.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 8 and ipatasertib (400 mg) on Study Day 10.

On Study Day 11, the patient experienced non-serious Grade 1 (initial intensity) diarrhea. On Study Day 14, the event of diarrhea worsened to Grade 3. Stool culture and coprological functional and parasitological examinations were performed (results were pending). She

received treatment with loperamide (2 mg every 4 hours) and also received dietary advice. On the same day (Study Day 14), the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis for diarrhea	4	PO	1	2
Diarrhea	12	PO	13	14
Prophylaxis for diarrhea	2	PO	30	50
Prophylaxis for diarrhea	2	PO	58	78
Prophylaxis for diarrhea	2	PO	87	104

Due to this event, there was no change in study treatment with paclitaxel, however, dose of ipatasertib was reduced to 300 mg from Study Day 14.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel

Event 2: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 101 and ipatasertib (300 mg) on Study Day 103.

On Study Day 104, the patient experienced non-serious Grade 3 diarrhea (20 episodes in last 24 hours). She did not have fever or hypotension. She received hydration and treatment with loperamide until Study Day 104. On Study Day 106, the event of diarrhea improved to Grade 1 and was considered resolved.

Due to this event, study treatment with ipatasertib and paclitaxel was permanently discontinued on Study Day 121 with the last dose of paclitaxel administered on Study Day 101 and ipatasertib administered on Study Day 105. The patient entered into the long-term follow-up.

The Investigator considered diarrhea to be unrelated to ipatasertib and paclitaxel and related to other unspecified causes.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Unspecified surgery of right breast	128	NA
Capecitabine (2 cycles)	156	Ongoing
Radiotherapy to right breast (dose: 4050 cGy, 15 fractions)	227	254

On Study Day 550, the patient withdrew consent from the study.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	1	Non-serious	2	3	Unrelated	Unrelated
Musculoskeletal pain	1	Non-serious	4	5	Unrelated	Related

Study Number/CRTN:	CO40016/318813	Patient number	1108
Demographics:	65-year-old White and American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER 2 negative right breast cancer (T1cN1aM1) on Study Day −60.

On Study Day −55, metastatic disease was confirmed with ER/PR and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included lung (right segment VI, left medial basal segment), right breast and lymph node (retroperitoneum paraaortic nodule).

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent conditions included insomnia, hypertension and arthralgia.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included clonazepam and tramadol.

Event: Neuropathy peripheral (neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel was administered on Study Day 57 and ipatasertib (300 mg) on Study Day 60. Ipatasertib was not given on Study Day 61 due to an unspecified adverse event.

On Study Day 62, the patient was diagnosed with non-serious Grade 1 neuropathy peripheral (presenting symptoms and diagnostic details not reported). On Study Day 68, the event worsened to Grade 2 and further to Grade 3 on Study Day 75. She received treatment with gabapentin. Grade changes for neuropathy are listed in the table below. The event of neuropathy peripheral remained unresolved at the time of patient's death.

Neuropathy peripheral grade changes:

Study Day	Neuropathy peripheral grade changes
68	2
75	3
91	2
109	3
174	2
309	1

Due to this event, there was no change in the study treatment with ipatasertib; however, study treatment with paclitaxel was initially reduced to 65 mg/m^2 on Study Day 85 and then permanently discontinued with the last dose given on Study Day 99.

The Investigator considered neuropathy peripheral to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 311, an overall response assessment showed disease progression with new lesion in right axillary lymph nodes.

On Study Day 371, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose given on Study Day 329. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Carboplatin (5 cycles)	443	Unknown

On Study Day 668, the patient died due to COVID-19 infection. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	2	Non-serious	3	151	Related	Unrelated
Asthenia	2	Non-serious	3	220	Unrelated	Unrelated
Abdominal pain	1	Non-serious	9	150	Related	Unrelated
Flatulence	1	Non-serious	34	Unresolved	Related	Unrelated
Nausea	1	Non-serious	34	136	Unrelated	Related
Alanine aminotransferase increased	2	Non-serious	71	92	Related	Unrelated
Aspartate aminotransferase increased	1	Non-serious	71	92	Related	Unrelated
Diarrhea	1	Non-serious	189	207	Related	Unrelated
Diarrhea	1	Non-serious	227	357	Related	Unrelated

Study Number/CRTN:	CO40016/318099	Patient number	1113
Demographics:	80-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Pulmonary embolism SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304776	Patient number	1123
Demographics:	55-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		

Cohort	Cohort A
Event (PT) Categories:	Large intestine perforation SAE, AE leading to study treatment discontinuation

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304623	Patient number	1142
Demographics:	72-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Categories:	Diarrhea SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/305120	Patient number	1154
Demographics:	65-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Diarrhea SAE, AE leading to study treatment discontinuation, Grade ≥ 3 diarrhea		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304627	Patient number	1162
Demographics:	67-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal and not otherwise specified histological subtype, poorly differentiated, ER/PR positive and HER 2-negative right breast cancer (T2N0M0) approximately 20 years prior to study entry, followed by the right breast ″other″ surgery and right axillary lymph node dissection performed on the same day.

On Study Day −92, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included pectoral muscle lymph node.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Adjuvant	Right breast (dose: 50 cGy, 25 fractions)	Approximately 19 years prior to study entry.	Approximately 19 years prior to study entry.
Radiotherapy	Adjuvant	Breast tumor bed (dose: 10 cGy, 5 fractions)	Approximately 19 years prior to study entry.	Approximately 19 years prior to study entry.
Cancer therapy	Adjuvant	Cyclophosphamide, methotrexate, and fluorouracil (6 cycles each)	Approximately 19 years prior to study entry.	Approximately 19 years prior to study entry.

The patient′s medical history included left ankle fracture. No surgical history was reported. Concurrent conditions included hypertension and anxiety.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included perindopril, amlodipine, alprazolam, cholecalciferol, and calcium carbonate.

Event: Peripheral sensory neuropathy

Prior to the event of peripheral sensory neuropathy, the most recent dose of paclitaxel was administered on Study Day 43 and ipatasertib (400 mg) on Study Day 44.

On Study Day 45, the patient was diagnosed with non-serious Grade 1 **peripheral sensory neuropathy** (symptoms and diagnostic details not reported). On Study Day 243, the event worsened to Grade 3. She received treatment with vitamin B-complex and duloxetine. The event of peripheral sensory neuropathy remained unresolved at the time of study discontinuation.

Due to this event, there was no change in study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 239.

The Investigator considered peripheral sensory neuropathy to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 673, the patient withdrew consent from the study treatment with the last dose of ipatasertib given on Study Day 672. The patient entered into the long-term follow-up.

On Study Day 778, a radiographic response assessment showed disease progression.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Radiotherapy to soft tissue (intra-pectoral lymph node) (dose: 3000 cGy, 10 fractions)	802	816

On Study Day 816, the patient was permanently discontinued from the study as per the physician’s decision (long term follow-up terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Edema peripheral	1	Non-serious	28	31	Unrelated	Related
Nausea	1	Non-serious	28	37	Related	Related
Sinus tachycardia	1	Non-serious	36	57	Unrelated	Unrelated
Nasal congestion	1	Non-serious	42	57	Unrelated	Related
Edema peripheral	2	Non-serious	57	400	Unrelated	Related
Vitamin B 12 Decreased	1	Non-serious	85	112	Unrelated	Unrelated
Weight increased	2	Non-serious	99	211	Unrelated	Related
Rash	1	Non-serious	123	131	Related	Related
Epistaxis	1	Non-serious	186	193	Unrelated	Related
Conjunctivitis	2	Non-serious	250	259	Unrelated	Unrelated
Diarrhea	2	Non-serious	286	296	Related	NA
Rash	1	Non-serious	334	400	Related	Related
Rash	1	Non-serious	334	564	Unrelated	Related
Rash	2	Non-serious	378	564	Related	NA
Pruritus	2	Non-serious	378	396	Related	NA
Nausea	1	Non-serious	463	463	Related	NA
Diarrhea	2	Non-serious	465	469	Related	NA
Vomiting	1	Non-serious	497	497	Unrelated	NA
Nausea	1	Non-serious	497	497	Related	NA
Diarrhea	2	Non-serious	500	502	Related	NA
Anxiety	1	Non-serious	535	Unresolved	Unrelated	Unrelated
Weight decreased	1	Non-serious	550	589	Unrelated	NA

Diarrhea	2	Non-serious	586	588	Related	NA
Edema peripheral	1	Non-serious	606	Unresolved	Unrelated	NA
Weight decreased	1	Non-serious	620	701	Unrelated	Unrelated
Diarrhea	2	Non-serious	664	668	Related	NA

Study Number/CRTN:	CO40016/318721	Patient number	1177
Demographics:	76-year-old female (race unknown)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea Grade $\geq$ 3 diarrhea		
Event 2 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal and not otherwise specified histological subtype, poorly differentiated, ER/PR negative and HER 2 equivocal left breast cancer (T1cN1M1) on Study Day −68.

On Study Day −44, metastatic disease was confirmed with ER/PR and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included breast (left axillary), left axillary lymph node, soft tissue (large left back muscle) and bone (thoracolumbar spine).

No past cancer treatments were reported.

The patient′s medical history included pericarditis, large intestine polyp and right breast cyst. Concurrent conditions included hypertension, adjustment disorder with depressed mood, spinal pain and fibrocystic breast disease.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. The same day, she also started loperamide prophylactically (total daily dose: 2 mg) for diarrhea.

Concomitant medications ongoing at Study Day 1 included paroxetine, atenolol, paracetamol, alprazolam, denosumab, calcium carbonate/cholecalciferol and pyridoxine.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 3.

On Study Day 4, the patient experienced non-serious Grade 1 intermittent diarrhea. Treatment with loperamide was maintained and she further received treatment with diosmectite. On Study Day 9, the event of diarrhea worsened to Grade 3. On Study Day 10, dose of loperamide was increased to 10 mg. On the same day (Study Day 10), the event of diarrhea improved to Grade 1. The event of diarrhea remained unresolved at the time of study discontinuation.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of Diarrhea	2	PO	1	5
Diarrhea	4	PO	6	6
Diarrhea	2	PO	7	7
Prophylaxis of Diarrhea	6	PO	8	8
Diarrhea	8	PO	9	9
Diarrhea	10	PO	10	10
Diarrhea	6	PO	11	12
Prophylaxis of Diarrhea	2	PO	13	13
Prophylaxis of Diarrhea	4	PO	14	14
Prophylaxis of Diarrhea	2	PO	15	15
Diarrhea	4	PO	16	19
Prophylaxis of Diarrhea	2	PO	20	21
Prophylaxis of Diarrhea	6	PO	24	24
Prophylaxis of Diarrhea	2	PO	27	27
Prophylaxis of Diarrhea	2	PO	30	32
Diarrhea	4	PO	33	33
Prophylaxis of Diarrhea	2	PO	34	34
Prophylaxis of Diarrhea	2	PO	36	36
Diarrhea	4	PO	37	39
Prophylaxis of Diarrhea	2	PO	40	46
Diarrhea	4	PO	47	48
Prophylaxis of Diarrhea	2	PO	49	50
Prophylaxis of Diarrhea	4	PO	51	51
Prophylaxis of Diarrhea	2	PO	52	55
Prophylaxis of Diarrhea	2	PO	58	61
Prophylaxis of Diarrhea	2	PO	59	60
Prophylaxis of Diarrhea	2	PO	63	64
Prophylaxis of Diarrhea	4	PO	65	65
Diarrhea	8	PO	66	66
Prophylaxis of Diarrhea	4	PO	67	67
Prophylaxis of Diarrhea	2	PO	68	71

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of Diarrhea	4	PO	72	72
Prophylaxis of Diarrhea	2	PO	73	76
Prophylaxis of Diarrhea	4	PO	77	77
Prophylaxis of Diarrhea	2	PO	78	85
Prophylaxis of Diarrhea	2	PO	86	87
Diarrhea	6	PO	91	91
Prophylaxis of Diarrhea	2	PO	92	92
Prophylaxis of Diarrhea	4	PO	93	93
Prophylaxis of Diarrhea	2	PO	94	94
Prophylaxis of Diarrhea	4	PO	95	95
Prophylaxis of Diarrhea	4	PO	98	98
Prophylaxis of Diarrhea	2	PO	99	101
Prophylaxis of Diarrhea	4	PO	102	103
Prophylaxis of Diarrhea	2	PO	105	110
Prophylaxis of Diarrhea	2	PO	113	113
Prophylaxis of Diarrhea	2	PO	114	115
Prophylaxis of Diarrhea	2	PO	117	120
Prophylaxis of Diarrhea	2	PO	122	123
Prophylaxis of Diarrhea	2	PO	125	132
Prophylaxis of Diarrhea	4	PO	133	133
Prophylaxis of Diarrhea	2	PO	134	137
Prophylaxis of Diarrhea	2	PO	139	139
Prophylaxis of Diarrhea	2	PO	141	141
Prophylaxis of Diarrhea	.	PO	142	142
Prophylaxis of Diarrhea	2	PO	147	148
Diarrhea	4	PO	150	150
Prophylaxis of Diarrhea	2	PO	151	152
Prophylaxis of Diarrhea	4	PO	153	153
Diarrhea	2	PO	154	155
Diarrhea	4	PO	156	156
Diarrhea	6	PO	157	157
Prophylaxis of Diarrhea	4	PO	158	158
Prophylaxis of Diarrhea	2	PO	159	160
Prophylaxis of Diarrhea	4	PO	161	161
Prophylaxis of Diarrhea	2	PO	162	162
Prophylaxis of Diarrhea	6	PO	163	163
Prophylaxis of Diarrhea	4	PO	164	164
Prophylaxis of Diarrhea	2	PO	165	165
Prophylaxis of Diarrhea	2	PO	169	169
Prophylaxis of Diarrhea	4	PO	170	170
Prophylaxis of Diarrhea	4	PO	173	173
Prophylaxis of Diarrhea	2	PO	179	180
Prophylaxis of Diarrhea	2	PO	183	183
Prophylaxis of Diarrhea	4	PO	184	186
Diarrhea	4	PO	189	192
Prophylaxis of Diarrhea	4	PO	204	204
Prophylaxis of Diarrhea	2	PO	206	206
Prophylaxis of Diarrhea	4	PO	207	207
Prophylaxis of Diarrhea	4	PO	210	211

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of Diarrhea	8	PO	213	213
Prophylaxis of Diarrhea	6	PO	214	214
Prophylaxis of Diarrhea	4	PO	215	215
Prophylaxis of Diarrhea	4	PO	217	218
Prophylaxis of Diarrhea	4	PO	220	220
Prophylaxis of Diarrhea	4	PO	225	225
Prophylaxis of Diarrhea	4	PO	230	230
Diarrhea	4	PO	233	234
Diarrhea	4	PO	238	238
Diarrhea	4	PO	240	243
Diarrhea	4	PO	246	247
Diarrhea	4	PO	257	257
Diarrhea	4	PO	262	262
Diarrhea	4	PO	268	268
Diarrhea	4	PO	275	275
Diarrhea	4	PO	285	285
Diarrhea	4	PO	291	291
Diarrhea	4	PO	293	293
Diarrhea	4	PO	295	300
Diarrhea	4	PO	303	303
Diarrhea	4	PO	307	307
Diarrhea	4	PO	313	315
Diarrhea	4	PO	317	318
Diarrhea	4	PO	320	328
Diarrhea	4	PO	330	330
Diarrhea	4	PO	339	339
Diarrhea	4	PO	347	347
Diarrhea	4	PO	349	349
Diarrhea	4	PO	355	355
Diarrhea	4	PO	369	369
Diarrhea	4	PO	379	380
Diarrhea	4	PO	382	382
Diarrhea	6	PO	385	386
Diarrhea	4	PO	387	387
Diarrhea	4	PO	394	394
Diarrhea	4	PO	400	400
Diarrhea	4	PO	404	404
Diarrhea	4	PO	407	407
Diarrhea	4	PO	409	410
Diarrhea	4	PO	414	414
Diarrhea	4	PO	430	430
Diarrhea	4	PO	438	438
Diarrhea	2	PO	439	439
Diarrhea	4	PO	440	440
Diarrhea	4	PO	443	444

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	456	456
Diarrhea	4	PO	461	462
Diarrhea	6	PO	464	464
Diarrhea	4	PO	465	465
Diarrhea	4	PO	470	470
Diarrhea	4	PO	487	487
Diarrhea	4	PO	494	494
Diarrhea	6	PO	497	497
Diarrhea	4	PO	498	499
Diarrhea	4	PO	511	511

Diarrhea grade changes:

Study Day	Diarrhea grade changes
7	2
8	1
9	3
10	1
11	2
12	1
15	1
16	2
17	1
29	1
32	1
33	2
36	1
37	2
39	1
47	3
48	2
49	1
55	1
65	3
67	1
91	2
94	1
150	2
156	2
157	1

Due to this event, study treatment with paclitaxel was reduced to 65 mg/m^2 on Study Day 85 and ipatasertib was reduced to 300 mg on Study Day 86.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

Event 2: Neuropathy peripheral (Neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel was administered on Study Day 43 and ipatasertib (400 mg) on Study Day 49.

On Study Day 58, the patient was diagnosed with non-serious Grade 3 neuropathy peripheral (presenting signs and symptoms not reported). Treatment for the event included pregabalin. On Study Day 85, the event of neuropathy peripheral improved to Grade 2. Grade changes for neuropathy peripheral are listed in the table below. The event of neuropathy peripheral remained unresolved at the time of study discontinuation.

Neuropathy peripheral grade changes:

Study Day	Neuropathy peripheral grade changes
85	2
148	1
183	2
223	1
254	3
268	2
422	2
436	1
444	2
505	3

Due to the event of neuropathy peripheral, there was no change in the study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 491.

The Investigator considered neuropathy peripheral to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 562, the patient was discontinued from the study as per physician's decision (no progression on RECIST; however, in view of clinical signs and trend to evolution, lesional progression). The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine (5 cycles)	570	Unknown

On Study Day 832, the patient was permanently discontinued from the study as per the physician's decision (long term follow-up terminated by Sponsor).

Other events experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Mucosal inflammation	2	Non-serious	8	58	Related	Unrelated
Neutropenia	3	Non-serious	13	15	Unrelated	Related
Folliculitis	2	Non-serious	15	29	Unrelated	Related
Neutropenia	2	Non-serious	15	27	Unrelated	Related
Vertigo	2	Non-serious	34	59	Unrelated	Unrelated
Rash pustular	2	Non-serious	43	58	Unrelated	Unrelated
Myalgia	2	Non-serious	43	Unresolved	Unrelated	Unrelated
Arthralgia	2	Non-serious	43	Unresolved	Unrelated	Unrelated
Alopecia	2	Non-serious	58	Resolving	Unrelated	Related
Anemia macrocytic	2	Non-serious	71	100	Related	Related
Asthenia	1	Non-serious	71	Unresolved	Related	Related
Nail dystrophy	1	Non-serious	85	100	Unrelated	Related
Urinary tract infection	2	Non-serious	100	120	Unrelated	Unrelated
Arthralgia	1	Non-serious	114	120	Unrelated	Unrelated
Neutropenia	3	Non-serious	118	120	Unrelated	Related
Insomnia	1	Non-serious	123	197	NA	NA
Neutropenia	3	Non-serious	126	140	Unrelated	Related
Neutropenia	3	Non-serious	154	170	Unrelated	Related
Neutropenia	3	Non-serious	182	183	Unrelated	Related
Osteoarthritis	1	Non-serious	272	Resolving	Unrelated	Unrelated
Neutropenia	2	Non-serious	294	296	Unrelated	Related
Urinary tract infection	2	Non-serious	295	302	Unrelated	Unrelated
Anemia	1	Non-serious	296	Resolving	Unrelated	Unrelated
Oedema peripheral	1	Non-serious	310	317	Unrelated	Unrelated
Urinary tract infection	2	Non-serious	333	333	Unrelated	Unrelated
Chest pain	2	Non-serious	447	Unresolved	Unrelated	Unrelated
Neutropenia	2	Non-serious	455	Resolving	NA	Related
Urinary tract infection	2	Non-serious	462	463	NA	Unrelated

Study Number/CRTN:	CO40016/305247	Patient number	1182
Demographics:	65-year-old female (race unknown)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER 2-negative right breast cancer (T1bN1aM0) approximately 7 years prior to study entry following right breast biopsy.

On Study Day −53, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included lymph nodes (left supraclavicular, right hilar and right ″LOGE 4″).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Adjuvant	Right breast (dose: 50Gy, 25 fractions)	Approximately 7 years prior to study entry	Approximately 6 years prior to study entry
Surgery	Curative	Right breast lumpectomy and axillary dissection	Approximately 7 years prior to study entry	NA
Cancer therapy	Adjuvant	Letrozole	Approximately 6 years prior to study entry	−22

The patient′s medical history included diverticulitis, ligament sprain (left knee) and left breast calcification. Surgical history included left breast tumor excision. Concurrent conditions included dermatitis contact, drug intolerance, hypertension, aortic valve incompetence, osteoarthritis, dyslipidemia and insomnia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included atorvastatin, ramipril, propranolol, bromazepam and hydroxyzine.

On Study Day 57, the patient was diagnosed Grade 1 foot neuropathy (preferred term: neuropathy peripheral; non-serious, related). On Study Day 68, she was diagnosed with Grade 1 hand neuropathy (preferred term: neuropathy peripheral; non-serious, related). No treatment was given for these events. On Study Day 134, the event of hand neuropathy was considered resolved.

Event: Neuropathy peripheral (Lower limbs peripheral neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel was administered on Study Day 215 and ipatasertib (400 mg) on Study Day 220.

On Study Day 221, the patient experienced Grade 1 asthenia (non-serious related). On the same day (Study Day 221), the patient's foot neuropathy was reassessed, and she was diagnosed with non-serious Grade 3 lower limbs peripheral neuropathy (symptoms and assessment details not reported). No treatment was given for these events. On Study Day 258, the event of asthenia was considered resolved. The event of neuropathy peripheral remained unresolved at the time of study discontinuation.

Due to this event, there was no change in study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 215.

The Investigator considered neuropathy peripheral to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 448, a radiographic assessment showed disease progression with new lesions in mediastinal lymph nodes.

On the same day (Study Day 448), study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose of ipatasertib given on Study Day 444. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Abemaciclib and anastrozole	467	522
Capecitabine (unknown cycles)	529	–

On Study Day 781, the patient was permanently discontinued from the study treatment as per the physician's decision (LTFU terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	3	19	Related	Related
Constipation	1	Non-serious	3	19	Related	Related
Headache	1	Non-serious	4	33	Related	Related
Alopecia	1	Non-serious	14	258	Unrelated	Related
Muscle spasms	1	Non-serious	19	258	Related	Related
Diarrhea	1	Non-serious	40	134	Related	Related
Epistaxis	1	Non-serious	69	134	Related	Related
Dyspnea exertional	1	Non-serious	80	Unresolved	Unrelated	Unrelated
Weight increased	1	Non-serious	117	124	Unrelated	Unrelated
Weight increased	1	Non-serious	131	Unresolved	Unrelated	Unrelated
Ear, nose and throat infection	1	Non-serious	141	150	Unrelated	Unrelated
Pruritus	1	Non-serious	142	160	Unrelated	Unrelated
Diarrhea	2	Non-serious	154	466	Related	Related
Conjunctivitis allergic	1	Non-serious	183	207	Unrelated	Unrelated
Erythema	2	Non-serious	208	209	Unrelated	Unrelated
Joint swelling	1	Non-serious	242	258	Unrelated	Unrelated
Edema peripheral	1	Non-serious	258	281	Unrelated	NA
Edema peripheral	1	Non-serious	314	Unresolved	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305629	Patient number	1192
Demographics:	71-year-old American Indian or Alaska native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ER/PR and HER2 negative left breast cancer (T3N0M1) (histopathology unknown), approximately 7 years prior to study entry.

The patient was diagnosed with metastatic disease on Study Day –46 with ER /PR unknown and HER2 not assessed in metastatic tissue. At screening, sites of disease involvement included bilateral breast, lymph nodes (superior mediastinal, left subclavian ganglion, right axillary and midline pericardium mediastinal), bilateral pleural effusion, and bone (left cervical ganglion).

Past cancer treatment is listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left radical mastectomy	Approximately 6 years prior to study entry	NA

No medical/surgical history was reported. The patient′s concurrent conditions included anemia and hypertension.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included bisoprolol and losartan.

Event: Neuropathy peripheral (peripheral neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel was administered on Study Day 261 and ipatasertib (400 mg) on Study Day 263.

On Study Day 264, the patient was diagnosed with non-serious Grade 2 neuropathy peripheral (presenting signs and symptoms not reported). No treatment was given for this event. On Study Day 285, the event of neuropathy peripheral improved to Grade 1.

On Study Day 464, the event of neuropathy peripheral was considered resolved.

Due to this event, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 303.

The Investigator considered neuropathy peripheral to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 474, a radiographic response assessment showed disease progression with new lesion in head (leptomeningeal infiltration).

On Study Day 474, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose given on Study Day 452. The patient entered into the long-term follow-up.

On Study Day 486, the patient died to disease progression. No information regarding autopsy was reported.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	2	Non-serious	3	9	Unrelated	Unrelated
Diarrhea	1	Non-serious	10	15	Related	Unrelated
Diarrhea	2	Non-serious	10	15	Related	Unrelated
Diarrhea	2	Non-serious	16	23	Related	Unrelated
Diarrhea	2	Non-serious	29	49	Related	Unrelated
Lipase increased	1	Non-serious	57	57	Unrelated	Unrelated
Amylase increased	1	Non-serious	57	57	Unrelated	Unrelated
Diarrhea	1	Non-serious	58	130	Related	Unrelated
Alopecia	1	Non-serious	67	97	Unrelated	Related
Alopecia	2	Non-serious	67	368	Unrelated	Related
Edema peripheral	2	Non-serious	103	190	Unrelated	Related

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Fungal skin infection	1	Non-serious	184	218	Unrelated	Unrelated
Gastritis	1	Non-serious	241	264	Unrelated	Unrelated
Syncope	1	Non-serious	241	241	Unrelated	Unrelated
Vomiting	1	Non-serious	290	293	Related	Related
Diarrhea	1	Non-serious	290	293	Related	Unrelated
Diarrhea	1	Non-serious	345	365	Related	Unrelated
Vomiting	1	Non-serious	379	389	Related	Unrelated
Vomiting	1	Non-serious	403	421	Related	Unrelated
Headache	1	Non-serious	453	459	Unrelated	Unrelated

Study Number/CRTN:	CO40016/318137	Patient number	1199
Demographics:	77-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Categories:	Diarrhea SAE, AE leading to study treatment discontinuation, Grade $\geq$ 3 diarrhea		
Event 2 (PT) Category:	Atrial fibrillation SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/307262	Patient number	1201
Demographics:	45-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Categories:	Erythema multiforme SAE, AE leading to study treatment discontinuation		
Event 2 (PT) Categories:	Hypersensitivity SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/320127	Patient number	1208
Demographics:	62-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Toxic neuropathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER2 negative left breast cancer (T2N1M0) on Study Day −792 following left radical mastectomy.

On Study Day −106, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included lymph nodes (left supraclavicular, right root of lung and midline perivascular).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	−758	−728
Cancer therapy	Adjuvant	Paclitaxel (4 cycles)	−728	−666
Radiotherapy	Adjuvant	Post-operative scar (site "other", dose: 46 cGy, 23 fractions)	−638	−607
Radiotherapy	Adjuvant	Parasternal lymph node (dose: 44 cGy, 21 fractions)	−638	−607
Radiotherapy	Adjuvant	Sub-supraclavicular and axillary lymph node (dose: 40 cGy, 20 fractions)	−638	−607

No medical history was reported. Surgical history included cholecystectomy and caesarean section. Concurrent conditions included osteoarthritis (knee), diabetes mellitus, hypertension, obesity, renal cyst (left kidney), hepatic cyst (liver segment VI).

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included metformin, indapamide/perindopril and bisoprolol.

Event: Toxic neuropathy (toxicity polyneuropathy)

Prior to the event of toxic neuropathy, the most recent dose of paclitaxel was administered on Study Day 71 and ipatasertib (400 mg) on Study Day 77.

On Study Day 81, the patient was diagnosed with non-serious Grade 1 toxic neuropathy. On Study Day 221, the event of toxic neuropathy, worsened to Grade 3. She received treatment with thioctic acid. The event of toxic neuropathy remained unresolved at the time of patient′s death (see narrative below).

Due to this event, there was no change in study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose of paclitaxel given on Study Day 218.

The Investigator considered toxic neuropathy to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 399, a radiographic response assessment showed disease progression with new lesion in right neck lymph node.

On Study Day 405, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose given on Study Day 386. The patient entered into the long-term follow-up.

On Study Day 700, the patient died due to disease progression. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Alanine aminotransferase increased	1	Non-serious	15	43	Related	Related
Diarrhea	1	Non-serious	18	18	Related	Unrelated
Diarrhea	1	Non-serious	60	64	Related	Unrelated
Alopecia	2	Non-serious	60	280	Unrelated	Related
Pneumonia	2	Non-serious	312	319	Unrelated	Unrelated

Study Number/CRTN:	CO40016/318813	Patient number	1210
Demographics:	62-year-old American Indian or Alaska native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal poorly differentiated ER/PR and HER2 negative right breast cancer (T1N0M0), approximately 2 years and 11 months prior to study entry.

The patient was diagnosed with metastatic disease on Study Day −7 with ER /PR negative and HER2 negative in metastatic tissue. At screening, sites of disease involvement included lung (left upper lobe) and chest (node at right arm level).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right lumpectomy	Approximately 2 years and 10 months prior to study entry	NA
Surgery	Curative	Right radical mastectomy	−888	NA

No medical/surgical history was reported. No concurrent conditions were reported.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 was reported.

Event: Neuropathy peripheral (peripheral neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel was administered on Study Day 71 and ipatasertib (400 mg) on Study Day 77.

On Study Day 82, the patient was diagnosed with non-serious Grade 1 neuropathy peripheral (presenting signs and symptoms not reported). On Study Day 218, the event of neuropathy peripheral worsened to Grade 2. She received treatment with gabapentin. On Study Day 300, the event of neuropathy peripheral improved to Grade 1.

On Study Day 442, the event of neuropathy peripheral was considered resolved.

Due to this event, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 239.

The Investigator considered neuropathy peripheral to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 765, the patient withdrew consent from study treatment with ipatasertib and study with the last dose given on Study Day 749.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	10	156	Related	Unrelated
Hypertriglyceridemia	2	Non-serious	141	183	Related	Unrelated
Blood cholesterol increased	1	Non-serious	141	183	Related	Unrelated
COVID-19	1	Non-serious	155	176	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305247	Patient number	1221
Demographics:	65-year-old female (Race unknown)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea Grade $\geq$ 3 diarrhea		
Event 2 (PT) Categories:	Diarrhea AE leading to study treatment discontinuation, Grade $\geq$ 3 diarrhea		
Event 3 (PT) Category:	Fatigue AE leading to study treatment discontinuation		
Event 4 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		
Event 5 (PT) Category:	Paronychia AE leading to study treatment discontinuation		
Event 6 (PT) Category:	Onycholysis AE leading to study treatment discontinuation		
Event 7 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR positive and HER2 negative left breast cancer (T1bN0M0), approximately 3 years and 9 months prior to study entry.

On Study Day −56, the patient was diagnosed with locally recurrent and metastatic disease with ER/PR and HER2 negative disease in recurrent/metastatic tissue. At screening, sites of disease involvement included left skin, bone (multiple lesions) and left internal mammal lymph node.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left partial mastectomy	Approximately 3 years and 8 months prior to study entry	NA

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Adjuvant	Inferior quadrant of left breast (dose: 66 cGy; 26 fractions)	Approximately 3 years and 6 months prior to study entry	Approximately 3 years and 5 months prior to study entry
Cancer therapy	Adjuvant	Letrozole	Approximately 3 years and 5 months prior to study entry	–30

The patient′s medical history included asthenia, hepatitis A, ectopic pregnancy with contraceptive device, hepatitis post transfusion, cervix carcinoma and pericarditis. Surgical history included hysterectomy. Concurrent conditions included hypercholesterolemia, factor V Leiden mutation, osteoporosis, meningioma, hypertension, scar pain, dyspnea, and insomnia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included melatonin, hydroxyzine, paracetamol, tinzaparin, verapamil and atorvastatin.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 2.

On Study Day 2, the patient experienced Grade 1 pyrexia (body temperature not reported), Grade 3 nausea, Grade 1 vomiting, Grade 2 decreased appetite (all non-serious, related). On Study Day 3, she experienced Grade 2 abdominal pain (non-serious, related) and non-serious Grade 3 diarrhea. She received treatment with loperamide and racecadotril for diarrhea, paracetamol for pyrexia and abdominal pain, metoclopramide and ondansetron for nausea and vomiting. On Study Day 10, the event of decreased appetite improved to Grade 1. On the same day (Study Day 10), the events of pyrexia, nausea, vomiting, abdominal pain and diarrhea were considered resolved. On Study Day 72, the event of decreased appetite was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	4	4
Diarrhea	6	PO	5	5
Diarrhea	10	PO	6	6
Diarrhea	4	PO	7	7
Diarrhea	6	PO	22	23
Diarrhea	2	PO	35	36

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	45	45
Diarrhea	4	PO	60	60
Diarrhea	4	PO	64	64

Due to the event of diarrhea, Cycle 1 Day 8 of paclitaxel was not administered; study treatment with ipatasertib was interrupted on Study Day 8. The next dose of paclitaxel and ipatasertib (at a reduced of 300 mg) was given on Study Day 22.

The Investigator considered diarrhea to be related to ipatasertib and paclitaxel.

On Study Day 26, the patient experienced Grade 1 (initial intensity) diarrhea (non-serious, related). She received treatment with racecadotril.

Diarrhea grade changes:

Study Day	Diarrhea grade changes
31	2
37	1
47	2

Event 2: Diarrhea
Event 3: Fatigue

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 64 and ipatasertib (200 mg) on Study Day 65.

On Study Day 66, the ongoing event of diarrhea worsened to non-serious Grade 3. She received treatment with racecadotril and loperamide.

Prior to the event of fatigue, the most recent dose of paclitaxel was administered on Study Day 64 and ipatasertib (200 mg) on Study Day 67.

On Study Day 68, the patient experienced non-serious Grade 3 fatigue. No treatment was given for the event of fatigue. On Study Day 72, the events of diarrhea and fatigue were considered resolved.

Due to the events of diarrhea and fatigue, Cycle 3 Day 15 dose of paclitaxel was delayed and later given on Study Day 78 (Cycle 3 Day 22). Study treatment with ipatasertib was permanently discontinued with the last dose given on Study Day 70.

The Investigator considered diarrhea and fatigue to be related to ipatasertib and unrelated to paclitaxel.

Event 4: Peripheral sensory neuropathy (Fingers sensitive neuropathy)

Prior to the event of peripheral sensory neuropathy, the most recent dose of paclitaxel was administered on Study Day 85.

On Study Day 86, the patient experienced non-serious Grade 1 peripheral sensory neuropathy of fingers**.** On Study Day 149, the event of peripheral sensory neuropathy worsened to Grade 2. No treatment was reported for this event. On Study Day 268, the event of peripheral sensory neuropathy improved to Grade 1. The event of peripheral sensory neuropathy remained unresolved at the time of study discontinuation.

Due to the event of peripheral sensory neuropathy, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 155.

The Investigator considered peripheral sensory neuropathy to be unrelated to ipatasertib and related to paclitaxel.

Event 5: Paronychia (Bilateral big toe paronychia)
Event 6: Onycholysis (Bilateral big toe onycholysis)

Prior to the events of onycholysis and paronychia, the most recent dose of paclitaxel was administered on Study Day 99.

On Study Day 101, the patient was diagnosed with non-serious Grade 2 bilateral big toe paronychia and non-serious Grade 2 bilateral big toe onycholysis. She received treatment with sodium hypochlorite, and clobetasol propionate and also dressing with duoderm. The events of paronychia and onycholysis remained unresolved at the time of study discontinuation.

Due to the events of paronychia and onycholysis, study treatment with paclitaxel was permanently discontinued.

The Investigator considered paronychia and onycholysis to be related to ipatasertib and paclitaxel.

Event 7: Neuropathy peripheral (Feet neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel was administered on Study Day 155.

On Study Day 156, the patient was diagnosed with non-serious Grade 2 neuropathy peripheral of feet. No treatment was reported for this event. The event of neuropathy peripheral remained unresolved at the time of study discontinuation.

Due to the event of neuropathy peripheral, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 155.

The Investigator considered neuropathy peripheral to be unrelated to ipatasertib and related to paclitaxel. The patient entered into the long-term follow-up.

On Study Day 461, a radiographic response assessment showed disease progression.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine	475	Ongoing

On Study Day 670, the patient was permanently discontinued from the study as per the physician's decision (LTFU terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Arthralgia	2	Non-serious	2	10	Related	Related
Alanine aminotransferase increased	2	Non-serious	7	21	Related	Related
Arthralgia	1	Non-serious	25	52	Related	Related
Dry mouth	1	Non-serious	25	65	Related	Related
Headache	2	Non-serious	30	55	Unrelated	Unrelated
Febrile Neutropenia	3	Non-serious	34	42	Related	Related
Pyrexia	1	Non-serious	47	50	Unrelated	Unrelated
Nausea	1	Non-serious	57	72	Related	Related
Headache	1	Non-serious	86	90	Unrelated	Unrelated
Anxiety	2	Non-serious	93	206	Unrelated	Unrelated
Constipation	2	Non-serious	115	142	Unrelated	Unrelated
Ageusia	1	Non-serious	118	206	Unrelated	Related
Decreased appetite	1	Non-serious	120	267	Unrelated	Unrelated
Neutropenia	2	Non-serious	126	133	Unrelated	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Weight decreased	2	Non-serious	141	267	Related	Related
Rash	1	Non-serious	156	165	Unrelated	Related

Study Number/CRTN:	CO40016/318101	Patient number	1231
Demographics:	81-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea SAE		
Event 2 (PT) Categories:	Diarrhea SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/318146	Patient number	1237
Demographics:	54-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Categories:	COVID-19 pneumonia SAE, COVID-19 SAE		
Event 2 (PT) Category:	Hyperglycemia AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/320127	Patient number	1248
Demographics:	69-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Polyneuropathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with not otherwise specified, moderately differentiated Grade 2 ER/PR negative and HER2 negative right breast cancer (T3N0M1) on Study Day −62.

On Study Day −62, the patient was diagnosed with pathological metastatic disease with ER /PR negative and HER2 negative disease followed by right breast biopsy performed on the same day. At screening, sites of disease involvement included bilateral mediastinum lymph node, left lymph node root of lung and right lateral breast.

No past cancer treatment was reported.

The patient′s medical history included chemical burn and skin graft. Surgical history included caesarean section and appendicectomy. Concurrent conditions included hyperglycemia, diabetes mellitus, hypertension, obesity, renal cyst, hiatus hernia, chronic gastritis, duodenogastric reflux and asthenia.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included indapamide, bisoprolol, amlodipine, empagliflozin, metformin/vildagliptin and metformin.

Event: Polyneuropathy

Prior to the event of polyneuropathy, the most recent dose of ipatasertib (300 mg) on Study Day 150 and paclitaxel on Study Day 157.

On Study Day 163, the patient was diagnosed with non-serious Grade 1 polyneuropathy. On Study Day 175, the event of polyneuropathy worsened to Grade 3. She received treatment with thioctic acid for polyneuropathy. The event of polyneuropathy remained unresolved at the time of study discontinuation.

Due to this event, there was no change in the study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose administered on Study Day 164.

The Investigator considered polyneuropathy to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 519, a radiographic response assessment showed disease progression with new lesion in right side of brain (cerebral hemisphere).

Study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose given on Study Day 512. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Radiotherapy for brain (dose: 30 cGy; 10 fractions)	542	559

On Study Day 682, the patient was discontinued from the study as the study was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	2	Non-serious	3	7	Related	Unrelated
Hyperglycemia	2	Non-serious	8	20	Related	Unrelated
Vomiting	1	Non-serious	70	70	Related	Unrelated
Alopecia	2	Non-serious	72	492	Unrelated	Related
Vomiting	1	Non-serious	134	134	Related	Unrelated
Vomiting	1	Non-serious	170	170	Related	Unrelated
Weight decreased	2	Non-serious	233	Unresolved	Unrelated	Unrelated
Hyperglycemia	2	Non-serious	261	265	Related	Unrelated
Lipase increased	3	Non-serious	323	405	Related	Unrelated

1.5 NARRATIVES FOR PATIENTS WHO BECAME PREGNANT WHILE IN THE STUDY

No patient became pregnant while in the study.

1.6 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥ 3 HYPERGLYCEMIA

Study Number/CRTN:	CO40016/304778	Patient number	1003
Demographics:	76-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Categories:	Pneumonia SAE, AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Hyperglycemia Grade ≥ 3 Hyperglycemia		
Event 3 (PT) Category:	Glucose tolerance impaired Grade ≥ 3 Hyperglycemia		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304787	Patient number	1028
Demographics:	65-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Hyperglycemia Grade ≥ 3 hyperglycemia		
Event 2 (PT) Categories:	Hyperglycemia SAE, Grade ≥ 3 hyperglycemia		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304879	Patient number	1084
Demographics:	62-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Hyperglycemia Grade ≥ 3 hyperglycemia		
Event 2 (PT) Category:	Edema AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

1.7 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE≥3 DIARRHEA

Study Number/CRTN:	CO40016/305632	Patient number	1010
Demographics:	80-year-old American Indian or Alaska Native/White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was diagnosed with medullary, poorly differentiated, ER/PR negative and HER 2 negative, locally advanced unresectable recurrent, left breast cancer (T4bN0M0), on Study Day –94.

At screening, sites of disease involvement included external inferior quadrant of left breast.

No past cancer treatments were reported.

The patient′s medical history included genital prolapse. Surgical history included prolapse repair. Concurrent conditions included nephrolithiasis, hypothyroidism, and hypertension.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included levothyroxine and losartan.

On Study Day 5, the patient experienced Grade 2 diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide. On Study Day 8, the event of diarrhea was considered resolved.

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 10 and ipatasertib (400 mg) on Study Day 13.

On Study Day 14, the patient experienced non-serious Grade 3 diarrhea (10 stools per day) and Grade 2 abdominal pain (non-serious, related to ipatasertib). She received treatment with loperamide for diarrhea and hyoscine for abdominal pain. On Study Day 16, the event of diarrhea improved to Grade 1 (3-4 stools per day). On Study Day 17, stool analysis was negative for infection. On the following day (On Study Day 18), the events of diarrhea and abdominal pain were considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Unit: mg)	Route	Start day	Stop day
Diarrhea	4	PO	1	4
Diarrhea	24	PO	5	8
Diarrhea	4	PO	9	13
Diarrhea	24	PO	14	18
Diarrhea	4	PO	19	25
Diarrhea	24	PO	26	28
Diarrhea	4	PO	29	117

Due to this event, there was no change in study treatment with paclitaxel; however, ipatasertib was interrupted on Study Day 14 and the next dose of ipatasertib was given at a reduced dose of 300 mg on Study Day 21.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 25, the patient experienced Grade 2 diarrhea (non-serious, related to ipatasertib). Treatment with loperamide was maintained. On Study Day 28, the event of diarrhea was considered resolved. Due to this event, study treatment with ipatasertib was further reduced to 200 mg on Study Day 34.

On Study Day 110, a radiographic response assessment showed disease progression with new lesion in right lung (segment III).

On Study Day 117, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 103 and ipatasertib on Study Day 109. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Gemcitabine and carboplatin	138	358
Capecitabine	358	Ongoing

On Study Day 1341, the patient was permanently discontinued from the study as per physician's decision (long term follow-up terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Asthenia	2	Non-serious	5	8	Related	Unrelated
Nausea	1	Non-serious	13	14	Related	Unrelated
Urinary tract infection	2	Non-serious	33	40	Unrelated	Unrelated
Alopecia	1	Non-serious	36	454	Unrelated	Related
Vomiting	1	Non-serious	37	42	Related	Related
Nausea	1	Non-serious	37	52	Related	Related
Pharyngitis	2	Non-serious	53	72	Unrelated	Unrelated
Insomnia	2	Non-serious	93	Unresolved	Unrelated	Unrelated
Peripheral sensory neuropathy	1	Non-serious	99	102	Unrelated	Related
Pain in extremity	1	Non-serious	1221	Unknown	NA	NA

Study Number/CRTN:	CO40016/304191	Patient number	1012
Demographics:	63-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Diarrhea Grade $\geq$ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was diagnosed with poorly differentiated (histological subtype: not otherwise specified), ER/PR negative and HER 2-negative, locally advanced unresectable, right breast cancer (T4bN2M0) on Study Day −58.

At screening, sites of disease involvement included right mammary gland and right axillary lymph nodes.

No past cancer treatments were reported.

The patient′s medical history included calculus urinary, leukocyturia, peptic ulcer, cholelithiasis, cholecystitis chronic, goiter and chronic gastritis. Surgical history included nephrectomy (right kidney). Concurrent conditions included hypertension, myocardial ischemia, arteriosclerosis coronary artery, cardiac failure chronic, hydronephrosis, cyst (abdominal cavity), anxiety, electrolyte imbalance and hypercalcemia.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included losartan and amlodipine.

On Study Day 8, the patient experienced Grade 2 diarrhea (non-serious, related). No treatment was given for the event. On Study Day 17, the event of diarrhea was considered resolved.

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 35 and ipatasertib (400 mg) on Study Day 39.

On Study Day 40, the patient experienced non-serious Grade 2 (initial intensity) diarrhea. She received treatment with loperamide (2 mg, PO) and dietary advice was given. On Study Day 43, the event of diarrhea worsened to Grade 3. Dose of loperamide was increased to 6 mg. Later, on the same day (Study Day 43), the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	40	42
Diarrhea	6	PO	43	43
Diarrhea	2	PO	47	47
Diarrhea	4	PO	60	62
Diarrhea	6	PO	63	65
Diarrhea	4	PO	67	81
Diarrhea	2	PO	84	117
Diarrhea	2	PO	178	178
Diarrhea	2	PO	187	187

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	192	192

Due to this event, Cycle 2 Day 15 of paclitaxel was delayed and ipatasertib was interrupted on Study Day 42. The next dose of paclitaxel was given on Study Day 49 and ipatasertib at a reduced dose of 300 mg (due to an event of Grade 2 hyperglycemia; non-serious, related to ipatasertib, onset day: Study Day 15 and resolution day: Study Day 154) on Study Day 56.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 284, study treatment with ipatasertib and paclitaxel was permanently discontinued as per physician′s decision (patient has achieved complete response according to RECIST assessment and is planned to undergo radical mastectomy) with the last dose of paclitaxel given on Study Day 266 and ipatasertib on Study Day 272. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Right breast ″other″ surgery	299	NA
Doxorubicin and cyclophosphamide (4 cycles each)	342	445
Radiotherapy to postoperative breast zone and regional lymph nodes zone (dose: 96 cGy, 1 fraction)	492	533

On Study Day 779, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Asthenia	2	Non-serious	9	322	Related	Related
Dyspepsia	1	Non-serious	9	29	Related	Related
Peripheral sensory neuropathy	1	Non-serious	9	92	Unrelated	Related
Alopecia	2	Non-serious	9	210	Related	Related
Dysphonia	1	Non-serious	17	210	Related	Related
Blood creatinine increased	1	Non-serious	42	47	Related	Unrelated
Diarrhea	1	Non-serious	47	47	Related	Unrelated

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	2	Non-serious	60	65	Related	Unrelated
Vomiting	1	Non-serious	60	60	Related	Related
Abdominal distension	2	Non-serious	67	81	Related	Unrelated
Diarrhea	2	Non-serious	70	73	Related	Unrelated
Diarrhea	2	Non-serious	78	78	Related	Unrelated
Constipation	2	Non-serious	82	117	Unrelated	Unrelated
Headache	1	Non-serious	92	104	Unrelated	Unrelated
Peripheral sensory neuropathy	2	Non-serious	92	652	Unrelated	Related
Dyspnea	1	Non-serious	127	Unresolved	Unrelated	Related
Arthralgia	2	Non-serious	127	134	Unrelated	Related
Arthralgia	1	Non-serious	142	143	Unrelated	Related
Arthralgia	1	Non-serious	149	150	Unrelated	Related
Headache	1	Non-serious	164	165	Unrelated	Unrelated
Abdominal distension	2	Non-serious	178	192	Unrelated	Related
Nail disorder	2	Non-serious	191	466	Related	Related
Hyperglycemia	1	Non-serious	196	203	Related	Unrelated
Pain in extremity	2	Non-serious	215	229	Related	Related
Rhinorrhea	1	Non-serious	222	295	Related	Related
Edema peripheral	1	Non-serious	227	295	Related	Related
Lacrimation increased	1	Non-serious	252	295	Related	Related
Hyperglycemia	1	Non-serious	266	284	Related	Unrelated
Pulmonary hypertension	1	Non-serious	284	Resolving	Related	Related

Study Number/CRTN:	CO40016/304778	Patient number	1079
Demographics:	64-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Hyperglycemia AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/307250	Patient number	1089
Demographics:	42 year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Diarrhea Grade $\geq$ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, lobular, moderately differentiated ER/PR and HER 2 negative right breast cancer (T3N3aM1), on Study Day –79 following right breast biopsy performed on the same day.

On Study Day –42, metastatic disease was confirmed with ER/PR and HER2 negative disease in metastatic tissue following right breast biopsy performed on the same day. At screening, sites of disease involvement included right breast lymph nodes and L3 bone.

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent conditions included hypertension, seasonal allergy, bipolar disorder, ventricular extrasystoles and right bundle branch block.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. The same day, she also started loperamide prophylactically (total daily dose: 4 mg) for diarrhea.

Concomitant medications ongoing at Study Day 1 included olmesartan, amlodipine, quetiapine, zolpidem, calcium carbonate/cholecalciferol/magnesium carbonate and denosumab.

On Study Day 3, the patient experienced Grade 1 intermittent nausea (non-serious, related). No treatment was given for this event. On the same day (Study Day 3), loperamide was given at a reduced dose of 2 mg (total daily dose).

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 4.

On Study Day 4, the patient experienced Grade 1 intermittent vomiting (non-serious, related). No treatment was given for this event. On Study Day 5, she experienced non-serious Grade 1 diarrhea. On Study Day 15, the event of diarrhea worsened to Grade 3. She received treatment with loperamide (details reported in the table below). On Study Day 16, the event of diarrhea was considered resolved. On Study Day 52, the events of nausea and vomiting were considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of Diarrhea	4	PO	1	2
Prophylaxis of Diarrhea	2	PO	3	3
Diarrhea	1	PO	6	6
Diarrhea	1	PO	9	10
Diarrhea	2	PO	11	11
Diarrhea	1	PO	12	14
Diarrhea	4	PO	15	15
Diarrhea	2	PO	22	22
Diarrhea	4	PO	23	23
Diarrhea	6	PO	24	24
Diarrhea	2	PO	25	26
Diarrhea	8	PO	27	27
Diarrhea	3	PO	28	28
Diarrhea	7	PO	29	29
Diarrhea	6	PO	30	30
Diarrhea	5	PO	31	31
Diarrhea	9	PO	32	32
Diarrhea	5	PO	33	33
Diarrhea	6	PO	34	34
Diarrhea	2	PO	35	35
Diarrhea	1	PO	36	38
Diarrhea	2	PO	39	39
Diarrhea	1	PO	40	40
Diarrhea	2	PO	41	42
Diarrhea	4	PO	43	43
Diarrhea	2	PO	44	44
Diarrhea	1	PO	45	48
Diarrhea	5	PO	49	49
Diarrhea	2	PO	50	50
Diarrhea	1	PO	51	54
Diarrhea	2	PO	55	55
Diarrhea	4	PO	56	56
Diarrhea	2	PO	57	57
Diarrhea	1	PO	58	58
Diarrhea	2	PO	59	59
Diarrhea	3	PO	60	60
Diarrhea	1	PO	62	62
Diarrhea	2	PO	63	63
Diarrhea	7	PO	64	64

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	10	PO	65	66
Diarrhea	4	PO	67	67
Diarrhea	2	PO	71	72
Diarrhea	6	PO	73	73
Diarrhea	2	PO	76	76
Diarrhea	6	PO	77	77
Diarrhea	4	PO	78	79
Diarrhea	6	PO	80	80
Diarrhea	4	PO	93	93
Diarrhea	4	PO	95	95
Diarrhea	6	PO	99	99
Diarrhea	4	PO	105	106
Diarrhea	2	PO	107	107
Diarrhea	6	PO	116	116
Diarrhea	4	PO	117	117
Diarrhea	6	PO	118	118
Diarrhea	4	PO	119	119
Diarrhea	4	PO	123	123
Diarrhea	8	PO	126	126

Due to this event, Cycle 1 Day 15 dose of paclitaxel was delayed and ipatasertib was interrupted on Study Day 15. The next dose of paclitaxel and ipatasertib was given on Study Day 22.

The Investigator considered diarrhea to be related to paclitaxel and ipatasertib.

On Study Day 148, the patient withdrew consent from the study treatment with the last dose of paclitaxel administered on Study Day 122 and ipatasertib on Study Day 128. The patient entered into the long-term follow-up.

On Study Day 241, an overall response assessment showed disease progression with new lesion in bilateral axillary lymph nodes and liver.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Paclitaxel (6 cycles)	323	371
Doxorubicin and cyclophosphamide (11 cycles)	385	644
Eribulin (7 cycles)	672	826
Vinorelbine (3 cycles)	854	882

On Study Day 896, the patient died due to disease progression. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	1	Non-serious	1	16	Unrelated	Unrelated
Dysgeusia	1	Non-serious	2	52	Related	Related
Abdominal distension	1	Non-serious	2	16	Unrelated	Unrelated
Peripheral sensory neuropathy	2	Non-serious	2	241	Unrelated	Related
Decreased appetite	1	Non-serious	3	129	Related	Related
Fatigue	1	Non-serious	3	129	Related	Related
Headache	1	Non-serious	3	129	Related	Related
Myalgia	1	Non-serious	3	52	Related	Related
Arthralgia	1	Non-serious	3	52	Related	Related
Back pain	1	Non-serious	11	52	Unrelated	Related
Splinter	1	Non-serious	12	72	Unrelated	Unrelated
White blood cell count decreased	3	Non-serious	15	22	Related	Related
Neutrophil count decreased	3	Non-serious	15	22	Related	Related
Alopecia	2	Non-serious	16	241	Unrelated	Related
Diarrhea	1	Non-serious	22	127	Related	Unrelated
White blood cell count decreased	2	Non-serious	52	94	Related	Related
Neutrophil count decreased	2	Non-serious	52	66	Related	Related
Edema	1	Non-serious	59	Unresolved	Unrelated	Related
Anemia	1	Non-serious	59	143	Unrelated	Related
Visual acuity reduced	1	Non-serious	81	Unresolved	Related	Related
Abdominal pain upper	1	Non-serious	81	87	Related	Related
Neutrophil count decreased	2	Non-serious	87	94	Related	Related
White blood cell count decreased	2	Non-serious	108	115	Related	Related
Neutrophil count decreased	2	Non-serious	108	115	Related	Related
Hypoalbuminemia	1	Non-serious	115	129	Unrelated	Unrelated
Anxiety	2	Non-serious	129	241	Related	Related

Study Number/CRTN:	CO40016/310604	Patient number	1094
Demographics:	35-year-old White Asian female		

Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)
Cohort	Cohort A
Event (PT) Category:	Diarrhea Grade ≥ 3 diarrhea

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, ER/PR and HER 2 negative left breast cancer (T3N1M1; histological grade unknown), on Study Day −47 following left breast biopsy performed on the same day.

On Study Day −23, metastatic disease was confirmed with ER/PR unknown and HER2 receptor not assessed in metastatic tissue. At screening, sites of disease involvement included left breast, left axillary lymph node and right lung multiple metastasis.

No past cancer treatments were reported.

The patient′s medical history included uterine leiomyoma and mastitis. Concurrent conditions included seasonal allergy, tumor pain and sensitive skin.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. The same day, she also started receiving loperamide prophylactically (total daily dose: 4 mg) for diarrhea.

Concomitant medications ongoing at Study Day 1 included loratadine, mucopolysaccharide polysulfuric acid ester and hydrocortisone.

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 7.

On Study Day 2, the patient experienced Grade 1 nausea (non-serious, related to paclitaxel). She received treatment with metoclopramide. On Study Day 8, she experienced non-serious Grade 1 diarrhea with most extreme Grade 3 on Study Day 102. Grade changes for the event of diarrhea are mentioned in the table below. She received treatment with loperamide (for dosing details please refer to the treatment details table below), unspecified probiotics and polycarbophil calcium for diarrhea and further received treatment with rabeprazole for nausea. On Study Day 162, the event of nausea was considered resolved. On the following day (on Study Day 163), the event of diarrhea was considered resolved.

Diarrhea grade changes:

Study Day	Diarrhea grade changes
8	1
75	2
79	1
101	2
102	3
105	1
123	2
124	1
125	2
129	1
130	2
131	1
134	2
136	1
150	2
151	1
152	2
153	3
154	2
156	3
157	2
159	1

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of Diarrhea	4	PO	1	3
Prophylaxis of Diarrhea	2	PO	4	4
Prophylaxis of Diarrhea	1	PO	5	6
Diarrhea	1	PO	8	8
Diarrhea	2	PO	9	16
Diarrhea	4	PO	17	17
Diarrhea	3	PO	18	18
Diarrhea	2	PO	19	20
Diarrhea	1	PO	21	21
Diarrhea	2	PO	22	23
Diarrhea	1	PO	24	24
Diarrhea	2	PO	25	27
Diarrhea	1	PO	28	28
Diarrhea	2	PO	29	36
Diarrhea	3	PO	37	38
Diarrhea	2	PO	39	41
Diarrhea	3	PO	42	42
Diarrhea	2	PO	43	50
Diarrhea	1	PO	51	53
Diarrhea	2	PO	57	57
Diarrhea	1	PO	58	58

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	59	59
Diarrhea	1	PO	60	60
Diarrhea	2	PO	61	68
Diarrhea	1	PO	69	70
Diarrhea	3	PO	70	71
Diarrhea	2	PO	72	72
Diarrhea	3	PO	73	74
Diarrhea	4	PO	75	75
Diarrhea	5	PO	76	77
Diarrhea	7	PO	78	78
Diarrhea	4	PO	79	79
Diarrhea	2	PO	80	81
Diarrhea	2	PO	85	85
Diarrhea	1	PO	86	86
Diarrhea	2	PO	87	87
Diarrhea	1	PO	88	88
Diarrhea	2	PO	89	89
Diarrhea	1	PO	90	90
Diarrhea	2	PO	91	91
Diarrhea	3	PO	92	92
Diarrhea	2	PO	93	95
Diarrhea	3	PO	96	96
Diarrhea	2	PO	97	97
Diarrhea	3	PO	98	99
Diarrhea	4	PO	100	100
Diarrhea	5	PO	101	101
Diarrhea	6	PO	102	103
Diarrhea	9	PO	104	104
Diarrhea	11	PO	105	105
Diarrhea	4	PO	106	106
Diarrhea	2	PO	107	107
Diarrhea	2	PO	113	117
Diarrhea	3	PO	118	119
Diarrhea	4	PO	120	120
Diarrhea	3	PO	121	123
Diarrhea	5	PO	124	125
Diarrhea	6	PO	126	126
Diarrhea	7	PO	127	127
Diarrhea	10	PO	128	128
Diarrhea	9	PO	129	129
Diarrhea	15	PO	130	130
Diarrhea	3	PO	131	131
Diarrhea	4	PO	132	132
Diarrhea	6	PO	133	133
Diarrhea	9	PO	134	135
Diarrhea	12	PO	136	136
Diarrhea	9	PO	137	137
Diarrhea	3	PO	138	138
Diarrhea	6	PO	141	141

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	5	PO	142	142
Diarrhea	3	PO	143	143
Diarrhea	2	PO	145	147
Diarrhea	3	PO	148	149
Diarrhea	9	PO	150	150
Diarrhea	5	PO	151	151
Diarrhea	9	PO	152	152
Diarrhea	12	PO	153	153
Diarrhea	9	PO	154	154
Diarrhea	12	PO	155	155
Diarrhea	16	PO	156	156
Diarrhea	8	PO	157	158
Diarrhea	8	PO	160	160
Diarrhea	6	PO	161	161

Due to this event, there was no change in study treatment with paclitaxel; however, study treatment with ipatasertib was interrupted on Study Day 157 and the next dose was given on Study Day 160.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 162, an overall response assessment showed disease progression. Subsequently, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 160 and ipatasertib given on Study Day 161. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Epirubicin, fluorouracil and cyclophosphamide (3 cycles each)	171	225
Bevacizumab and paclitaxel (2 cycles each)	247	281
Eribulin (3 cycles)	308	330
Atezolizumab and paclitaxel albumin (2 cycles each)	337	351

On Study Day 356, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	1	Non-serious	2	8	Unrelated	Unrelated
Treatment	Not	Non-serious	2	2	Not reported	Not

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Noncompliance	reported					reported
Treatment noncompliance	Not reported	Non-serious	4	6	Not reported	Not reported
Stomatitis	1	Non-serious	6	57	Unrelated	Related
Peripheral sensory neuropathy	1	Non-serious	8	161	Unrelated	Related
Hot flush	1	Non-serious	8	8	Unrelated	Related
Epistaxis	1	Non-serious	9	134	Unrelated	Related
Treatment noncompliance	Not reported	Non-serious	10	10	Not reported	Not reported
Treatment noncompliance	Not reported	Non-serious	12	13	Not reported	Not reported
Neutrophil count decreased	2	Non-serious	15	22	Unrelated	Related
Treatment noncompliance	Not reported	Non-serious	17	17	Not reported	Not reported
Alopecia	2	Non-serious	19	Unresolved	Unrelated	Related
Treatment noncompliance	Not reported	Non-serious	19	21	Not reported	Not reported
Hot flush	2	Non-serious	22	22	Unrelated	Related
Dyspnea	2	Non-serious	22	22	Unrelated	Related
Edema	1	Non-serious	26	134	Unrelated	Related
Treatment noncompliance	Not reported	Non-serious	34	34	Not reported	Not reported
Hot flush	1	Non-serious	36	36	Unrelated	Related
Treatment noncompliance	Not reported	Non-serious	40	41	Not reported	Not reported
Solar dermatitis	2	Non-serious	47	99	Unrelated	Unrelated
Hot flush	1	Non-serious	50	50	Unrelated	Related
Dyspnea	1	Non-serious	50	50	Unrelated	Related
Treatment noncompliance	Not reported	Non-serious	62	62	Not reported	Not reported
Treatment noncompliance	Not reported	Non-serious	67	67	Not reported	Not reported
Treatment noncompliance	Not reported	Non-serious	76	76	Not reported	Not reported
Hot flush	1	Non-serious	92	92	Unrelated	Related
Hot flush	1	Non-serious	99	99	Unrelated	Related
Treatment noncompliance	Not reported	Non-serious	118	118	Not reported	Not reported
Hemorrhoids	2	Non-serious	122	133	Unrelated	Unrelated
Pyrexia	1	Non-serious	129	134	Unrelated	Related
Vomiting	1	Non-serious	131	132	Unrelated	Related
Menopausal symptoms	2	Non-serious	135	Unresolved	Unrelated	Unrelated
Neutrophil count decreased	3	Non-serious	148	160	Unrelated	Related
Stomatitis	1	Non-serious	149	165	Unrelated	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nausea	1	Non-serious	171	174	Unrelated	Unrelated
Decreased appetite	1	Non-serious	171	176	Unrelated	Unrelated
Dysgeusia	1	Non-serious	171	178	Unrelated	Unrelated
Malaise	1	Non-serious	171	178	Unrelated	Unrelated

Study Number/CRTN:	CO40016/ 305247	Patient number	1095
Demographics:	59-year-old female (Race unknown)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 3 (PT) Category:	Glaucoma SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/305631	Patient number	1104
Demographics:	41-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Categories:	Diarrhea AE leading to study treatment discontinuation, Grade ≥ 3 diarrhea		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/304623	Patient number	1142
Demographics:	72-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Categories:	Diarrhea SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/305120	Patient number	1154
Demographics:	65-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Diarrhea SAE, AE leading to study treatment discontinuation, Grade ≥ 3 diarrhea		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/318721	Patient number	1177
Demographics:	76-year-old female (race unknown)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/304787	Patient number	1193
Demographics:	28-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was diagnosed with ductal, moderately differentiated, ER/PR and HER 2 negative locally advanced unresectable left breast cancer (T2N1M0), on Study Day −45. At screening, sites of disease involvement included lateral upper quadrant of left breast and left axillary lymph node.

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent condition included gastritis.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

Prior to event of Grade 3 diarrhea, the patient experienced multiple events of non-serious diarrhea (please refer to table below for details). She received treatment with loperamide (for detailed dosing please refer to table below). There was no change in the study treatments due to these events.

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	2	47	Related	Related
Diarrhea	1	Non-serious	57	78	Related	Related
Diarrhea	1	Non-serious	86	108	Related	Related
Diarrhea	2	Non-serious	129	129	Related	Related

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 127 and ipatasertib (400 mg) on Study Day 129.

On Study Day 130, the patient experienced non-serious Grade 3 diarrhea. On Study Day 131, the dose of ongoing loperamide was increased to 12 mg (total daily dose). On Study Day 132, the event of diarrhea improved to Grade 2 and was considered resolved on Study Day 133.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of Diarrhea	2	PO	2	13
Diarrhea	2	PO	16	18
Diarrhea	2	PO	20	21
Diarrhea	4	PO	29	31
Diarrhea	2	PO	32	32
Diarrhea	4	PO	33	35
Diarrhea	4	PO	37	38
Prophylaxis of Diarrhea	4	PO	40	40
Prophylaxis of Diarrhea	4	PO	43	46
Diarrhea	4	PO	48	49
Prophylaxis of Diarrhea	4	PO	57	67
Prophylaxis of Diarrhea	4	PO	69	77
Diarrhea	4	PO	85	95
Diarrhea	4	PO	97	110
Diarrhea	4	PO	113	130
Diarrhea	12	PO	131	131
Diarrhea	10	PO	132	133
Diarrhea	4	PO	141	142
Diarrhea	4	PO	147	148

There was no change in study treatment due to this event.

The Investigator considered diarrhea to be related to ipatasertib and paclitaxel.

On Study Day 144, an overall response assessment showed disease progression.

On Study Day 169, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 141 and ipatasertib on Study Day 147. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Surgery for a target lesion on left breast	179	NA
Radiotherapy of left breast (dose: 5000 cGy, 25 fractions)	229	NA
Capecitabine	291	Ongoing

On Study Day 732, the patient was permanently discontinued from the study as LTFU was terminated by Sponsor.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious/ Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Nausea	1	Non-serious	2	13	Related	Related
Vomiting	1	Non-serious	74	76	Related	Related
Myalgia	1	Non-serious	86	89	Related	Related
Myalgia	1	Non-serious	93	98	Related	Related
Pain	1	Non-serious	129	132	Related	Related
Pain in extremity	1	Non-serious	141	144	Related	Related
Diarrhea	1	Non-serious	141	143	Related	Related
Diarrhea	1	Non-serious	146	153	Related	Related

Study Number/CRTN:	CO40016/318137	Patient number	1199
Demographics:	77-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Categories:	Diarrhea SAE, AE leading to study treatment discontinuation, Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Atrial fibrillation SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/305247	Patient number	1221
Demographics:	65-year-old female (Race unknown)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Categories:	Diarrhea AE leading to study treatment discontinuation, Grade ≥ 3 diarrhea		
Event 3 (PT) Category:	Fatigue AE leading to study treatment discontinuation		
Event 4 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		
Event 5 (PT) Category:	Paronychia AE leading to study treatment discontinuation		
Event 6 (PT) Category:	Onycholysis AE leading to study treatment discontinuation		
Event 7 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/305252	Patient number	1242
Demographics:	66-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Dyspnea SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/305649	Patient number	1247
Demographics:	53-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Categories:	Diarrhea SAE, Grade ≥ 3 diarrhea		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

1.8 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥ 2 COLITIS/ ENTEROCOLITIS

Study Number/CRTN:	CO40016/318540	Patient number	1188
Demographics:	33-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Colitis Grade ≥ 2 colitis/enterocolitis		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER 2-negative, metastatic left breast cancer (T2NXM1), on Study Day –57. At screening, sites of disease involvement included upper right lobe of lung, left axilla lymph node, bone (left rib and femoral diaphysis) and left breast.

No past cancer treatments were reported.

The patient′s medical history included non-Hodgkin′s lymphoma. Surgical history included cholecystectomy. Concurrent conditions included thyroid mass and gastritis.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications were ongoing at Study Day 1.

On Study Day 3, the patient experienced Grade 1 diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide.

Event: Colitis

Prior to the event of colitis, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 15.

On Study Day 16, the patient experienced fever (body temperature not reported; approximately every 8 hours). Later, she took the scheduled dose of ipatasertib and 2 hours after the dose she experienced vomiting (non-serious; 3 episodes) and blood in stools (3 episodes). Subsequently, she was diagnosed with non-serious Grade 3 colitis (diagnostic test not reported). She received treatment with metoclopramide, ciprofloxacin, metronidazole and ibuprofen. Dietary advice was

also given. On the same day (Study Day 16), the event of diarrhea was considered resolved. On Study Day 17, a laboratory work-up showed RBC count 5×10^{12}/L, WBC count 4.7×10^{9}/L and platelet count was 361×10^{9}/L (normal ranges not reported). Stool culture showed common flora. On Study Day 19, the event of colitis was considered resolved.

Due to this event, there was no change in the study treatment with paclitaxel; however, ipatasertib was interrupted on Study Day 18 and the next dose was given at a reduced dose of 300 mg on Study Day 29.

The Investigator considered colitis to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 107, a radiographic assessment showed disease progression with new lesions in bone (multiple osteoblastic lesions in the spine, sacrum, iliac and femur).

On Study Day 113, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 99 and ipatasertib on Study Day 105. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine (8 cycles), pamidronate, anastrozole (1 cycle), leuprorelin, carboplatin and gemcitabine (unknown cycles)	122	Ongoing

On Study Day 446, the patient died due to disease progression. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Flushing	1	Non-serious	2	3	Unrelated	Related
Pain in extremity	1	Non-serious	4	4	Unrelated	Related
Flushing	1	Non-serious	9	40	Unrelated	Related
Vomiting	1	Non-serious	13	13	Related	Unrelated
Diarrhea	1	Non-serious	19	24	Related	Unrelated
Erythema	1	Non-serious	28	Unresolved	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	41	46	Related	Unrelated
Diarrhea	2	Non-serious	49	50	Related	Unrelated
Vomiting	1	Non-serious	60	60	Related	Unrelated
Diarrhea	1	Non-serious	75	77	Related	Unrelated
Constipation	1	Non-serious	86	88	Unrelated	Unrelated

1.9 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥ 3 RASH

Study Number/CRTN:	CO40016/304776	Patient number	1070
Demographics:	66-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Febrile neutropenia SAE		
Event 2 (PT) Categories:	Rash AE leading to study treatment discontinuation, Grade ≥ 3 rash		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/307234	Patient number	1071
Demographics:	66-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Rash Grade ≥ 3 rash		

The patient was randomized on Study Day −1.

The patient was diagnosed with ductal, ER/PR and HER-2 negative, metastatic right breast cancer (T2N1M1, histological grade unknown), on Study Day −85. At screening, sites of disease involvement included liver (right lobe), right breast and right axillary lymph node.

No past cancer treatment was reported.

The patient′s medical history included appendicitis. No surgical history was reported. Concurrent conditions included uterine leiomyoma and thyroid mass.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included loxoprofen, rebamipide and cefdinir.

Event: Rash (skin rash)

Prior to the event of rash, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 9.

On Study Day 10, the patient experienced non-serious Grade 1 (initial intensity) rash with redness and eczema around the left upper arm port construction site. She was started on treatment with betamethasone. On Study Day 11, she experienced rash on both upper limbs and medial thigh. On Study Day 13, the event of rash worsened to Grade 3 with skin eruption extended from the limbs to the neck. A skin biopsy was performed which revealed infiltration of inflammatory cells centered in lymphocytes and eosinophils in the superficial layer of the dermis. Epidermal individual cell necrosis was also observed, and it was concluded as drug rash. Virus tests result showed HSV IgG/EIA 26.5, HSV IGM/EIA 0.60 and mycoplasma/CF < 4 times. She further received treatment with difluprednate and fexofenadine. On Study Day 21, rash improved to Grade 2 and to Grade 1 on Study Day 27. On Study Day 41, the event of rash was considered resolved.

Due to this event, study treatment with paclitaxel was interrupted from Cycle 1 Day 8 and the next dose was given on Study Day 27 (Cycle 2 Day 1). Ipatasertib was initially interrupted on Study Day 12 and was resumed at a reduced dose of 300 mg on Study Day 34. On the same day (Study Day 34), the patient had accidental overdose (she took 300 mg ipatasertib at site and 300 mg at home) following which ipatasertib was again interrupted on Study Day 35. On Study Day 36, ipatasertib was resumed at a dose of 300 mg.

The Investigator considered rash to be related to paclitaxel and ipatasertib.

On Study Day 191, a radiographic response assessment showed disease progression. Subsequently, study treatment with ipatasertib and paclitaxel was permanently discontinued with the last dose of paclitaxel given on Study Day 181 and ipatasertib on Study Day 189. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine (8 cycles)	223	391
Unspecified investigational drug	428	484
Bevacizumab (5 cycles)	813	979
Gimeracil/oteracil/tegafur	986	–

On Study Day 1049, the patient was permanently discontinued from the study as per physician's decision (long term follow-up terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	2	13	Related	Related
Nausea	1	Non-serious	3	219	Unrelated	Related
Alopecia	2	Non-serious	14	Unresolved	Unrelated	Related
Diarrhea	1	Non-serious	43	196	Related	Related
Neuropathy peripheral	1	Non-serious	60	Unresolved	Unrelated	Related
Ligament sprain	1	Non-serious	64	73	Unrelated	Unrelated
Nasopharyngitis	1	Non-serious	78	86	Unrelated	Unrelated
Weight decreased	1	Non-serious	84	181	Related	Related
Neutrophil count decreased	2	Non-serious	97	106	Related	Related
Neutrophil count decreased	2	Non-serious	133	139	Related	Related
Nasopharyngitis	1	Non-serious	163	177	Unrelated	Unrelated

1.10 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥ 2 PNEUMONITIS

No patient experienced Grade ≥ 2 pneumonitis while in the study.

1.11 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥ 3 HEPATOTOXICITY

Study Number/CRTN:	CO40016/304878	Patient number	1005
Demographics:	59-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Category:	Fracture SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/305632	Patient number	1017
Demographics:	41-year-old American Indian or Alaska Native and White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity		

The patient was randomized on Study Day 1.

The patient was diagnosed with ductal, moderately differentiated, ER/PR and HER 2 negative, locally advanced unresectable right breast cancer (T4dN2M0) on Study Day −124. At screening, sites of disease involvement included external right quadrant of right breast and right armpit lymph node.

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent conditions included tumor pain and hypertriglyceridemia.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included tramadol, paracetamol, and atorvastatin.

Event: Alanine aminotransferase increased

Prior to the event of alanine aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 29 and ipatasertib (400 mg) on Study Day 35.

On Study Day 36, a laboratory work-up showed ALT 178 U/L (normal range: 6-30 U/L) and AST 111 U/L (normal range: 9-31 U/L). The patient was diagnosed with non-serious Grade 3 alanine aminotransferase increased**,** and Grade 2 aspartate aminotransferase increased (non-serious, related). She was asymptomatic with no clinical jaundice and abdominal pain. No treatment was reported for these events. On Study Day 43, the event of alanine aminotransferase increased improved to Grade 2 and aspartate aminotransferase increased to Grade 1. On Study Day 64, the event of alanine aminotransferase increased further improved to Grade 1. On Study Day 78, the event of alanine aminotransferase increased worsened to Grade 2, which improved back to Grade 1 on Study Day 92. On Study Day 150, the events of alanine aminotransferase and aspartate aminotransferase increased were considered resolved.

Relevant lab values are listed in the table below:

Study Day	**AST** (normal range: 9-31 U/L)	**ALT** (normal range: 6-30 U/L)	**Total bilirubin** (normal range: 0.1-1 mg/dL)	**ALP** (normal range: 35-104 U/L)
Screening	57	57	0.87	118
28	107	118	1.05	144
36	111	178	1.32	197.5
43	57	110	1.55	181.2
50	71	132	1.15	185.9
64	39	75	1.04	143.6
78	71	114	1.24	146.3
92	61	60	1.35	116
106	52	78	1.4	150.8
120	41	43	1.21	138.8

Study Day	AST (normal range: 9-31 U/L)	ALT (normal range: 6-30 U/L)	Total bilirubin (normal range: 0.1-1 mg/dL)	ALP (normal range: 35-104 U/L)
150	45	52	1.86	176.2

Due to this event, Cycle 2 Day 8 of paclitaxel was delayed and ipatasertib was interrupted on Study Day 37. The next dose of paclitaxel and ipatasertib (at a reduced dose of 300 mg; reduction due to the event of aspartate aminotransferase increased) was given on Study Day 43.

The Investigator considered alanine aminotransferase increased to be related to ipatasertib and paclitaxel.

On Study Day 150, study treatment with paclitaxel and ipatasertib was permanently discontinued as per physician′s decision (two scans showed an increase in the target lesions although the increase did not exceed 20%) with the last dose of paclitaxel given on Study Day 134 and ipatasertib given on Study Day 140. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Gemcitabine and carboplatin (9 cycles each)	170	346
Other surgery of right breast	379	NA

On Study Day 1312, the patient was permanently discontinued from the study as per physician's decision (long term follow-up terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	5	6	Related	Related
Asthenia	1	Non-serious	5	6	Related	Related
Epistaxis	1	Non-serious	6	6	Unrelated	Unrelated
Hyperglycemia	1	Non-serious	8	28	Related	Unrelated
Nasopharyngitis	2	Non-serious	15	18	Unrelated	Unrelated
Rash	1	Non-serious	18	20	Related	Unrelated
Diarrhea	1	Non-serious	21	22	Related	Related

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Peripheral sensory neuropathy	1	Non-serious	30	369	Unrelated	Related
Hyperglycemia	1	Non-serious	36	50	Related	Unrelated
Nasopharyngitis	1	Non-serious	68	76	Unrelated	Unrelated
Urinary tract infection	2	Non-serious	71	78	Unrelated	Unrelated
Diarrhea	1	Non-serious	102	102	Related	Related
Headache	2	Non-serious	108	108	Related	Related
Diarrhea	1	Non-serious	130	130	Related	Related
Diarrhea	1	Non-serious	146	146	Related	Related
Pain in extremity	1	Non-serious	1164	Unknown	Unrelated	Unrelated

Study Number/CRTN:	CO40016/306203	Patient number	1047
Demographics:	70-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Category:	Abscess jaw SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304638	Patient number	1058
Demographics:	39-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		

Event (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity

The patient was randomized on Study Day 1.

The patient was initially diagnosed with poorly differentiated, ER/PR and HER 2 negative right breast cancer (T2N0M1; histological subtype not otherwise specified), on Study Day −45 following right breast biopsy performed on the same day.

On Study Day −35, metastatic disease was confirmed with ER/PR and HER 2-negative in metastatic tissue. At screening, sites of disease involvement included lungs (left subpleural and lateral 8th right segment), bone (multiple) and liver (segments 4/A and 7th).

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent conditions included metastases to bone, abdominal pain upper, hepatic enzyme increased, neck pain and headache.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included nimesulide, calcium carbonate/cholecalciferol and zoledronic acid.

Event: Alanine aminotransferase increased (ALT elevation)

Prior to the event of alanine aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 6.

On Study Day 7, a laboratory work-up showed AST 100 U/L (normal range: 0-31 U/L) and ALT 186 U/L (normal range: 0-31 U/L) and the patient was diagnosed with Grade 2 aspartate aminotransferase increased (non-serious, related to ipatasertib) and non-serious Grade 3 alanine aminotransferase increased. She had ongoing condition of Grade 1 hepatic enzyme increased. No treatment was reported for these events. On Study Day 14, the event of aspartate aminotransferase increased improved to Grade 1 and alanine aminotransferase increased improved to Grade 2. Relevant laboratory values are reported in the table below. On Study Day 21, the event of aspartate aminotransferase increased again worsened to Grade 2. On Study Day 28. the event of aspartate aminotransferase increased improved to Grade 1 and on Study Day 35, the event of alanine aminotransferase increased improved to Grade 1. The events of alanine aminotransferase increased, and aspartate aminotransferase increased remained unresolved at the time of patient′s death.

Relevant lab values are listed in the table below:

Study Day	AST (normal range: 0-31 U/L)	ALT (normal range: 0-31 U/L)	ALP (normal range: 35-104 U/L)	Bilirubin (normal range: 0-21 μmol/L)
Screening	61	68	138	11.3
1	70	70	156	10.8
7	100	186	152	10.4
14	69	125	153	8.3
21	96	108	311	4.9
28	70	115	216	12.8
35	54	75	189	5.9
42	56	70	297	5.6
67	91	98	321	9.0

There was no change in study treatment due to this event.

The Investigator considered alanine aminotransferase increased to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 55, an overall response assessment showed disease progression.

On Study Day 67, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 43 and ipatasertib on Study Day 49. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Radiotherapy: whole brain irradiation and to bone (cervical I-II vertebrae) (dose: 3000 cGy, 10 fractions each)	68	81
Radiotherapy to bone: lumbar IV vertebra (dose: 2000 cGy, 5 fractions)	75	81
Cyclophosphamide, methotrexate and fluorouracil (1 cycle each)	83	90
Unspecified palliative surgery of small intestine	113	NA
Talazoparib	142	260
Radiotherapy to lymph nodes: left side of the neck (dose: 3000 cGy, 10 fractions)	231	245
Cisplatin (1 cycle)	284	284

On Study Day 294, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Vomiting	1	Non-serious	5	5	Related	Related
Diarrhea	1	Non-serious	5	5	Related	Unrelated
Fatigue	1	Non-serious	8	Unresolved	Related	Related
Mucosal inflammation	1	Non-serious	9	29	Related	Unrelated
Headache	2	Non-serious	10	12	Unrelated	Unrelated
Vomiting	1	Non-serious	11	11	Related	Related
Neutropenia	3	Non-serious	14	21	Unrelated	Related
Bone pain	1	Non-serious	22	36	Unrelated	Unrelated
Neck pain	1	Non-serious	22	218	Unrelated	Unrelated
Diarrhea	1	Non-serious	26	26	Unrelated	Related
Diarrhea	1	Non-serious	33	33	Unrelated	Related
Vomiting	1	Non-serious	34	34	Unrelated	Related
Diarrhea	1	Non-serious	38	40	Unrelated	Related
Diarrhea	1	Non-serious	45	45	Unrelated	Related
Diarrhea	1	Non-serious	48	48	Unrelated	Related

Study Number/CRTN:	CO40016/304641	Patient number	1075
Demographics:	75-year old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Categories:	Alanine aminotransferase increased AE leading to study treatment discontinuation, Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Categories:	Alanine aminotransferase increased AE leading to study treatment discontinuation, Grade ≥ 3 hepatotoxicity		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/307253	Patient number	1116
Demographics:	38-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Category:	Gamma-glutamyltransferase increased Grade ≥ 3 hepatotoxicity		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR and HER 2 negative left breast cancer (T1N0M0), on Study Day −880.

On Study Day −63, the patient was diagnosed with metastatic disease with ER/PR and HER 2-negative disease in metastatic tissue. At screening, sites of disease involvement included posterior left cervical and supraclavicular lymph node and pericardial effusion.

Past cancer treatments are listed in the table below:

Type of treatment	**Therapy Setting/Intent**	**Treatments details**	**Start Day**	**Stop Day**
Surgery	Curative	Left simple mastectomy	−814	NA
Cancer therapy	Adjuvant	Epirubicin, cyclophosphamide and docetaxel (4 cycles each)	Approximately 1 year and 10 months prior to study entry	Approximately 1 year and 10 months prior to study entry

No medical or surgical history was reported. Concurrent conditions included hepatic steatosis and cancer pain.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included loxoprofen.

Event 1: Alanine aminotransferase increased (ALT increased)
Event 2: Gamma-glutamyltransferase increased (GGT increased)

Prior to the events of alanine aminotransferase and gamma-glutamyl transferase increased, the most recent dose of paclitaxel was administered on Study Day 14 and ipatasertib (400 mg) on Study Day 22.

On Study Day 27, a laboratory work-up showed ALT 59 U/L (normal range: 7-23 U/L), AST 42 U/L (normal range: 13-30 U/L), ALP 556 U/L (normal range: 106-322 U/L), and GGT 413 U/L (normal range: 9-32 U/L). The patient was diagnosed with non-serious Grade 1 (initial intensity) alanine aminotransferase increased and Grade 3 (initial intensity) gamma-glutamyl transferase increased, Grade 1 aspartate aminotransferase increased, and Grade 1 blood alkaline phosphatase increased (both non-serious, related). On Study Day 41, the patient was noted with Grade 1 blood bilirubin increased with total bilirubin 1.6 mg/dL (normal range: 0.4-1.5 mg/dL; non-serious, related). No treatment was given for these events. On Study Day 48, the event of blood bilirubin increased was considered resolved. On Study Day 83, the event of alanine aminotransferase increased worsened to Grade 3. On Study Day 195, the event of gamma-glutamyl transferase increased worsened to Grade 4 with GGT 648 U/L (normal range: 9-32 U/L). Grade changes for alanine aminotransferase and gamma-glutamyl transferase increased are listed in the table below. The events of aspartate aminotransferase increased, alkaline phosphatase increased, alanine aminotransferase increased and gamma-glutamyl transferase increased remained unresolved at the time of patient's death.

Grade changes:

Study Day	Grade changes for alanine aminotransferase increased	Grade changes for gamma-glutamyltransferase increased
48	2	—
83	3	—
91	2	—
97	1	—
139	2	—
195	—	4
203	—	3

Relevant lab values are listed in the table below:

Study Day	AST (normal range: 13-30 U/L)	ALT (normal range: 7-23 U/L)	ALP (normal range: 106-322 U/L)	Bilirubin (normal range: 0.4-1.5 mg/dL)
Screening	35	54	352	1.3
14	27	33	237	0.6
27	42	59	556	0.7
35	32	46	432	0.9
41	40	49	326	1.6
48	64	99	405	1.3

Study Day	AST (normal range: 13-30 U/L)	ALT (normal range: 7-23 U/L)	ALP (normal range: 106-322 U/L)	Bilirubin (normal range: 0.4-1.5 mg/dL)
55	39	68	348	1.1
69	62	84	456	0.9
83	67	117	567	1.3
91	–	78	–	–
97	38	57	417	1.4
104	40	56	383	1.5
111	36	58	337	1.0
139	53	86	545	0.9
167	46	64	376	0.8
195	52	79	519	0.8
217	42	47	414	1.2

There was no change in study treatment due to the event of gamma-glutamyltransferase increased.

Due to the event of alanine aminotransferase increased, study treatment with paclitaxel was reduced to 65 mg/m^2 and ipatasertib was reduced to 300 mg on Study Day 98.

The Investigator considered alanine aminotransferase increased to be related to ipatasertib and paclitaxel.

The Investigator considered gamma-glutamyltransferase increased to be unrelated to ipatasertib and paclitaxel and related to concurrent illness (hepatic steatosis).

On Study Day 196, an overall response assessment showed disease progression with new lesion in brain (left cerebellum).

On Study Day 203, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 181 and ipatasertib on Study Day 189. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Radiotherapy to brain (cyber knife) (dose: 2000 cGy, 1 fraction)	217	217
Eribulin (3 cycles)	238	301
Capecitabine	315	428
Radiotherapy to neck (dose: unknown, 10 fractions)	380	393
Bevacizumab and paclitaxel	479	581
Radiotherapy to brain (dose: unknown, 7 fractions)	617	623

On Study Day 631, the patient died due to disease progression. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Accidental overdose	Not reported	Non-serious	1	1	Not reported	Not reported
Upper respiratory tract Infection	2	Non-serious	3	5	Unrelated	Unrelated
Diarrhea	2	Non-serious	5	Unresolved	Related	Unrelated
Rash	2	Non-serious	25	Unresolved	Related	Related
Stomatitis	2	Non-serious	28	Unresolved	Related	Related
Upper respiratory tract Infection	2	Non-serious	154	217	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305634	Patient number	1169
Demographics:	57-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event (PT) Category:	Aspartate aminotransferase increased Grade $\geq$ 3 hepatotoxicity		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER/PR and HER 2 negative right breast cancer (T2N1aM0; histological grade unknown), on Study Day −918.

On Study Day −50, the patient was diagnosed with locally recurrent, metastatic disease with ER/PR and HER2 negative disease in recurrent/metastatic tissue. At screening, sites of disease involvement included lymph nodes (right supraclavicular, pectoral and midline adjacent to superior vena cava).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neo-adjuvant	Doxorubicin, cyclophosphamide (4 cycles each) and paclitaxel (12 cycles)	−866	−744
Surgery	Curative	Right modified radical mastectomy	−694	NA
Radiotherapy	Adjuvant	Right chest wall (dose unknown; 25 fractions)	−660	−626

No medical or surgical history was reported. Concurrent condition included hypertension.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

Event: Aspartate aminotransferase increased (AST elevation)

Prior to the event of aspartate aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 7.

On Study Day 8, a laboratory work-up showed ALT 168 U/L (normal range: 0-55 U/L) and AST 218 U/L (normal range: 5-34 U/L) and she was diagnosed with Grade 2 alanine aminotransferase increased (initial intensity Grade 1) (non-serious, unrelated) and non-serious Grade 3 aspartate aminotransferase increased. No treatment was given for these events. On Study Day 29, the events of alanine aminotransferase increased, and aspartate aminotransferase increased were considered resolved.

Relevant lab values are listed in the table below:

Study Day	AST (normal range: 5-34 U/L)	ALT (normal range: 0-55 U/L)	Bilirubin (normal range: 0.2-1.2 mg/dL)	ALP (normal range: 40-150 U/L)
Screening	21	24	0.48	95
1	19	21	0.44	94
8	218	168	0.92	142
15	211	154	0.83	185
29	18	31	0.44	117

There was no change in study treatment due to this event.

The Investigator considered aspartate aminotransferase increased to be unrelated to ipatasertib and paclitaxel and related to disease under study.

On Study Day 231, an overall response assessment showed disease progression with new lesion in right supraclavicular lymph node.

On Study Day 245, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 239 and ipatasertib on Study Day 245. The patient entered into the long-term follow-up.

On Study Day 573, the patient died due to unknown cause. It was unknown if an autopsy was performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	58	67	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	84	Unresolved	Unrelated	Unrelated
Lymphoedema	1	Non-serious	84	Unresolved	Unrelated	Unrelated

Study Number/CRTN:	CO40016/318146	Patient number	1195
Demographics:	48-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Alanine aminotransferase increased Grade $\geq$ 3 hepatotoxicity		
Event 2 (PT) Category:	Gamma-glutamyl transferase increased Grade $\geq$ 3 hepatotoxicity		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with moderately differentiated, ER/PR and HER 2-negative bilateral breast cancer (T3N2M1; histological subtype: other), on Study Day −61.

On Study Day −59, metastatic disease was confirmed with ER/PR and HER 2-negative disease in metastatic tissue. At screening, sites of disease involvement included bilateral lung and breast nodules, bilateral armpit lymph nodes and pulmonary hilum lymph nodes.

No past cancer treatments were reported.

The patient′s medical history included cholelithiasis. No surgical history and concurrent conditions were reported.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications were ongoing at Study Day 1.

Event 1: Alanine aminotransferase increased (increased alanine aminotransaminase)
Event 2: Gamma glutamyltransferase increased (increased gamma-glutamyl transferase)

Prior to the events of alanine aminotransferase increased and gamma glutamyl transferase increased, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 6.

On Study Day 7, the patient was noted to have Grade 3 alanine aminotransferase increased (ALT 606.1 U/L; normal range: 0-41 U/L) and Grade 3 gamma glutamyltransferase increased (GGT on Study Day 8: 246 U/L; normal range: 5-35 U/L). No treatment was reported for these events. On Study Day 15, the event of alanine aminotransferase increased was considered resolved. On Study Day 16, the event of gamma glutamyltransferase increased improved to Grade 2 (GGT: 149 U/L). On Study Day 34, the event of gamma glutamyltransferase increased was considered resolved.

Relevant lab values are listed in the table below:

Study Day	**AST** (normal range: 0-40 U/L)	**ALT** (normal range: 0-41 U/L)	**ALP** (normal range: 40-129 U/L)	**Bilirubin** (normal range: 0-1.2 mg/dL)
Screening	19.4	25.4	95.6	0.4
7	118.2	606.1	178.7	0.4
8	66	438	166	Not done
16	20.9	70.9	112.9	0.2
28	26.2	41.6	107.2	0.3
35	22.5	46	106.5	0.4

There was no change in study treatment due to these events.

The Investigator considered alanine aminotransferase increased and gamma glutamyl transferase increased to be related to ipatasertib and paclitaxel.

On Study Day 52, an overall response assessment showed disease progression with new lesion in mediastinal lymph node.

On Study Day 85, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 71 and ipatasertib on Study Day 79. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Doxorubicin and cyclophosphamide (4 cycles each)	94	Ongoing
Radiotherapy to brain (dose unknown; 10 fractions)	105	120

On Study Day 396, the patient died due to an unknown cause. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	2	Non-serious	1	4	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	2	3	Unrelated	Related
Nausea	2	Non-serious	2	3	Unrelated	Related
Rash	1	Non-serious	31	99	Related	Unrelated
Back pain	2	Non-serious	32	57	Unrelated	Unrelated
Gamma-glutamyltransferase Increased	2	Non-serious	58	Resolving	Related	Related
Mastitis	2	Non-serious	63	71	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304786	Patient number	1245
Demographics:	45-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Categories:	COVID-19 SAE, COVID-19 SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

1.12 NARRATIVES FOR PATIENTS WHO EXPERIENCED POTENTIAL DRUG-INDUCED LIVER INJURY AS DEFINED BY HY'S LAW

No patient experienced potential drug-induced liver injury as defined by Hy's law while in the study.

1.13 NARRATIVES FOR PATIENTS WHO EXPERIENCED SUSPECTED TRANSMISSION OF AN INFECTIOUS AGENT BY THE STUDY DRUG

No patient experienced suspected transmission of an infectious agent by the study drug while in the study.

1.14 NARRATIVES FOR PATIENTS WHO EXPERIENCED COVID-19 SAE

Study Number/CRTN:	CO40016/318146	Patient number	1237
Demographics:	54-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Categories:	COVID-19 pneumonia SAE, COVID-19 SAE		
Event 2 (PT) Category:	Hyperglycemia AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304786	Patient number	1245
Demographics:	45-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort A		
Event 1 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Categories:	COVID-19 SAE, COVID-19 SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

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1. NARRATIVES

1.1 NARRATIVES FOR PATIENTS WHO DIED DUE TO ADVERSE EVENT(S)

Study Number/CRTN:	CO40016/305629	Patient number	2008
Demographics:	76-year-old American Indian or Alaska native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Categories:	Diarrhea SAE, AESI: Grade $\geq$ 3 diarrhea		
Event 2 (PT) Categories:	Hyperglycemia SAE, AE leading to study treatment discontinuation, AESI: Grade $\geq$ 3 hyperglycemia		
Event 3 (PT) Category:	Dehydration SAE		
Event 4 (PT) Category:	Hypoglycemia SAE		
Event 5 (PT) Categories:	Respiratory distress Death due to AE, SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal and other unspecified subtype (NOS), moderately differentiated, ER/PR positive and HER2 negative left breast cancer (T4bN1M0), approximately 5 years prior to study entry.

The patient was diagnosed with metastatic disease, approximately 1 year and 4 months prior to study entry with ER/PR unknown and HER2 was not assessed in metastatic tissue.

At screening, sites of disease included liver (lateral edge and medial border of segment VI), right upper breast and chest (upper trachea), lung (bilateral nodules), pelvis (bilateral adenopathy of obturator groups), bone (blastic lesions at right costal, lumbar 5th, sacrum and left iliac) and retroperitoneal lymph node. The patient was assessed by the Investigator to have endocrine resistant disease and visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neo-adjuvant	Cyclophosphamide, doxorubicin, and paclitaxel	Approximately 5 years prior to study entry	Approximately 4 years and 7 months prior to study entry
Surgery	Curative	Left modified radical mastectomy	Approximately 4 years and 6 months prior to study entry	—
Radiotherapy	Adjuvant	Left breast (total dose: 4500 cGy)	Approximately 4 years and 6 months prior to study entry	Approximately 4 years and 4 months prior to study entry
Cancer therapy	Adjuvant	Anastrozole	Approximately 4 years and 6 months prior to study entry	−512
Cancer therapy	Metastatic	Exemestane	−512	−92

No medical or other surgical history was reported. The patient′s concurrent conditions included Parkinson′s disease, and left ilium fracture.

At screening, the patient′s ECOG Performance Status was 1. Her vitals showed pulse rate 100 beats/min, respiratory rate 19 breaths/min and blood pressure 100/60 mmHg.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. The same day, she also started loperamide prophylactically (total daily dose: 4 mg) for diarrhea.

Concomitant medication ongoing at Study Day 1 included zoledronic acid.

The patient was noted with Grade 2 hyperglycemia (non-serious, related to ipatasertib) from Study Days 8-11 for which ipatasertib was interrupted until levels resolved to Grade 1 and she received metformin (425 mg, PO, BID). She experienced Grade 1 diarrhea (non-serious, related to ipatasertib) from Study Days 12-16. Treatment with loperamide was maintained at 4 mg total daily dose. She also had an episode of Grade 1 hyperglycemia (non-serious, related to ipatasertib; glucose 139 mg/dL) from Study Days 14-18, for which metformin was continued but at an increased dose of 425 mg, PO, TID from Study Day 16 until Study Day 29 (patient was non-compliant). Relevant laboratory values are reported in the table below.

Event 1: Diarrhea
Event 2: Hyperglycemia

Event 3: Dehydration
Event 4: Hypoglycemia

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 29 and ipatasertib (400 mg) on Study Day 34.

Prior to the events of hyperglycemia, dehydration and hypoglycemia, the most recent dose of paclitaxel was administered on Study Day 29 and ipatasertib on Study Day 40.

On Study Day 40, the patient attended clinic in preparation for her Cycle 2 Day 8 visit and was noted with dehydration and diarrhea (started on Study Day 35, Grade 3, treatment with loperamide maintained at 4 mg). Laboratory work-up showed fasting glucose level at 411 mg/dL (normal range: 70-110 mg/dL) and the patient was diagnosed with Grade 3 hyperglycemia. On Study Day 41, the patient presented with persisting Grade 3 diarrhea, and she was also diagnosed with Grade 3 dehydration. She was hospitalized for management of diarrhea, hyperglycemia and dehydration. Stool examination showed presence of yeasts. She received treatment with insulin, ceftriaxone, sodium chloride and ranitidine, and was given dietary and hydration advice. After treatment with insulin, glucose value was noted to be 279 mg/dL, and the event of hyperglycemia was considered to have improved to Grade 2. Later, the same day (Study Day 41), the event of hyperglycemia was considered resolved. On Study Day 42, loperamide dose was increased to 8 mg. The same day (Study Day 42), the event of dehydration was considered resolved.

On Study Day 43, the patient was noted with Grade 2 hypoglycemia (glucose 60 mg/dL) leading to prolongation of hospitalization. No treatment was reported for this event. On Study Day 44, the event of diarrhea was considered resolved. Hypoglycemia resolved on the following day (Study Day 45). Treatment with loperamide was stopped and the patient was given dietary and hydration advice. On Study Day 46, she was discharged from the hospital.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of Diarrhea	4	PO	1	42
Diarrhea	8	PO	42	46

Hyperglycemia treatment details:

Treatment	Indication	Dose (Units: mg)	Route	Frequency	Start day	Stop day
Metformin	Hyperglycemia	425	PO	BID	8	16
Metformin	Hyperglycemia	425	PO	TID	16	29
Ranitidine	Hyperglycemia	50	IV	TID	41	42

Treatment	Indication	Dose (Units: mg)	Route	Frequency	Start day	Stop day
Insulin	Hyperglycemia	20*	SC	PRN	41	41
Ceftriaxone	Hyperglycemia and diarrhea	2	IV	QD	42	45
Ranitidine	Hyperglycemia	300	PO	QD	43	Ongoing

*Units: IU

Relevant laboratory work-up:

Study Day	Glucose Normal range: 70-110 mg/dL)	HbA1c Normal range: 2-6%	Sodium Normal range: 133-145 mEq/L	Potassium Normal range: 3.3-5.1 mEq/L
Screening	80	5.8	140	4.18
8	210	—	135.1	4.17
11	98	—	—	—
14	139	—	138	3.7
18	78	—	—	—
40	411	—	132	3.7
41	279	—	—	—
42	86	—	—	—
43	60	—	—	—
44	70	—	—	—
45	77	—	—	—
46	70	—	—	—

Due to the events of diarrhea, dehydration and hypoglycemia, study treatment with ipatasertib and paclitaxel was interrupted; however, due to the event of hyperglycemia, study treatment was permanently discontinued with the last dose of paclitaxel administered on Study Day 29 and ipatasertib on Study Day 40.

The Investigator considered diarrhea and hyperglycemia to be related to ipatasertib and unrelated to paclitaxel.

The Investigator considered dehydration to be unrelated to ipatasertib and paclitaxel and related to other unspecified cause.

The Investigator considered hypoglycemia to be unrelated to ipatasertib and paclitaxel and related to other cause (antidiabetic treatment given during hospitalization).

Event 5: Respiratory distress

Prior to the event of respiratory distress, study treatment had already been discontinued.

On Study Day 54, the patient developed respiratory distress with cough and vomiting. Her condition worsened, and she was transferred to the hospital nearby. Reportedly, she did not have any problems until Study Day 53 after getting discharged on Study Day 46. No treatment was reported for the event. The same day (Study Day 54), she died due to respiratory distress. It was unknown whether an autopsy was performed or not. Details regarding death certificate were not available.

The Investigator considered respiratory distress to be unrelated to ipatasertib and paclitaxel and related to disease under study.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious/ Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Alopecia	2	Non-serious	20	Unresolved	Unrelated	Related
Mucosal inflammation	1	Non-serious	41	46	Unrelated	Related
Rash maculo-papular	2	Non-serious	42	46	Unrelated	Unrelated

Study Number/CRTN:	CO40016/310803	Patient number	2033
Demographics:	76-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Categories:	Death Death due to AE, SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was diagnosed with lobular, moderately differentiated, ER/PR positive and HER2 negative locally advanced unresectable right breast cancer (T4N3M0) on Study Day −56.

At screening sites of disease involvement included right breast (middle), and lymph nodes (right supraclavicular and axillary).

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent conditions included hypertension, pulmonary fibrosis (diffuse basal pneumosclerosis and lung root fibrosis), endometrial hyperplasia, uterine leiomyoma, cholelithiasis, supraventricular extrasystoles, left ventricular hypertrophy, aortic arteriosclerosis, aortic valve sclerosis, mitral valve sclerosis, pericardial effusion, proteinuria, glycosuria, blood calcium increased, serum ferritin increased, glycosylated hemoglobin increased, hepatomegaly, pancreatic steatosis, hyperplasia adrenal, pyelocaliectasis and renal cyst.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included indapamide.

Event: Death (Unexplained death)

Prior to death, the most recent dose of paclitaxel was administered on Study Day 15 and ipatasertib (400 mg) on Study Day 20.

On Study Day 21, the patient died. The cause of death remained unexplained. It was reported that disease under study could not be a cause of death as the patient had a good response to the treatment on last visits. An autopsy was performed. Note from the local pathology department reported acute pneumonia as the cause of death; however, this was not considered appropriate by the investigator because no clinical signs, elevated body temperature or CT-scan results were reported, which could detect pneumonia. According to the investigator, pneumonia as a cause of death was mentioned by default and was without any evidence.

The patient received the last dose of paclitaxel on Study Day 15 and ipatasertib on Study Day 21.

The Investigator considered death to be unrelated to paclitaxel and ipatasertib and related to other cause (unspecified).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	2	Non-serious	5	6	Related	Unrelated
Nausea	1	Non-serious	7	7	Unrelated	Related
Diarrhea	1	Non-serious	9	9	Related	Unrelated
Nausea	1	Non-serious	11	14	Unrelated	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Blood lactate dehydrogenase increased	1	Non-serious	15	21	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305250	Patient number	2078
Demographics:	66-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Categories:	Road traffic accident Death due to AE, SAE		
Event 2 (PT) Categories:	General physical health deterioration Death due to AE, SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, left breast cancer (T1cN1M0; histological grade unknown), approximately 25 years prior to study entry followed by left lumpectomy and axillary lymph node dissection. ER and PR status was unknown and HER2 status was not assessed.

The patient was diagnosed with locally recurrent disease followed by left radical mastectomy approximately 20 years prior to study entry. On Study Day –341, the patient was diagnosed with metastatic disease (ER positive, PR negative and HER2 negative in recurrent/metastatic tissue). At screening sites of disease involvement included liver (segment III). The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Vindesine, cyclophosphamide, epirubicin, fluorouracil and tamoxifen	Approximately 24 years prior to study entry	Approximately 24 years prior to study entry

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Adjuvant	Breast, internal mammal chain and supraclavicular fossa (4500 cGy; fractions not reported)	Approximately 24 years prior to study entry	Approximately 24 years prior to study entry
Cancer therapy	Adjuvant	Epirubicin	Approximately 19 years prior to study entry	Approximately 19 years prior to study entry
Cancer therapy	Adjuvant	Exemestane and letrozole	Approximately 6 years prior to study entry	Approximately 4 years prior to study entry
Cancer therapy	Adjuvant	Anastrozole, docetaxel and cyclophosphamide	Approximately 4 years and 4 months prior to study entry	Approximately 3 years and 10 months prior to study entry
Cancer therapy	Metastatic	Exemestane and everolimus	−331	−228
Cancer therapy	Metastatic	Palbociclib and fulvestrant	−228	−24
Surgery	Curative	Left axillary lymph node dissection	−156	NA

The patient′s medical history included hiatus hernia and intervertebral disc protrusion. Other surgical history included hysterectomy. Concurrent conditions included sinus tachycardia, retinal disorder and lymphedema.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included bisoprolol, calcium carbonate and docosahexaenoic acid/eicosapentaenoic acid.

On Study Day 392, radiographic response assessment showed disease progression.

On the same day (Study Day 392), study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and ipatasertib given on Study Day 365 and Study Day 385, respectively. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Pegylated liposomal doxorubicin	399	399

Event 1: Road traffic accident (Deterioration of general condition due to car accident)
Event 2: General physical health deterioration (Deterioration of general condition due to car accident)

Prior to the events of road traffic accident and general physical health deterioration, study treatment had been already discontinued.

On Study Day 410, the patient died due to general physical health deterioration following road traffic accident. No treatment and diagnostic tests were reported. An autopsy was not performed.

The Investigator considered road traffic accident and general physical health deterioration to be unrelated to ipatasertib and paclitaxel and related to other causes.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Arthralgia	1	Non-serious	3	33	Unrelated	Unrelated
Diarrhea	2	Non-serious	6	33	Related	Unrelated
Abdominal pain upper	2	Non-serious	16	47	Unrelated	Unrelated
Asthenia	1	Non-serious	16	378	Unrelated	Related
Pyrexia	2	Non-serious	20	21	Unrelated	Unrelated
Pyrexia	1	Non-serious	22	27	Unrelated	Unrelated
Urinary tract infection	2	Non-serious	26	51	Unrelated	Unrelated
Cough	1	Non-serious	26	33	Unrelated	Unrelated
Alopecia	2	Non-serious	33	211	Unrelated	Related
Diarrhea	1	Non-serious	41	41	Related	Unrelated
Neutropenia	3	Non-serious	43	54	Unrelated	Related
White blood cell count decreased	3	Non-serious	43	54	Unrelated	Related
Fracture pain	2	Non-serious	55	88	Unrelated	Unrelated
Fall	2	Non-serious	55	88	Unrelated	Unrelated
Vascular access site pain	1	Non-serious	65	Unresolved	Unrelated	Unrelated
Diarrhea	1	Non-serious	67	67	Related	Unrelated
Neutropenia	3	Non-serious	69	82	Unrelated	Related
Diarrhea	1	Non-serious	74	85	Related	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Neutropenia	3	Non-serious	97	110	Unrelated	Related
Abdominal pain upper	1	Non-serious	121	378	Unrelated	Related
Neutropenia	3	Non-serious	125	138	Unrelated	Related
Nasopharyngitis	2	Non-serious	133	161	Unrelated	Unrelated
Vulvovaginal pruritus	2	Non-serious	140	150	Unrelated	Related
Cough	2	Non-serious	144	161	Unrelated	Unrelated
Urinary tract infection	2	Non-serious	170	172	Unrelated	Unrelated
Arthralgia	1	Non-serious	197	215	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	197	Unresolved	Unrelated	Related
Diarrhea	1	Non-serious	209	264	Related	Unrelated
Spinal osteoarthritis	1	Non-serious	222	281	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	242	Unresolved	Unrelated	Related
Conjunctival hemorrhage	1	Non-serious	277	280	Unrelated	Unrelated
Dry eye	1	Non-serious	281	Unresolved	Unrelated	Related
Photosensitivity reaction	1	Non-serious	283	303	Unrelated	Unrelated
Pruritus	1	Non-serious	283	291	Unrelated	Unrelated
Bronchitis	2	Non-serious	293	328	Unrelated	Unrelated
Neutropenia	2	Non-serious	321	334	Unrelated	Related
Pneumonia	2	Non-serious	328	336	Unrelated	Unrelated
Neutropenia	2	Non-serious	349	364	Unrelated	Related

Study Number/CRTN:	CO40016/305637	Patient number	2161
Demographics:	59-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Neutropenia SAE		
Event 2 (PT) Categories:	Febrile neutropenia Death due to AE, SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER, PR positive and HER2 negative right breast cancer (T1N1M0), approximately 3 years and 5 months prior to study entry.

On Study Day −34, the patient was diagnosed with metastatic disease (ER and PR status was unknown and HER2 status was not assessed in metastatic tissue). At screening sites of disease involvement included liver (segments IV and VII), lung (apical lobe) and bone (bilateral axial skeleton; multiple lesions). The patient was assessed by the Investigator to have visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right radical mastectomy and axillary lymph node dissection	Approximately 3 years and 3 months prior to study entry	NA
Cancer therapy	Adjuvant	Cyclophosphamide, epirubicin and fluorouracil	Approximately 3 years and 2 months prior to study entry	−703
Cancer therapy	Adjuvant	Docetaxel	Approximately 2 years and 11 months prior to study entry	Approximately 2 years and 9 months prior to study entry

No medical and other surgical history was reported. Concurrent condition included back pain, hypercholesterolemia, and hypertriglyceridemia.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included paracetamol and bezafibrate.

Event 1: Neutropenia
Event 2: Febrile neutropenia (Neutropenic fever)

Prior to the events of neutropenia and febrile neutropenia, the most recent dose of paclitaxel was administered on Study Day 8 and ipatasertib on Study Day 13.

On Study Day 14, a laboratory work-up for Cycle 1 Day 15 dose of paclitaxel showed Grade 4 neutropenia (neutrophil count $0.09 \times 10^3/\mu L$; normal range: $1.69\text{-}7.16 \times 10^3/\mu L$). The patient was asymptomatic. Treatment for the event included filgrastim.

Due to the event of neutropenia, study treatment with paclitaxel and ipatasertib was interrupted after Study Day 8 and Study Day 14, respectively.

On Study Day 22, the patient presented with fever (body temperature not reported) and she was assessed to have Grade 4 (initial intensity) febrile neutropenia, leading to hospitalization. She received unspecified antibiotics. On an unspecified day, she experienced nausea, vomiting and fatigue. Reportedly, neutrophil levels did not increase even after continuous treatment with filgrastim and the patient did not respond to antibiotics treatment and continued having fever. A specific source of infection was unknown. On Study Day 28, the patient died due to febrile neutropenia. It was reported that she had detrimental functional status with sepsis (blood culture not reported) that evolved to septic shock and finally led to death, which was related to neutropenia. An autopsy was not performed.

The patient received the last dose of paclitaxel on Study Day 8 and ipatasertib on Study Day 14.

Relevant laboratory work-up:

Study Day	**WBC count** Normal range: $4.1\text{-}12.6 \times 10^3/\mu L$	**Neutrophil count** Normal range: $1.69\text{-}7.16 \times 10^3/\mu L$	**Body temperature** °C
Screening	14.43	11.52	—
	—	—	36.5
8	3.48	2.48	36.9
14	0.52	0.09	—

The Investigator considered neutropenia and febrile neutropenia to be related to ipatasertib and paclitaxel.

Other AE experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Hyperbilirubinemia	1	Non-serious	1	27	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305649	Patient number	2208
Demographics:	58-year-old female (race unknown)		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Pleural effusion SAE		
Event 2 (PT) Category:	Lower respiratory tract infection SAE		
Event 3 (PT) Categories:	Pneumonia Death due to AE, SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER positive, PR and HER2 negative right breast cancer (T4bN1M0) on Study Day -722.

On Study Day -48, the patient was diagnosed with metastatic disease with ER positive, PR negative and HER2 negative disease in metastatic tissue. At screening, sites of disease included lung (left lung lingula), bone (sternal, parietal region, vertebral column D11, D5, D3 and L5; third medium of right radius, 9th and 10th right costal arch), lymph nodes (left axillary, prevascular and pretracheal), pleura (ipsilateral left pleural effusion and paramedian left pleural grease) and soft tissue (right pre and retro sternal space with extension to subcutaneous tissue and skin). The patient was assessed by the Investigator to have endocrine resistant disease and visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neo-adjuvant	Doxorubicin and cyclophosphamide	-613	-541
Cancer therapy	Neo-adjuvant	Paclitaxel	-519	-430
Surgery	Curative	Right modified radical mastectomy and axillary lymph node dissection	-358	NA
Radiotherapy	Adjuvant	Right breast, axillary and supraclavicular lymph nodes (total dose: 5000 cGy; 25 fractions)	-324	-287
Cancer therapy	Adjuvant	Anastrozole	-324	-83

The patient′s medical history included chronic gastritis. No other surgical history was reported. Concurrent conditions included cough, dyspnea, cardiac failure, hypertension, hepatic steatosis, and back pain.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included irbesartan, carvedilol, hydrochlorothiazide, and spironolactone.

On Study Day 9, the patient experienced Grade 2 diarrhea infectious and dehydration (both non-serious, unrelated). On Study Day 10, she was noted to have Grade 2 worsening hypertension (non-serious, unrelated, blood pressure value not provided for this day). She received treatment with irbesartan and carvedilol for hypertension; loperamide and ondansetron for diarrhea and sodium chloride and unspecified electrolytes for dehydration. Dehydration resolved on the same day (Study Day 10). On Study Day 13, she was diagnosed with Grade 2 dehydration and Grade 3 hypokalemia (both non-serious, unrelated and relevant laboratory values not provided for this day). On the same day (Study Day 13), her blood pressure was 150/80 mmHg. She received treatment with sodium chloride, glucose and unspecified electrolytes for dehydration and potassium chloride for hypokalemia and metamizole, ceftriaxone and amikacin for diarrhea.

Event 1: Pleural effusion

Prior to the event of pleural effusion, the most recent dose of paclitaxel was administered on Study Day 8 and ipatasertib (400 mg) on Study Day 14.

On Study Day 15, the patient presented with ongoing dyspnea. A chest X-ray and an ultrasound showed Grade 2 pleural effusion. Subsequently, she was hospitalized, and thoracentesis was

performed. It was reported that fluid overload due to the management of hypertension and hypokalemia was considered as antecedent of class I heart failure. She received treatment with isosorbide dinitrate, spironolactone, potassium citrate and furosemide. On Study Day 16, dehydration was considered resolved. On Study Day 17, diarrhea infectious resolved. The event of hypokalemia resolved on Study Day 18. On Study Day 19, pleural effusion was considered as resolved, and the patient was discharged from the hospital. At the time of discharge, the patient had Grade 1 dyspnea, however, it was ongoing prior to study start and was considered as a symptom of disease under study. She further received treatment with captopril and on Study Day 34, worsening hypertension was considered as resolved.

There was no change in the study treatment due to the event of pleural effusion.

The Investigator considered pleural effusion to be unrelated to ipatasertib and paclitaxel and related to disease under study, concurrent illness and other causes.

Event 2: Lower respiratory tract infection (Infection of low respiratory routes)

Prior to the event of lower respiratory tract infection, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 22.

On Study Day 23, the patient presented to the hospital with dyspnea. Chest X-ray results were suggestive of inflammatory process; however, surgeons discarded the suspicion, and diagnosis of Grade 2 lower respiratory tract infection was established. Subsequently, she was hospitalized due to persistent symptoms. She received treatment with ceftriaxone, ciprofloxacin, meropenem, vancomycin, trimethoprim/sulfamethoxazole and prednisone. On Study Day 40, the event of lower respiratory tract infection was considered as resolved and the patient was discharged from the hospital.

Relevant laboratory work-up:

Study Day	**WBC count** Normal range: 4.5-11 $\times 10^9$/L	**Absolute neutrophil count** Normal range: 0-0.5 $\times 10^9$/L	**Absolute lymphcyte count** Normal range: 1-4.8 $\times 10^9$/L
Screening	9.16	7.79	0.82
22	14.03	12.49	0.84
25	3.88	3.53	0.08
34	15.1	13.59	0.75
40	17.49	12.59	1.22
48	13.34	10.27	1.57
49	14.54	11.92	1.31
51	15.82	14.55	0.79
54	12.16	10.95	0.73

Due to the event of lower respiratory tract infection, study treatment with paclitaxel and ipatasertib was interrupted after Study Day 22.

The Investigator considered lower respiratory tract infection to be unrelated to ipatasertib and paclitaxel and related to disease under study, concurrent illness and other causes.

Event 3: Pneumonia (Hospital-acquired pneumonia)

Prior to the event of pneumonia, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 22.

On Study Day 48, the patient presented to the hospital with cough with green expectoration and increased dyspnea. A chest tomography revealed consolidation and pleural effusion and the patient was hospitalized with Grade 2 pneumonia. Sputum culture was positive for *Staphylococcus aureus* and the event was reassessed as hospital-acquired pneumonia. She received treatment with meropenem and vancomycin. On Study Day 59, she was diagnosed with decompensated intrahepatic cholangiocarcinoma and cardiorenal failure (symptoms and diagnostic details not provided).

Due to the event of pneumonia, study treatment was permanently discontinued with the last dose of paclitaxel and ipatasertib administered on Study Day 22.

On Study Day 60, the patient was hypotensive (blood pressure not provided) and in pain. On the same day, at 13:10 hours, the patient died due to hospital-acquired pneumonia. Cardiogenic shock due to myocardial infarction was also considered one of the cause of death, however no autopsy was performed to confirm the final cause; thus hospital-acquired pneumonia was considered the primary cause of death.

The Investigator considered pneumonia to be unrelated to ipatasertib and paclitaxel and related to other cause.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Back pain	1	Non-serious	3	4	Unrelated	Related
Vomiting	1	Non-serious	4	7	Related	Unrelated
Constipation	1	Non-serious	7	7	Unrelated	Unrelated
Headache	2	Non-serious	9	10	Unrelated	Unrelated
Vomiting	1	Non-serious	14	15	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Urinary retention	2	Non-serious	18	18	Unrelated	Unrelated
Diarrhea	1	Non-serious	19	21	Related	Unrelated
Vomiting	1	Non-serious	20	21	Unrelated	Unrelated
Hypokalemia	3	Non-serious	22	40	Unrelated	Unrelated
Hypocalcemia	1	Non-serious	22	30	Unrelated	Unrelated
Blood bicarbonate Increased	2	Non-serious	22	27	Unrelated	Unrelated
Hypomagnesaemia	1	Non-serious	22	29	Unrelated	Unrelated
Urinary tract Infection	2	Non-serious	24	36	Unrelated	Unrelated
Hyperglycemia	2	Non-serious	25	27	Unrelated	Unrelated
Gastritis	2	Non-serious	25	39	Unrelated	Unrelated
Hypoalbuminemia	1	Non-serious	25	Resolving	Unrelated	Unrelated
Hypophosphatemia	3	Non-serious	25	34	Unrelated	Unrelated
Angina unstable	2	Non-serious	29	34	Unrelated	Unrelated
Anemia	2	Non-serious	30	34	Unrelated	Unrelated
Skin infection	1	Non-serious	49	51	Unrelated	Unrelated

1.2 NARRATIVES FOR PATIENTS WHO DIED DUE TO DISEASE PROGRESSION

Study Number/CRTN:	CO40016/304193	Patient number	2005
Demographics:	62-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Alanine aminotransferase increased AESI: Grade ≥ 3 hepatotoxicity		

Event 2 (PT) Category:	Aspartate aminotransferase increased AESI: Grade ≥ 3 hepatotoxicity
Additional category:	Death due to disease progression

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal and lobular, moderately differentiated, ER positive/PR status unknown and HER2 negative left breast cancer (T2N3M0), approximately 3 years 5 months prior to study entry following left breast biopsy.

On Study Day −79, the patient was diagnosed with metastatic disease with ER positive/PR negative and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included liver (multiple lesions including segments 3 and 6) and bone (multiple). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	″Other″ (site: left breast)	Approximately 3 years 4 months prior to study entry	NA
Cancer therapy	Adjuvant	Docetaxel and doxorubicin	Approximately 3 years 3 months prior to study entry	Approximately 2 years 11 months prior to study entry
Radiotherapy	Adjuvant	Lymph nodes (cervico-supraclavicular, axillary and parasternal) and left chest wall (total dose: 46 cGy; 2 fractions)	Approximately 3 years prior to study entry	Approximately 2 years 10 months prior to study entry
Cancer therapy	Adjuvant	Tamoxifen	Approximately 2 years 9 months prior to study entry	−30

No medical history was reported. Other surgical history included oophorectomy and appendicectomy. Concurrent conditions included alanine aminotransferase increased, aspartate aminotransferase increased, chronic pancreatitis, chronic cholecystitis, gastric ulcer, diabetes mellitus, hypertension, coronary artery arteriosclerosis, chronic pyelonephritis, seroma, vaginal prolapse, upper abdominal pain, asthenia, and back pain.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included loperamide, ademetionine, metformin, bisoprolol, losartan and omeprazole.

The patient was noted with worsening of pre-existing condition of aspartate aminotransferase increased to Grade 2 (non-serious, related) from Study Day 117 to Study Day 131. No treatment was given for this event. Relevant laboratory parameters reported in the table below.

On Study Day 145, a laboratory work-up again showed worsening of pre-existing condition of aspartate aminotransferase increased (non-serious, related) to Grade 2. She received treatment with ademetionine and thioctic acid. She also received calcium chloride/potassium chloride/sodium chloride, potassium chloride and ascorbic acid for hepatopathy prophylaxis. Relevant laboratory parameters reported in the table below.

Event 1: Alanine aminotransferase increased
Event 2: Aspartate aminotransferase increased

Prior to the events of alanine aminotransferase increased and aspartate aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 153 and ipatasertib (300 mg) on Study Day 158.

On Study Day 159, the patient was noted with worsening of pre-existing condition of alanine aminotransferase increased and ongoing event of aspartate aminotransferase increased to Grade 3 (both non-serious) with ALT 288 U/L and AST 292 U/L. Treatment with thioctic acid was maintained and she received additional treatment with glycyrrhizic acid/phospholipids, calcium chloride/potassium chloride/sodium chloride, potassium chloride and prednisolone. On Study Day 167, she experienced Grade 2 asthenia and decreased appetite (both non-serious, unrelated). No treatment was administered for asthenia and decreased appetite. The events of alanine aminotransferase increased, aspartate aminotransferase increased, asthenia and decreased appetite remained unresolved at the time of patient′s death (see narrative below).

Relevant chemistry work-up:

Study Day	**AST** Normal range: 10-40 U/L	**ALT** Normal range: 10-40 U/L	**ALP** Normal range: 115-306 U/L	**Bilirubin** Normal range: 5.5-20.5 μmol/L
Screening	85	116	311	9.5
103	76	123	331	25
117	145	146	453	6.9
131	77	129	427	10.5
145	199	197	495	9.1
159	292	288	531	13.6
173	382	598	1260	104

Due to the events of alanine aminotransferase increased and aspartate aminotransferase increased, study treatment with ipatasertib was interrupted from Study Day 160 and Cycle 6 Day 15 dose of paclitaxel was not administered.

The Investigator considered alanine aminotransferase increased and aspartate aminotransferase increased, to be related to ipatasertib and paclitaxel.

On Study Day 173, a radiographic response assessment showed disease progression with new lesions in brain (cerebellum) and liver.

On Study Day 174, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and ipatasertib given on Study Day 153 and Study Day 159, respectively. The patient entered into long-term follow-up.

On Study Day182, the patient died due to disease progression. It was unknown whether an autopsy was performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Hyperhidrosis	1	Non-serious	2	Unresolved	Related	Related
Diarrhea	2	Non-serious	13	14	Related	Unrelated
Abdominal pain	1	Non-serious	13	14	Related	Related
Epistaxis	1	Non-serious	16	16	Related	Related
Hyperglycemia	2	Non-serious	28	61	Related	Related
Hypomagnesemia	1	Non-serious	47	61	Related	Related
Hypomagnesemia	1	Non-serious	75	145	Related	Related
Anemia	1	Non-serious	89	99	Unrelated	Related
Hyperglycemia	2	Non-serious	99	117	Related	Related
Hypocalcemia	1	Non-serious	103	117	Related	Related
Hyperbilirubinemia	1	Non-serious	103	117	Related	Related
Anemia	1	Non-serious	117	131	Related	Related
Supraventricular extrasystoles	2	Non-serious	145	Unresolved	Related	Related
Hypomagnesaemia	1	Non-serious	152	173	Related	Related
Neuropathy peripheral	1	Non-serious	153	Unresolved	Related	Related
Diarrhea	1	Non-serious	153	153	Related	Related
Neutropenia	2	Non-serious	159	Unresolved	Related	Related
Ataxia	1	Non-serious	167	Unresolved	Unrelated	Unrelated
Bone swelling	1	Non-serious	167	Unresolved	Unrelated	Unrelated
Eastern cooperative oncology group performance status worsened	1	Non-serious	167	Unresolved	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Blood creatinine increased	3	Non-serious	173	Unresolved	Related	Related
Hyponatremia	3	Non-serious	173	Unresolved	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305626	Patient number	2043
Demographics:	48-year-old female (race unknown)		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Category:	Death due to disease progression		

The patient was randomized on Study Day 1.

The patient was diagnosed with poorly differentiated, ER negative/PR positive and HER2 negative metastatic right breast cancer (T4N3M1; histological subtype: not otherwise specified) on Study Day −36.

At screening, sites of disease involvement included right breast (external quadrant), lymph nodes (right axillary adenopathy, retro pectoral adenopathy and group IV right neck adenopathy), neck (adenopathy in left group IV of the neck) and chest (left axillary adenopathy).

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent condition included neck pain.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

On Study Day 121, a radiographic response assessment showed disease progression with new lesions in brain (two nodular enhancement zones of 0.9 cm and 0.4 cm located in the left frontal parasagittal region).

On Study Day 125, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and ipatasertib given on Study Day 113 and Study Day 118, respectively. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Radiotherapy to brain (holocranial fields; 3000 cGy, 10 fractions)	129	141

On Study Day 146, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Vomiting	1	Non-serious	4	5	Related	Unrelated
Diarrhea	2	Non-serious	9	19	Related	Unrelated
Dyspepsia	1	Non-serious	9	19	Unrelated	Unrelated
Abdominal distension	1	Non-serious	9	19	Unrelated	Unrelated
Diarrhea	2	Non-serious	20	36	Related	Unrelated
Dry skin	1	Non-serious	69	84	Related	Unrelated
Influenza	1	Non-serious	81	84	Unrelated	Unrelated
Diarrhea	2	Non-serious	101	101	Related	Unrelated
Diarrhea	1	Non-serious	102	110	Unrelated	Unrelated
Hepatic vein thrombosis	1	Non-serious	106	119	Unrelated	Unrelated
Headache	1	Non-serious	113	113	Unrelated	Unrelated
Depression	1	Non-serious	113	Unresolved	Unrelated	Unrelated
Vomiting	2	Non-serious	119	119	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304754	Patient number	2073
Demographics:	66-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Category:	Death due to disease progression		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER positive, PR negative and HER2 negative right breast cancer (TxNxMx), approximately 23 years prior to study entry.

The patient was diagnosed with locally recurrent disease, metastatic disease and locally advanced unresectable disease, approximately 3 years prior to study entry, with ER/PR positive and HER2 negative disease in recurrent/metastatic tissue. At screening sites of disease involvement included liver (porta), bone (calotte and bilateral femur), right lateral chest wall and pleura. The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right radical mastectomy	Approximately 23 years prior to study entry	NA
Cancer therapy	Metastatic	Anastrozole and Denosumab	Approximately 3 years prior to study entry	Approximately 2 years prior to study entry
Cancer therapy	Metastatic	Fulvestrant and palbociclib	Approximately 2 years prior to study entry	Approximately 8 months prior to study entry
Radiotherapy	Metastatic	Right femur (total dose: 38 cGy; 15 fractions)	−17	−6

No medical or other surgical history was reported. The patient′s concurrent conditions included hypothyroidism, hypertension, bone pain and decreased appetite.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included dexamethasone, levothyroxine and metamizole.

On Study Day 125, a radiographic response assessment showed disease progression with new lesions in lymph nodes (mediastinal and para-aortal) and pleural carcinosis (pleural effusion).

On Study Day 126, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and ipatasertib given on Study Day 100 and Study Day 105, respectively. The patient entered into the long-term follow-up.

On Study Day 131, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	2	Non-serious	6	106	Related	Unrelated
Vomiting	2	Non-serious	15	Resolving	Related	Related
Cystitis	2	Non-serious	20	43	Unrelated	Unrelated
Alopecia	2	Non-serious	36	57	Unrelated	Related
Cystitis	2	Non-serious	55	Unresolved	Unrelated	Unrelated
Anemia	2	Non-serious	57	69	Unrelated	Unrelated
Dyspnea	2	Non-serious	85	Unresolved	Unrelated	Unrelated
Fatigue	1	Non-serious	98	100	Unrelated	Unrelated

Study Number/CRTN:	CO40016/307256	Patient number	2102
Demographics:	39-year-old Asian female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade $\geq$ 3 diarrhea		
Event 2 (PT) Category:	Diarrhea AESI: Grade $\geq$ 3 diarrhea		
Additional category:	Death due to disease progression		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER/PR positive and HER2 negative left breast cancer (T2N0M0; histological grade unknown) on Study Day −966.

On Study Day −54, the patient was diagnosed with metastatic disease (no results were available for hormone and HER2 receptor status in recurrent/metastatic tissue). At screening sites of disease involvement included lung (bilateral lung cancerous lymphangiopathy), liver (bilateral lobe; multiple), bone, lymph nodes (left axillary) and pericardial cavity (bilateral pleural

effusion). The patient was assessed by the Investigator to have endocrine resistance and visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left partial mastectomy	−890	NA
Radiotherapy	Adjuvant	Left breast (total dose: 6000 cGy; 30 fractions)	−834	−793
Cancer therapy	Adjuvant	Tamoxifen	−793	−63

No medical or other surgical history was reported. The patient′s concurrent conditions included hyperlipidemia, hypothyroidism, depression, seasonal allergy, and cough.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included duloxetine, aripiprazole, levothyroxine, and atorvastatin.

On Study Day 1, the patient started receiving loperamide prophylactically (total daily dose: 4 mg). On Study Day 3, loperamide dose was reduced to 3 mg, which was further reduced to 1 mg (total daily dose) on Study Day 4.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 4.

On Study Day 5, the patient experienced non-serious Grade 2 (initial intensity) diarrhea. Loperamide dose was increased to 2 mg (total daily dose). On the following day (Study Day 6), diarrhea improved to Grade 1. On Study Day 11, loperamide dose was increased to 3 mg (total daily dose). On Study Day 13, diarrhea worsened to Grade 3. On Study Day 15, loperamide dose was further increased to 6 mg (total daily dose). On Study Day 16, the event of diarrhea was considered resolved and the patient continued on loperamide prophylactically (total daily dose: 4 mg).

Loperamide details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea prophylaxis	4	PO	1	2
Diarrhea prophylaxis	3	PO	3	3
Diarrhea prophylaxis	1	PO	4	4
Diarrhea	2	PO	5	10

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	3	PO	11	12
Diarrhea	4	PO	13	14
Diarrhea	6	PO	15	15
Diarrhea prophylaxis	4	PO	16	24

Due to the event of diarrhea, there was no change in study treatment with paclitaxel; however, ipatasertib was initially interrupted on Study Day 15 and then resumed at a reduced dose of 300 mg on Study Day 22.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

After resolution of Grade 3 diarrhea, the patient experienced multiple non-serious events of diarrhea detailed in the table below. There was no change in study treatment due to these events. Treatment included loperamide (details reported in table below), probiotics (from Study Day 29 to Study Day 127) and Tsumura Hangeshashinto extract (from Study Day 43 to Study Day 168).

Most extreme Grade	Onset day	Resolution day/Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
2	25	29	Related	Unrelated
1	39	52	Related	Unrelated
2	80	102	Related	Related

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	25	25
Diarrhea	6	PO	26	28
Diarrhea prophylaxis	6	PO	29	37
Diarrhea prophylaxis	4	PO	38	38
Diarrhea	6	PO	39	41
Diarrhea	8	PO	42	43
Diarrhea	6	PO	44	44
Diarrhea	8	PO	45	50
Diarrhea	6	PO	51	51
Diarrhea prophylaxis	6	PO	52	52
Diarrhea prophylaxis	4	PO	53	53
Diarrhea prophylaxis	6	PO	54	56
Diarrhea prophylaxis	8	PO	57	62
Diarrhea prophylaxis	6	PO	63	63
Diarrhea prophylaxis	6	PO	71	73
Diarrhea prophylaxis	4	PO	74	74
Diarrhea prophylaxis	6	PO	75	79
Diarrhea	6	PO	80	84
Diarrhea	4	PO	85	88
Diarrhea	6	PO	89	91
Diarrhea	8	PO	92	92

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea prophylaxis	8	PO	93	93
Diarrhea prophylaxis	6	PO	94	95
Diarrhea prophylaxis	4	PO	96	96
Diarrhea prophylaxis	6	PO	97	100
Diarrhea	6	PO	101	101
Diarrhea prophylaxis	6	PO	102	115

Event 2: Diarrhea

Prior to the event of diarrhea (second episode), the most recent dose of paclitaxel was administered on Study Day 129 and ipatasertib (300 mg) on Study Day 130. The patient received loperamide 4 mg (total daily dose) prophylactically on Study Day 130.

On Study Day 131, the patient experienced non-serious Grade 3 diarrhea. Loperamide dose was increased to 6 mg (total daily dose). She also received probiotics and Tsumura Hangeshashinto extract. On the following day (Study Day 132), loperamide dose was increased to 12 mg (total daily dose) and diarrhea improved to Grade 2. On Study Day 134, loperamide dose was reduced to 10 mg (total daily dose) and on Study Day 136, further reduced to 8 mg (total daily dose). On Study Day 137, the event of diarrhea was considered resolved and the patient was started on loperamide prophylactically (total daily dose: 6 mg).

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea prophylaxis	4	PO	116	128
Diarrhea prophylaxis	2	PO	129	129
Diarrhea prophylaxis	4	PO	130	130
Diarrhea	6	PO	131	131
Diarrhea	12	PO	132	133
Diarrhea	10	PO	134	135
Diarrhea	8	PO	136	136
Diarrhea prophylaxis	6	PO	137	138
Diarrhea prophylaxis	8	PO	139	139
Diarrhea prophylaxis	6	PO	140	148
Diarrhea prophylaxis	4	PO	149	154
Diarrhea	8	PO	155	155
Diarrhea	6	PO	156	156
Diarrhea	6	PO	157	165
Diarrhea prophylaxis	4	PO	166	166
Diarrhea prophylaxis	6	PO	167	178
Diarrhea prophylaxis	4	PO	179	181
Diarrhea	4	PO	182	182
Diarrhea	6	PO	183	184
Diarrhea prophylaxis	4	PO	185	207
Diarrhea	6	PO	208	208
Diarrhea prophylaxis	6	PO	209	209

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea prophylaxis	4	PO	210	218
Diarrhea prophylaxis	2	PO	219	219
Diarrhea prophylaxis	4	PO	220	229
Diarrhea prophylaxis	2	PO	230	230
Diarrhea prophylaxis	4	PO	231	232
Diarrhea prophylaxis	2	PO	233	237
Diarrhea prophylaxis	4	PO	238	238
Diarrhea prophylaxis	2	PO	239	241
Diarrhea	4	PO	242	242
Diarrhea prophylaxis	2	PO	243	257

Due to the event of diarrhea, there was no change in study treatment with paclitaxel; however, ipatasertib was interrupted on Study Day 132 and resumed on Study Day 141.

The Investigator considered diarrhea to be related to ipatasertib and paclitaxel.

After resolution of second episode of Grade 3 diarrhea, the patient experienced multiple non-serious events of diarrhea detailed in the table below. There was no change in study treatment due to these events. Treatment included loperamide (details reported in table above) and probiotics (from Study Day 169 to Study Day 260).

Most extreme Grade	Onset day	Resolution day/Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
1	155	166	Related	Related
1	182	185	Related	Related
1	208	209	Related	Related
1	242	243	Related	Related

On Study Day 252, a radiographic response assessment showed disease progression.

On Study Day 258, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and ipatasertib given on Study Day 232 and Study Day 236, respectively. The patient entered into long-term follow-up.

On Study Day 263, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Peripheral sensory neuropathy	1	Non-serious	2	3	Unrelated	Related
Nausea	1	Non-serious	3	15	Unrelated	Related
White blood cell count decreased	2	Non-serious	8	63	Related	Related
Dysgeusia	1	Non-serious	9	10	Unrelated	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Angular cheilitis	1	Non-serious	11	189	Related	Related
Alopecia	2	Non-serious	15	Unresolved	Unrelated	Related
Neutrophil count decreased	2	Non-serious	15	29	Related	Related
Arthralgia	1	Non-serious	17	216	Unrelated	Related
Headache	1	Non-serious	31	33	Unrelated	Unrelated
Lacrimation increased	2	Non-serious	35	Unresolved	Unrelated	Related
Nail discoloration	1	Non-serious	35	Unresolved	Unrelated	Related
Peripheral sensory neuropathy	1	Non-serious	38	Unresolved	Unrelated	Related
Stomatitis	1	Non-serious	46	53	Related	Related
Oropharyngeal pain	2	Non-serious	47	57	Related	Related
Pruritus	1	Non-serious	50	57	Related	Related
Pyrexia	1	Non-serious	63	70	Unrelated	Unrelated
White blood cell count decreased	3	Non-serious	71	249	Related	Related
Product dose omission	NA	NA	74	74	NA	NA
Nasopharyngitis	2	Non-serious	88	100	Unrelated	Unrelated
Neutrophil count decreased	2	Non-serious	92	99	Related	Related
Headache	1	Non-serious	126	127	Unrelated	Unrelated
Neutrophil count decreased	2	Non-serious	129	148	Related	Related
Pruritus	1	Non-serious	137	142	Related	Related
Rash	1	Non-serious	152	169	Related	Related
Neutrophil count decreased	2	Non-serious	155	176	Related	Related
Edema	1	Non-serious	165	Unresolved	Related	Related
Cough	2	Non-serious	198	Unresolved	Unrelated	Unrelated
Pyrexia	1	Non-serious	199	206	Related	Related
Treatment non-compliance	NA	NA	200	200	NA	NA
Neutrophil count decreased	2	Non-serious	211	225	Related	Related
Product dose omission	NA	NA	237	237	NA	NA
Neutrophil count decreased	3	Non-serious	238	249	Related	Related
Pyrexia	1	Non-serious	251	253	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305427	Patient number	2108
Demographics:	55-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		

Cohort:	Cohort B
Category:	Death due to disease progression

The patient was randomized on Study Day -1.

The patient was initially diagnosed with lobular, moderately differentiated, ER/PR positive and HER2 negative right breast cancer (T3N1M0), approximately 4 years 2 months prior to study entry.

On Study Day -273, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included liver (segment IV and VIII) and bone (axial skeletal). The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neo-adjuvant	Paclitaxel	Approximately 3 years 11 months prior to study entry	Approximately 3 years 9 months prior to study entry
Cancer therapy	Neo-adjuvant	Fluorouracil, epirubicin and cyclophosphamide	Approximately 3 years 8 months prior to study entry	Approximately 3 years 6 months prior to study entry
Surgery	Curative	Right radical mastectomy and right axillary lymph node dissection	Approximately 3 years 5 months prior to study entry	NA
Cancer therapy	Adjuvant	Tamoxifen	Approximately 3 years 2 months prior to study entry	–973
Radiotherapy	Adjuvant	Breast (side and dose unknown)	Approximately 3 years 3 months prior to study entry	Approximately 3 years 3 months prior to study entry
Cancer therapy	Adjuvant	Letrozole	–973	–273
Radiotherapy	Adjuvant	Bone (D7) (total dose: 40 cGy; single fraction)	–193	–193

No medical or other surgical history was reported. The patient′s concurrent condition included back pain.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included zoledronic acid.

On Study Day 26, the patient showed symptomatic deterioration (worsening asthenia, nausea, chronic headache and vomiting). On the same day (Study Day 26), a radiographic response assessment showed disease progression with new lesions in the brain. Subsequently, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and ipatasertib given on Study Day 15 and Study Day 21, respectively. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatment	Start Day	Stop Day
Radiotherapy to bone (Holocranial; total dose: 30 cGy)	33	43

On Study Day 46, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Back pain	2	Non-serious	1	Unresolved	Unrelated	Unrelated
Nausea	1	Non-serious	1	Unresolved	Related	Unrelated
Vomiting	2	Non-serious	1	25	Related	Unrelated
Neuropathy peripheral	1	Non-serious	15	Unresolved	Unrelated	Related
Diarrhea	1	Non-serious	15	15	Related	Related
Asthenia	2	Non-serious	15	Unresolved	Unrelated	Unrelated
Anxiety	1	Non-serious	15	Unresolved	Unrelated	Unrelated
Headache	1	Non-serious	29	Unresolved	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304195	Patient number	2180
Demographics:	57-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		
Additional category:	Death due to disease progression		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative right breast cancer (T2N1M0), approximately 4 years prior to study entry followed by right radical mastectomy.

On Study Day −29, the patient was diagnosed with metastatic disease (ER/PR unknown and HER2 receptor not assessed in metastatic tissue). At screening, sites of disease involvement included liver (segment 2 and 6), bone (vertebrae TH12, L1, L2) and liver (bilateral lobes). The patient was assessed by the Investigator to have visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Adjuvant	Supraclavicular and parasternal lymph node (dose: 40 cGy, 20 fractions)	Approximately 4 years prior to study entry.	Approximately 4 years prior to study entry.
Cancer therapy	Adjuvant	Cyclophosphamide, methotrexate and fluorouracil	Approximately 4 years prior to study entry.	Approximately 3 years prior to study entry

No medical or surgical history was reported. Concurrent conditions included goiter, renal hamartoma, osteoarthritis (right hip) and spinal pain (lumbar spine).

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included dexamethasone and ketorolac.

Event: Neuropathy peripheral (Neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 253.

On Study Day 253, the patient was diagnosed with non-serious Grade 3 (initial intensity Grade 1) neuropathy peripheral (presenting signs and symptoms not reported). No treatment was given for this event.

Due to this event, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose given on Study Day 267.

On Study Day 281, the event of neuropathy peripheral worsened to Grade 3 and on Study Day 349, improved to Grade 1, which remained unresolved at the time of patient′s death (see narrative below).

The Investigator considered neuropathy peripheral, to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 349, the patient showed symptomatic deterioration (fatigue and weakness).

On the same day (Study Day 349), study treatment with ipatasertib was permanently discontinued due to symptomatic deterioration with the last dose administered on Study Day 329. The patient entered into the long-term follow-up.

On Study Day 350, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	4	22	Related	Related
Alopecia	2	Non-serious	27	Unresolved	Unrelated	Related

Study Number/CRTN:	CO40016/306642	Patient number	2192

Demographics:	53-year-old White female
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)
Cohort:	Cohort B
Event (PT) Categories:	Febrile neutropenia SAE, AE leading to study treatment discontinuation
Additional category:	Death due to disease progression

The patient was randomized on Study Day –2.

The patient was initially diagnosed with lobular, moderately differentiated ER/PR positive and HER2 negative left breast cancer (T3N1M1) on Study Day –43 following left breast biopsy.

At screening sites of disease involvement included liver (segment V, VI and VII), bone and left axillary lymph node. The patient was assessed by the Investigator to have visceral crisis.

Past cancer treatment is listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Metastatic	Bone (lumbar region; total dose: 3000 cGy; 10 fractions)	-34	-16

The patient′s medical history included depression and non-cardiac chest pain. No other surgical history was reported. Concurrent condition included nausea.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included denosumab, fentanyl, metoclopramide, calcium carbonate, alprazolam, fluoxetine, and paracetamol.

Event: Febrile neutropenia

Prior to the event of febrile neutropenia, the most recent dose of paclitaxel was administered on Study Day 148 and ipatasertib (400 mg) on Study Day 149.

On Study Day 151, the patient experienced fever (body temperature not provided) and was noted with Grade 2 stomatitis (non-serious, unrelated). A laboratory work-up revealed Grade 3

febrile neutropenia (neutrophil count 0.78 $\times$ $10^3/\mu L$; normal range: 1.6-7.5 $\times$ $10^3/\mu L$). Reportedly, fever lasted for 30 minutes on Study Day 151. She received treatment with filgrastim. The following day (Study Day 152), she experienced Grade 1 diarrhea (non-serious, related) and her body temperature was 38.2°C. Reportedly, the patient refused hospitalization on Study Day 152 and started outpatient treatment with amoxicillin and ciprofloxacin for possible neutropenic sepsis. However, on Study Day 153, she was feeling unwell. Vitals showed tachycardia (heart rate 125 beats/minute), hypotension (blood pressure 80/60 mmHg) and fever (body temperature 37.2°C). Blood gas analysis showed oxygen saturation 94.6%, pH 7.45, pCO_2 33.1 and pO_2 48.7. Subsequently, she was hospitalized with neutropenic sepsis and for further investigations and treatment. Laboratory work-up also showed Grade 3 thrombocytopenia (ongoing since Study Day 112; non-serious, related), Grade 3 anemia (ongoing since Study Day 29; non-serious, related), increased lactate (34 mg/dL; normal range not reported) and increased C-reactive protein (CRP: 12.72 mg/dL, normal value $\leq$ 0.3 mg/dL). Blood and urine cultures were negative. It was reported that during her admission, she remained hemodynamically stable. She also received treatment with filgrastim, meropenem, fluconazole, benzydamine, miconazole, acyclovir, 2 units of red blood cells and intravenous fluids and showed rapid clinical improvement.

On Study Day 155, she was noted with Grade 2 sinus tachycardia (non-serious, unrelated; heart rate: 125 beats/minute) for which she received treatment with metoprolol and bisoprolol. The same day (Study Day 155), diarrhea was considered resolved. On Study Day 156, she experienced Grade 2 cough (non-serious, unrelated) for which she was given budesonide. Her chest X-ray revealed blunting of the costophrenic angle. Due to persistent fever and productive cough, a CT scan was performed which showed evidence of pneumonia. She received treatment with amikacin. Sputum cultures were positive for hemolytic *Streptococcus*. On Study Day 159, she was also diagnosed with Grade 2 lower respiratory tract infection (non-serious, unrelated). She received treatment with furosemide and fresh frozen plasma with significant improvement for edema peripheral, vancomycin, cefixime and levofloxacin for lower respiratory tract infection and ivabradine for sinus tachycardia. On the same day (Study Day 159), the event of febrile neutropenia was considered as resolved. On Study Day 161, stomatitis and cough resolved and the patient was discharged from the hospital. On Study Day 167, the event of lower respiratory tract infection resolved. The events of anemia, thrombocytopenia and sinus tachycardia remained unresolved at the time of patient's death (see narrative below).

Relevant laboratory work-up:

Study Day	**WBC count** Normal range: 4-10 $\times$ $10^3/\mu L$	**Absolute neutrophil count** Normal range: 1.6-7.5 $\times$ $10^3/\mu L$	**Absolute lymphocyte count** Normal range:0.8-4.5 $\times$ $10^3/\mu L$	**C-reactive protein** Normal range: $\leq$ 0.3 mg/dL
Screening	6.07	4.86	0.55	—
151	1.69	0.78	0.82	8.25

Study Day	WBC count Normal range: 4-10 $\times 10^3/\mu L$	Absolute neutrophil count Normal range: 1.6-7.5 $\times 10^3/\mu L$	Absolute lymphocyte count Normal range:0.8-4.5 $\times 10^3/\mu L$	C-reactive protein Normal range: $\leq$ 0.3 mg/dL
153	1.83	0.65	1	12.72
154	2.81	1.31	1.19	12.95
155	10.54	5	4.36	—
156	22.48	12.57	6.75	9.03
157	28.21	18.3	7.4	—
158	33.74	22.01	9.13	5.34
159	24.07	15.49	6.54	4.4
160	15.26	10.06	3.83	3.73
161	12.62	8.35	3.26	3.85
169	8.57	6.63	0.94	—

Vital signs:

Study Day	Blood pressure Units: mmHg	Heart rate Units: beats/minute	Body temperature Units: °C
Screening	125/80	87	37.2
151	—	—	36.2
152	—	—	38.2
153	80/60	125	37.2
154	110/80	110	37.2
155	110/70	125	37.4
156	110/70	120	37.2
157	120/80	110	37.2
158	120/70	102	37.7
159	130/80	102	37.4
160	120/80	82	36.2
161	120/80	82	37.1
169	110/70	89	37.3

Due to the event of febrile neutropenia, study treatment with ipatasertib was interrupted on Study Day 152 and resumed on Study Day 169 at a reduced dose of 300 mg; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 148.

The Investigator considered febrile neutropenia to be related to ipatasertib and paclitaxel.

On Study Day 195, the patient was noted to have symptomatic deterioration [fatigue, ascites (pleural effusion), elevated liver enzymes, jaundice, hemolysis and lethargy].

On Study Day 198, study treatment with ipatasertib was permanently discontinued due to symptomatic deterioration with the last dose administered on Study Day 189. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Letrozole	198	202

On Study Day 203, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	2	Non-serious	2	93	Unrelated	Unrelated
Vomiting	1	Non-serious	7	7	Related	Unrelated
Vomiting	1	Non-serious	9	9	Related	Related
Vomiting	1	Non-serious	14	14	Related	Related
Neutropenia	2	Non-serious	14	29	Related	Related
Sciatica	1	Non-serious	15	27	Unrelated	Unrelated
Chest pain	1	Non-serious	15	67	Unrelated	Unrelated
Vomiting	1	Non-serious	17	18	Related	Unrelated
Pollakiuria	1	Non-serious	33	44	Unrelated	Unrelated
Abdominal pain	1	Non-serious	33	40	Unrelated	Unrelated
Sciatica	2	Non-serious	42	70	Unrelated	Unrelated
Hypercholesterolemia	1	Non-serious	57	141	Related	Related
Diarrhea	1	Non-serious	66	66	Related	Unrelated
Diarrhea	1	Non-serious	70	70	Related	Unrelated
Back pain	1	Non-serious	70	100	Unrelated	Unrelated
Non-cardiac chest pain	1	Non-serious	70	Unresolved	Unrelated	Unrelated
Abdominal pain upper	1	Non-serious	74	74	Related	Unrelated
Nausea	1	Non-serious	74	74	Related	Unrelated
Thrombocytopenia	1	Non-serious	85	99	Related	Related

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	2	Non-serious	95	97	Related	Unrelated
Diarrhea	1	Non-serious	101	103	Related	Unrelated
Constipation	1	Non-serious	104	142	Unrelated	Unrelated
Abdominal pain upper	1	Non-serious	105	105	Related	Unrelated
Neuritis	1	Non-serious	121	Resolving	Unrelated	Related
Fatigue	1	Non-serious	121	Unresolved	Related	Related
Diarrhea	1	Non-serious	124	125	Related	Related
Neutropenia	2	Non-serious	127	141	Related	Related
Diarrhea	1	Non-serious	127	138	Related	Related
Decreased appetite	1	Non-serious	130	145	Unrelated	Unrelated
Depression	2	Non-serious	143	Unresolved	Unrelated	Unrelated
Anxiety disorder	2	Non-serious	143	Unresolved	Unrelated	Unrelated
Nausea	2	Non-serious	146	Unresolved	Unrelated	Unrelated
Edema peripheral	1	Non-serious	157	165	Unrelated	Unrelated
Edema peripheral	2	Non-serious	159	Unresolved	Unrelated	Unrelated
Hemolysis	1	Non-serious	196	Unresolved	NA	NA
Lethargy	1	Non-serious	198	Unresolved	NA	NA
Oliguria	3	Non-serious	198	Unresolved	NA	NA
Urinary tract infection	2	Non-serious	200	Unresolved	Unrelated	NA

1.3 NARRATIVES FOR PATIENTS WHO EXPERIENCED SERIOUS ADVERSE EVENT(S)

Study Number/CRTN:	CO40016/307263	Patient number	2001
Demographics:	63-year-old Asian female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Abdominal abscess SAE		
Event 2 (PT) Category:	Pneumonia SAE		

The patient was randomized on Study Day −2.

The patient was diagnosed with ductal, poorly differentiated, ER/PR positive and HER2 negative, locally advanced unresectable metastatic left breast cancer (T4cN3cM1) on Study Day −47.

At screening, sites of disease involvement included left breast, bilateral lung, bone (multiple lesions) and left sub-clavicular and right axillary lymph nodes. The patient was assessed by the Investigator to have visceral crisis.

No past cancer treatments were reported.

The patient′s medical history included facial paralysis. No surgical history was reported. Concurrent conditions included hypertension, cancer pain and skin ulcer.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included amlodipine/irbesartan, teprenone, metronidazole, loxoprofen and cefmetazole.

Event 1: Abdominal abscess

Prior to the event of abdominal abscess, the most recent dose of paclitaxel was administered on Study Day 45 and ipatasertib (400 mg) on Study Day 51.

On Study Day 59, the patient experienced right lower abdominal pain. A laboratory work-up showed elevated C-reactive protein at 10.19 mg/dL (normal range not provided). An abdominal CT-scan showed Grade 3 appendicitis (non-serious, unrelated) and Grade 3 abdominal abscess, leading to hospitalization. Necrotizing appendicitis rupture was also suspected. On Study Day 74, laparoscopic ileocolic resection was performed. She further received treatment with calcium chloride dihydrate/glucose/potassium chloride/sodium acetate, cyanocobalamin/pyridoxine/thiamine disulfide, amino acids/electrolytes/glucose/thiamine, carbohydrates/potassium chloride/sodium chloride/sodium lactate, magnesium citrate, sennoside A+B calcium, calcium chloride dihydrate/potassium chloride/sodium acetate trihydrate/ sodium chloride, carbazochrome sodium sulfonate, tranexamic acid, glycerol, remifentanil, rocuronium, propofol, flurbiprofen, ephedrine, phenylephrine, sugammadex, dexamethasone, calcium gluconate monohydrate/glucose/magnesium chloride hexahydrate/potassium chloride/sodium acetate/sodium chloride/sodium citrate dihydrate, glucose/magnesium chloride hexahydrate/potassium chloride/potassium phosphate monobasic/sodium acetate trihydrate/sodium chloride, ascorbic acid and fentanyl citrate. On Study Day 80, it was reported that the patient had a good postoperative care. On the same day (Study Day 80), her symptoms recovered; the events of abdominal abscess and appendicitis improved to Grade 1 and she was discharged from the hospital. On Study Day 94, the events of abdominal abscess and appendicitis were considered resolved.

Due to the event of abdominal abscess, study treatment with ipatasertib was interrupted on Study Day 59 and paclitaxel was interrupted at Cycle 3. The next dose of ipatasertib and paclitaxel was administered on Study Day 87.

The Investigator considered abdominal abscess to be unrelated to ipatasertib and paclitaxel and related to other cause (appendicitis).

Event 2: Pneumonia

Prior to the event of pneumonia, the most recent dose of paclitaxel was administered on Study Day 269 and ipatasertib (400 mg) on Study Day 275.

On Study Day 278, during tumor assessment week 40 visit, the patient presented with cough. A CT-scan showed opaque area over the lower right lung field and the patient was diagnosed with Grade 2 pneumonia (initial intensity Grade 1). On the same day (Study Day 278), she was also reported with disease progression with new lesions in right lung (confirmed after subsequent scan on Study Day 334). She was started on treatment with levofloxacin and L-carbocisteine for pneumonia. On Study Day 311, a repeat CT-scan showed deterioration of right lung field opaque area. On Study Day 317, she was hospitalized for bronchoscopy to differentiate breast cancer metastasis, inflammation and lung cancer. She received treatment with midazolam, flumazenil, and lidocaine. Bronchoscopy was performed, and biopsy showed metastatic breast cancer. On Study Day 318, the patient was discharged from the hospital. On Study Day 334, CT-scan showed reduced invasion opaque area. On the same day (Study Day 334), a

radiographic response assessment confirmed new lesion in right lung. On Study Day 338, the event of pneumonia was considered resolved.

Relevant laboratory work-up:

Study Day	**WBC count** Normal range: 4-9 $\times$ 10^9/L	**Neutrophils** Normal range: 38-58%	**Lymphocytes** Normal range: 26-47%
Screening	78.1	69.6	24.7
283	58.5	65.5	26.8
311	78.6	76	17.3

There was no change in study treatment due to the event of pneumonia.

The Investigator considered pneumonia to be unrelated to ipatasertib and paclitaxel and related to other cause (unspecified).

On Study Day 339, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 325 and ipatasertib on Study Day 331. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Fulvestrant	348	348
Fulvestrant and Abemaciclib	369	485
Fulvestrant	493	689
Eribulin	695	997
Capecitabine	1004	1249
Paclitaxel and Bevacizumab	1262	Ongoing

On Study Day 1395, the patient was discontinued from the study as per physician decision (study was terminated by the Sponsor).

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious/ Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Diarrhea	1	Non-serious	5	348	Related	Unrelated
Stomatitis	2	Non-serious	16	348	Unrelated	Related
Butterfly rash	1	Non-serious	38	348	Unrelated	Related
Periodontitis	1	Non-serious	68	290	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Dermatitis contact	2	Non-serious	220	348	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305629	Patient number	2008
Demographics:	76-year-old American Indian or Alaska native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Categories:	Diarrhea SAE, AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Categories:	Hyperglycemia SAE, AE leading to study treatment discontinuation, AESI: Grade ≥ 3 hyperglycemia		
Event 3 (PT) Category:	Dehydration SAE		
Event 4 (PT) Category:	Hypoglycemia SAE		
Event 5 (PT) Categories:	Respiratory distress Death due to AE, SAE		

A narrative for this patient is available under Section 1.1; Narratives for patients who died due to adverse event(s).

Study Number/CRTN:	CO40016/305631	Patient number	2029
Demographics:	50-year-old female (race unknown)		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Categories:	Pneumonitis SAE, AE leading to study treatment discontinuation, AESI: Grade ≥ 2 Pneumonitis		

The patient was randomized on Study Day 1.

The patient was diagnosed with ER/PR positive and HER2 negative left breast cancer (T3N3M1; histological grade unknown and subtype: not otherwise specified) on Study Day −34.

At screening sites of disease involvement included breast (left external quadrant), left axillary lymph nodes and bone (right scapula, right fourth coastal posterior arch, right ninth costal posterior arch and midline vertebra lumbar 3).

No past cancer treatments were reported.

The patient′s medical history included arachnoid cyst. Surgical history included ventriculoperitoneal shunt placement and cholecystectomy. Concurrent conditions included hypertension and insomnia.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included pregabalin, cyclobenzaprine, tramadol, and losartan.

Event: Pneumonitis

Prior to the event of pneumonitis, the most recent dose of paclitaxel was administered on Study Day 15 and ipatasertib (400 mg) on Study Day 21.

On Study Day 28, the patient experienced dyspnea. A laboratory work-up showed Grade 3 lymphopenia (lymphocyte count $0.58 \times 10^3/\mu L$, normal range: 1-$4.8 \times 10^3/\mu L$) and Grade 2 anemia (hemoglobin 9.9 g/dL, normal range not provided). Chest X-ray showed interstitial basal infiltrate with right para cardiac basal predominance and obturation of costophrenic angles. She was diagnosed with Grade 2 pneumonitis.

On Study Day 29, during scheduled Cycle 2 visit, the patient′s oxygen saturation was 78% and she had fever (body temperature 39.2°C). She also experienced pain in lower limbs. Her ECOG Performance status was 2. CT scan showed multiple bilateral parenchymal opacities distributed diffusely (predominantly in upper lobes); suggestive of inflammatory parenchymal process. Subsequently, she was hospitalized for worsening of pneumonitis to Grade 3. The same day (Study Day 29), blood and urine cultures were negative. During hospitalization, she received oxygen support by nasal cannula and received treatment with meropenem, trimethoprim/sulfamethoxazole, oseltamivir, hydrocortisone, furosemide, enoxaparin, midazolam and levofloxacin. She also received dietary and hydration advice. On Study Day 34, the event of pneumonitis improved to Grade 2. On Study Day 37, her ECOG Performance status improved to Grade 1. On the same day (Study Day 37), the event of pneumonitis was considered resolved and she was discharged from the hospital.

On Study Day 45, study treatment was permanently discontinued as per the physician decision due to the event of pneumonitis with the last dose of paclitaxel administered on Study Day 15 and ipatasertib on Study Day 21. The patient entered into long-term follow-up.

The Investigator considered pneumonitis to be related to ipatasertib and unrelated to paclitaxel.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Paclitaxel	51	Ongoing

On Study Day 206, the patient withdrew consent from the study.

No other AEs were experienced by the patient during the study.

Study Number/CRTN:	CO40016/305386	Patient number	2032
Demographics:	51-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Hyperglycemia AESI: Grade $\geq$ 3 hyperglycemia		
Event 2 (PT) Categories:	Hyperglycemia AE leading to study treatment discontinuation, AESI: Grade $\geq$ 3 hyperglycemia		
Event 3 (PT) Category:	Deep vein thrombosis SAE		
Event 4 (PT) Category:	Extravasation SAE		

The patient was randomized on Study Day −1.

The patient was diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative metastatic right breast cancer (T2NXM1) Study Day −102, following right palliative lumpectomy. At screening sites of disease involvement included lung (right upper lobe and bilateral nodes), bone (axial skeleton) and pericardial effusion. The patient was assessed by the Investigator to have visceral crisis.

No past cancer treatments were reported.

No medical history was reported. The patient′s other surgical history included cholecystectomy, caesarean section and intrauterine device (copper T) installation. Concurrent conditions included hypertension and type II diabetes mellitus.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included enalapril, propranolol, hydrochlorothiazide, metformin, ethinyl estradiol/gestodene and pamidronate.

Event 1: Hyperglycemia (Asymptomatic hyperglycemia)

Prior to the event of hyperglycemia, the most recent dose of paclitaxel was administered on Study Day 43 and ipatasertib (400 mg) on Study Day 48.

On Study Day 57, the patient presented for scheduled Cycle 3 Day 1 visit. Her laboratory work-up showed non-serious Grade 3 hyperglycemia (glucose 272 mg/dL; normal range: 70-100 mg/dL). No new treatment was reported for the event; however, treatment with metformin (ongoing medication from prior to study start) and glibenclamide (started on Study Day 7) was maintained for her pre-existing condition of diabetes mellitus (for treatment details please refer to table below). Relevant laboratory work-up has been reported in the table below. On Study Day 62, the event of hyperglycemia improved to Grade 2. On Study Day 70, the event of hyperglycemia was considered resolved.

Due to the event of hyperglycemia, there was no change in treatment with paclitaxel; however, treatment with ipatasertib was interrupted on Study Day 57 and was resumed at a reduced dose of 300 mg on Study Day 70.

The Investigator considered hyperglycemia to be unrelated to paclitaxel and related to ipatasertib and concurrent illness.

Event 2: Hyperglycemia

Prior to the event of hyperglycemia, the most recent dose of paclitaxel was administered on Study Day 70 and ipatasertib (300 mg) on Study Day 76.

On Study Day 85, the patient presented for scheduled Cycle 4 Day 1 visit and was reported with non-serious Grade 3 hyperglycemia (no supporting glucose value corresponding to Grade 3 was available). Reportedly, she maintained poor metabolic control due to incorrect eating habits. No additional treatment was reported other than concomitant metformin and glibenclamide (for treatment details please refer to table below), however ipatasertib was not administered, and home glucose monitoring started.

Hyperglycemia treatment details:

Treatment	Indication	Dose (Units: mg)	Route	Frequency	Start day	Stop day
Metformin	Diabetes mellitus	850	PO	BID	Approximately 3 years prior to study entry	43
Glibenclamide	Diabetes mellitus	5	PO	TID	7	Ongoing
Metformin	Diabetes mellitus	850	PO	TID	43	Ongoing

On Study Day 155, the event of hyperglycemia improved to Grade 1. On Study Day 168, the event of Grade 3 hyperglycemia was considered resolved; however, the patient then had a subsequent event of Grade 2 hyperglycemia (non-serious, unrelated) from Study Day 169; ipatasertib remain interrupted. Although glucose levels remained at Grade 2 and levels did not resolve between these events, site considered these separate events, with differing causality noted. Per site feedback: the patient did not have proper diet even when educated about it. The event of hyperglycemia improved and worsened multiple times (reported in table below with most extreme intensity as Grade 3 on Study Day 508); however, remained unresolved at the time of study discontinuation.

Hyperglycemia grade changes:

Study Day	Hyperglycemia grade changes
253	1
281	2
307	1
335	2
365	1
421	2
508	3
537	2
567	3
606	2

Relevant laboratory work-up:

Study Day	Glucose Normal range: 70-100 mg/dL	HbA1c Normal range: 2-6%
Screening	147	7.3
57	272	11.9
62	218	—
70	147	—

Study Day	Glucose Normal range: 70-100 mg/dL	HbA1c Normal range: 2-6%
85	200	—
92	194	—
112	192	9.4
120	174	—
126	172	—
141	171	9.2
148	178	—
155	130	—
169	204	—
176	172	—
181	166	—
197	172	—
204	204	—
211	162	—
225	199	8.3
253	145	—
281	162	—
308	160	8.6
335	202	—
365	152	—
393	201	9.6
421	199	—
449	193	—
477	223	11.2
508	255	—
537	230	—
567	293	13.7
606	193	—

Due to the event of hyperglycemia, there was no change in study treatment with paclitaxel; however, ipatasertib was permanently discontinued with the last dose administered on Study Day 76.

The Investigator considered hyperglycemia to be unrelated to paclitaxel and related to ipatasertib and concurrent illness.

On Study Day 316, during Cycle 12 Day 8 paclitaxel administration, the patient developed Grade 1 extravasation on left arm (non-serious, related to paclitaxel), which was considered to be a local infusion site reaction. The event was also considered to be related to procedure. On Study Day 324, extravasation worsened to Grade 3. She underwent central catheter placement and also received treatment with fluticasone. On Study Day 344, the event of extravasation improved to Grade 1. She further received treatment with pregabalin and serrapeptase.

Event 3: Deep vein thrombosis (Deep vein thrombosis right leg)

Prior to the event of deep vein thrombosis, the most recent dose of paclitaxel was administered on Study Day 435; ipatasertib had already been discontinued.

On Study Day 438, the patient experienced edema and change in color of skin on right leg. She was hospitalized with the suspicion of thrombosis. On Study Day 440, an ECHO doppler was performed and the patient was diagnosed with Grade 3 deep vein thrombosis. On Study Day 442, the patient was discharged from the hospital. On Study Day 448, she was started on treatment with enoxaparin which remained ongoing. Platelet count remained normal throughout the course of the event. On Study Day 516, event of deep vein thrombosis improved to Grade 1. On Study Day 622 (partial day), the event of deep vein thrombosis was considered resolved.

There was no change in study treatment with paclitaxel due to the event of deep vein thrombosis.

The Investigator considered deep vein thrombosis to be unrelated to paclitaxel and ipatasertib and related to disease under study.

Event 4: Extravasation (Left arm extravasation)

Prior to the event of extravasation, the most recent dose of paclitaxel was administered on Study Day 463; ipatasertib had already been discontinued.

On Study Day 476, the patient felt pain and sensation on her left arm, making it difficult for her to perform self-care activities of daily living. The ongoing event of extravasation was assessed as serious Grade 3 and was considered to cause significant disability. She was started on physiotherapy (twice per week) and was asked to put on compression sleeve. Therapy kinesics focused on manual lymphatic lymph drainage and education. The patient evolved favorably to the treatment, and her pain decreased. On Study Day 516, the event of extravasation improved to Grade 2; however, remained unresolved at the time of study discontinuation.

There was no change in study treatment with paclitaxel due to the event of extravasation.

The Investigator considered extravasation to be unrelated to ipatasertib and related to paclitaxel and other unspecified procedure.

On Study Day 658, study treatment with paclitaxel was permanently discontinued as per the physician’s decision (patient stop attending visits, assessment CT scan, bone scan) with study treatment with the last dose administered on Study Day 621. The patient entered into the long term follow-up.

On the same day (Study Day 658), the patient withdrew the consent from the study.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	2	Non-serious	12	60	Related	Unrelated
Incorrect dose administered	1	Non-serious	22	25	Related	Unrelated
Nasopharyngitis	2	Non-serious	34	37	Unrelated	Unrelated
Alopecia	2	Non-serious	35	Resolving	Unrelated	Related
Myalgia	2	Non-serious	62	155	Unrelated	Related
Fatigue	2	Non-serious	138	347	Unrelated	Related
Neuropathy peripheral	2	Non-serious	206	Unresolved	Unrelated	Related
Hypertriglyceridemia	2	Non-serious	477	Unresolved	Unrelated	Unrelated
Hypercholesterolemia	1	Non-serious	477	Unresolved	Unrelated	Unrelated
Diarrhea	1	Non-serious	502	506	Unrelated	Unrelated
Neutropenia	1	Non-serious	508	Unresolved	Unrelated	Related

Study Number/CRTN:	CO40016/310803	Patient number	2033
Demographics:	76-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Categories:	Death Death due to AE, SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.1; Narratives for patients who died due to adverse event(s).

Study Number/CRTN:	CO40016/304879	Patient number	2037
Demographics:	42-year-old Asian female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Hypersensitivity SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER/PR positive, right breast cancer (T2N1MX; histological grade unknown, HER 2-status not assessed), approximately 7 years prior to study entry.

On Study Day −377, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative disease in metastatic tissue. At screening sites of disease involvement included left breast, skin (bilateral breast and chest wall) and lymph node (left breast axillary nodes). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neo-adjuvant	Doxorubicin, cyclophosphamide, and docetaxel	Approximately 7 years prior to study entry	Approximately 7 years prior to study entry
Cancer therapy	Neo-adjuvant	Goserelin	Approximately 7 years prior to study entry	Approximately 7 years prior to study entry
Cancer therapy	Adjuvant	Tamoxifen	Approximately 7 years prior to study entry	Approximately 1 year 4 months prior to study entry
Surgery	Curative	Right simple mastectomy	Approximately 7 years prior to study entry	NA
Cancer therapy	Metastatic	Letrozole and goserelin	−350	−20

No medical or other surgical history was reported. Concurrent condition included back pain.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. On the same day (Study Day 1), she was started on famotidine, chlorphenamine and dexamethasone as prophylaxis for hypersensitivity.

No concomitant medications ongoing at Study Day 1 were reported.

On Study Day 9, the patient experienced Grade 2 rash (non-serious, related to ipatasertib and unrelated to paclitaxel). She received treatment with bepotastine besilate, chlorpheniramine, hydrocortisone, and methylprednisolone. On Study Day 16, the patient received azelastine as prophylaxis for itching. On the same day (Study Day 16), rash resolved.

Event: Hypersensitivity (Hypersensitivity reaction)

On Study Day 17, the patient received ipatasertib (400 mg) as scheduled. On the same day, prior to scheduled Cycle 1 Day 15 dose of paclitaxel, vital signs showed body temperature 36.7°C, pulse rate 69 beats/min, respiratory rate 18 breaths/min and blood pressure 109/58 mmHg. Prophylactic medications included montelukast sodium and hydrocortisone sodium succinate for hypersensitivity and ondansetron for nausea.

At 14:49 hours, the patient started receiving paclitaxel infusion. During the paclitaxel infusion, she experienced Grade 1 myalgia (non-serious, related to paclitaxel), Grade 2 pruritus (non-serious, related to paclitaxel) and Grade 2 rash (non-serious, related). She was diagnosed with Grade 2 hypersensitivity (local infusion site reaction). Subsequently, paclitaxel infusion was interrupted. She received treatment with intravenous chlorphenamine, which resulted in improvement of symptoms. Treatment with bepotastine besilate, hydrocortisone and methylprednisolone was also maintained for rash. At an unspecified time, paclitaxel infusion was restarted slowly (rate not provided); however, it was interrupted again at 16:30 hours due to recurrence of rash and pruritus. Subsequently, the patient was hospitalized for close monitoring and paclitaxel desensitization. On the same day (Study Day 17), the event of myalgia was considered resolved without any treatment. On Study Day 18, she received fexofenadine and ketotifen fumarate for paclitaxel hypersensitivity and she completed remaining dose of paclitaxel. On Study Day 19, the event of rash improved to Grade 1. The same day (Study Day 19), the event of hypersensitivity was considered resolved, and the patient was discharged from the hospital. On Study Day 31, the event of pruritus was considered resolved. On Study Day 38, the patient received prophylactic intravenous dexamethasone for hypersensitivity reaction and the event of rash was considered resolved.

Due to the event of hypersensitivity, study treatment with ipatasertib was interrupted on Study Day 18 and the next dose of ipatasertib- was given on Study Day 21.

The Investigator considered hypersensitivity to be unrelated ipatasertib and related to paclitaxel and other causes (unspecified).

On Study Day 333, a radiographic response assessment showed disease progression.

On Study Day 344, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 325 and ipatasertib on Study Day 331. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Vinorelbine	368	Ongoing

On Study Day 444, the patient died due to disease progression. An autopsy was performed (details not provided)

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nausea	2	Non-serious	3	16	Related	Related
Vomiting	2	Non-serious	3	8	Related	Related
Neutrophil count decreased	2	Non-serious	8	10	Unrelated	Related
Pyrexia	2	Non-serious	9	10	Related	Related
Stomatitis	2	Non-serious	10	16	Related	Related
Pharyngitis	2	Non-serious	10	16	Related	Related
Alopecia	1	Non-serious	15	Unresolved	Related	Related
Neutrophil count decreased	2	Non-serious	17	24	Unrelated	Related
Stomatitis	1	Non-serious	17	126	Related	Related
Pharyngitis	1	Non-serious	17	23	Related	Related
Diarrhea	1	Non-serious	21	24	Related	Unrelated
Neutrophil count decreased	4	Non-serious	31	38	Unrelated	Related
Diarrhea	2	Non-serious	46	293	Related	Unrelated
Headache	1	Non-serious	49	126	Unrelated	Unrelated
Edema	1	Non-serious	58	Unresolved	Unrelated	Related
Rash	1	Non-serious	59	64	Related	Unrelated
Myalgia	1	Non-serious	70	126	Unrelated	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Eczema	1	Non-serious	86	88	Unrelated	Unrelated
Urinary tract infection	2	Non-serious	91	143	Unrelated	Related
Herpes zoster	1	Non-serious	132	289	Unrelated	Unrelated
Post herpetic neuralgia	2	Non-serious	132	161	Unrelated	Unrelated
Nasopharyngitis	1	Non-serious	151	234	Unrelated	Unrelated
Neutrophil count decreased	3	Non-serious	157	199	Unrelated	Related
Headache	1	Non-serious	170	Unresolved	Unrelated	Unrelated
Myalgia	1	Non-serious	179	Unresolved	Unrelated	Related
Neck pain	1	Non-serious	183	227	Unrelated	Unrelated
Dyspepsia	2	Non-serious	193	200	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	227	Unresolved	Unrelated	Related
Upper respiratory tract infection	2	Non-serious	234	294	Unrelated	Unrelated
Skin disorder	1	Non-serious	251	Unresolved	Unrelated	Unrelated
Rash	1	Non-serious	280	Resolving	Related	Unrelated
Hot flush	1	Non-serious	308	343	Unrelated	Unrelated
Upper respiratory tract infection	1	Non-serious	318	338	Unrelated	Unrelated
Vomiting	2	Non-serious	343	Resolving	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304332	Patient number	2039
Demographics:	59-year-old White female		

Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)
Cohort:	Cohort B
Event (PT) Category:	Pathological fracture SAE

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative left breast cancer (T4N1M0), approximately 5 years prior to study entry followed by left simple mastectomy.

On Study Day −559, the patient was diagnosed with metastatic disease (ER/PR status was unknown and HER2 status not assessed in metastatic tissue). At screening sites of disease involvement included lung (bilateral including left S3 and S6), lymph nodes (aortic arch, right root, upper clavicular, bronchopulmonary, mediastinal and sternal), liver (segment VIII), chest (soft tissue), bilateral adrenal gland, bone and mediastinum. The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Tamoxifen	Approximately 5 years prior to study entry	−79
Radiotherapy	Adjuvant	Scar after left mastectomy (dose: 38 cGy), left axillary region (dose: 16 cGy), left upper clavicular and parasternal regions (each at 40 cGy)	Approximately 4 years 11 months prior to study entry	Approximately 4 years 11 months prior to study entry
Radiotherapy	Metastatic	Bone (hip joint at 38 cGy, pelvis at 18 cGy, right chest and vertebrae; each at 20 cGy)	−554	−320
Cancer therapy	Metastatic	Letrozole	−77	−24

No medical or other surgical history was reported. Concurrent conditions included cough, dyspnea, and pathological fracture (left femoral neck).

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

Event: Pathological fracture (Pathological fracture of the middle third bone of left femur)

Prior to the event of pathological fracture, the most recent dose of paclitaxel was administered on Study Day 15 and ipatasertib (400 mg) on Study Day 21.

On Study Day 23, the patient presented with pain in left leg. A CT was performed, and she was diagnosed with Grade 3 pathological fracture of the middle third bone of left femur with slight displacement of debris. The event of pathological fracture led to persistent or significant disability. The patient had no history of osteopenia or osteoporosis.

On Study Day 27, a repeat CT scan was performed, and she was also diagnosed with Grade 2 right femoral neck fracture (non-serious, unrelated). On Study Day 30, she was hospitalized and underwent intramedullary blocked osteosynthesis of the left femur. No treatment medications were reported for pathological and right femoral neck fractures. On Study Day 43, the event of pathological fracture was considered resolved and the patient was discharged from the hospital. The patient received zoledronic acid prophylactically for bone fractures. The event of femoral neck fracture remained unresolved at the time of patient's death.

Due to the event of pathological fracture, Cycle 2 Day 1 of paclitaxel was delayed and ipatasertib was interrupted on Study Day 29. The patient received the next dose of ipatasertib (400 mg) and paclitaxel on Study Day 50.

The Investigator considered pathological fracture to be unrelated to ipatasertib and paclitaxel and related to disease under study.

On Study Day 195, a radiographic response assessment showed disease progression with new lesions in liver (S7). Subsequently, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 190 and ipatasertib on Study Day 196. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Epirubicin	213	280

On Study Day 373, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Arthralgia	2	Non-serious	3	3	Unrelated	Related
Diarrhea	1	Non-serious	3	4	Related	Unrelated
Vomiting	1	Non-serious	4	5	Related	Related
Thrombocytopenia	1	Non-serious	6	15	Unrelated	Related
Nausea	1	Non-serious	6	6	Related	Related
Diarrhea	1	Non-serious	6	21	Related	Unrelated
Alopecia	2	Non-serious	17	171	Unrelated	Related
Anemia	2	Non-serious	50	210	Unrelated	Related
Diarrhea	2	Non-serious	50	70	Related	Unrelated
Pain in extremity	1	Non-serious	50	70	Related	Related
Neutropenia	2	Non-serious	64	76	Unrelated	Related
Arthralgia	2	Non-serious	78	83	Related	Related
Pain in extremity	2	Non-serious	96	Unresolved	Unrelated	Unrelated
Herpes zoster	2	Non-serious	147	181	Unrelated	Unrelated
Bone pain	2	Non-serious	185	185	Unrelated	Related
Cerebral ischemia	2	Non-serious	199	199	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304335	Patient number	2072
Demographics:	53-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Diarrhea AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Paresthesia AE leading to study treatment discontinuation		
Event 3 (PT) Category:	Blood creatine phosphokinase increased SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER/PR positive and HER2 negative, left breast cancer (T1cN1M0; histological grade unknown), approximately 4 years 5 months prior to study entry following left partial mastectomy.

On Study Day −247, the patient was diagnosed with metastatic disease with ER positive/ PR negative and HER2 negative disease in metastatic tissue. At screening sites of disease involvement included liver (segment II and III) and lymph node (left axilla, lumbo-aortic, subpectoral, site of the neck, celiac site, retrocaval site, retrocrural, and inter-aortic). The patient was assessed by the Investigator to have endocrine resistance and visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Docetaxel	Approximately 4 years 4 months prior to study entry	Approximately 3 year 11 months prior to study entry
Cancer therapy	Metastatic	Palbociclib and fulvestrant	−236	−41

No medical or surgical history and concurrent conditions were reported.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib.

No concomitant medications ongoing at Study Day 1 were reported.

Event 1: Diarrhea
Event 1: Paresthesia (Paresthesia lower limbs)
Event 2: Blood creatine phosphokinase increased (creatine kinase increased)

Prior to the event of diarrhea, the most recent dose of ipatasertib was administered on Study Day 1.

On Study Day 1, the patient experienced non-serious Grade 2 diarrhea. She received treatment with loperamide (details in the table below).

On Study Day 9 (Cycle 1 Day 1 dose was interrupted due to Grade 2 diarrhea), the patient received her first study treatment with paclitaxel.

Prior to the event of paresthesia, the most recent dose of paclitaxel was administered on Study Day 175 and ipatasertib (400 mg) on Study Day 181.

On Study Day 182, the patient experienced non-serious Grade 2 paresthesia in lower limbs (initial intensity Grade 1) along with Grade 1 asthenia and Grade 1 nail disorder (non-serious, related to paclitaxel). She received treatment with thioctic acid for paresthesia and tioconazole for nail disorder. On Study Day 189, the event of nail disorder worsened to Grade 2. She further received treatment with hydrogen peroxide and chlortetracycline for nail disorder.

Prior to the event of blood creatine phosphokinase increased, the most recent dose of paclitaxel was administered on Study Day 294 and ipatasertib (400 mg) on Study Day 307.

On Study Day 314, the patient was hospitalized with Grade 2 blood creatine phosphokinase increased (CPK 414 U/L). She was asymptomatic. Electrocardiogram (ECG) was performed (results not provided). No treatment was given for the event. On the same day (Study Day 314), the event of asthenia was considered resolved. No information regarding the patient′s discharge was provided. The events of diarrhea, paresthesia, nail disorder and blood creatine phosphokinase increased remained unresolved at the time of study discontinuation.

Relevant laboratory work-up:

Study Day	**Creatine kinase** Normal range: <170 U/L
Screening	234
314	414
349	489

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	6	PO	1	1
Diarrhea	4	PO	2	3
Diarrhea	2	PO	4	15
Diarrhea	2	PO	4	86
Diarrhea	2	PO	30	50
Diarrhea	2	PO	122	122
Diarrhea	2	PO	124	124
Diarrhea	2	PO	128	128
Diarrhea	2	PO	130	131
Diarrhea	2	PO	134	135
Diarrhea	2	PO	159	162
Diarrhea	2	PO	214	216
Diarrhea	2	PO	221	223
Diarrhea	2	PO	240	240
Diarrhea	2	PO	246	247
Diarrhea	2	PO	258	380
Diarrhea	2	PO	259	259
Diarrhea	2	PO	261	261
Diarrhea	2	PO	267	267
Diarrhea	2	PO	269	269
Diarrhea	2	PO	271	279
Diarrhea	2	PO	271	393
Diarrhea	2	PO	287	295
Diarrhea	2	PO	297	297
Diarrhea	2	PO	299	301
Diarrhea	2	PO	305	307
Diarrhea	2	PO	324	325
Diarrhea	2	PO	328	328
Diarrhea	2	PO	331	331
Diarrhea	2	PO	334	334
Diarrhea	2	PO	336	336
Diarrhea	2	PO	339	341
Diarrhea	2	PO	355	355

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	358	359
Diarrhea	2	PO	362	362
Diarrhea	2	PO	364	365
Diarrhea	2	PO	368	369
Diarrhea	2	PO	377	377
Diarrhea	2	PO	383	383
Diarrhea	2	PO	385	387
Diarrhea	2	PO	391	391
Diarrhea	2	PO	395	395
Diarrhea	2	PO	397	397

Due to the events of diarrhea and paresthesia, there was no change in treatment with ipatasertib; however due to the event of blood creatine phosphokinase increased, dose of ipatasertib was reduced to 300 mg on Study Day 349.

Due to the event of blood creatine phosphokinase increased, study treatment with paclitaxel was interrupted from Cycle 12 and later permanently discontinued due to the events of diarrhea and paresthesia with the last dose administered on Study Day 294.

The Investigator considered diarrhea to be unrelated to paclitaxel and related to ipatasertib.

The Investigator considered paresthesia to be related to paclitaxel and ipatasertib.

The Investigator considered blood creatine phosphokinase increased to be unrelated to paclitaxel and ipatasertib and related to other causes (unknown).

On Study Day 406, a radiographic response assessment showed disease progression.

On Study Day 412, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 397. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine and exemestane	448	Ongoing

On Study Day 1240, the patient was permanently discontinued from the study as per the physician’s decision (LTFU terminated by Sponsor)

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Blood lactate dehydrogenase increased	1	Non-serious	8	99	Unrelated	Unrelated
Leukopenia	2	Non-serious	44	132	Unrelated	Unrelated
Neutropenia	2	Non-serious	44	58	Unrelated	Unrelated
Urinary tract infection	2	Non-serious	59	73	Unrelated	Unrelated
Anemia	1	Non-serious	65	99	Unrelated	Unrelated
Neutropenia	2	Non-serious	71	118	Unrelated	Unrelated
Leukopenia	2	Non-serious	146	153	Unrelated	Unrelated
Pyrexia	1	Non-serious	177	179	Unrelated	Unrelated
Leukopenia	1	Non-serious	230	237	Unrelated	Related

Study Number/CRTN:	CO40016/305250	Patient number	2078
Demographics:	66-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Categories:	Road traffic accident Death due to AE, SAE		
Event 2 (PT) Categories:	General physical health deterioration Death due to AE, SAE		

A narrative for this patient is available under Section 1.1; Narratives for patients who died due to adverse event(s).

Study Number/CRTN:	CO40016/304335	Patient number	2092
Demographics:	37-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Abdominal pain SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative right breast cancer (T4dN2M0), approximately 3 years 3 months prior to study entry.

On Study Day −233, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative disease in metastatic tissue. At screening sites of disease involvement included liver (segment VII and VIII). The patient was assessed by the Investigator to have endocrine resistance disease and visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right radical mastectomy and right axillary lymph node dissection	Approximately 3 years prior to study entry	NA
Cancer therapy	Neo-adjuvant	Epirubicin, cyclophosphamide	Approximately 3 years 3 months prior to study entry	Approximately 3 years 1 month prior to study entry
Cancer therapy	Adjuvant	Paclitaxel	Approximately 2 years 10 months prior to study entry	Approximately 2 years 8 months prior to study entry
Cancer therapy	Adjuvant	Leuprorelin and letrozole	Approximately 2 years 7 months prior to study entry	Approximately 9 months prior to study entry
Radiotherapy	Adjuvant	Breast, chest and lymph nodes (dose unknown)	−961	−926

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Metastatic	Palbociclib, fulvestrant and leuprorelin	Approximately 8 months prior to study entry	Approximately 2 months prior to study entry

No medical or other surgical history was reported. Concurrent condition included back pain.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medication ongoing on Study Day 1 was reported.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of ipatasertib (400 mg) and paclitaxel was administered on Study Day 8.

On Study Day 8, within 24 hours after end of paclitaxel infusion, the patient experienced non-serious Grade 1 (initial intensity) diarrhea (considered to be systemic infusion reaction). She received treatment with loperamide (total daily dose: 4 mg), metoclopramide and hydration. On Study Day 9, dose of loperamide was increased to 6 mg. On Study Day 10, diarrhea worsened to Grade 3 and loperamide dose was further increased to 8 mg and then to 12 mg on Study Day 11. On Study Day 63, the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	8	8
Diarrhea	6	PO	9	9
Diarrhea	8	PO	10	10
Diarrhea	12	PO	11	14
Diarrhea	4	PO	15	16
Diarrhea	8	PO	17	17
Diarrhea	12	PO	18	18
Diarrhea	4	PO	19	24
Diarrhea	2	PO	25	25
Diarrhea	4	PO	31	31
Diarrhea	4	PO	34	34
Diarrhea	6	PO	36	36
Diarrhea	4	PO	37	37

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	6	PO	42	42
Diarrhea	8	PO	43	43
Diarrhea	4	PO	44	44
Diarrhea	4	PO	46	48
Diarrhea	6	PO	49	49

Due to the event of diarrhea, there was no change in treatment with paclitaxel; however, dose of ipatasertib was reduced to 300 mg on Study Day 29.

The Investigator considered diarrhea to be related to paclitaxel and ipatasertib.

Event 2: Abdominal pain

Prior to the event of abdominal pain, the most recent dose of paclitaxel was administered on Study Day 56 and ipatasertib (300 mg) on Study Day 62.

On Study Day 70, the patient experienced Grade 3 abdominal pain. On Study Day 74, she was hospitalized with worsening abdominal pain. It was reported that abdominal pain was suspected to be due to sub-occlusive state. Abdominal CT-scan was performed (results not provided). On Study Day 77, abdominal X-ray was performed (results not provided). She received treatment with ketorolac trometamol.

Due to the event of abdominal pain, study treatment with ipatasertib and paclitaxel was interrupted.

On Study Day 80, a radiographic response assessment showed disease progression with new lesions (bilateral pleural effusion, lung upper, lateral and lower; hepatic and pelvic).

On Study Day 87, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 56 and ipatasertib on Study Day 62. The patient entered into long-term follow-up.

On Study Day 100, the patient was discharged from the hospital. The event of abdominal pain remained unresolved at the patient′s death.

The Investigator considered abdominal pain to be unrelated to paclitaxel and ipatasertib and related to disease under study.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Vinorelbine and capecitabine	88	177

On Study Day 264, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Gamma-glutamyltransferase increased	2	Non-serious	8	Unresolved	Related	Related
Aspartate aminotransferase increased	1	Non-serious	8	Unresolved	Related	Related
Alanine aminotransferase increased	1	Non-serious	8	Unresolved	Related	Related
Leukopenia	1	Non-serious	8	29	Related	Related
Anemia	1	Non-serious	8	Unresolved	Related	Related
Blood alkaline phosphatase increased	1	Non-serious	29	55	Related	Related
Leukopenia	2	Non-serious	43	Unresolved	Related	Related
Neutropenia	2	Non-serious	43	55	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304331	Patient number	2093
Demographics:	55-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Cholecystitis acute SAE		

The patient was randomized on Study Day -1.

The patient was initially diagnosed with right breast cancer (T2N1M0; histological grade unknown and subtype: not otherwise specified), approximately 2 years 9 months prior to study entry following right breast biopsy. Her ER/PR status was unknown and HER2 receptor status was not assessed.

On Study Day −38, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative disease in metastatic tissue. At screening sites of disease involvement included lymph nodes (sub-cardiac, right axillary node with diameter 18 x 17 mm, left axillary node with diameter 15 x 15 mm and subaortic lymph node with diameter 14 x 13 mm), bilateral lungs (multiple lesions of 5, 10, 13 mm in size), bilateral pleural cavity (effusion in the pleural cavity with thickness 18 mm) and bone (lesions in thoracic and lumbar vertebra, pelvic bones, right side ribs, sternum and cranium). The patient was assessed by the Investigator to have visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Neo-adjuvant	Breast (right breast and lymph efflux route; 4000 cGy)	Approximately 2 years 9 months prior to study entry	−979
Surgery	Curative	Right mastectomy and right axillary lymph node dissection	−953	NA
Radiotherapy	Adjuvant	Other (unspecified; 2800 cGy)	−927	−909
Cancer therapy	Adjuvant	Doxorubicin, fluorouracil and cyclophosphamide	−878	−744

The patient′s medical history included chronic cholecystitis. Other surgical history included bilateral pleural cavity aspiration. Concurrent conditions included essential hypertension, myocardial fibrosis, left bundle branch block, mitral valve incompetence, tricuspid valve incompetence, cardiac failure, varicose vein, osteoarthritis (right knee and hip joint), obesity, hepatosplenomegaly, arterial disorder and renal cyst.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included losartan, ivabradine, spironolactone, torasemide and trimetazidine.

On Study Day 204, the patient was noted with Grade 1 hyperbilirubinemia (non-serious, related; bilirubin 25.8 μmol/L). She received treatment with ademetionine and *Cynara cardunculus* extract.

Event: Cholecystitis acute (Acute calculous cholecystitis)

Prior to the event of cholecystitis acute, the most recent dose of paclitaxel was administered on Study Day 204 and ipatasertib (400 mg) on Study Day 207.

On Study Day 208, the patient experienced acute pain in right hypochondrium and increased temperature (up to 37.8°C). She was transferred to the hospital. An abdominal ultrasound was performed, and she was diagnosed with Grade 3 acute calculous cholecystitis, leading to hospitalization. She received treatment with dexketoprofen trometamol, drotaverine, ceftriaxone, calcium chloride/potassium chloride/sodium chloride, diclofenac, metoclopramide, metamizole and enoxaparin. On Study Day 209, laparoscopic cholecystectomy was performed. She also received concomitant therapy with meldonium for cardiotoxicity prevention, calcium chloride/magnesium chloride/potassium chloride/sodium chloride/sodium lactate/sorbitol as detoxification therapy and dressings in surgery department. On Study Day 218, the event of cholecystitis acute was considered resolved. On Study Day 219, she was discharged from the hospital. On Study Day 225, the event of hyperbilirubinemia was considered resolved.

Relevant chemistry work-up:

Study Day	**AST** Normal range: 5-34 U/L	**ALT** Normal range: 4-36 U/L	**Bilirubin** Normal range: 3.4-20.4 μmol/L	**ALP** Normal range: 35-123 U/L
Screening	32	30	24.7	127
204	21	26	25.8	153
225	24	27	11.6	191

Due to the event of cholecystitis acute, study treatment with ipatasertib and paclitaxel was interrupted and later never resumed (details below).

The Investigator considered cholecystitis acute to be related to ipatasertib, paclitaxel and concurrent illness.

On Study Day 224, a radiographic response assessment showed disease progression with multiple new lesions in bilateral brain with left frontal lobe lesion measuring 15 x 13 mm in size.

On Study Day 269, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 204 and ipatasertib on Study Day 208. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Lomustine	239	473
Letrozole	239	504

On Study Day 564, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Alanine aminotransferase increased	1	Non-serious	8	43	Related	Related
Alopecia	2	Non-serious	38	Unresolved	Related	Related
Diarrhea	1	Non-serious	81	83	Related	Related
Diarrhea	1	Non-serious	90	91	Related	Related
Diarrhea	1	Non-serious	94	96	Related	Related
Polyneuropathy	1	Non-serious	103	Unresolved	Related	Related
Diarrhea	1	Non-serious	124	125	Related	Related
Diarrhea	1	Non-serious	144	144	Related	Related
Diarrhea	1	Non-serious	172	172	Related	Related
Diarrhea	1	Non-serious	181	181	Related	Related
Hyperbilirubinemia	1	Non-serious	183	197	Related	Related

Study Number/CRTN:	CO40016/304195	Patient number	2107
Demographics:	70-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Categories:	Cerebrovascular accident SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER negative, PR positive and HER2 negative right breast cancer (T4N1M0; histological grade unknown), approximately 2 years and 10 months prior to study entry.

On Study Day −62, the patient was diagnosed with metastatic disease with ER/PR status unknown and HER2 status not assessed in metastatic tissue. At screening, sites of disease involvement included bone, right lung root, peritoneum (mesentery and omentum), pleural effusion (left hemithorax), liver (segment V) and soft tissue (right chest). The patient was assessed by the Investigator to have visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neo-adjuvant	Cyclophosphamide and Doxorubicin	Approximately 2 years and 10 months prior to study entry	−875
Surgery	Curative	Right radical mastectomy	−862	NA
Radiotherapy	Adjuvant	Parasternal and supraclavicular lymph nodes (40 cGy, 16 fractions)	−825	−801
Cancer therapy	Adjuvant	Tamoxifen	Approximately 2 years and 2 months prior to study entry	Approximately 2 months prior to study entry

No medical or other surgical history or concurrent condition was reported.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included ranitidine, diphenhydramine, ondansetron and dexamethasone.

Event: Cerebrovascular accident

Prior to the event of cerebrovascular accident, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 15.

On Study Day 16, the patient experienced speech disorder. A CT scan showed ischemic cerebral circulation in the left temporal lobe and she was diagnosed with Grade 2 cerebrovascular accident (considered life-threatening and causing persistent or significant disability/incapacity). No treatment was reported for this event. The event of cerebrovascular accident remained unresolved at the time of study discontinuation.

Due to this event, study treatment was permanently discontinued with the last dose of paclitaxel given on Study Day 15 and ipatasertib on Study Day 17.

The Investigator considered cerebrovascular accident, to be unrelated to ipatasertib and paclitaxel and related to disease under study.

Other AE experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel
Diarrhea	1	Non-serious	8	19	Related	Related

Study Number/CRTN:	CO40016/304634	Patient number	2113
Demographics:	68-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Renal impairment SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER positive, PR negative and HER2 negative right breast cancer (T1cN0M0), approximately 7 years prior to study entry followed by lumpectomy and axillary lymph node dissection.

On Study Day −34, the patient was diagnosed with metastatic disease (ER/PR status unknown and HER2 status was not assessed in metastatic tissue). At screening, sites of disease involvement included bone (multiple lesions including soft tissue in the left hip bone), whole left and right lung, lymph node (midline aorto-pulmonary window, left gastric artery and right axillary) and infiltration in the left pleural cavity. The patient was assessed by the Investigator to have visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Adjuvant	Right breast and boost to the area of the tumor bed (dose: 4250 cGy, 17 fractions)	Approximately 7 years prior to study entry	Approximately 7 years prior to study entry
Cancer therapy	Adjuvant	Tamoxifen	Approximately 7 years prior to study entry	Approximately 1 year and 9 months prior to study entry

The patient′s medical history included cough and dyspnea exertional. No other surgical history was reported. Concurrent conditions included asthenia, hypothyroidism and type 2 diabetes mellitus.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included levothyroxine, metformin, and ranitidine.

On Study Day 279, the patient experienced Grade 2 decreased appetite (non-serious, unrelated). She was started on treatment with megestrol.

Event: Renal impairment (acute renal dysfunction)

Prior to the event of renal impairment, the most recent dose of paclitaxel was administered on Study Day 295 and ipatasertib (400 mg) on Study Day 297.

On Study Day 297, the patient was reported with exacerbation of pre-existing asthenia to Grade 3 (non-serious, related to paclitaxel), Grade 1 diarrhea (non-serious, related to ipatasertib), Grade 2 urinary tract infection (diagnostic details not reported) and Grade 1 right upper limb lymphedema (both non-serious, unrelated). On Study Day 298, she presented with ongoing events. A laboratory work-up showed sodium 125 mmol/L (normal range: 132-145 mmol/L), glucose 199 mg/dL (normal range: 70-99 mg/dL), creatinine 2.91 mg/dL (normal range: 0.6-1.1 mg/dL), urea 149 mg/dL (normal range: 10-50 mg/dL) and CRP 209.2 mg/L (normal range: 0.10–5 mg/L). Subsequently, she was hospitalized with Grade 3 renal impairment along with dehydration. An ECG showed left axis deviation. She was started on treatment with metronidazole, lactobacillus acidophilus, insulin aspart, isophane insulin human, metoprolol, electrolytes (unspecified), potassium chloride, furosemide, dexamethasone, ceftriaxone, hydroxyzine and drotaverine. On the same day (Study Day 298), diarrhea was considered resolved. On Study Day 300, chest X-ray showed 2.5 mm lesion in the right lung with little pleural effusion in the left lung. On Study Day 307, chest and pelvis CT was consistent with metastatic changes in bones and she was also suspected with renal cyst. During the hospitalization, she was also reported with renal colic (diagnostic test not reported) with lumbar pain. It was reported that following treatment, her condition improved. On Study Day 308, the event of renal impairment was considered resolved and she was discharged from the hospital on etamsylate, potassium chloride, metoprolol, drotaverine and dexamethasone. On Study Day 321, the event of urinary tract infection was considered resolved. On Study Day 337, the event of asthenia exacerbation resolved. On Study Day 360, the event of decreased appetite was considered resolved. The event of lymphedema remained unresolved at the time of study discontinuation.

Relevant laboratory work-up:

Study Day	Sodium Normal range: 136-146 mmol/L	Potassium Normal range: 3.5-5.1 mmol/L	Glucose Normal range: 70-99 mg/dL	Creatinine Normal range: 0.6-1.1 mg/dL	Urea Normal range: 10-50 mg/dL	CRP Normal range: 0.10-5 mg/L
Screening	140.7	4.57	124	0.73^	31.1#	—
295	135.6	3.94	123	1.09^	47.8#	—
298	125*	—	199**	2.91	149	209.2
299	—	—	—	3.07	164	199.6
301	—	—	—	2.13	86	155
303	—	—	—	1.82	131	—
306	—	—	—	1.31	66	8.5
309	143.4	4.26	74	1.12^	69#	—

*normal range: 132-145 mmol/L, **normal range: 74-106 mg/dL, ^normal range: 0.51-0.95 mg/dL, # normal range: 17-43 mg/dL

There was no change in study treatment due to the event of renal impairment.

The Investigator considered renal impairment, to be unrelated to ipatasertib and paclitaxel and related to other causes (unspecified).

On Study Day 849, study treatment was permanently discontinued due to symptomatic deterioration (deterioration of general health and recurrent anemia) with the last dose of paclitaxel and ipatasertib given on Study Day 828 and Study Day 834, respectively. The patient entered into the long-term follow-up.

Later, on the same day (Study Day 849), the patient withdrew consent from the study.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	8	10	Related	Unrelated
Back pain	2	Non-serious	10	Unresolved	Unrelated	Unrelated
Diarrhea	2	Non-serious	11	11	Related	Unrelated
Diarrhea	1	Non-serious	12	14	Related	Unrelated
Anemia	2	Non-serious	29	380	Unrelated	Related
Diarrhea	2	Non-serious	36	46	Related	Unrelated
Decreased appetite	2	Non-serious	43	107	Unrelated	Related

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	59	59	Related	Unrelated
Diarrhea	1	Non-serious	63	65	Related	Unrelated
Diarrhea	2	Non-serious	66	66	Related	Unrelated
Affect lability	1	Non-serious	71	75	Unrelated	Unrelated
Diarrhea	1	Non-serious	71	74	Related	Unrelated
Alopecia	2	Non-serious	88	Unresolved	Unrelated	Related
Polyneuropathy	2	Non-serious	117	Unresolved	Unrelated	Related
Imperception	1	Non-serious	309	334	Unrelated	Unrelated
Anemia	1	Non-serious	394	408	Unrelated	Related
Diarrhea	2	Non-serious	402	409	Unrelated	Unrelated
Anemia	2	Non-serious	422	Unresolved	Unrelated	Related
Diarrhea	2	Non-serious	460	463	Related	Unrelated
Fluid retention	2	Non-serious	518	646	Unrelated	Related
Headache	1	Non-serious	782	791	Unrelated	Unrelated
Upper respiratory tract infection	2	Non-serious	841	847	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305252	Patient number	2116
Demographics:	78-year-old female (Race unknown)		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		
Event 2 (PT) Categories:	Diarrhea SAE, AESI: Grade $\geq$ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative right breast cancer (T1cNXM0), approximately 15 years prior to study entry.

The patient was diagnosed with locally recurrent disease, approximately 3 years 4 months prior to study entry. She was diagnosed with metastatic disease on Study Day −183 with ER positive/PR unknown and HER2 negative disease in recurrent/metastatic tissue. At screening, sites of disease involvement included left mediastinal lymph nodes and liver (segment V and VI). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right lumpectomy	Approximately 15 years prior to study entry	NA
Radiotherapy	Adjuvant	Right breast (50 cGy, 25 fractions)	Approximately 15 years prior to study entry	Approximately 15 years prior to study entry
Cancer therapy	Adjuvant	Tamoxifen	Approximately 15 years prior to study entry	Approximately 14 years prior to study entry
Cancer therapy	Adjuvant	Exemestane	Approximately 10 years prior to study entry	Approximately 8 years prior to study entry
Cancer therapy	Adjuvant	Exemestane	Approximately 3 years 3 months prior to study entry	−833
Cancer therapy	Metastatic	Exemestane and Everolimus	−833	−175
Cancer therapy	Metastatic	Palbociclib and Fulvestrant	−175	−83

The patient′s medical history included left breast cancer, contusion, skin abrasion and wrist fracture. Other surgical history included hysterectomy. Concurrent conditions included dyslipidemia, dyspnea, and restless legs syndrome.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

On Study Day 1, the patient started receiving loperamide (total daily dose: 4 mg, PO) for diarrhea.

Prior to onset of Grade 3 diarrhea (serious), the patient experienced multiple non-serious events of diarrhea detailed in the table below. Treatment included loperamide (details reported in table below), diosmectite and racecadotril.

Most extreme Grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Action taken (Ipatasertib)	Action taken (Paclitaxel)
2	10	15	Related	Unrelated	Drug interrupted on Study Day 12 and resumed on Study Day 29 at a reduced dose of 300 mg	Cycle 1 Day 15 dose interrupted
2	35	52	Related	Unrelated	Drug interrupted on Study Day 37 and resumed on Study Day 44 at a reduced dose of 200 mg	Dose reduced to 65 mg/m^2 on Study Day 37
1	54	57	Related	Unrelated	None	None
1	68	69	Related	Unrelated	None	None
1	72	73	Related	Unrelated	None	None
2	75	79	Related	Unrelated	None	None

Event 1: Neuropathy peripheral (neuropathy)
Event 2: Diarrhea

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel was administered on Study Day 71 and ipatasertib (200 mg) on Study Day 77.

On Study Day 85, the patient was diagnosed with Grade 2 (initial intensity) peripheral neuropathy (presenting symptoms not reported).

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 85 and ipatasertib (200 mg) on Study Day 95.

On Study Day 96, the patient experienced Grade 2 (initial intensity) diarrhea, Grade 3 nausea (non-serious, unrelated) and vomiting. On Study Day 97, she experienced Grade 2 asthenia (non-serious, related). She received loperamide (for detailed dosing please refer to table below) for diarrhea and treatment with diosmectite was maintained. No treatment was administered for asthenia. On Study Day 98, diarrhea improved to Grade 1. On Study Day 99, the patient experienced Grade 2 mucosal inflammation (non-serious, related). She further received metoclopramide for nausea and amphotericin B, fluconazole, and pantoprazole for mucosal inflammation.

On Study Day 103, the patient presented with Grade 4 vomiting (non-serious, unrelated), nausea, dehydration, alteration of general state and worsening of diarrhea to Grade 3. She was reported to have lost 2 kg weight in four days. Subsequently, she was hospitalized. Stool culture was performed (results not provided). It was reported that nausea and vomiting were probably due to mucosal inflammation. On the same day (Study Day 103), the event of peripheral neuropathy was reported to have worsened to Grade 3. No treatment was given for neuropathy peripheral. She received dietary advice for diarrhea. On Study Day 111, the events of nausea

and vomiting were considered resolved and she was discharged from the hospital. On Study Day 113, the event of asthenia and diarrhea resolved. On Study Day 141, the event of mucosal inflammation was considered resolved. The event of peripheral neuropathy remained unresolved at the time of study discontinuation.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	1	2
Diarrhea	4	PO	7	7
Diarrhea	6	PO	8	8
Diarrhea	8	PO	9	12
Diarrhea	4	PO	13	14
Diarrhea	4	PO	16	18
Diarrhea	2	PO	19	21
Diarrhea	4	PO	30	30
Diarrhea	2	PO	33	34
Diarrhea	6	PO	35	35
Diarrhea	4	PO	36	36
Diarrhea	2	PO	44	44
Diarrhea	4	PO	45	46
Diarrhea	6	PO	47	48
Diarrhea	8	PO	49	49
Diarrhea	6	PO	50	51
Diarrhea	4	PO	52	53
Diarrhea	10	PO	52	52
Diarrhea	4	PO	53	53
Diarrhea	6	PO	54	56
Diarrhea	2	PO	57	57
Diarrhea	2	PO	59	60
Diarrhea	2	PO	63	64
Diarrhea	2	PO	67	67
Diarrhea	4	PO	68	68
Diarrhea	4	PO	68	68
Diarrhea	2	PO	69	69
Diarrhea	4	PO	72	72
Diarrhea	2	PO	73	76
Diarrhea	4	PO	77	77
Diarrhea	4	PO	79	79
Diarrhea	2	PO	88	88
Diarrhea	4	PO	91	92
Diarrhea	2	PO	93	94
Diarrhea	4	PO	95	95
Diarrhea	2	PO	96	96
Diarrhea	4	PO	97	97
Diarrhea	2	PO	98	98
Diarrhea	6	PO	99	99
Diarrhea	8	PO	100	100
Diarrhea	4	PO	101	101

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	6	PO	102	102
Diarrhea	2	PO	123	123
Diarrhea	2	PO	125	125
Diarrhea	4	PO	127	129
Diarrhea	2	PO	130	130
Diarrhea	2	PO	132	134
Diarrhea	2	PO	136	136
Diarrhea	2	PO	139	139
Diarrhea	2	PO	143	143
Diarrhea	2	PO	145	146
Diarrhea	4	PO	147	147
Diarrhea	2	PO	148	148
Diarrhea	2	PO	150	150
Diarrhea	2	PO	154	155
Diarrhea	4	PO	157	158
Diarrhea	2	PO	158	158
Diarrhea	2	PO	160	163
Diarrhea	2	PO	160	160
Diarrhea	2	PO	168	169

Due to the event of diarrhea, there was no change in study treatment with paclitaxel; however, ipatasertib was interrupted on Study Day 97 and was resumed on Study Day 99 and then again interrupted on Study Day 102 and resumed on Study Day 113.

Due to the event of peripheral neuropathy, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 99.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

The Investigator considered peripheral neuropathy to be related to paclitaxel and unrelated to ipatasertib.

The patient experienced another episode of Grade 1 diarrhea (non-serious, related to ipatasertib) from Study Day 117 to Study Day 118. Treatment with diosmectite was maintained for diarrhea.

On Study Day 169, a radiographic response assessment showed disease progression with new lesions in liver. Subsequently, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 162. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatment	Start Day	Stop Day
Cyclophosphamide and epirubicin	176	288
Cyclophosphamide	330	434
Eribulin	470	673
Capecitabine	694	992
Etoposide	1028	–

On Study Day 1156, the patient was permanently discontinued from the study as LTFU was terminated by Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	1	Non-serious	1	3	Unrelated	Unrelated
Vomiting	1	Non-serious	10	15	Related	Unrelated
Nausea	1	Non-serious	10	28	Related	Unrelated
Anemia	2	Non-serious	27	61	Unrelated	Related
Neuropathy peripheral	2	Non-serious	34	43	Unrelated	Related
Mucosal inflammation	2	Non-serious	35	43	Related	Related
Nausea	1	Non-serious	35	43	Unrelated	Unrelated
Gastroesophageal reflux disease	1	Non-serious	35	43	Unrelated	Unrelated
Escherichia urinary tract infection	2	Non-serious	111	141	Unrelated	Unrelated
Asthenia	1	Non-serious	113	120	Unrelated	Related

Study Number/CRTN:	CO40016/304640	Patient number	2120
Demographics:	63-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Categories:	Pneumonitis SAE, Grade ≥ 3 pneumonitis		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER/PR positive and HER 2 negative right breast cancer (TXNXMX, histological grade unknown), approximately 10 years prior to study entry followed by right partial mastectomy.

The patient was diagnosed with locally recurrent disease approximately 3 years prior to study entry followed by right simple mastectomy. On Study Day −656, she was diagnosed with metastatic disease with ER/PR positive and HER 2-negative disease in recurrent/metastatic tissue. At screening, sites of disease involvement included in midline liver (segment 7), soft tissue (porto-cavalis) and bone (multiple sclerotic lesions). The patient was assessed by the Investigator to have visceral crisis.

No other past cancer treatments were reported.

No medical history was reported. Surgical history included cholecystectomy. Concurrent conditions included asthma, hypothyroidism, hyperuricemia, hypertonia, type 2 diabetes mellitus, dyspepsia, and back pain.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included cetirizine, perindopril, levothyroxine, allopurinol, metformin, budesonide/formoterol, fecosterol /ipratropium, methylprednisolone, ivabradine, metamizole, paracetamol/tramadol, ascorbic acid/beta carotene/biotin/calcium/carbohydrates(unspecified)chloride/choline/chromium;copper/cyanocobalamin/fats (unspecified) fiber dietary/fluorine/folic acid/ iodine/ iron/ magnesium/ manganese/ molybdenum/ nicotinamide/pantothenic acid/ phosphorus/potassium/ proteins (unspecified)/pyridoxine/ riboflavin/selenium/ sodium/thiamine/vitamin D (unspecified);vitamin E (unspecified)/zinc, aceclofenac and anastrozole.

Event: Pneumonitis

Prior to the event of pneumonitis, the most recent dose of paclitaxel was administered on Study Day 158 and ipatasertib (300 mg) on Study Day 164.

On Study Day 167, the patient experienced fever (maximum body temperature: 40.1°C) and cough. On Study Day 172, X-ray was performed, and she was hospitalized with the diagnosis of Grade 2 pneumonitis. On the same day (Study Day 172), an ultrasound was also performed (results not reported). She received treatment with moxifloxacin and ongoing methylprednisolone. On Study Day 177, a repeat X-ray was performed (results not reported). On the following day (Study Day 178), the event of pneumonitis was considered resolved and she was discharged from the hospital.

Due to the event of pneumonitis, study treatment with ipatasertib was interrupted on Study Day 172 and was resumed at a reduced dose of 200 mg on Study Day 193; dose of paclitaxel was also reduced to 65 mg/m^2 from Study Day 193.

The Investigator considered pneumonitis to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 484, study treatment was permanently discontinued due to symptomatic deterioration (peripheral neuropathy) with the last dose of paclitaxel and ipatasertib given on Study Day 437 and Study Day 476, respectively. The patient entered into long-term follow-up.

On Study Day 725, the patient died due to disease progression. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	2	Non-serious	4	14	Related	Unrelated
Epistaxis	1	Non-serious	5	64	Unrelated	Unrelated
Flushing	1	Non-serious	8	9	Unrelated	Related
Cystitis	2	Non-serious	8	23	Unrelated	Related
Neutropenia	2	Non-serious	15	29	Unrelated	Related
Alopecia	1	Non-serious	23	26	Unrelated	Related
Aphthous ulcer	2	Non-serious	23	27	Unrelated	Related
Flushing	1	Non-serious	58	60	Unrelated	Related
Arthralgia	1	Non-serious	59	63	Unrelated	Related
Swelling face	1	Non-serious	78	221	Unrelated	Unrelated
Joint swelling	1	Non-serious	78	221	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Paresthesia	2	Non-serious	78	221	Unrelated	Unrelated
Dermatitis	1	Non-serious	78	81	Unrelated	Related
Rash	2	Non-serious	89	148	Related	Unrelated
Herpes virus infection	1	Non-serious	120	124	Unrelated	Unrelated
Catarrh	2	Non-serious	131	146	Unrelated	Unrelated
Urinary tract infection	1	Non-serious	157	164	Unrelated	Unrelated
Cystitis	2	Non-serious	262	270	Unrelated	Unrelated
Cystitis	1	Non-serious	306	311	Unrelated	Unrelated
Pollakiuria	1	Non-serious	319	339	Unrelated	Unrelated
Rhinorrhea	1	Non-serious	319	324	Unrelated	Unrelated
Abdominal pain upper	2	Non-serious	332	334	Unrelated	Unrelated
Diarrhea	2	Non-serious	336	339	Related	Unrelated
Sinusitis	2	Non-serious	353	356	Unrelated	Related
Pain	2	Non-serious	363	364	Unrelated	Unrelated
Cystitis	2	Non-serious	383	386	Unrelated	Related
Paronychia	2	Non-serious	383	409	Related	Unrelated
Back pain	1	Non-serious	385	409	Unrelated	Unrelated
Oral herpes	2	Non-serious	389	396	Unrelated	Unrelated
Abdominal pain upper	2	Non-serious	423	454	Unrelated	Unrelated
Neuropathy peripheral	3	Non-serious	450	Unresolved	Unrelated	Related

Study Number/CRTN:	CO40016/305633	Patient number	2122
Demographics:	70-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Categories:	COVID-19 SAE, AE leading to study treatment discontinuation, COVID-19 SAE		

The patient was randomized on Study Day 1.

The patient was diagnosed with lobular, poorly differentiated, ER/PR positive and HER2-negative metastatic left breast cancer (T3N1M1) on Study Day −35.

At screening, sites of disease involvement included mediastinum (left pre-tracheal nodule), ascites, bone (left scapula, ilium, and sacrum), and lymph node (left axillary),.

No past cancer treatment was reported.

No medical/surgical history was reported. The patient′s concurrent conditions included ascites, peripheral venous disease, anemia, and hypoalbuminemia.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included spironolactone.

Event: COVID-19 (COVID-19 infection)

Prior to the event of COVID-19, the most recent dose of paclitaxel was administered on Study Day 668 and ipatasertib (400 mg) on Study Day 671.

On Study Day 672, the presented to the emergency room due to fever (body temperature not reported). She denied any respiratory difficulty and had adequate oxygen saturation. A relevant diagnostic included hematology, urinalysis, and hepatic examination (results not reported) were performed. A rapid antigen test was positive for COVID-19. Subsequently, she was hospitalized with the diagnosis of mild Grade 1 COVID-19. She received treatment with ketoprofen, dimenhydrinate, ceftriaxone, azithromycin, and enoxaparin. On Study Day 673, a chest X-ray was normal. On Study Day 674, the event of COVID-19 was considered resolved and she was discharged from the hospital.

Due to this event, study treatment with paclitaxel and ipatasertib was permanently discontinued with the last dose given on Study Day 668 and Study Day 671, respectively. The patient entered into long-term follow-up.

The Investigator considered COVID-19, to be unrelated to ipatasertib, paclitaxel and related other cause.

On Study Day 721, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	1	23	Related	Unrelated
Anemia	3	Non-serious	1	Unresolved	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nausea	1	Non-serious	11	11	Unrelated	Related
Conjunctivitis	1	Non-serious	13	14	Unrelated	Unrelated
Abdominal pain upper	1	Non-serious	18	19	Unrelated	Related
Diarrhea	1	Non-serious	34	51	Related	Unrelated
Diarrhea	1	Non-serious	57	68	Related	Unrelated
Neuropathy peripheral	1	Non-serious	101	Unresolved	Unrelated	Related
Chronic gastritis	1	Non-serious	123	169	Unrelated	Unrelated
Abdominal pain	1	Non-serious	189	189	Unrelated	Unrelated
Diarrhea	1	Non-serious	202	202	Related	Unrelated
Diarrhea	1	Non-serious	229	238	Related	Unrelated
Urinary tract infection	1	Non-serious	239	245	Related	Related
Diarrhea	1	Non-serious	270	670	Related	Related
Leukopenia	1	Non-serious	533	617	Related	Related
Ascites	3	Non-serious	579	590	Related	Related
Ascites	3	Non-serious	623	627	Related	Related
Blood creatinine increased	2	Non-serious	681	Unresolved	Related	Related
Blood creatinine increased	1	Non-serious	687	Unresolved	Related	Related
Venous thrombosis limb	2	Non-serious	694	Unresolved	Related	Related
Abdominal pain	2	Non-serious	699	Unresolved	Related	Related

Study Number/CRTN:	CO40016/304640	Patient number	2135
Demographics:	59-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Rash AESI: Grade $\geq$ 3 rash		
Event 2 (PT) Category:	Dyspnea SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative left breast cancer (T3N1aM0), approximately 3 years 6 months prior to study entry.

On Study Day −38, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative in metastatic tissue. At screening, sites of disease involvement included liver (left S7 and 8) and bone (right scapula). The patient was assessed by the Investigator to have visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neo-adjuvant	Cyclophosphamide, goserelin and letrozole	Approximately 3 years 5 months prior to study entry	Approximately 3 years prior to study entry
Surgery	Curative	Left simple mastectomy	Approximately 3 years prior to study entry	NA
Radiotherapy	Adjuvant	Breast (left chest wall) (5000 cGy)	Approximately 2 years 10 months prior to study entry	Approximately 2 years 9 months prior to study entry

No medical history or concurrent conditions were reported. Surgical history included tonsillectomy, abdominoplasty, and caesarean section.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

Event 1: Rash
Event 2: Dyspnea

Prior to the events of rash and dyspnea, the most recent dose of paclitaxel was administered on Study Day 209 and ipatasertib (400 mg) on Study Day 215.

On Study Day 223, the patient came to hospital for Cycle 9 Day 1 visit. She was noted with Grade 3 rash and received treatment with methylprednisolone and famotidine.

On Study Day 226, she presented to the hospital with heavy breathing and was hospitalized with Grade 3 dyspnea. Chest X-ray showed hydrothorax. A chest drain was placed, and 3000 mL of fluid was removed. No medications were given for dyspnea.

On Study Day 230, CT-scan showed disease progression with new lesions in mediastinal lymph nodes. On Study Day 231, the event of dyspnea resolved. On the same day (Study Day 231), chest drain was removed, and the patient was discharged from the hospital in a good condition. On Study Day 237, the event of rash resolved.

Due to the event of dyspnea, there was no change in study treatment; however, due to the event of rash, study treatment with ipatasertib and paclitaxel was interrupted.

On Study Day 237, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 209 and ipatasertib on Study Day 215. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine	234	Ongoing

The Investigator considered rash to be unrelated to paclitaxel and related to ipatasertib and disease under study.

The Investigator considered dyspnea to be unrelated to ipatasertib and paclitaxel and related to disease under study.

On Study Day 938, the patient died due to disease progression. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	1	97	Unrelated	Related
Musculoskeletal chest pain	1	Non-serious	1	41	Unrelated	Related
Muscle spasms	1	Non-serious	4	8	Related	Unrelated
Epistaxis	1	Non-serious	13	55	Related	Unrelated
Chest pain	1	Non-serious	29	29	Unrelated	Unrelated
Dyspnea	1	Non-serious	29	29	Unrelated	Unrelated
Dizziness	1	Non-serious	29	30	Unrelated	Unrelated
Dyspnea	2	Non-serious	48	64	Unrelated	Unrelated
Generalized edema	2	Non-serious	48	65	Unrelated	Unrelated
Flatulence	2	Non-serious	48	Unresolved	Unrelated	Unrelated
Face edema	1	Non-serious	55	65	Unrelated	Unrelated
Nausea	1	Non-serious	55	97	Unrelated	Unrelated
Vomiting	1	Non-serious	57	57	Unrelated	Unrelated
Hypertonia	2	Non-serious	65	Unresolved	Unrelated	Unrelated
Arthralgia	1	Non-serious	83	Unresolved	Unrelated	Unrelated
Diabetes mellitus	1	Non-serious	90	Unresolved	Unrelated	Unrelated
Muscle spasms	2	Non-serious	90	Unresolved	Unrelated	Unrelated
Musculoskeletal chest pain	1	Non-serious	131	Unresolved	Unrelated	Related
Laryngitis	2	Non-serious	153	Unresolved	Unrelated	Unrelated
Blood cholesterol increased	1	Non-serious	167	Unresolved	Related	Unrelated
Eczema	2	Non-serious	183	Unresolved	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304786	Patient number	2136

Demographics:	48-year-old White male
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)
Cohort:	Cohort B
Event 1 (PT) Category:	Anxiety SAE
Event 2 (PT) Category:	Alanine aminotransferase increased AESI: Grade $\geq$ 3 hepatotoxicity
Event 3 (PT) Category:	Nausea AE leading to study treatment discontinuation
Event 4 (PT) Category:	Asthenia AE leading to study treatment discontinuation
Event 5 (PT) Category:	Fatigue AE leading to study treatment discontinuation

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated ER/PR positive and HER2 negative, left breast cancer (T2N1M0), approximately 4 years prior to study entry.

On Study Day −172, the patient was diagnosed with metastatic disease (ER and PR status was unknown and HER2 status was not assessed in metastatic tissue). At screening, sites of disease involvement included lung (bilateral including left hilar and right subpleural regions). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left modified radical mastectomy	Approximately 3 years 10 months prior to study entry	NA
Cancer therapy	Adjuvant	Doxorubicin and Cyclophosphamide	Approximately 3 years 8 months prior to study entry	Approximately 3 years 6 months prior to study entry
Cancer therapy	Adjuvant	Docetaxel	Approximately 3 years 5 months prior to study entry	Approximately 3 years 3 months prior to study entry
Cancer therapy	Adjuvant	Tamoxifen	Approximately 3 years 2 months prior to study entry	−172
Radiotherapy	Adjuvant	Left breast (5040 cGy)	Approximately 3 years prior to study entry	Approximately 2 years 11 months prior to study entry

The patient′s medical history included thrombosis. Other surgical history included tonsillectomy and cholecystectomy. Concurrent conditions included spondylitis, anxiety, and bipolar disorder.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received his first study treatment with ipatasertib and paclitaxel. On the same day (Study Day 1), he experienced Grade 1 nausea and Grade 1 asthenia (both non-serious, related).

Concomitant medications ongoing at Study Day 1 included alprazolam and valproate.

Event 1: Anxiety (Anxiety crisis)

Prior to the event of anxiety, the most recent dose of paclitaxel was administered on Study Day 7 and ipatasertib (400 mg) on Study Day 10.

On Study Day 11, the patient presented with Grade 3 chest and lumbar pain (unrelated to ipatasertib), Grade 1 sweating (unrelated to ipatasertib), Grade 1 diarrhea (non-serious, related to ipatasertib), Grade 1 vomiting (non-serious, related to paclitaxel), Grade 1 nausea and worsening of his concurrent condition of anxiety to Grade 3, resulting in hospitalization. On the same day, the event of asthenia (non-serious, causality re-assessed as related to paclitaxel and unrelated to ipatasertib) worsened to Grade 2. Laboratory work-up was negative for creatine kinase (CK) and creatine kinase-MB (CKMB) enzymes (values not provided). Hematology and chemistry tests were considered not clinically significant. ECG and chest X-ray were normal. He received treatment with isosorbide dinitrate and treatment with alprazolam was maintained for

anxiety. Treatment for diarrhea included loperamide. No treatment was given for nausea, vomiting and asthenia. The event of vomiting was considered resolved on the same day (Study Day 11). On Study Day 12, the events of anxiety and asthenia were considered resolved and the patient was discharged from the hospital. On Study Day 13, diarrhea resolved.

Due to the event of anxiety, there was no change in study treatment with paclitaxel; however, ipatasertib was interrupted on Study Day 12 and was resumed on Study Day 13.

The Investigator considered anxiety to be unrelated to ipatasertib and paclitaxel and related to concurrent illness.

Event 2: Alanine aminotransferase increased (ALT increased)

Prior to the event of alanine aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 7 and ipatasertib (400 mg) on Study Day 13.

On Study Day 14, at scheduled Cycle 1 Day 15 visit, a laboratory work-up showed AST level at 76.4 U/L and ALT level at 228.8 U/L and the patient was noted with non-serious Grade 3 alanine aminotransferase increased. No treatment was administered for the event. On Study Day 27, the event of alanine aminotransferase increased was considered resolved.

Relevant laboratory work-up:

Study Day	**AST** Normal range: 8-33 U/L	**ALT** Normal range: 4-36 U/L	**Bilirubin** Normal range: 2-21 μmol/L	**ALP** Normal range: 40-129 U/L
Screening	23	19.1	0.78	51
1	22	19.1	0.49	49
7	40	39	1.13	45
14	76.4	228.8	0.52	105
28	21.7	37.6	0.39	90

There was no change in study treatment due to the event of alanine aminotransferase increased.

The Investigator considered alanine aminotransferase increased to be unrelated to ipatasertib and paclitaxel and related to other causes (unspecified).

On Study Day 30, the patient experienced Grade 1 fatigue (non-serious, related to paclitaxel). On Study Day 43, fatigue worsened to Grade 2 and on Study Day 53 improved to Grade 1.

On Study Day 148, the event of nausea was considered resolved. On Study Day 158, the patient experienced another event of Grade 1 nausea (non-serious, related).

Event 3: Nausea

Event 4: Asthenia
Event 5: Fatigue

Prior to the event of nausea, the most recent dose of paclitaxel was administered on Study Day 237 and ipatasertib (300 mg) on Study Day 239.

On Study Day 240, the ongoing event of nausea worsened to Grade 2 (non-serious). The same day, the patient also experienced Grade 2 constipation (non-serious, unrelated) and Grade 2 muscle spasms (non-serious, related). The patient received treatment with metoclopramide and ondansetron for nausea, unspecified medication for muscle spasms and no treatment was given for constipation.

Prior to the events of asthenia and fatigue, the most recent dose of paclitaxel was administered on Study Day 237 and ipatasertib (300 mg) was administered on Study Day 244.

On Study Day 250, the ongoing events of asthenia and fatigue worsened to Grade 2 (both non-serious). No treatment was administered for the events of fatigue and asthenia. On Study Day 256, the event of muscle spasms was considered resolved. On Study Day 308, the events of nausea, constipation, asthenia, and fatigue were considered resolved.

Due to the events of nausea, asthenia and fatigue, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 280.

The Investigator considered nausea and asthenia to be related to ipatasertib and paclitaxel.

The Investigator considered fatigue to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 389, a radiographic response assessment showed disease progression.

On Study Day 393, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 384. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Anastrozole and goserelin	393	Ongoing

On Study Day 1120, the patient was permanently discontinued from the study as the LTFU was terminated by Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Arthralgia	1	Non-serious	1	9	Related	Related
Myalgia	1	Non-serious	1	11	Related	Related
Muscle spasms	1	Non-serious	1	14	Related	Related
Constipation	1	Non-serious	1	10	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	18	Resolving	Unrelated	Related
Arthralgia	1	Non-serious	30	42	Unrelated	Related
Diarrhea	2	Non-serious	38	40	Unrelated	Related
Hyperglycemia	2	Non-serious	42	43	Related	Unrelated
Arthralgia	2	Non-serious	43	52	Unrelated	Related
Hyperglycemia	2	Non-serious	44	280	Related	Unrelated
Insomnia	1	Non-serious	44	52	Unrelated	Related
Pneumonia	2	Non-serious	52	62	Unrelated	Unrelated
Arthralgia	1	Non-serious	53	56	Unrelated	Related
Arthralgia	2	Non-serious	57	68	Unrelated	Related
Insomnia	1	Non-serious	63	79	Unrelated	Unrelated
Diarrhea	1	Non-serious	67	78	Related	Unrelated
Arthralgia	1	Non-serious	69	148	Unrelated	Related
Diarrhea	1	Non-serious	85	88	Related	Unrelated
Diarrhea	2	Non-serious	89	90	Unrelated	Unrelated
Diarrhea	1	Non-serious	91	91	Related	Unrelated
Diarrhea	2	Non-serious	92	96	Related	Unrelated
Diarrhea	1	Non-serious	97	148	Related	Unrelated
Upper respiratory tract infection	2	Non-serious	135	142	Unrelated	Unrelated
Erectile dysfunction	2	Non-serious	148	308	Unrelated	Unrelated
Paronychia	1	Non-serious	189	194	Related	Related
Paresthesia oral	1	Non-serious	197	308	Unrelated	Related
Upper respiratory tract infection	2	Non-serious	226	233	Unrelated	Unrelated
Phlebitis	2	Non-serious	237	243	Unrelated	Related
Phlebitis	1	Non-serious	244	258	Unrelated	Related
Gastritis	1	Non-serious	270	Resolving	Related	Unrelated
Chest pain	1	Non-serious	281	282	Unrelated	Unrelated
Neck pain	1	Non-serious	281	282	Unrelated	Unrelated

Study Number/CRTN:	CO40016/307260	Patient number	2142
Demographics:	74-year-old Asian female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Decreased appetite SAE		
Event 3 (PT) Category:	Erythema multiforme SAE		
Event 4 (PT) Category:	Decreased appetite SAE		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, poorly differentiated, left breast cancer (T1N0M0) on an unknown day. Her ER and PR status was unknown and HER2 status was not assessed.

The patient was diagnosed with metastatic disease approximately 4 years prior to study entry following left breast biopsy with ER/PR positive and HER2 negative disease in metastatic tissue. At screening sites of disease involvement included left breast skin, bone (multiple metastatic lesions) and lymph nodes (mediastinal and right axillary; multiple lesions). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left partial mastectomy	Approximately 27 years prior to study entry	—
Cancer therapy	Adjuvant	Tamoxifen	Approximately 27 years prior to study entry	Approximately 26 years prior to study entry
Cancer therapy	Metastatic	Letrozole and palbociclib	Approximately 4 years prior to study entry	−652

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Metastatic	Fulvestrant and unspecified PI3KA-specific inhibitor	−596	−372
Cancer therapy	Metastatic	Exemestane and unspecified HDAC inhibitor	−337	−250
Cancer therapy	Metastatic	Toremifene and everolimus	−231	−56

No medical or surgical history was reported. The patient′s concurrent conditions included hypertension, dry eye, constipation, blood cholesterol increased, dry skin, glaucoma, and hyperglycemia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. She also received prophylactic loperamide (2 mg) for diarrhea on Study Days 1-2.

Concomitant medications ongoing at Study Day 1 included amlodipine, telmisartan, rosuvastatin, magnesium oxide, denosumab, hyaluronate sodium and brinzolamide/timolol.

Event 1: Peripheral sensory neuropathy

Prior to the event of peripheral sensory neuropathy, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 7.

On Study Day 8, the patient was diagnosed with Grade 1 peripheral sensory neuropathy (signs and symptoms not reported). No treatment was reported for the event. On Study Day 163, the event of peripheral sensory neuropathy worsened to Grade 2, which remained unresolved at the time of patient's death (see narrative below).

Due to the event of peripheral sensory neuropathy, there was no change in treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 154.

The Investigator considered peripheral sensory neuropathy to be related to paclitaxel and unrelated to ipatasertib.

Event 2: Decreased appetite (Anorexia)

Prior to the event of decreased appetite, the most recent dose of paclitaxel was administered on Study Day 14 and ipatasertib (400 mg) on Study Day 15.

On Study Day 10, the patient experienced Grade 1 (initial intensity) diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide (1 mg). On Study Day 14, she experienced Grade 1 vomiting (non-serious, related to ipatasertib), and the following day (Study Day 15), diarrhea worsened to Grade 2 (6 times/day). Loperamide dose was increased to 3 mg. On the same day (Study Day 15), she experienced Grade 1 nausea (non-serious, related to ipatasertib) and Grade 2 (initial intensity) decreased appetite. No treatment was reported for nausea and vomiting. On Study Day 16, the event of diarrhea improved to Grade 1 (1-2 times/day). Details regarding loperamide treatment are reported in the table below.

On Study Day 21, the patient presented with ongoing vomiting and diarrhea (2 times a day) and worsening of decreased appetite to Grade 3 resulting in hospitalization. Reportedly, worsening of decreased appetite was secondary to diarrhea and vomiting. She received treatment with calcium chloride dihydrate/potassium chloride/sodium acetate trihydrate/sodium chloride and amino acids unspecified/electrolytes unspecified/glucose/thiamine for decreased appetite and diarrhea. The same day (Study Day 21), vomiting resolved. She further received carbohydrates unspecified/potassium chloride/sodium chloride/sodium lactate, calcium chloride dihydrate/glucose/potassium chloride/sodium acetate, potassium chloride and lactomin. On Study Day 22, the event of decreased appetite improved to Grade 2 after ipatasertib interruption. On Study Day 23, nausea resolved, and the event of decreased appetite further improved to Grade 1. The patient was advised to not to have dinner. On Study Day 27, she resumed eating; however, diarrhea occurred again. Therefore, meal prohibition was advised. Further treatment for decreased appetite included cyanocobalamin/pyridoxine/thiamine and ascorbic acid. On Study Day 34, the patient started to have porridge and vegetable diet. The following day, fluid replacement was decreased. On Study Day 37, the event of diarrhea resolved. On Study Day 38, the patient did not require IV drip infusion. On Study Day 40, her food intake was increased. On Study Day 44, the event of decreased appetite resolved, and the patient was discharged from the hospital.

Due to the event of decreased appetite, study treatment with paclitaxel was interrupted on Cycle 2 Day 1 and Cycle 2 Day 8 and ipatasertib was interrupted from Study Days 22-48. Reportedly, as light headedness due to dehydration occurs in patients on anti-hypertensive medications, therefore, amlodipine and telmisartan were also interrupted.

The next dose of paclitaxel and ipatasertib (at reduced dose of 300 mg) was administered on Study Day 41 and Study Day 49, respectively. On Study Day 45, treatment with amlodipine and telmisartan were resumed.

Loperamide details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	1	PO	10	10
Diarrhea	2	PO	12	12
Diarrhea	1	PO	14	14
Diarrhea	3	PO	15	15

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	16	18
Diarrhea	3	PO	19	19
Diarrhea	6	PO	20	20
Diarrhea	2	PO	21	21
Diarrhea	5	PO	22	23
Diarrhea	2	PO	24	25
Diarrhea	2	PO	28	28
Diarrhea	4	PO	29	31
Diarrhea	2	PO	32	32

The Investigator considered decreased appetite to be unrelated to paclitaxel and related to ipatasertib.

Event 3: Erythema multiforme

Prior to the event of erythema multiforme, the most recent dose of paclitaxel was administered on Study Day 14 and ipatasertib (400 mg) on Study Day 21.

On Study Day 24, whilst hospitalized for the event of decreased appetite, the patient experienced pruritus (site unspecified) for which she received topical petrolatum. On Study Day 26, she experienced rash maculopapular on face, oral mucosa and whole body along with wheals, and was diagnosed with Grade 2 erythema multiforme (confirmed by clinical course of the event). She was started on fexofenadine. On the following day (Study Day 27), the event of erythema multiforme worsened to Grade 3, leading to prolongation of hospitalization. She was started on betamethasone, heparinoid and hydrocortisone. On an unspecified day, she also developed epidermolysis on palmar and dorsum of the hand. On Study Day 28, erythema gradually spread to buccal cavity and itching worsened. Skin biopsy was performed. Treatment with olopatadine was started and the event of erythema multiforme improved to Grade 2 on Study Day 29.

On Study Day 30, the patient had strong itching in buccal cavity and erythema on trunks and limbs became discolored. She also had scaling of skin. On Study Day 34, itching improved, erythema on face almost disappeared and was residual on forearms. However, scaling on whole body persisted. She further received treatment with white soft paraffin. On Study Day 37, the event of erythema multiforme further improved to Grade 1 with almost disappearance of erythema on whole body; however, the patient had scaling persisting on forearms and trunk. Epidermolysis on palmar and dorsum of the hand progressed. On Study Day 43, erythema disappeared and the same day, biopsy results showed interface dermatitis. The following day (Study Day 44), the patient was discharged from the hospital. She further received treatment with diphenhydramine. On Study Day 49, she again experienced pruritus. She received fexofenadine. On Study Day 63, the event of erythema multiforme was considered resolved.

Relevant laboratory work-up:

Study Day	**Eosinophils** Normal range: 0-10%
Screening	2.7
21	0.9*
23	1.3*
27	3.9*
29	3.6
34	11.1*
37	9.4
41	10.8
49	14.3
63	5.3

*Normal range not reported

Due to the event of erythema multiforme, there was no change in treatment with paclitaxel; however, ipatasertib remained interrupted and the next dose was given on Study Day 49 at a reduced dose of 300 mg.

The Investigator considered erythema multiforme to be unrelated to paclitaxel and related to ipatasertib.

Event 4: Decreased appetite (Anorexia; second episode)

Prior to the event of decreased appetite, the most recent dose of paclitaxel was administered on Study Day 154 and ipatasertib (300 mg) on Study Day 155.

On Study Day 145, the patient experienced Grade 1 diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide (details reported in table below). On Study Day 155, she experienced Grade 2 (initial intensity) decreased appetite. The following day (Study Day 156), she experienced Grade 1 nausea (non-serious, related to ipatasertib) for which she received treatment with metoclopramide. On Study Day 163, the event of decreased appetite worsened to Grade 3, leading to hospitalization. Laboratory work-up showed Grade 2 hypokalemia (potassium value not reported, non-serious, related to ipatasertib). She received treatment with potassium chloride of hypokalemia, sodium chloride and unspecified amino acids/electrolytes unspecified/glucose/thiamine of dehydration. The following day (Study Day 164), blood work-up showed CRP 2.64 and WBC count 3500 (units and normal range not reported). On Study Day 165, vitals showed body temperature 37.7°C. On Study Day 166, fever persisted, and the patient also experienced muddy stool. She was suspected with enteritis. She was put on fasting and treatment with unspecified amino acids/electrolytes unspecified/glucose/thiamine for dehydration was continued. On

Study Day 167, repeat laboratory work-up showed CRP 1.03 and WBC count 6700 (units and normal range not reported). On Study Day 168, the event of hypokalemia resolved. On Study Day 170, the patient passed normal stool, and she started having meals. On Study Day 174, after resumption of diet, she did not have any abdominal symptom or fever. Fluid replacement was stopped. On Study Day 183, the event of decreased appetite was considered resolved and the patient was discharged from the hospital. On Study Day 189, the events of diarrhea and nausea were considered resolved.

Loperamide details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	145	145
Diarrhea	4	PO	146	146
Diarrhea	2	PO	148	150
Diarrhea	4	PO	151	152
Diarrhea	6	PO	153	153
Diarrhea	2	PO	154	154
Diarrhea	6	PO	155	155
Diarrhea	4	PO	156	156
Diarrhea	2	PO	157	158
Diarrhea	4	PO	159	159
Diarrhea	2	PO	160	160
Diarrhea	6	PO	161	162
Diarrhea	4	PO	163	165
Diarrhea	2	PO	168	168

Due to the event of decreased appetite, paclitaxel was interrupted after Study Day 154 and never resumed; ipatasertib was interrupted from Study Day 169 and resumed at a reduced dose of 200 mg on Study Day 203.

The Investigator considered decreased appetite to be related to ipatasertib and paclitaxel.

On Study Day 254, radiographic response assessment showed disease progression with new lesions in lateral segment of liver.

On Study Day 268, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 245. The patient entered into the long-term follow-up

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Anastrozole and abemaciclib	294	384

On Study Day 457, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	1	Non-serious	1	7	Unrelated	Related
Stomatitis	1	Non-serious	8	49	Related	Related
Alopecia	2	Non-serious	13	Unresolved	Unrelated	Related
Edema peripheral	1	Non-serious	29	37	Unrelated	Unrelated
Hyponatremia	3	Non-serious	29	34	Related	Unrelated
Hyperglycemia	2	Non-serious	29	394	Related	Unrelated
Treatment non-compliance	N/A	Non-serious	49	N/A	N/A	N/A
Constipation	1	Non-serious	50	63	Unrelated	Unrelated
Hemorrhoids	2	Non-serious	50	Unresolved	Unrelated	Unrelated
Treatment non-compliance	N/A	Non-serious	51	N/A	N/A	N/A
Pruritus	1	Non-serious	77	Unresolved	Unrelated	Related
Accidental overdose	N/A	Non-serious	78	N/A	N/A	N/A
Wrong schedule	N/A	Non-serious	84	N/A	N/A	N/A
Diarrhea	1	Non-serious	97	98	Related	Unrelated
Diarrhea	1	Non-serious	99	109	Related	Unrelated
Diarrhea	1	Non-serious	124	137	Related	Unrelated
Nausea	1	Non-serious	129	130	Related	Unrelated
Edema peripheral	1	Non-serious	196	Unresolved	Unrelated	Unrelated
Malaise	1	Non-serious	250	Unresolved	Related	Unrelated
C-reactive protein increased	3	Non-serious	252	357	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304880	Patient number	2148
Demographics:	74-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Categories:	Diarrhea SAE, AESI: Grade $\geq$ 3 diarrhea		
Event 2 (PT) Category:	Febrile neutropenia AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER positive, PR negative and HER2 negative left breast cancer (T2N0M0; histological grade unknown), approximately 6 years prior to study entry.

On Study Day −673, the patient was diagnosed with locally recurrent disease. On Study Day −278, she was diagnosed with metastatic disease with ER positive, PR negative and HER2 negative disease in recurrent/metastatic tissue. At screening, sites of disease involvement included lung (multiple lesions in bilateral lower lobes). The patient was assessed by the Investigator to have endocrine resistant.

Past cancer treatments are listed in the table below:

Type of treatment	**Therapy Setting/Intent**	**Treatments details**	**Start Day**	**Stop Day**
Surgery	Curative	Left simple mastectomy	Approximately 6 years prior to study entry	NA
Cancer therapy	Adjuvant	Cyclophosphamide, methotrexate, and fluorouracil	Approximately 6 years prior to study entry	Approximately 5 years prior to study entry
Cancer therapy	Adjuvant	Letrozole	Approximately 5 years prior to study entry	−668
Surgery	Palliative	Left breast ″other″ surgery	−644	NA

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Tamoxifen	−617	−183
Radiotherapy	Adjuvant	Left supraclavicular lymph nodes and left chest wall (dose: 5000 cGy, 25 fractions)	−607	−573
Radiotherapy	Adjuvant	Breast (tumor bed) (dose: 1000 cGy, 5 fractions)	−572	−566
Surgery	Palliative	Left axillary lymph node dissection	−226	NA
Cancer therapy	Metastatic	Exemestane	−183	−91

No medical or surgical history was reported. Concurrent conditions included hypertension, dyslipidemia, angina pectoris and hypothyroidism.

At screening, the patient's ECOG Performance Status was 0.

Relevant laboratory work-up included:

Study Day	WBC count Normal range: 4-10 × $10^3/\mu L$	Neutrophil count Normal range: 2-7 × $10^3/\mu L$	Body temperature °C
Screening	4.69	2.49	36.5

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. She also received prophylactic loperamide (4 mg, PO) for diarrhea on Study Days 1-8.

Concomitant medications ongoing at Study Day 1 included atorvastatin, levothyroxine, acetylsalicylic acid, trimetazidine and rebamipide.

Event 1: Diarrhea
Event 2: Febrile neutropenia

Prior to the event of diarrhea, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 7.

On Study Day 8, the patient experienced Grade 1 (initial intensity) diarrhea. On Study Day 21, she experienced Grade 1 nausea (non-serious, related to paclitaxel). She received treatment with loperamide (treatment details in the table below), tiropramide, diosmectite for diarrhea, metoclopramide, and cimetidine for nausea.

On Study Day 34, the patient experienced Grade 1 dizziness (non-serious, related to paclitaxel). No treatment was given for dizziness. On Study Day 121, the event of dizziness was considered resolved. On Study Day 160, the events of diarrhea and nausea worsened to Grade 2. She further received treatment with octreotide for nausea. On Study Day 166, the events of diarrhea and nausea improved to Grade 1.

Prior to the event of febrile neutropenia that led to ipatasertib and paclitaxel discontinuation, the patient was noted with multiple non-serious events of neutrophil count decreased detailed in the table below:

Most extreme grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Action taken (Ipatasertib)	Action taken (Paclitaxel)
4	14	21	Unrelated	Related	Treatment interrupted from Study Day 14 to Study Day 21 and the next dose was given on Study Day 22 at reduced dose of 300 mg	Cycle 1 Day 15 dose was interrupted, and the next dose given at a reduced dose of 65 mg/m^2 on Study Day 22
3	43	50	Unrelated	Related	Treatment interrupted from Study Day 43 to Study Day 49 and the next dose was given on Study Day 50 at reduced dose of 200 mg	Cycle 2 Day 15 dose was interrupted, and the next dose was given on Study Day 50 (Cycle 2 Day 22)

Most extreme grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Action taken (Ipatasertib)	Action taken (Paclitaxel)
3	57	70	Unrelated	Related	None	Cycle 3 administration was delayed, and one dose was interrupted; the next dose was given on Study Day 71
2	86	92	Unrelated	Related	None	Cycle 4 administration was delayed by a week and the next dose was given on Study Day 92

Prior to the event of febrile neutropenia, the most recent dose of paclitaxel was administered on Study Day 183 and ipatasertib (200 mg) on Study Day 186.

On Study Day 187, the event of diarrhea worsened to Grade 3, leading to hospitalization. On the same day (Study Day 187), the patient experienced fever (body temperature not reported). Her fecal occult blood test was negative. She was diagnosed with non-serious Grade 3 febrile neutropenia (neutrophil count not reported). She further received treatment with sodium chloride, paracetamol, glucose, piperacillin, metoclopramide and filgrastim for febrile neutropenia alanine/arginine/calcium chloride/glucose/glycine/histidine/isoleucine/leucine/lysine/magnesium chloride/methionine/phenylalanine/potassium phosphate dibasic/proline/serine/sodium acetate/sodium chloride/threonine/tryptophan, L-tyrosine/valine, amino acids/electrolytes (unspecified)/glucose, chromic chloride/copper sulfate/manganese sulfate/zinc sulfate, vitamins (unspecified), potassium chloride, paracetamol/tramadol and cefpodoxime for diarrhea. On Study Day 189, the event of febrile neutropenia (body temperature and neutrophil count not reported) was considered resolved. On Study Day 190, she was discharged from the hospital. On Study Day 191, the event of diarrhea improved to Grade 1. On Study Day 220, the events of diarrhea and nausea were considered resolved.

Loperamide details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	6	PO	9	9
Diarrhea	8	PO	10	10
Diarrhea	4	PO	11	11
Diarrhea	8	PO	12	13
Diarrhea	4	PO	14	15
Diarrhea	12	PO	16	16
Diarrhea	8	PO	17	17
Diarrhea	4	PO	18	28
Diarrhea	10	PO	30	30
Diarrhea	2	PO	31	33
Diarrhea	2	PO	35	35
Diarrhea	4	PO	36	36
Diarrhea	6	PO	37	37
Diarrhea	8	PO	38	38
Diarrhea	12	PO	40	41
Diarrhea	8	PO	42	42
Diarrhea	4	PO	43	43
Diarrhea	6	PO	45	45
Diarrhea	4	PO	46	47
Diarrhea	2	PO	50	50
Diarrhea	4	PO	55	55
Diarrhea	4	PO	57	59
Diarrhea	4	PO	61	61
Diarrhea	4	PO	63	63
Diarrhea	4	PO	69	69
Diarrhea	4	PO	72	72
Diarrhea	8	PO	74	75
Diarrhea	8	PO	77	77
Diarrhea	4	PO	78	78
Diarrhea	8	PO	80	81
Diarrhea	8	PO	84	84
Diarrhea	4	PO	85	85
Diarrhea	4	PO	87	87
Diarrhea	4	PO	92	92

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	8	PO	95	95
Diarrhea	2	PO	96	96
Diarrhea	12	PO	97	97
Diarrhea	4	PO	98	98
Diarrhea	4	PO	105	105
Diarrhea	4	PO	113	113
Diarrhea	2	PO	117	118
Diarrhea	4	PO	121	121
Diarrhea	2	PO	124	124
Diarrhea	2	PO	126	126
Diarrhea	4	PO	127	127
Diarrhea	4	PO	129	129
Diarrhea	8	PO	130	130
Diarrhea	4	PO	131	131
Diarrhea	12	PO	132	132
Diarrhea	2	PO	133	133
Diarrhea	4	PO	141	141
Diarrhea	2	PO	148	148
Diarrhea	4	PO	150	151
Diarrhea	8	PO	154	154
Diarrhea	4	PO	157	157
Diarrhea	8	PO	158	163
Diarrhea	2	PO	164	164
Diarrhea	8	PO	165	165
Diarrhea	2	PO	166	166
Diarrhea	2	PO	175	175
Diarrhea	4	PO	176	176
Diarrhea	4	PO	180	181
Diarrhea	6	PO	182	182
Diarrhea	14	PO	183	183
Diarrhea	20	PO	184	184
Diarrhea	8	PO	185	185
Diarrhea	12	PO	186	186

Due to the event of diarrhea, study treatment with paclitaxel was interrupted; ipatasertib was interrupted on Study Day 187 and the next dose was given on Study Day 191.

Due to the event of febrile neutropenia, study treatment with paclitaxel and ipatasertib was permanently discontinued with the last dose of paclitaxel and ipatasertib given on Study Day 183 and Study Day 192, respectively. The patient entered into long-term follow-up.

The Investigator considered diarrhea, to be unrelated to paclitaxel and related to ipatasertib.

The Investigator considered febrile neutropenia, to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 335, radiographic response assessment showed disease progression with new lesions in left pelvis (sternum, T spine and left pelvic bone).

The patient received follow-up anti-cancer therapies as listed in table below:

Treatment	Start Day	Stop Day
Giredestrant	364	419
Doxorubicin and cyclophosphamide	435	Ongoing

On Study Day 745, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Myalgia	1	Non-serious	2	8	Unrelated	Related
Stomatitis	1	Non-serious	25	121	Unrelated	Related
Vomiting	1	Non-serious	34	34	Unrelated	Related
Vomiting	3	Non-serious	48	48	Related	Related
Arthralgia	1	Non-serious	53	Unresolved	Unrelated	Related
Dyspnea	1	Non-serious	53	Unresolved	Unrelated	Unrelated
Breast pain	1	Non-serious	64	Unresolved	Unrelated	Unrelated
Lymphoedema	1	Non-serious	113	Unresolved	Unrelated	Unrelated
Dyspepsia	1	Non-serious	113	Unresolved	Unrelated	Unrelated
Peripheral sensory neuropathy	1	Non-serious	121	Unresolved	Unrelated	Related
Insomnia	1	Non-serious	141	148	Unrelated	Unrelated
Vomiting	2	Non-serious	160	162	Related	Related
Edema	1	Non-serious	165	220	Unrelated	Related

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nail discoloration	1	Non-serious	183	Unresolved	Unrelated	Related

Study Number/CRTN:	CO40016/305626	Patient number	2149
Demographics:	76-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Abdominal hernia SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with moderately differentiated, ER/PR positive and HER2 negative right breast cancer (T2N2M0; histological subtype: not otherwise specified), approximately 3 years prior to study entry.

On Study Day –61, the patient was diagnosed with metastatic disease, with ER/PR positive and HER2 negative in metastatic tissue. At screening, sites of disease involvement included left axillary adenopathy, left group IV ganglion conglomerate, left retro-pectoral adenopathy, left group VB adenopathy, left group III adenopathy, left pre-vascular adenopathy and adenopathy in mammary chain. The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right radical mastectomy	Approximately 2 years 10 months prior to study entry	NA
Cancer therapy	Adjuvant	Doxorubicin and cyclophosphamide	Approximately 2 years 8 months prior to study entry	–909
Cancer therapy	Adjuvant	Paclitaxel	–880	–775
Cancer therapy	Adjuvant	Anastrozole	–766	–37

The patient's medical history included inguinal and umbilical hernia. Surgical history included surgery for inguinal and umbilical hernia. Concurrent condition included cataract.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

Event: Abdominal hernia

Prior to the event of abdominal hernia, the most recent dose of paclitaxel was administered on Study Day 177 and ipatasertib (200 mg) on Study Day 181.

On Study Day 184, the patient presented with abdominal pain. She was hospitalized with Grade 3 abdominal hernia (diagnostic details not available). An unspecified procedure/surgery was performed. She received treatment with paracetamol and simethicone. On Study Day 185, the event of abdominal hernia was considered resolved and she was discharged from the hospital.

Due to the event of abdominal hernia, study treatment with ipatasertib and paclitaxel was interrupted.

On Study Day 208, a radiographic response assessment showed disease progression.

On Study Day 253, study treatment was permanently discontinued as patient withdrew consent from the study. The patient received the last dose of paclitaxel on Study Day 177 and ipatasertib on Study Day 181.

The Investigator considered abdominal hernia to be unrelated to ipatasertib and paclitaxel and related to other causes (unspecified).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Vomiting	1	Non-serious	4	4	Related	Unrelated
Diarrhea	2	Non-serious	5	7	Related	Unrelated
Diarrhea	2	Non-serious	40	45	Related	Unrelated
Asthenia	2	Non-serious	57	62	Unrelated	Related
Urinary tract infection	2	Non-serious	97	111	Unrelated	Unrelated
Paresthesia	1	Non-serious	116	253	Unrelated	Related
Skin lesion	1	Non-serious	163	253	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Skin lesion	1	Non-serious	177	253	Unrelated	Unrelated
Skin lesion	1	Non-serious	177	253	Unrelated	Unrelated
Skin lesion	1	Non-serious	177	253	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304622	Patient number	2150
Demographics:	76-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Categories:	Neutropenia SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated ER/PR positive, bilateral breast cancer (T2N1miM0; HER2 receptor status not assessed), approximately 7 years prior to study entry followed by left partial mastectomy.

The patient was diagnosed with locally recurrent disease approximately 3 years 6 months prior to study entry. She was diagnosed with metastatic disease on Study Day −151 with ER positive/PR negative and HER2 negative disease in recurrent/metastatic tissue. At screening, sites of disease involvement included liver (bilateral lobe). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Doxorubicin and cyclophosphamide	Approximately 7 years prior to study entry	Approximately 6 years prior to study entry
Cancer therapy	Adjuvant	Letrozole	Approximately 6 years prior to study entry	Approximately 3 years 5 months prior to study entry
Radiotherapy	Adjuvant	Left breast (5000 cGy and 6600 cGy, 33 fractions)	Approximately 6 years prior to study entry	Approximately 6 years prior to study entry

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Tamoxifen	Approximately 3 years 4 months prior to study entry	Approximately 3 years 2 months prior to study entry
Cancer therapy	Adjuvant	Anastrozole	Approximately 3 years 2 months prior to study entry	Approximately 2 years 8 months prior to study entry
Cancer therapy	Adjuvant	Letrozole	Approximately 2 years 8 months prior to study entry	Approximately 1 years 6 months prior to study entry
Cancer therapy	Adjuvant	Fulvestrant	−509	−56

No medical or other surgical history was reported. Concurrent conditions included hypertension, urinary incontinence, carpal tunnel syndrome, diabetes mellitus, hyperuricemia and hyperlipidemia.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included hydrochlorothiazide/telmisartan, acetylsalicylic acid/glycine, solifenacin, pregabalin, metformin, allopurinol, rosuvastatin and bisoprolol.

On Study Day 1, the patient experienced Grade 2 diarrhea (non-serious, related to ipatasertib). She received loperamide (total daily dose: 4 mg).

Event: Neutropenia

Prior to the event of neutropenia, the most recent dose of paclitaxel was administered on Study Day 7 and ipatasertib (400 mg) on Study Day 8.

On Study Day 7, a laboratory work-up showed creatinine 196 μmol/L (normal range: 49-90 μmol/L), urea 19.7 mmol/L (normal range: 2.8-8.1 mmol/L) and the patient was diagnosed with Grade 2 renal failure (non-serious, related to ipatasertib). She received hydration with sodium chloride.

On Study Day 9, the patient experienced fever (body temperature 38.3°C), shivering, and confusion. Her ECOG Performance Status was 3 and blood pressure was 130/85 mmHg. On physical examination, she was conscious and anicteric without cyanosis. She had overall deterioration and could not walk properly. Brain CT-scan done due to suspected stroke or metastasis was normal. A laboratory work-up was performed, and she was noted with Grade 2 hyperglycemia (non-serious, related to ipatasertib; glucose 13.2 mmol/L; normal range: 3-5.6 mmol/L) and Grade 3 neutropenia (neutrophil count 0.91 x 10^9/L, normal range not provided). The patient had high creatine kinase, myoglobin and troponin value (values not provided). Subsequently, she was hospitalized. She received treatment with tiapride,

piperacillin/tazobactam sodium, spironolactone, and furosemide for neutropenia. No treatment was given for hyperglycemia. On Study Day 10, she was diagnosed with Grade 3 rhabdomyolysis (non-serious, related to ipatasertib). On Study Day 11, the event of rhabdomyolysis was considered resolved without any treatment. On Study Day 12, the event of neutropenia was considered resolved. On Study Day 31, the patient was discharged from the hospital. It was reported that she was feeling much better after one week and could walk with help. The events of diarrhea, renal failure and hyperglycemia were reported as unresolved at the time of patient's death (see narrative below).

Relevant laboratory work-up:

Study Day	**WBC count** Normal range: 4-10 $\times$ 10^9/L	**Neutrophil count** Normal range: 2-7 $\times$ 10^9/L
Screening	4.92	2.66
7	4.13	1.87
9	—	0.91*

*Normal range not reported

Due to the event of neutropenia, study treatment with ipatasertib and paclitaxel was permanently discontinued on Study Day 46 with the last dose of paclitaxel administered on Study Day 7 and ipatasertib on Study Day 8. The patient entered into long-term follow-up.

The Investigator considered neutropenia to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 57, a radiographic response assessment showed disease progression with new lesions in liver (bilateral lobes).

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	**Start Day**	**Stop Day**
Paclitaxel and carboplatin	77	84

On Study Day 89, the patient died due to disease progression. An autopsy was not performed.

No other AEs were experienced by the patient during the study.

Study Number/CRTN:	CO40016/304332	Patient number	2160
Demographics:	51-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Erysipelas SAE		

The patient was randomized on Study Day 1.

The patient was diagnosed with lobular, moderately differentiated, ER positive, PR negative and HER2 negative metastatic left breast cancer (T4N3M1) on Study Day −27.

At screening, sites of disease involvement included bone (L2 and TH7), bilateral breast, liver (segment VI), lymph node (multiple lesions in left axillary, left upper sub clavicular and clavicular, left interpectoral, mediastinal, and right axillary) and right pleural effusion. The patient was assessed by the Investigator to have visceral crisis.

No past cancer treatment was reported.

The patient′s medical history included Hodgkin′s disease, skin cancer (left breast) and pneumonia. Surgical history included lung lobectomy (left lower lobe), Caesarean section and female sterilization. Concurrent conditions included osteochondrosis, scoliosis, uterine leiomyoma, autonomic nervous system imbalance and anemia.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included bisoprolol.

Event: Erysipelas (erysipelas of right leg)

Prior to the event of erysipelas, the most recent dose of paclitaxel was administered on Study Day 401 and ipatasertib (400 mg) on Study Day 403.

On Study Day 404, the patient experienced fever (body temperature 39°C), fatigue and was noted with erythematosus rash and edema in right leg. Subsequently, she was diagnosed with Grade 3 erysipelas. On Study Day 407, she was hospitalized. Her WBC count was 12.5×10^9/L (normal range not reported). She received treatment with ceftriaxone, clemastine, diosmin/hesperidin, phospholipids, probiotics (unspecified) and diclofenac for the event of

erysipelas. On Study Day 419, the event of erysipelas was considered resolved and she was discharged from the hospital.

Relevant laboratory work-up:

Study Day	**WBC count** Normal range: 4-9 × 10^9/L	**Neutrophil count** Normal range: 1.96-6.93 × 10^9/L	**Body temperature** °C
Screening	7.46	5.55	36.5
404	—	—	39
407	12.5*	—	—

*Normal range not reported

Due to the event of erysipelas, there was no change in study treatment with ipatasertib, however, Cycle 15 Day 15 of paclitaxel was not administered, and the next dose was given on Study Day 422.

The Investigator considered erysipelas, to be unrelated to ipatasertib and paclitaxel and related to concurrent illness (unspecified).

On Study Day 555, a radiographic response assessment showed disease progression with new lesions in right breast, right pleura, and bones. Subsequently, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose administered on Study Day 512 and Study Day 534 respectively. The patient entered into long-term follow-up.

On Study Day 582, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious / non-serious**	**Onset Day**	**Resolution Day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Diarrhea	1	Non-serious	12	14	Related	Unrelated
Alopecia	2	Non-serious	16	259	Unrelated	Related
Food poisoning	3	Non-serious	22	24	Unrelated	Unrelated
Weight decreased	2	Non-serious	29	Unresolved	Unrelated	Unrelated
Edema peripheral	1	Non-serious	38	Unresolved	Unrelated	Related

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Blood glucose increased	1	Non-serious	184	198	Unrelated	Unrelated
Blood glucose increased	1	Non-serious	240	254	Related	Unrelated
Fatigue	2	Non-serious	419	426	Unrelated	Unrelated
Back pain	2	Non-serious	531	536	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305637	Patient number	2161
Demographics:	59-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Neutropenia SAE		
Event 2 (PT) Categories:	Febrile neutropenia Death due to AE, SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.1; Narratives for patients who died due to adverse event(s).

Study Number/CRTN:	CO40016/306642	Patient number	2192
Demographics:	53-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Categories:	Febrile neutropenia SAE, AE leading to study treatment discontinuation		
Additional category:	Death due to disease progression		

A narrative for this patient is available under Section 1.2; Narratives for patients who died due to disease progression.

Study Number/CRTN:	CO40016/318833	Patient number	2199
Demographics:	59-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Chronic gastritis SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER positive/PR positive and HER 2-receptor equivocal right breast cancer (T1aN0M0) approximately 6 years prior to study entry, followed by right simple mastectomy.

On Study Day −979, the patient was diagnosed with locally recurrent disease. On Study Day −8, she was diagnosed with metastatic disease with ER /PR positive and HER 2-receptor negative disease in metastatic/recurrent tissue. At screening, sites of disease involvement included lateral aspect of right breast and lung (right upper lobe, lateral segment of right middle lobe, multiple pulmonary nodules in bilateral lung parenchyma and mediastinum lymphadenopathy in right hilar area). The patient was assessed by the Investigator to have endocrine resistant disease and visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Tamoxifen	Approximately 6 years prior to study entry	Approximately 4 years prior to study entry
Radiotherapy	Adjuvant	Right breast (dose unknown, 45 fractions)	Approximately 6 years prior to study entry	Approximately 6 years prior to study entry

The patient′s medical history included ovarian neoplasm. Surgical history included hysterosalpingogram-oophorectomy. Concurrent conditions included diabetes mellitus and breast injury.

At screening, the patient′s ECOG performance status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing on Study Day 1 were reported. The patient received prophylactic loperamide (4 mg, PO) for diarrhea on Study Days 1-4.

On Study Day 5, the patient experienced Grade 2 diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide. On Study Day 6, the event of diarrhea improved to Grade 1. On Study Day 15, the event of diarrhea was considered resolved.

Event 1: Diarrhea
Event 2: Chronic gastritis

Prior to the event of diarrhea, the most recent dose paclitaxel was administered on Study Day 36 and ipatasertib (400 mg) on Study Day 41.

On Study Day 42, the patient experienced non-serious Grade 1 diarrhea (initial intensity). She received treatment with loperamide (details in the table below). On Study Day 99, she experienced Grade 2 weight decreased (non-serious, unrelated).

Prior to the event of chronic gastritis, the most recent dose of paclitaxel was administered on Study Day 99 and ipatasertib (400 mg) on Study Day 104.

On Study Day 105, the patient complained of post-prandial epigastric pain since 3 weeks and she was diagnosed with Grade 2 (initial intensity) chronic gastritis. On Study Day 112, esophagogastroduodenoscopy showed reflux esophagitis (Grade IA), shallow gastric ulcers, gastric polyps and duodenitis. On Study Day 115, the event of chronic gastritis improved to Grade 1. On Study Day 135, the event of diarrhea worsened to Grade 3. On the following day (Study Day 136), the event of diarrhea improved to Grade 2

On Study Day 137, in the morning, she experienced severe epigastralgia, abdominal bloating and acid regurgitation after eating. On the same day (Study Day 137), at 18:00 hours, the event of chronic gastritis worsened to Grade 3, leading to hospitalization. Upon hospitalization, her vitals showed body temperature 37°C, heart rate 92 beats/minute, respiratory rate 22 breaths/min and blood pressure 128/80 mmHg. Upon physical examination, her abdominal was soft with dull and colic epigastric pain migrating to right upper quadrant which improved on bending knee. On auscultation, hypoactive bowel sound were heard. Laboratory work-up showed elevated ALP 118 U/L (normal range: 35-104 U/L), GGT 146 U/L (normal range not reported) and Grade 2 hypokalemia (potassium 3.0 mmol/L, normal range: 3.7-5.3 mmol/L; non-serious, unrelated). Her amylase/lipase and troponin I were within normal range. Standing abdominal X-ray showed no free air; however, some air-fluid level at intestine. She received treatment with potassium chloride, pantoprazole and morphine. Reportedly, due to suspected ileus, probably due to ongoing loperamide, frequency of loperamide was changed to as needed, which the patient did not use as the event of diarrhea improved Grade 1 on Study Day 138. She was started on clear liquid diet and then advanced to bland diet. Her abdominal pain was improving, and she could tolerate food. She further received treatment with lansoprazole, aluminum hydroxide/calcium carbonate/magnesium carbonate/oxetacaine. On Study Day 139,

upper abdominal ultrasound showed multiple new liver lesions (up to 1.6 cm), with no evidence of cholecystitis or common bile duct (CBD) dilatation. On Study Day 140, the event of hypokalemia (potassium value not reported) was considered resolved. On Study Day 141, the event of chronic gastritis improved to Grade 2. On the same day (Study Day 141), the event of diarrhea was considered resolved and she was discharged from the hospital.

On Study Day 143, the patient again experienced Grade 1 diarrhea (non-serious, related to ipatasertib) and Grade 1 lipase increased (non-serious, unrelated; lipase: 86 U/L, normal range: 13-60 U/L). She further received treatment with metoclopramide, *Bifidobacterium bifidum/Enterococcus faecalis/Lactobacillus acidophilus* and pancreatin for chronic gastritis. On Study Day 227, the event of lipase increased was considered resolved (lipase: 36 U/L). On Study Day 255, the event of chronic gastritis was considered resolved. The events of weight decreased, and Grade 1 diarrhea remained unresolved at the time of study discontinuation.

Loperamide details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	6	PO	5	5
Diarrhea	4	PO	6	15
Diarrhea	4	PO	16	21
Diarrhea	2	PO	22	23
Diarrhea	2	PO	29	42
Diarrhea	4	PO	43	56
Diarrhea	4	PO	57	84
Diarrhea	4	PO	85	114
Diarrhea	4	PO	115	135
Diarrhea	4	PO	143	170
Diarrhea	4	PO	171	196
Diarrhea	4	PO	197	226
Diarrhea	4	PO	227	254
Diarrhea	4	PO	255	282
Diarrhea	4	PO	283	Ongoing

Due to the event of diarrhea, there was no change in the study treatment with paclitaxel, however, dose of ipatasertib was reduced to 300 mg on Study Day 143.

There was no change in the study treatment due to the event of chronic gastritis.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

The Investigator considered chronic gastritis to be unrelated to ipatasertib and paclitaxel and related to other causes (unspecified).

On Study Day 338, the patient withdrew consent from study treatment (physician discussed with the patient, the options to continue current clinical trial vs switching to alternative treatment with palbociclib and anastrozole, patient elected to discontinue current trial) with the last dose of paclitaxel administered on Study Day 324 and ipatasertib on Study Day 332. The patient entered into long-term follow up.

On Study Day 531, the patient withdrew consent from the study.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Alopecia	2	Non-serious	23	Unresolved	Unrelated	Related
Hordeolum	1	Non-serious	53	63	Unrelated	Unrelated
Hyperglycemia	1	Non-serious	71	115	Related	Unrelated
Neuropathy peripheral	2	Non-serious	134	Unresolved	Unrelated	Related
Influenza like illness	1	Non-serious	251	283	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305629	Patient number	2201
Demographics:	68-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Categories:	Diarrhea SAE, AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Categories:	Diarrhea SAE, AESI: Grade ≥ 3 diarrhea		
Event 3 (PT) Categories:	Enterocolitis SAE, AESI: Grade ≥ 2 enterocolitis/colitis		
Event 4 (PT) Category:	Intestinal obstruction SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER2-negative bilateral breast cancer (T2N1M0), approximately 9 years prior to study entry followed by bilateral axillary dissection.

On Study Day −29, the patient was diagnosed with metastatic disease with ER positive/PR unknown and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included nodal liver, bilateral lung and mediastinal ganglion. The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/ Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Paclitaxel, cyclophosphamide, doxorubicin and exemestane	Approximately 9 years prior to study entry.	Approximately 8 years prior to study entry.
Radiotherapy	Neo-adjuvant	Breast (66cGy: 66 fractions)	Approximately 8 years prior to study entry.	Approximately 8 years prior to study entry
Radiotherapy	Adjuvant	Armpit lymph node (50 cGy 50 fractions)	Approximately 8 years prior to study entry.	Approximately 8 years prior to study entry

Type of treatment	Therapy Setting/ Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Anastrozole	Approximately 6 years prior to study entry	–725

The patient's medical history included asymptomatic bacteriuria. No surgical history and concurrent conditions were reported.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

On Study Day 2, the patient experienced Grade 1 diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide (2 mg, PO). On Study Day 7, the event of diarrhea was considered resolved.

On Study Day 11, the patient experienced Grade 2 diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide (2 mg, PO). On Study Day 17, the event of diarrhea improved to Grade 1. On Study Day 18, she experienced Grade 1 decreased appetite (related to paclitaxel). No treatment was given for event of decreased appetite. On Study Day 30, the event of diarrhea was considered resolved.

On Study Day 37, the patient experienced Grade 1 mucosal inflammation (non-serious, related to paclitaxel). No treatment was given for this event.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 36 and ipatasertib (400 mg) on Study Day 37.

On Study Day 38, the patient experienced Grade 1 (initial intensity) diarrhea. She received treatment with loperamide (details in the table below). On Study Day 46, the event of mucositis was considered resolved.

On Study Day 79, the event of diarrhea (associated with oral intolerance) worsened to Grade 3, leading to hospitalization. Treatment with loperamide was maintained and she also received hydration therapy. On Study Day 80, the event of diarrhea was considered resolved. On Study Day 81, the event of decreased appetite was considered resolved. On Study Day 83, she was discharged from the hospital.

Loperamide details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	2	6
Diarrhea	2	PO	15	16
Diarrhea	2	PO	19	20
Diarrhea	4	PO	38	67
Diarrhea	4	PO	91	92
Diarrhea	2	PO	96	98
Diarrhea	4	PO	106	107

Due to the event of diarrhea, study treatment with ipatasertib was interrupted on Study Day 83 and Cycle 4 Day 1 of paclitaxel was delayed. The next dose of paclitaxel and ipatasertib (at a reduced dose of 300 mg) was given on Study Day 90.

The investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

Event 2: Diarrhea
Event 3: Enterocolitis
Event 4: Intestinal obstruction

Prior to the events of diarrhea, enterocolitis and intestinal obstruction, the most recent dose of paclitaxel was administered on Study Day 161 and ipatasertib (300 mg) on Study Day 166.

On Study Day 173, the patient experienced abdominal pain and Grade 3 diarrhea. On Study Day 174, she was hospitalized for antibiotic management and hydration. She received treatment with ceftriaxone, hyoscine, metamizole and morphine. On Study Day 176, the event of diarrhea was considered resolved, however due to abdominal pain she remained hospitalized. On Study Day 177, a CT scan was performed and she was diagnosed with Grade 3 enterocolitis and Grade 4 intestinal obstruction, leading to prolonged hospitalization. The event of enterocolitis was considered to cause significant disability. She further received treatment with meropenem and vancomycin. On Study Day 183, the events of enterocolitis and intestinal obstruction were considered resolved and she was discharged from the hospital.

Due to the events of diarrhea, enterocolitis and intestinal obstruction, study treatment with paclitaxel and ipatasertib was interrupted after Study Day 161 and Study Day 166, respectively.

The investigator considered diarrhea to be related to paclitaxel and unrelated to ipatasertib.

The investigator considered enterocolitis and intestinal obstruction to be related to ipatasertib and paclitaxel.

On Study Day 224, study treatment with paclitaxel and ipatasertib was permanently discontinued as per physician′s decision (patient presented adverse event of Grade 3 colitis, which led to other complications and its determinant as limiting toxicity) with the last dose of paclitaxel administered on Study Day 161 and ipatasertib on Study Day 166. The patient entered into long-term follow up.

On Study Day 601, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nausea	1	Non-serious	2	6	Unrelated	Related
Alopecia	2	Non-serious	18	Unresolved	Unrelated	Related
Neuropathy peripheral	1	Non-serious	58	Unresolved	Unrelated	Related
Dry skin	1	Non-serious	98	Unresolved	Related	Unrelated
Diarrhea	1	Non-serious	99	103	Related	Unrelated
Fatigue	1	Non-serious	107	133	Unrelated	Related

Study Number/CRTN:	CO40016/305649	Patient number	2208
Demographics:	58-year-old female (race unknown)		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Pleural effusion SAE		
Event 2 (PT) Category:	Lower respiratory tract infection SAE		
Event 3 (PT) Categories:	Pneumonia Death due to AE, SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.1; Narratives for patients who died due to adverse event(s).

Study Number/CRTN:	CO40016/318958	Patient number	2209
Demographics:	59-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Cellulitis SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal well differentiated ER positive, PR negative, and HER2-negative left breast cancer (T1cN0M0) approximately 7 years prior to study entry, following left sentinel lymph node biopsy and left partial mastectomy performed on the same day.

On Study Day −893, the patient was diagnosed with metastatic disease with ER/PR status unknown and HER 2-not assessed in metastatic tissue. At screening, sites of disease involvement included bilateral lung, lymph nodes (left axillary, and left supraclavicular), and bone (midline sternum). The patient was assessed by the Investigator to have endocrine resistant.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Adjuvant	Left breast (dose unknown)	Approximately 7 years prior to study entry	Approximately 7 years prior to study entry
Cancer therapy	Adjuvant	Tamoxifen	Approximately 7 years prior to study entry	−900
Cancer therapy	Metastatic	Letrozole	−884	−642
Cancer therapy	Metastatic	Fulvestrant	−641	−472
Cancer therapy	Metastatic	Letrozole and palbociclib (11 cycles)	−443	−130
Cancer therapy	Metastatic	Exemestane and everolimus	−121	−35

No medical/surgical history was reported. The patient′s concurrent conditions included pneumonia, atrial septal defect, and tumor pain.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 was reported.

On Study Day 83, the patient experienced Grade 1 lymphedema of left arm (non-serious, unrelated). No treatment was given for the event.

Event: Cellulitis (Cellulitis; left arm)

Prior to the event of cellulitis, the most recent dose of paclitaxel was administered on Study Day 911 and ipatasertib (400 mg) on Study Day 916.

On Study Day 917, the patient′s left arm was hot, and she experienced fever (body temperature 40°C). On Study Day 918, laboratory work-up showed WBC count 14.54 $\times$ 10^9/L (normal range: 3.3-8. 6 $\times$ 10^9/L), and C-reactive protein 18.15 mg/dL (normal range: $<$ 0.14 mg/dL). A quantitative antigen test for SARS-CoV-2 was negative. She was diagnosed with Grade 3 cellulitis. On Study Day 919, she was hospitalized due to cellulitis. She received treatment with ibuprofen, cefazolin, and cefaclor. On Study Day 926, she was discharged from the hospital. On Study Day 932, the event of cellulitis was considered resolved. The event of lymphedema remained unresolved at the time of study discontinuation.

Due to this event, Cycle 34 of the study treatment with paclitaxel was delayed and study treatment with ipatasertib was interrupted after Study Day 917. The next dose was given on Study Day 932.

Relevant lab values are listed in the table below:

Study Day	**WBC count** (normal range: 3.3-8.6 $\times$ 10^9/L)	**Neutrophils** (normal range: 45-70%)	**Lymphocytes** (normal range: 20-45%)	**C-reactive protein** (normal range: $<$ 0.14 mg/dL)
Screening	5.67	58.2	32.1	
918	14.54	95.2*	4^	18.15
922	3.8	52.6*	32.4	2.53
926	3.28	–	–	0.51
932	4.97	–	–	0.53

*normal range: 39.7-70.6% and ^normal range: 23.1-49.9%

The Investigator considered cellulitis, to be unrelated to ipatasertib and paclitaxel and related to other cause (ongoing lymphedema).

On Study Day 1290, symptomatic deterioration assessment showed elevation of CEA and CA 15-3.

On Study Day 1296, study treatment and study was permanently discontinued due to symptomatic deterioration with the last dose of paclitaxel administered on Study Day 1275 and ipatasertib on Study Day 1281.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	7	1296	Related	Unrelated
Neutrophil count decreased	2	Non-serious	8	36	Related	Related
White blood cell count decreased	2	Non-serious	8	29	Related	Related
Alopecia	2	Non-serious	22	Unresolved	Unrelated	Related
Peripheral sensory neuropathy	1	Non-serious	22	Unresolved	Unrelated	Related
Neutrophil count decreased	3	Non-serious	43	50	Related	Related
White blood cell count decreased	2	Non-serious	43	50	Related	Related
Neutrophil count decreased	3	Non-serious	64	71	Related	Related
White blood cell count decreased	2	Non-serious	64	71	Related	Related
Dysgeusia	1	Non-serious	83	Unresolved	Unrelated	Related
Decreased appetite	1	Non-serious	83	Unresolved	Unrelated	Related
Neutrophil count decreased	3	Non-serious	85	92	Related	Related
White blood cell count decreased	2	Non-serious	85	92	Related	Related
Pharyngitis	2	Non-serious	101	106	Unrelated	Related
Neutrophil count decreased	3	Non-serious	106	113	Related	Related
White blood cell count decreased	2	Non-serious	106	113	Related	Related
Product dose omission issue	–	Non-serious	106	112	–	–
Constipation	1	Non-serious	197	201	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Neutrophil count decreased	2	Non-serious	211	225	Related	Related
White blood cell count decreased	2	Non-serious	211	219	Related	Related
Neutrophil count decreased	2	Non-serious	232	240	Related	Related
White blood cell count decreased	2	Non-serious	232	240	Related	Related
White blood cell count decreased	2	Non-serious	246	260	Related	Related
Neutrophil count decreased	3	Non-serious	253	260	Related	Related
Neutrophil count decreased	2	Non-serious	267	274	Related	Related
White blood cell count decreased	2	Non-serious	267	274	Related	Related
Product dose omission issue	–	Non-serious	267	273	–	–
Nasopharyngitis	1	Non-serious	286	292	Related	Related
Oral herpes	1	Non-serious	292	302	Unrelated	Related
Abdominal discomfort	1	Non-serious	330	337	Related	Related
Neutrophil count decreased	2	Non-serious	337	344	Related	Related
White blood cell count decreased	2	Non-serious	379	393	Related	Related
Neutrophil count decreased	2	Non-serious	379	393	Related	Related
Rash	1	Non-serious	390	400	Related	Related
Abdominal pain	1	Non-serious	405	406	Related	Related
Neutrophil count decreased	2	Non-serious	407	414	Related	Related
White blood cell count decreased	2	Non-serious	407	414	Related	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Oral herpes	1	Non-serious	413	422	Unrelated	Related
Neutrophil count decreased	2	Non-serious	428	435	Related	Related
White blood cell count decreased	2	Non-serious	428	435	Related	Related
Rash	1	Non-serious	430	448	Related	Related
Neutrophil count decreased	2	Non-serious	449	456	Related	Related
White blood cell count decreased	2	Non-serious	449	456	Related	Related
Abdominal discomfort	1	Non-serious	464	Unresolved	Related	Related
White blood cell count decreased	2	Non-serious	477	484	Related	Related
Neutrophil count decreased	2	Non-serious	491	498	Related	Related
White blood cell count decreased	2	Non-serious	491	498	Related	Related
Rash	1	Non-serious	495	504	Related	Related
Rash	1	Non-serious	530	545	Related	Related
Neutrophil count decreased	2	Non-serious	533	540	Related	Related
White blood cell count decreased	2	Non-serious	533	540	Related	Related
Product dose omission issue	–	Non-serious	590	590	–	–
Nasopharyngitis	2	Non-serious	607	613	Related	Related
Neutrophil count decreased	2	Non-serious	631	645	Related	Related
White blood cell count decreased	2	Non-serious	631	645	Related	Related
Rash	1	Non-serious	641	652	Related	Related
Neutrophil count decreased	2	Non-serious	674	680	Related	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Neutrophil count decreased	2	Non-serious	687	701	Related	Related
White blood cell count decreased	2	Non-serious	687	701	Related	Related
Oral herpes	1	Non-serious	713	725	Unrelated	Related
Abdominal pain	2	Non-serious	723	725	Related	Related
White blood cell count decreased	2	Non-serious	729	736	Related	Related
Neutrophil count decreased	2	Non-serious	757	764	Related	Related
White blood cell count decreased	2	Non-serious	757	764	Related	Related
White blood cell count decreased	2	Non-serious	771	778	Related	Related
Neutrophil count decreased	2	Non-serious	792	799	Related	Related
White blood cell count decreased	2	Non-serious	792	799	Related	Related
Neutrophil count decreased	2	Non-serious	884	890	Related	Related
White blood cell count decreased	2	Non-serious	884	890	Related	Related
Constipation	1	Non-serious	900	901	Unrelated	Unrelated
Vomiting	1	Non-serious	901	901	Unrelated	Unrelated
Anemia	2	Non-serious	918	932	Unrelated	Related
Oral herpes	1	Non-serious	919	925	Unrelated	Related
Hypertension	2	Non-serious	932	939	Unrelated	Unrelated
Pyrexia	1	Non-serious	985	986	Unrelated	Unrelated
Oropharyngeal discomfort	1	Non-serious	994	1002	Unrelated	Unrelated
Cellulitis	2	Non-serious	1082	1093	Unrelated	Unrelated
Oral herpes	1	Non-serious	1085	1090	Unrelated	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Folliculitis	1	Non-serious	1085	1090	Unrelated	Unrelated
Neutrophil count decreased	2	Non-serious	1093	1100	Related	Related
White blood cell count decreased	2	Non-serious	1093	1100	Related	Related
Herpes zoster	2	Non-serious	1151	1163	Unrelated	Related
Post herpetic neuralgia	2	Non-serious	1151	1173	Unrelated	Unrelated
White blood cell count decreased	3	Non-serious	1191	1205	Related	Related
Neutrophil count decreased	3	Non-serious	1191	1205	Related	Related
Myalgia	1	Non-serious	1223	Unresolved	Unrelated	Unrelated
Neutrophil count decreased	2	Non-serious	1233	1240	Related	Related
White blood cell count decreased	2	Non-serious	1233	1240	Related	Related

Study Number/CRTN:	CO40016/304792	Patient number	2218
Demographics:	58-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Eyelid edema SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal and ″other″ histological subtype, poorly differentiated, ER/PR positive and HER2 negative, left breast cancer (T2N1M0), approximately 3 years 6 months prior to study entry.

On Study Day –46, the patient was diagnosed with metastatic disease with ER and PR status was unknown and HER2 status was not assessed in metastatic tissue). At screening, sites of disease involvement included lung (expansive pulmonary formation inferior lingula, bilateral

solid, medullary and cortical pulmonary nodular formations, and expansive formation amorphous in correspondence with the right hilar region accompanying peri-bronchovascular bundles in the medial aspect of the anterior segment of the right upper lobe), lymph nodes (pre vascular-lymphadenopathy, prominent lymph nodes and enlargement in several mediastinal chains as well as bilateral hilar lymph nodes and retrocrural, peri-gastric, celiac, superior mesenteric, left para-aortic and inter-aortocaval prominent lymph nodes), and liver (nodular lesions). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left modified radical mastectomy	Approximately 3 years 5 months prior to study entry	NA
Cancer therapy	Adjuvant	Doxorubicin, cyclophosphamide and docetaxel	Approximately 3 years 5 months prior to study entry	Approximately 2 years 10 months prior to study entry
Radiotherapy	Adjuvant	Left breast (dose unknown, 25 fractions)	Approximately 1 year 9 months prior to study entry	Approximately 1 year 8 months prior to study entry
Cancer therapy	Adjuvant	Anastrozole	Approximately 1 years 8 months prior to study entry	−32

No medical or other surgical history was reported. Concurrent condition included dyspnea.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

Event: Eyelid edema (Bi-palpebral edema)

On Study Day 45, the patient received ipatasertib (400 mg) and Cycle 2 Day 8 of paclitaxel as scheduled. Within 24 hours after the end of paclitaxel infusion, the patient experienced Grade 2 urticaria (non-serious, related to paclitaxel) and hypersensitivity reaction (both considered as systemic infusion reaction) manifested with Grade 2 eyelid edema (serious; medically significant) and throat pruritus. She received treatment with hydrocortisone. On the same day (Study Day 45), the events of urticaria and eyelid edema were considered resolved.

There was no change in study treatment due to the event of eyelid edema.

The Investigator considered eyelid edema to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 115, a radiographic response assessment showed disease progression with new lesions in bone (skullcap, manubrium and sternal body, several vertebrae, sacrum, iliac bilaterally, lower branch of the left pubis and heterogeneous uptake in costal arches).

On Study Day 122, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 108 and ipatasertib on Study Day 113. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Fulvestrant	133	296
Denosumab and palbociclib	199	296
Cisplatin	324	394

On Study Day 470, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	8	31	Related	Related
Alopecia	2	Non-serious	21	Unresolved	Unrelated	Related
Asthenia	1	Non-serious	24	221	Unrelated	Related
Diarrhea	2	Non-serious	60	61	Related	Related
Neuropathy peripheral	1	Non-serious	93	Unresolved	Unrelated	Related
Back pain	1	Non-serious	115	221	Unrelated	Unrelated

1.4 NARRATIVES FOR PATIENTS WHO EXPERIENCED ADVERSE EVENTS LEADING TO STUDY TREATMENT DISCONTINUATION

Study Number/CRTN:	CO40016/307264	Patient number	2003
Demographics:	69-year-old Asian female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Diarrhea AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Stomatitis AE leading to study treatment discontinuation		
Event 3 (PT) Category:	Vomiting AE leading to study treatment discontinuation		

The patient was randomized on Study Day −2.

The patient was diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative metastatic right breast cancer (T4bN3aM1) on Study Day −323.

At screening sites of disease involvement included liver (multiple lesions including S3 and S4) and bone (multiple). The patient was assessed by the Investigator to have visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Metastatic	Letrozole	−294	−80
Surgery	Palliative	Right partial mastectomy and axillary sampling of lymph node	−209	—

The patient's medical history included nausea. No other surgical history was reported. Concurrent condition included seasonal allergy.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. The same day, she also started loperamide prophylactically (total daily dose: 4 mg) for diarrhea.

No concomitant medications ongoing at Study Day 1 were reported.

On Study Day 2, the patient experienced Grade 2 nausea (non-serious, related).

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 8.

On Study Day 9, the patient experienced non-serious Grade 2 diarrhea (intermittent). She received treatment with loperamide (details reported in table below) for diarrhea. On Study Day 10, she experienced Grade 2 vomiting (non-serious, related). She received treatment with ramosetron, metoclopramide and carbohydrates/potassium chloride/sodium chloride/sodium lactate for nausea and vomiting. On Study Day 23, the event of diarrhea improved to Grade 1. On Study Day 30, the event of diarrhea again worsened to Grade 2. On Study Day 37, the events of nausea and vomiting were considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of diarrhea	4	PO	1	4
Diarrhea	4	PO	18	18
Diarrhea	4	PO	26	26
Diarrhea	2	PO	29	29
Diarrhea	4	PO	30	31
Diarrhea	2	PO	32	32
Diarrhea	4	PO	33	33
Diarrhea	2	PO	50	56

Event 2: Stomatitis
Event 3: Vomiting

Prior to the events of stomatitis and vomiting, the most recent dose of paclitaxel was administered on Study Day 50 and ipatasertib (400 mg) on Study Day 51.

On Study Day 52, the patient experienced non-serious Grade 1 stomatitis and Grade 1 vomiting. No treatment was reported for these events. On Study Day 53, the event of vomiting was considered resolved. On Study Day 56, the ongoing event of diarrhea was considered resolved. On Study Day 59, the event of stomatitis was considered resolved.

Due to the events of diarrhea, stomatitis and vomiting, there was no change in study treatment with paclitaxel; however, ipatasertib was permanently discontinued with the last dose administered on Study Day 54.

The Investigator considered diarrhea, stomatitis, and vomiting, to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 386, a radiographic response assessment showed disease progression with new lesion in liver (right S5).

On Study Day 412, study treatment with paclitaxel was permanently discontinued due to disease progression with the last dose administered on Study Day 384. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Eribulin	414	958
Fulvestrant and Palbociclib	972	Ongoing

On Study Day 1384, the patient was discontinued from the study as per physician's decision (study was terminated by the Sponsor). Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	1	Non-serious	2	7	Unrelated	Unrelated
Hyperglycemia	2	Non-serious	8	93	Unrelated	Unrelated
Neutropenia	2	Non-serious	15	22	Related	Related
Alopecia	2	Non-serious	15	Unresolved	NA	Related
Neutropenia	3	Non-serious	64	71	Unrelated	Related
Neuropathy peripheral	1	Non-serious	64	Unresolved	NA	Related
Pyrexia	1	Non-serious	70	74	NA	Related
Neutropenia	2	Non-serious	86	93	NA	Related
Nail discoloration	1	Non-serious	93	Unresolved	NA	Related
Neutropenia	2	Non-serious	100	111	NA	Related
Neutropenia	3	Non-serious	125	139	NA	Related
Vomiting	1	Non-serious	134	135	Unrelated	Unrelated
Neutropenia	3	Non-serious	153	167	NA	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Neutropenia	2	Non-serious	209	216	NA	Related
Neutropenia	2	Non-serious	239	251	NA	Related
Eczema asteatotic	2	Non-serious	248	285	NA	Unrelated
Neutropenia	2	Non-serious	265	272	NA	Related
Diarrhea	1	Non-serious	284	285	NA	Unrelated
Nasopharyngitis	1	Non-serious	307	350	NA	Unrelated
Neutropenia	2	Non-serious	321	328	NA	Related
Neutropenia	2	Non-serious	335	342	NA	Related
Neutropenia	2	Non-serious	370	384	NA	Related
Nail bed inflammation	2	Non-serious	372	Unresolved	NA	Related

Study Number/CRTN:	CO40016/305629	Patient number	2008
Demographics:	76-year-old American Indian or Alaska native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Categories:	Diarrhea SAE, AESI: Grade $\geq$ 3 diarrhea		
Event 2 (PT) Categories:	Hyperglycemia SAE, AE leading to study treatment discontinuation, AESI: Grade $\geq$ 3 hyperglycemia		
Event 3 (PT) Category:	Dehydration SAE		
Event 4 (PT) Category:	Hypoglycemia SAE		
Event 5 (PT) Categories:	Respiratory distress Death due to AE, SAE		

A narrative for this patient is available under Section 1.1; Narratives for patients who died due to adverse event(s).

Study Number/CRTN:	CO40016/305300	Patient number	2012
Demographics:	54-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR positive and HER2-negative left breast cancer (T2N1miM0), approximately 7 years prior to study entry.

On Study Day −31, the patient was diagnosed with metastatic disease with ER positive, PR negative and HER2-negative disease in metastatic tissue. At screening, sites of disease involvement included bone (sternum), liver (segment V and VII), left lung (lingula) and right hilar lymph node. The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	″Other″ surgery of left breast and left axillary lymph node sampling	Approximately 7 years prior to study entry	NA
Cancer therapy	Adjuvant	Docetaxel, doxorubicin, and cyclophosphamide	Approximately 7 years prior to study entry	Approximately 7 years prior to study entry
Cancer therapy	Adjuvant	Tamoxifen	Approximately 7 years prior to study entry	−28

No medical or other surgical history was reported. Concurrent conditions included hypercholesterolemia, bone pain and spinal pain.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included loperamide, lorazepam, omeprazole, simvastatin and tramadol.

On Study Day 106, the patient developed Grade 1 palmo-plantar neuropathy (preferred term: peripheral neuropathy; non-serious, related to paclitaxel; symptoms not reported). On Study Day 299, the event of neuropathy peripheral was considered resolved without any

treatment. On Study Day 314, she again developed Grade 1 (initial intensity) palmo-plantar neuropathy (non-serious, related to paclitaxel). No treatment was administered for this event. On Study Day 454, palmo-plantar neuropathy worsened to Grade 2. On Study Day 455, dose of paclitaxel was reduced to 65 mg/m^2. On Study Day 488, the event of neuropathy peripheral was considered resolved.

Event: Neuropathy peripheral (palmo-plantar neuropathy)

Prior to the event of Grade 2 neuropathy peripheral which led to paclitaxel discontinuation, the most recent dose of paclitaxel was administered on Study Day 553 and ipatasertib (300 mg) on Study Day 559.

On Study Day 566, the patient developed non-serious Grade 2 palmo-plantar neuropathy (preferred term: **neuropathy peripheral**; presenting signs and symptoms not reported). No treatment was reported for this event. On Study Day 593, the event of neuropathy peripheral improved to Grade 1. On Study Day 788, the event of neuropathy peripheral was considered resolved.

Due to this event, there was no change in study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 553.

The Investigator considered neuropathy peripheral, to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 894, a radiographic response assessment showed disease progression.

On Study Day 901, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose of ipatasertib given on Study Day 895. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Camizestrant and Palbociclib	929	984
Capecitabine	1028	Ongoing

On Study Day 1112, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Vomiting	1	Non-serious	7	16	Related	Related
Diarrhea	2	Non-serious	9	20	Related	Related
Vomiting	1	Non-serious	19	19	Related	Related
Alopecia	1	Non-serious	28	124	Related	Related
Diarrhea	1	Non-serious	33	34	Related	Related
Vomiting	1	Non-serious	34	34	Related	Related
Diarrhea	1	Non-serious	42	90	Related	Related
Anemia	1	Non-serious	55	173	Related	Related
Diarrhea	1	Non-serious	106	106	Related	Unrelated
Hematocrit decreased	1	Non-serious	125	138	Related	Related
Catarrh	1	Non-serious	140	153	Unrelated	Unrelated
Odynophagia	2	Non-serious	147	174	Related	Related
Cough	2	Non-serious	147	174	Related	Related
Upper respiratory tract infection	1	Non-serious	154	293	Unrelated	Unrelated
Cough	1	Non-serious	175	293	Related	Related
Odynophagia	1	Non-serious	175	293	Unrelated	Related
Anemia	1	Non-serious	271	286	Related	Related
Neutrophil count decreased	1	Non-serious	271	286	Related	Related
Asthenia	1	Non-serious	300	313	Related	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Anemia	1	Non-serious	440	467	Related	Related
Paresthesia	1	Non-serious	510	565	Unrelated	Related
Asthenia	1	Non-serious	510	788	Related	Related
Lymphocyte count decreased	1	Non-serious	566	593	Unrelated	Related
Onycholysis	1	Non-serious	649	704	Unrelated	Related
Blood cholesterol increased	1	Non-serious	649	676	Unrelated	Unrelated
Asthenia	1	Non-serious	817	949	Related	NA
Back pain	1	Non-serious	870	908	Unrelated	NA
Neuropathy peripheral	1	Non-serious	873	929	Unrelated	Related

Study Number/CRTN:	CO40016/305245	Patient number	2017
Demographics:	52-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Neurotoxicity AE leading to study treatment discontinuation		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with lobular, ER/PR positive and HER2 negative right breast cancer (T2N1M0; histological grade unknown) approximately 4 years prior to study entry, followed by right modified radical mastectomy.

On Study Day −420, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative disease in metastatic tissue. At screening sites of disease involvement included

pleura (right parietal, right posterior and bilateral), para-sternal subcutaneous nodule and peritoneum (peritoneal carcinomatosis). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Docetaxel, doxorubicin and cyclophosphamide	Approximately 4 years prior to study entry	Approximately 3 years 9 months prior to study entry
Cancer therapy	Adjuvant	Tamoxifen	Approximately 3 years 8 months prior to study entry	Approximately 1 year prior to study entry
Cancer therapy	Metastatic	Letrozole and goserelin	Approximately 1 year prior to study entry	Approximately 7 months prior to study entry

No medical or other surgical history was reported. Concurrent conditions included sarcoidosis, hypertension and gamma-glutamyltransferase increased.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included prednisone, codeine, paracetamol, atenolol, citalopram and lormetazepam.

Event: Neurotoxicity (neurotoxicity in hands and feet)

Prior to the event of neurotoxicity, the most recent dose of paclitaxel was administered on Study Day 203 and ipatasertib (400 mg) on Study Day 209.

On Study Day 210, the patient was reported with non-serious Grade 2 neurotoxicity in hands and feet (signs and symptoms not provided). No details regarding evaluation was provided. No treatment was reported for the event. The event of neurotoxicity remained unresolved at the time of patient′s death (see narrative below).

Due to the event of neurotoxicity, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 210.

The Investigator considered neurotoxicity to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 276, a radiographic response assessment showed disease progression with new lesions in liver (hepatic parenchyma) and bilateral pleural effusion.

On Study Day 296, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose of administered on Study Day 271. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Abemaciclib	297	458
Surgery (palliative; Other unspecified; site: breast)	416	NA
Liposomal doxorubicin and cyclophosphamide	464	Ongoing

On Study Day 537, the patient died due to disease progression. It was unknown whether an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	1	Non-serious	1	3	Unrelated	Unrelated
Rash	1	Non-serious	2	2	Unrelated	Related
Diarrhea	1	Non-serious	5	19	Related	Related
Hypertransaminasemia	3	Non-serious	7	21	Related	Related
Blood alkaline phosphatase increased	1	Non-serious	8	20	Related	Related
Respiratory tract infection	2	Non-serious	41	49	Unrelated	Unrelated
Epistaxis	1	Non-serious	42	56	Unrelated	Related
Hemoglobin decreased	2	Non-serious	56	Unresolved	Related	Related
Cough	1	Non-serious	56	311	Unrelated	Unrelated
Gastritis	1	Non-serious	63	83	Related	Related
Pruritus	1	Non-serious	168	Unresolved	Related	Related
Blood triglycerides increased	1	Non-serious	196	223	Related	Related
Blood cholesterol increased	1	Non-serious	224	251	Related	Related
Amylase increased	1	Non-serious	224	251	Related	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Lipase increased	1	Non-serious	224	253	Related	Related

Study Number/CRTN:	CO40016/304776	Patient number	2019
Demographics:	46-year-old Asian female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Neutrophil count decreased AE leading to study treatment discontinuation		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, ER positive/PR negative and HER2 negative left breast cancer (T2NXM0; histological grade unknown), approximately 5 years 6 months prior to study entry following left breast biopsy.

On Study Day −146, the patient was diagnosed with metastatic disease with ER positive/ PR negative and HER2 negative disease in metastatic tissue. At screening sites of disease involvement included chest (left parasternal region and left anterior mediastinum), bone (multiple) and bilateral lung (multiple nodules). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neo-adjuvant	Cyclophosphamide, epirubicin and fluorouracil	Approximately 5 years prior to study entry	Approximately 5 years prior to study entry
Cancer therapy	Neo-adjuvant	Docetaxel	Approximately 5 years prior to study entry	Approximately 5 years 2 prior to study entry
Surgery	Curative	Left modified radical mastectomy and axillary lymph node dissection	Approximately 5 years prior to study entry	NA
Cancer therapy	Adjuvant	Tamoxifen	Approximately 5 years prior to study entry	−133

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Adjuvant	Breast (left chest wall with bolus) and lymph nodes (left supraclavicular) (dose: each at 5000 cGy, 25 fractions)	Approximately 4 years 11 months prior to study entry	Approximately 4 years 10 months prior to study entry
Radiotherapy	Metastatic	Bone (L2-S3 spine and bilateral SI joints) (dose: 3000 cGy, 15 fractions)	–47	–33

No medical history was reported. Other surgical history included central venous catheterization and bilateral oophorectomy. Concurrent condition included neuropathy peripheral.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

Prior to the event of neutrophil count decreased due to which study treatment with paclitaxel was discontinued, the patient was noted with multiple events of neutrophil count decreased and an event of white blood cell count decreased (please refer to table below for details). She received treatment with filgrastim. Relevant laboratory work-up has been reported in the table below.

Event	Most extreme grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Action taken (Ipatasertib)	Action taken (Paclitaxel)
Neutrophil count decreased	2	7	13	Unrelated	Related	None	Cycle 1 Day 15 dose interrupted
Neutrophil count decreased	3	14	20	Unrelated	Related	Drug Interrupted on Study Day 14 and resumed on Study Day 21	Cycle 1 Day 15 dose interrupted
Neutrophil count decreased	2	21	55	Unrelated	Related	None	None

Event	Most extreme grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Action taken (Ipatasertib)	Action taken (Paclitaxel)
Neutrophil count decreased	2	71	76	Related	Related	Drug Interrupted on Study Day 71 and resumed on Study Day 77	Cycle 3 Day 15 dose interrupted
White blood cell count decreased	2	84	142	Unrelated	Related	None	None
Neutrophil count decreased	3	91	97	Related	Related	Drug interrupted from Study Days 91-97 and dose reduced to 300 mg on Study Day 98	Dose delayed and reduced to 65 mg/m^2 on Study Day 98
Neutrophil count decreased	2	112	120	Related	Related	Drug interrupted on Study Day 112 and resumed at a reduced dose of 200 mg (due to the event of Grade 2 diarrhea) on Study Day 121	Cycle 5 Day 1 dose interrupted

Event	Most extreme grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Action taken (Ipatasertib)	Action taken (Paclitaxel)
Neutrophil count decreased	3	136	142	Unrelated	Related	Drug interrupted on Study Day 136 and resumed on Study Day 143	Cycle 5 Day 22 dose interrupted
Neutrophil count decreased	2	171	177	Unrelated	Related	Drug interrupted on Study Day 171 and resumed on Study Day 178	Cycle 7 Day 1 dose interrupted

Event: Neutrophil count decreased

Prior to the event of neutrophil count decreased, the most recent dose of paclitaxel was administered on Study Day 185 and ipatasertib (200 mg) on Study Day 191.

On Study Day 192, the patient was noted with Grade 2 white blood cell count decreased (WBC count 2.39 $\times$ $10^3/\mu L$, non-serious, related to paclitaxel) and non-serious Grade 3 neutrophil count decreased (neutrophils 39%). No treatment was reported for the events. On Study Day 198, the events of neutrophil count decreased, and white blood cell count decreased were considered resolved.

Relevant laboratory work-up:

Study Day	WBC count Normal range: 3.54-9.06 $\times$ $10^3/\mu L$	Neutrophils Normal range: 38.3-71.1%
Screening	3.6	67.2
7	2.41	58.5
14	1.81	45.3
21	2.62	47.7
28	3.79	63.4
35	2.48	59.7
42	2.56	56.7
56	3.43	63.4
71	2.63	44.5
77	4.54	49
84	2.85	54.3
91	2.31	27.7
98	2.98	52.4
105	3.43	54.5

Study Day	WBC count Normal range: 3.54-9.06 × $10^3/\mu L$	Neutrophils Normal range: 38.3-71.1%
112	2.1	52.3
136	2.4	38.7
143	3.82	58.9
171	2.73	44.3
192	2.39	39
199	3.38	56.4

Due to the event of neutrophil count decreased, study treatment with ipatasertib was interrupted on Study Day 192 and next dose was given on Study Day 206; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 185.

The Investigator considered neutrophil count decreased to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 276, a radiographic response assessment showed disease progression with new lesions in lung (left pleura).

On Study Day 315, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 282. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Exemestane and everolimus	315	Ongoing

On Study Day 1129, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nausea	1	Non-serious	2	Unresolved	Related	Related
Rash	1	Non-serious	2	30	Unrelated	Unrelated
Constipation	1	Non-serious	5	11	Unrelated	Unrelated
Diarrhea	2	Non-serious	8	111	Related	Unrelated
Constipation	1	Non-serious	58	101	Unrelated	Unrelated
Flatulence	1	Non-serious	65	164	Related	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Anemia	2	Non-serious	84	118	Unrelated	Related
Rash	1	Non-serious	87	Unresolved	Unrelated	Related
Neuropathy peripheral	3	Non-serious	112	199	Unrelated	Related

Study Number/CRTN:	CO40016/304878	Patient number	2022
Demographics:	57-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative right breast cancer (T2N3aM0), approximately 2 years and 11 months prior to study entry.

On Study Day −257, the patient was diagnosed with metastatic disease with ER positive, PR negative and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included lymph node (left axillary and internal mammary). The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Doxorubicin, Cyclophosphamide and Docetaxel	Approximately 2 years and 10 months prior to study entry	−880
Surgery	Curative	Right axillary lymph node dissection and partial mastectomy	−855	NA
Cancer therapy	Adjuvant	Tamoxifen	−832	−238
Radiotherapy	Adjuvant	Right chest wall (dose: 5000 cGy, 25 fractions)	−819	−783
Radiotherapy	Adjuvant	Supraclavicular lymph node (dose: 4500 cGy, 25 fractions)	−819	−814
Radiotherapy	Adjuvant	Right chest wall and axillary region (dose: 1500 cGy, 6 fractions)	−779	−771
Cancer therapy	Metastatic	Anastrozole	−237	−20

No medical or other surgical history was reported. Concurrent conditions included joint stiffness, hypertension, and hypothyroidism.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included amlodipine and levothyroxine.

Event: Peripheral sensory neuropathy

Prior to the event of peripheral sensory neuropathy, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 2.

On Study Day 3, the patient experienced Grade 1 fatigue (non-serious, related), Grade 1 myalgia (non-serious, related to paclitaxel) and was diagnosed with non-serious Grade 1 (initial intensity) peripheral sensory neuropathy (assessment details not reported). She was started on treatment with gabapentin for peripheral sensory neuropathy; no treatment was reported for fatigue and myalgia. On Study Day 19, the event of myalgia resolved.

On Study Day 100, the event of peripheral sensory neuropathy worsened to Grade 2 and further to Grade 3 (most extreme intensity) on Study Day 270. She further received treatment with duloxetine and pregabalin. On Study Day 276, the event of peripheral sensory neuropathy improved to Grade 2. On Study Day 478, the patient developed Grade 1 peripheral motor neuropathy (non-serious, related to paclitaxel). No treatment was reported for this event. On Study Day 503, the event of peripheral sensory neuropathy again worsened to Grade 3.

Due to the event of peripheral sensory neuropathy, there was no change in study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 493.

On Study Day 537, peripheral sensory neuropathy improved to Grade 2 which further improved Grade 1 on Study Day 618. On Study Day 1343, the event of fatigue was considered resolved. The events of peripheral sensory and motor neuropathy remained unresolved at the time of study discontinuation.

The Investigator considered peripheral sensory neuropathy to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 1346, study treatment with ipatasertib was permanently discontinued as per physician decision (tumor evaluation showed complete response) with the last dose of ipatasertib administered on Study Day 1338. The patient entered into long-term follow-up.

On Study Day 1381, the patient was discontinued from the study as per physician's decision (study was terminated by the Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Influenza like illness	1	Non-serious	4	14	Unrelated	Unrelated
Stomatitis	1	Non-serious	18	33	Related	Related
Alopecia	2	Non-serious	18	1343	Unrelated	Related
Abdominal pain upper	1	Non-serious	18	46	Related	Related
Pruritus	1	Non-serious	22	29	Related	Related
Productive cough	1	Non-serious	28	29	Unrelated	Unrelated
Cough	1	Non-serious	35	37	Unrelated	Unrelated
Pruritus	1	Non-serious	38	415	Related	Related
Edema	1	Non-serious	54	64	Related	Related
Diarrhea	1	Non-serious	60	62	Related	Related
Dyspepsia	1	Non-serious	64	136	Related	Related
Localized edema	1	Non-serious	98	Unresolved	Unrelated	Related
Rash maculo-papular	1	Non-serious	100	363	Related	Related
Diarrhea	1	Non-serious	103	104	Related	Unrelated
Stomatitis	1	Non-serious	110	130	Related	Related

Event	Most extreme grade	Serious / Non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Productive cough	1	Non-serious	167	239	Related	Related
Cellulitis	2	Non-serious	170	176	Unrelated	Unrelated
Rhinitis allergic	1	Non-serious	175	181	Related	Related
Oropharyngeal pain	1	Non-serious	175	181	Related	Related
Diarrhea	1	Non-serious	180	182	Related	Related
Stomatitis	1	Non-serious	189	196	Related	Related
Diarrhea	1	Non-serious	201	201	Related	Unrelated
Skin hyperpigmentation	1	Non-serious	205	786	Related	Related
Diarrhea	1	Non-serious	215	216	Related	Unrelated
Productive cough	1	Non-serious	282	295	Unrelated	Related
Herpes zoster	2	Non-serious	294	337	Unrelated	Unrelated
Diplopia	1	Non-serious	299	391	Unrelated	Unrelated
Decreased appetite	1	Non-serious	299	774	Related	Related
Diarrhea	1	Non-serious	327	329	Related	Related
Diarrhea	1	Non-serious	355	359	Related	Related
Productive cough	1	Non-serious	362	386	Unrelated	Unrelated
Stomatitis	1	Non-serious	391	416	Related	Related
Embolism	2	Non-serious	398	Unresolved	Related	Related
Productive cough	1	Non-serious	398	410	Unrelated	Unrelated
Diarrhea	1	Non-serious	419	420	Related	Related
Hyperlipidemia	1	Non-serious	429	Unresolved	Unrelated	Related
Stomatitis	1	Non-serious	439	442	Related	Related
Diarrhea	1	Non-serious	440	442	Related	Related
Pruritus	1	Non-serious	440	754	Related	Related
Dry Eye	1	Non-serious	450	Unresolved	Unrelated	Unrelated
Diarrhea	1	Non-serious	452	453	Related	Related
Diarrhea	1	Non-serious	471	472	Related	Related
Diarrhea	1	Non-serious	496	501	Related	Related
Diarrhea	1	Non-serious	506	507	Related	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Upper respiratory tract infection	2	Non-serious	518	520	Related	Unrelated
Cellulitis	1	Non-serious	521	537	Unrelated	NA
Productive cough	1	Non-serious	525	531	Related	Unrelated
Diarrhea	1	Non-serious	536	537	Related	NA
Nausea	1	Non-serious	536	582	Related	NA
Tinea Pedis	1	Non-serious	548	567	Unrelated	NA
Diarrhea	1	Non-serious	555	556	Related	NA
Diarrhea	1	Non-serious	565	567	Related	NA
Productive cough	1	Non-serious	577	596	Related	NA
Productive cough	1	Non-serious	643	651	Unrelated	NA
Diarrhea	1	Non-serious	650	652	Related	Unrelated
Constipation	1	Non-serious	693	754	Unrelated	NA
Productive cough	1	Non-serious	702	711	Related	NA
Diarrhea	1	Non-serious	783	784	Related	Unrelated
Rash	1	Non-serious	854	Unresolved	Related	NA
Productive cough	1	Non-serious	926	935	Unrelated	NA
Productive cough	1	Non-serious	954	Unresolved	Unrelated	NA
Deafness	1	Non-serious	1004	Unresolved	Unrelated	NA
Cellulitis	2	Non-serious	1075	1085	Unrelated	NA
Diarrhea	1	Non-serious	1086	1087	Related	NA
Diarrhea	1	Non-serious	1101	1102	Related	NA
Diarrhea	1	Non-serious	1110	1112	Related	NA
Diarrhea	1	Non-serious	1116	1117	Related	NA
Dermatitis bullous	2	Non-serious	1165	1171	Related	NA
Pruritus	1	Non-serious	1226	1338	Related	NA
Oropharyngeal pain	1	Non-serious	1229	1242	Unrelated	NA

Study Number/CRTN:	CO40016/305631	Patient number	2029
Demographics:	50-year-old female (race unknown)		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Categories:	Pneumonitis SAE, AE leading to study treatment discontinuation, AESI: Grade ≥ 2 Pneumonitis		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/305386	Patient number	2032
Demographics:	51-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Hyperglycemia AESI: Grade ≥ 3 hyperglycemia		
Event 2 (PT) Categories:	Hyperglycemia AE leading to study treatment discontinuation, AESI: Grade ≥ 3 hyperglycemia		
Event 3 (PT) Category:	Deep vein thrombosis SAE		
Event 4 (PT) Category:	Extravasation SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/310803	Patient number	2033
Demographics:	76-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Categories:	Death Death due to AE, SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.1; Narratives for patients who died due to adverse event(s).

Study Number/CRTN:	CO40016/305213	Patient number	2040
Demographics:	64-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Neurotoxicity AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER positive, PR negative and HER2 negative left breast cancer (T1bN0M0) on Study Day −770.

On Study Day −156, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included right liver lobe, multiple lesions in bone and mediastinal lymph nodes. The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left lumpectomy	−741	NA
Surgery	Diagnostic	Left sentinel lymph node biopsy	−741	NA
Cancer therapy	Adjuvant	Doxorubicin, cyclophosphamide (4 cycles each) and paclitaxel (6 cycles)	−694	−625

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Adjuvant	Left breast (dose: 4860 cGy, 18 fractions)	−496	−469
Cancer therapy	Adjuvant	Letrozole	−469	−152
Cancer therapy	Metastatic	Palbociclib and fulvestrant (4 cycles each)	−139	−31

The patient′s medical history included hepatitis C, thyroiditis, and decreased appetite. No other surgical history was reported. Concurrent conditions included chronic gastritis, vitamin D deficiency, back pain, asthenia, and osteoporosis.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included denosumab, paracetamol, calcium and calcifediol.

Event: Neurotoxicity

Prior to the event of neurotoxicity, the most recent dose of paclitaxel was administered on Study Day 35 and ipatasertib (400 mg) on Study Day 41.

On Study Day 42, the patient was diagnosed with non-serious Grade 1 (initial intensity) neurotoxicity (presenting signs and symptoms and diagnostic details not reported). On Study Day 156, the event worsened to Grade 2. No treatment was reported for this event. On Study Day 397, the event of neurotoxicity was considered resolved.

Due to this event, there was no change in study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 211.

The Investigator considered neurotoxicity, to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 1344, study treatment with ipatasertib and study was permanently discontinued as per physician’s decision (enter post trial access program) with the last dose given on Study Day 1336.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Accidental overdose	1	Non-serious	1	Unresolved	NA	NA
Diarrhea	1	Non-serious	3	68	Related	Related
Headache	1	Non-serious	9	26	Unrelated	Unrelated
Constipation	2	Non-serious	64	Unresolved	Unrelated	Related
Nausea	1	Non-serious	71	112	Related	Related
Pruritus	1	Non-serious	71	112	Related	Related
Asthenia	1	Non-serious	71	112	Related	Related
Alopecia	2	Non-serious	121	252	Unrelated	Related
Back pain	1	Non-serious	142	168	Unrelated	Unrelated
Upper respiratory tract infection	2	Non-serious	183	203	Unrelated	Unrelated
Rhinitis allergic	1	Non-serious	281	336	Unrelated	NA
Pruritus	2	Non-serious	396	Unresolved	Related	Unrelated
Headache	1	Non-serious	861	923	Unrelated	NA

Study Number/CRTN:	CO40016/305631	Patient number	2046
Demographics:	73-year-old female (race unknown)		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade ≥ 3 Diarrhea		
Event 2 (PT) Categories:	Diarrhea AE leading to study treatment discontinuation, AESI: Grade ≥ 3 Diarrhea		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal and subtype: not otherwise specified, poorly differentiated, ER/PR positive and HER2 negative metastatic left breast cancer (T3N3M1) on an unknown date.

At screening site of disease involvement included lung (right pleural cavity, subpleural in the basal lateral segment) and mediastinum (subcarinal lesion). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right radical mastectomy	Approximately 28 years prior to study entry	NA
Cancer therapy	Metastatic	Fulvestrant	−714	−98
Surgery	Curative	Left radical mastectomy	−49	NA

The patient′s medical history included metastasis in right thigh. Other surgical history included lung lobectomy, caesarean section, tonsillectomy, and hysterectomy. Concurrent conditions included hypertension, dyslipidemia, anemia, and constipation.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included enalapril.

The patient underwent enema for pre-existing constipation. After which, she experienced Grade 2 diarrhea (non-serious, unrelated) from Study Day 4 to Study Day 7. She received loperamide (details reported in the table below).

Event 1: Diarrhea (Grade 3)

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 8 and ipatasertib (400 mg) on Study Day 11.

On Study Day 12, the patient experienced non-serious Grade 3 diarrhea (10 times per day). Reportedly, she had no fever. Coproculture was negative. Treatment with loperamide was maintained (details in table below) and she received additional treatment with ciprofloxacin, *Saccharomyces boulardii*, pargeverine, oral electrolytes, levosulpiride, ranitidine, dimenhydrinate, magnesium sulphate and hydration with sodium chloride and potassium chloride. She was also given unspecified corticosteroids and dietary advice. On Study Day 15, the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	5	6
Diarrhea	4	PO	7	7
Diarrhea	6	PO	8	10
Diarrhea	12	PO	11	35

Due to the event of diarrhea, study treatment with ipatasertib was interrupted on Study Day 12 and resumed at a reduced dose of 300 mg on Study Day 19; Cycle 1 Day 15 dose of paclitaxel was delayed by a week and administered at a reduced dose of 65 mg/m^2 on Study Day 23.

The Investigator considered Grade 3 diarrhea to be unrelated to paclitaxel and related to ipatasertib and disease under study.

Event 2: Diarrhea (Grade 3; second episode)

Prior to the event of diarrhea (Grade 3, second episode), the most recent dose of paclitaxel was administered on Study Day 30 and ipatasertib (300 mg) on Study Day 33.

On Study Day 34, the patient experienced non-serious Grade 2 (initial intensity) diarrhea. On Study Day 35, the event of diarrhea worsened to Grade 3. She received treatment with loperamide and hydration with sodium chloride and potassium chloride. On Study Day 36, the patient visited for consultation and physical examination. Diarrhea was reported to be controlled considerably by that time and was considered resolved on the same day (Study Day 36).

Due to the event of diarrhea, study treatment with ipatasertib was permanently discontinued on Study Day 36 with the last dose administered on Study Day 35.

On Study Day 36, study treatment with paclitaxel was permanently discontinued as the patient withdrew consent from the study with the last dose administered on Study Day 30. The patient entered long-term follow-up.

The Investigator considered Grade 3 diarrhea (second episode) to be related to ipatasertib and unrelated to paclitaxel.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Paclitaxel	43	Ongoing

On Study Day 451, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Rash	1	Non-serious	29	Resolving	Unrelated	Unrelated
Rash	1	Non-serious	46	51	Unrelated	Related

Study Number/CRTN:	CO40016/304634	Patient number	2047
Demographics:	53-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Polyneuropathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with mucinous, moderately differentiated, ER/PR positive and HER2 negative left breast cancer (T1cN2aM0) on Study Day −904.

On Study Day −266, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included soft tissue (midline sternum) and skin (right abdominal wall). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left lumpectomy and axillary lymph node dissection	−860	NA
Cancer therapy	Adjuvant	Doxorubicin, and cyclophosphamide	−813	−741
Cancer therapy	Adjuvant	Paclitaxel	−713	−657
Surgery	Curative	Left simple mastectomy	−637	NA
Cancer therapy	Adjuvant	Tamoxifen	−628	−266

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Adjuvant	Lymph node (left arm pit) and scar after mastectomy (each at 45 cGy, 20 fractions)	−573	−545
Cancer therapy	Metastatic	Letrozole and ribociclib	−218	−28

No medical or other surgical history was reported. Concurrent conditions included hypertension and anxiety disorder.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included nebivolol.

Event: Polyneuropathy

Prior to the event of polyneuropathy, the most recent dose of paclitaxel was administered on Study Day 127 and ipatasertib (400 mg) on Study Day 132.

On Study Day 133, the patient was diagnosed with non-serious Grade 1 polyneuropathy (signs and symptoms not reported). She was started on treatment with cyanocobalamin/pyridoxine/thiamine. On Study Day 220, the event of polyneuropathy worsened to Grade 3. She further received treatment with pregabalin. On Study Day 249, the event of polyneuropathy improved to Grade 2 and remained unresolved at the time of patient's death.

Due to the event of polyneuropathy; there was no change in study treatment with ipatasertib; however, paclitaxel dose was first reduced to 65 mg/m^2 on Study Day 141 and then permanently discontinued with the last dose administered on Study Day 213.

The Investigator considered polyneuropathy, to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 273, a radiographic response assessment showed disease progression with new lesions in skin (midline new nodules).

On Study Day 281, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose of administered on Study Day 273 The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Liposomal doxorubicin and cyclophosphamide	284	Ongoing

On Study Day 542, the patient was lost to follow-up. On Study Day 584, she died (as per public records).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	10	22	Related	Unrelated
Diarrhea	2	Non-serious	32	32	Related	Unrelated
Diarrhea	2	Non-serious	34	35	Related	Unrelated
Diarrhea	2	Non-serious	39	42	Related	Unrelated
Diarrhea	2	Non-serious	45	49	Related	Unrelated
Diarrhea	2	Non-serious	88	89	Related	Unrelated
Diarrhea	2	Non-serious	94	96	Related	Unrelated
Asthenia	2	Non-serious	100	Unresolved	Unrelated	Related
Diarrhea	2	Non-serious	101	101	Related	Unrelated
Diarrhea	2	Non-serious	103	103	Related	Unrelated
Rash papular	1	Non-serious	103	164	Related	Unrelated
Diarrhea	2	Non-serious	105	105	Related	Unrelated
Anemia	1	Non-serious	127	176	Unrelated	Related
Diarrhea	1	Non-serious	129	134	Related	Unrelated
Diarrhea	1	Non-serious	150	154	Related	Unrelated
Diarrhea	1	Non-serious	157	163	Related	Unrelated
Diarrhea	1	Non-serious	171	175	Related	Unrelated
Diarrhea	1	Non-serious	177	182	Related	Unrelated
Palpitations	1	Non-serious	183	Unresolved	Unrelated	Related
Diarrhea	1	Non-serious	185	191	Related	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	199	205	Related	Unrelated
Diarrhea	1	Non-serious	208	212	Related	Unrelated
Diarrhea	1	Non-serious	214	219	Related	Unrelated
Pneumonitis	1	Non-serious	219	Unresolved	Related	Unrelated
Diarrhea	1	Non-serious	226	247	Related	Unrelated
Diarrhea	1	Non-serious	269	269	Related	Unrelated
Diarrhea	1	Non-serious	273	273	Related	Unrelated

Study Number/CRTN:	CO40016/304191	Patient number	2051
Demographics:	68-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade $\geq$ 3 diarrhea		
Event 2 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was diagnosed with moderately differentiated, ER/PR positive and HER2 negative metastatic left breast cancer (T4bN2M1; histological subtype: not otherwise specified) on Study Day -47.

At screening site of disease involvement included left breast (2 lesions), left axillary lymph node, right pleura and bilateral lung. The patient was assessed by the Investigator to have visceral crisis.

No past cancer treatments were reported.

The patient′s medical history included chronic gastritis, chronic pancreatitis, cholelithiasis, chronic cholecystitis, hiatus hernia, gastroesophageal reflux disease, deafness neurosensory, cardiovascular somatic symptom disorder, intervertebral disc protrusion, seasonal allergy,

autoimmune thyroiditis, goitre, varicose vein, gout and vaginal prolapse. No surgical history was reported. Concurrent conditions included hypertension, breast pain, asthenia, and anxiety.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included enalapril, levothyroxine and loperamide.

On the same day (Study Day 1), the patient started receiving loperamide prophylactically (total daily dose: 2 mg).

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 8.

On Study Day 9, the patient experienced non-serious Grade 1 (initial intensity) diarrhea and Grade 2 asthenia (non-serious, related). On Study Day 43, she was reported with Grade 1 discolored feces (non-serious, related to ipatasertib) and worsening of diarrhea to most extreme Grade 3 intensity. Stool culture was performed (results not provided). She received treatment with loperamide. Grade changes and loperamide treatment details for the event of diarrhea reported in the table below. On Study Day 45, she experienced Grade 1 flatulence (non-serious, related to ipatasertib). On Study Day 127, the event of discolored feces was considered resolved. On Study Day 140, the events of diarrhea and flatulence were considered resolved.

Grade changes for diarrhea:

Study Day	Grade changes for diarrhea
43	3
45	1
72	2
73	1
78	2
79	1

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of diarrhea	2	PO	1	141
Diarrhea	4	PO	43	43
Diarrhea	2	PO	72	78

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of diarrhea	2	PO	163	163
Prophylaxis of diarrhea	2	PO	179	179
Prophylaxis of diarrhea	2	PO	183	183
Diarrhea	2	PO	215	220

Due to the event of diarrhea, ipatasertib dose was reduced to 300 mg on Study Day 86 and paclitaxel dose was reduced to 65 mg/m^2 from Study Day 92.

The Investigator considered diarrhea to be related to paclitaxel and ipatasertib.

The patient developed Grade 1 peripheral sensory neuropathy (non-serious, related to paclitaxel) from Study Day 43 to Study Day 56 for which she did not receive any treatment.

Event 2: Peripheral sensory neuropathy

Prior to the event of peripheral sensory neuropathy, the most recent dose of paclitaxel was administered on Study Day 71 and ipatasertib (400 mg) on Study Day 73.

On Study Day 74, the patient was diagnosed with Grade 1 (initial intensity) peripheral sensory neuropathy (presenting symptoms not reported). Grade changes for the event of peripheral sensory neuropathy are reported in the table below. She received treatment with vitamin B1 in combination with vitamin B6 and/or vitamin B12 and meloxicam.

Grade changes for peripheral sensory neuropathy:

Study Day	Grade changes for peripheral sensory neuropathy
102	3
110	2
268	3
415	2

Due to the event of peripheral sensory neuropathy, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 267.

The Investigator considered peripheral sensory neuropathy to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 397, a radiographic response assessment showed disease progression.

On Study Day 400, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 392. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Exemestane and everolimus	419	Ongoing

On Study Day 898, the events of peripheral sensory neuropathy and asthenia were considered resolved.

On Study Day 1269, the patient was permanently discontinued from the study as per physician's and Sponsor's decision.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nausea	1	Non-serious	30	145	Related	Related
Arthralgia	1	Non-serious	43	62	Related	Related
Rash	1	Non-serious	44	51	Related	Related
Onycholysis	1	Non-serious	64	127	Unrelated	Related
Onycholysis	1	Non-serious	64	127	Unrelated	Related
Dysgeusia	2	Non-serious	72	78	Unrelated	Related
Lip dry	1	Non-serious	94	316	Related	Related
Vertigo	1	Non-serious	101	106	Related	Related
Onychoclasis	2	Non-serious	113	428	Related	Related
Arthralgia	2	Non-serious	121	372	Unrelated	Related
Lacrimation increased	1	Non-serious	134	322	Related	Related
Edema peripheral	1	Non-serious	160	898	Related	Related
Abdominal distension	1	Non-serious	163	163	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Abdominal distension	1	Non-serious	179	179	Related	Unrelated
Abdominal distension	1	Non-serious	183	183	Related	Unrelated
Diarrhea	2	Non-serious	215	220	Related	Unrelated
Rash	1	Non-serious	220	239	Related	Related
Constipation	1	Non-serious	240	344	Unrelated	Related
Pulmonary hypertension	1	Non-serious	400	Resolving	Related	Unrelated

Study Number/CRTN:	CO40016/304335	Patient number	2064
Demographics:	48-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Category:	Anemia AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Gamma-glutamyl transferase increased Grade $\geq$ 3 hepatotoxicity		
Event 3 (PT) Category:	Leukopenia AE leading to study treatment discontinuation		
Event 4 (PT) Category:	Neutropenia AE leading to study treatment discontinuation		

The patient was randomized on Study Day −1.

The patient was diagnosed with ductal, ER/PR positive and HER 2 negative, locally advanced unresectable, metastatic left breast cancer (T1N0M1; histological grade unknown) on Study Day −377.

At screening, sites of disease involvement included left breast, multiple bone lesions and bilateral pleural nodules. The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Metastatic	Bone: Sacrum (8 cGy, 1 fraction)	−363	−363
Radiotherapy	Metastatic	Bone: D10 (8 cGy, 1 fraction)	−358	−358
Cancer therapy	Metastatic	Ribociclib, letrozole and goserelin	−327	−63

No medical or surgical history was reported. Concurrent conditions included hypertension and headache.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included denosumab and chlorphenamine.

On Study Day 28, the patient was noted to have Grade 1 gamma-glutamyl transferase increased (non-serious, unrelated, GGT value not reported). No treatment was given for this event.

Event 1: Anemia
Event 2: Gamma-glutamyl transferase increased (GGT increased)

Event 3: Leukopenia
Event 4: Neutropenia

Prior to the event of anemia, the most recent dose of ipatasertib (400 mg) was administered on Study Day 21 and paclitaxel on Study Day 29.

On Study Day 35, the patient was diagnosed with non-serious Grade 1 anemia (hemoglobin: 11.6 g/dL). She received treatment with epoetin alfa and lactoferrin for anemia. On the same day (Study Day 35), Grade 1 event of gamma-glutamyl transferase increased was considered resolved.

Prior to the event of gamma-glutamyl transferase increased, the most recent dose of paclitaxel was administered on Study Day 36 and ipatasertib (400 mg) on Study Day 42.

On Study Day 43, the patient was noted with Grade 1 alanine aminotransferase increased (non-serious, unrelated; ALT 59 U/L) and non-serious Grade 2 (initial intensity) gamma-glutamyl transferase increased (GGT value not reported). On Study Day 52, the event of gamma-glutamyl transferase increased worsened to Grade 3. On Study Day 57, the event of alanine aminotransferase increased was considered resolved. No treatment was reported for these events. Relevant laboratory work-up is detailed in the table below.

Prior to the events of leukopenia and neutropenia that led to paclitaxel discontinuation, the patient was noted with multiple non-serious events of leukopenia and neutropenia detailed in the table below. She received GCSF prophylactically on Study Day 174 and Study Day 229. Relevant laboratory work-up is detailed in the table below.

Event	Most extreme grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Action taken (Ipatasertib)	Action taken (Paclitaxel)
Neutropenia	2	14	28	Unrelated	Unrelated	None	Cycle 1 Day 15 interrupted and next dose was given on Study Day 29 (Cycle 2 Day 1)
Leukopenia	2	14	28	Unrelated	Unrelated	None	None
Leukopenia	2	42	52	Related	Related	None	None
Neutropenia	2	43	52	Related	Related	None	None
Neutropenia	1	70	84	Unrelated	Unrelated	Dose reduced to 300 mg from Study Day 85	Cycle 3 Day 15 interrupted and next dose was given on Study Day 85 (Cycle 4 Day 1)
Leukopenia							
Leukopenia	2	98	112	Unrelated	Related	None	Cycle 4 Day 15 interrupted and next dose was given on Study Day 113 (Cycle 5 Day 1)
Neutropenia				Unrelated	Unrelated		
Leukopenia	1	126	147	Unrelated	Unrelated	None	None
Neutropenia	2	126	147	Unrelated	Unrelated	None	None
Leukopenia	2	126	182	Related	Unrelated	None	None
Neutropenia	1	175	182	Related	Related	None	None
Leukopenia	2	203	231	Unrelated	Related	None	None
Neutropenia	1	210	224	Related	Related	None	None

Prior to the event of leukopenia and neutropenia which led to study treatment discontinuation, the most recent dose of paclitaxel was administered on Study Day 260 and ipatasertib (300 mg) was administered on Study Day 265.

On Study Day 266, the patient was noted to have non-serious Grade 2 leukopenia and Grade 1 neutropenia (WBC count and neutrophil count for this day not reported). No treatment was reported for these events. Relevant laboratory work-up is detailed in the table below. On study Day 367, the event of gamma glutamyl transferase increased was considered resolved. On Study Day 394, the events of neutropenia and leukopenia were considered resolved. On Study Day 507, the event of anemia was considered resolved.

Relevant chemistry work-up:

Study Day	**AST** Normal range 4-32 U/L	**ALT** Normal range 4-33 U/L	**Total bilirubin** Normal range: 0-1.2 mg/dL	**ALP** Normal range: 35-105 U/L
Screening	21	33	0.50	62
35	19	44	0.50	54
43	28	59	0.30	73
57	16	29	0.50	75
70	17	28	0.30	62
84	18	25	0.50	86
98	17	25	0.50	64
112	17	26	0.50	76
140	16	23	0.40	77
168	15	26	0.40	84
196	16	21	0.4	81
224	14	24	0.50	87
252	16	22	0.30	82
282	15	29	0.40	74
311	21	23	0.50	74
337	19	18	0.5	60
338	15	24	0.30	56
394	14	20	0.5	66

Study Day	AST Normal range 4-32 U/L	ALT Normal range 4-33 U/L	Total bilirubin Normal range: 0-1.2 mg/dL	ALP Normal range: 35-105 U/L
423	23	29	0.6	93

Relevant hematology work-up:

Study Day	Hemoglobin Normal range: 12-16 g/dL	WBC count Normal range: 4.8-10.8 $\times$ $10^3/\mu L$	Neutrophil count Normal range: 1.9-8$\times 10^3/\mu L$
Screening	12.9	4.87	3.1
28	12.3	6.97	4.8
35	11.6	5.55	3.9
43	11.9	2.59	1.3
57	11.2	4.13	2.7
70	11.1	2.71	1.7
84	11.2	4.05	2.4
98	12.2	2.75	1.4
112	12.6	5.75	3.2
140	11.3	2.53	1.3
168	11.1	3.73	2.3
196	10.7	4.89	3.2
224	11	3.95	2.3
252	10.2	4.26	2.5
282	11.1	3.41	1.8
311	11.3	4.7	2.4
338	11.4	4.86	2.9
367	11.5	3.26	1.8
394	11.6	3.59	2.2
423	11.4	3.93	2.3

There was no change in study treatment due to the event of gamma-glutamyl transferase increased.

Due to the events of anemia, leukopenia and neutropenia, there was no change in the study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 267.

The investigator considered anemia to be related to paclitaxel, ipatasertib and other causes (unspecified).

The investigator considered gamma-glutamyl transferase increased to be unrelated to paclitaxel and ipatasertib and related to other causes (unspecified).

The investigator considered neutropenia and leucopenia to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 1361, the patient was permanently discontinued from the study as the patient entered post trial access program.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	2	6	24	Related	Unrelated
Aspartate aminotransferase increased	1	14	28	Unrelated	Unrelated
Alanine aminotransferase increased	1	14	28	Unrelated	Unrelated
Diarrhea	1	24	36	Unrelated	Unrelated
Erythema	2	29	36	Unrelated	Unrelated
Blood triglycerides increased	2	35	52	Unrelated	Unrelated
Diarrhea	2	40	40	Related	Related
Paresthesia	1	54	64	Unrelated	Unrelated
Blood triglycerides increased	2	57	70	Unrelated	Unrelated
Diarrhea	2	57	Unresolved	Unrelated	Unrelated
Hypercholesterolemia	1	63	84	Unrelated	Unrelated
Blood triglycerides increased	2	84	98	Unrelated	Unrelated
Abdominal pain	1	85	89	Unrelated	Unrelated
Constipation	1	85	89	Unrelated	Unrelated
Abdominal pain	1	91	91	Unrelated	Unrelated
Abdominal pain	1	99	141	Unrelated	Unrelated

Event	Most extreme grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Dyspepsia	1	99	127	Unrelated	Unrelated
Blood triglycerides increased	2	112	175	Unrelated	Unrelated
Pyrexia	1	130	131	Unrelated	Unrelated
Pyrexia	1	159	161	Unrelated	Unrelated
Blood cholesterol increased	1	168	182	Related	Related
Blood thyroid stimulating hormone increased	1	168	196	Related	Related
Neuropathy peripheral	1	170	197	Related	Related
Hypertension	1	191	204	Unrelated	Unrelated
Blood triglycerides increased	2	203	252	Unrelated	Unrelated
Nail disorder	2	253	282	Related	Related
Myalgia	1	253	282	Related	Related
Abdominal pain	2	253	260	Related	Related
Dyspepsia	2	253	260	Related	Related
Hypercholesterolemia	1	282	394	Unrelated	Unrelated
Blood triglycerides increased	2	282	394	Unrelated	NA
Mucosal inflammation	2	359	373	Related	NA
Hypertriglyceridemia	1	570	Unresolved	Related	NA
Flatulence	1	598	598	Unrelated	NA
Hypercholesterolemia	1	654	682	Related	NA
Sinus tachycardia	1	924	924	Unrelated	NA
Vomiting	1	924	924	Related	NA
Abdominal pain upper	1	1000	1000	Unrelated	NA
Gamma-glutamyltransferase increased	1	1046	Unresolved	Unrelated	NA
Hyperuricemia	1	1102	1165	Unrelated	NA

Study Number/CRTN:	CO40016/304335	Patient number	2072
Demographics:	53-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Diarrhea AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Paresthesia AE leading to study treatment discontinuation		
Event 3 (PT) Category:	Blood creatine phosphokinase increased SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304792	Patient number	2085
Demographics:	58-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was diagnosed with poorly differentiated, ER/PR positive and HER2 negative, metastatic right breast cancer (T3N0M1; histological subtype not otherwise specified) on Study Day −84.

At screening, sites of disease involvement included lymph nodes (prominent lymph nodes in axillary and intraperitoneal regions), diffuse asymmetry in the upper quadrant of the right breast, lung (rare micronodules distributed by the pulmonary cortex, non-specific) and bone (disseminated bone blast lesions, lytic lesions in frontal bone and in the vertebral body of D4). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Metastatic	Zoledronic acid and anastrozole	−56	−26
Radiotherapy	Metastatic	Lumbar spine (dose unknown, 1 fraction)	−28	−15

No medical or surgical history was reported. Concurrent conditions included hypertension, dyslipidemia, labyrinthitis and arthralgia.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included amiloride/hydrochlorothiazide, codeine/paracetamol and rosuvastatin.

Event: Neuropathy peripheral (Peripheral neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel was administered on Study Day 72 and ipatasertib (400 mg) on Study Day 79.

On Study Day 86, the patient was diagnosed with Grade 1 (initial intensity) neuropathy peripheral (signs and symptoms not reported). On Study Day 134, the event of neuropathy peripheral worsened to Grade 2, which further worsened to Grade 3 on Study Day 162. No treatment was reported for the event. The event of neuropathy peripheral remained unresolved at the time of patient′s death.

Due to the event of neuropathy peripheral, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 161.

The Investigator considered neuropathy peripheral to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 232, a radiographic response assessment showed disease progression with new lesions in right liver (secondary aspect lesions).

On Study Day 253, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose of administered on the same day (Study Day 253). The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Cisplatin and gemcitabine	254	304
Anastrozole	329	366

On Study Day 367, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Asthenia	1	Non-serious	3	Unresolved	Unrelated	Related
Vomiting	1	Non-serious	11	11	Unrelated	Related
Leukopenia	3	Non-serious	15	57	Unrelated	Related
Neutropenia	3	Non-serious	15	16	Unrelated	Related
Alopecia	2	Non-serious	35	Unresolved	Unrelated	Related
Vomiting	1	Non-serious	72	73	Unrelated	Related
Diarrhea	2	Non-serious	77	88	Related	Unrelated
Anemia	1	Non-serious	97	118	Unrelated	Related
Bone pain	2	Non-serious	105	Unresolved	Unrelated	Unrelated
Diarrhea	1	Non-serious	129	219	Related	Related

Study Number/CRTN:	CO40016/304332	Patient number	2098
Demographics:	57-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Rash erythematous AESI: Grade ≥ 3 rash		
Event 2 (PT) Category:	Aspartate aminotransferase increased AESI: Grade ≥ 3 hepatotoxicity		

Event 3 (PT) Categories:	Alanine aminotransferase increased AE leading to study treatment discontinuation, AESI: Grade ≥ 3 hepatotoxicity

The patient was randomized on Study Day 1.

The patient was initially diagnosed with lobular, moderately differentiated, ER/PR positive and HER2 negative left breast cancer (T2N0M0), approximately 9 years prior to study entry following right radical mastectomy.

On Study Day -438, the patient was diagnosed with metastatic disease (ER and PR status was unknown and HER2 status was not assessed in metastatic tissue). At screening sites of disease involvement included bone (chest bone, C7, bilateral head of the shoulder bones, body of lumbar vertebra, bilateral pelvis and head of the left femur) and liver (S6 and S8). The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Tamoxifen	Approximately 9 years prior to study entry	Approximately 7 years prior to study entry
Cancer therapy	Metastatic	Letrozole	−430	−62

No medical or other surgical history was reported. Concurrent conditions included chronic gastritis and pain.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medication ongoing at Study Day 1 was reported.

Event 1: Rash erythematous (Erythematosus rash on whole body)

Prior to the event of rash erythematous, the most recent dose of paclitaxel was administered on Study Day 15 and ipatasertib (400 mg) on Study Day 19.

On Study Day 20, the patient experienced Grade 3 rash erythematous on whole body. She received treatment with chloropyramine. On Study Day 37, the event of rash erythematous was considered as resolved.

Due to the event of rash erythematous; there was no change in study treatment with paclitaxel; however, ipatasertib was interrupted on Study Day 28 and resumed on Study Day 38 at a reduced dose of 300 mg.

The Investigator considered rash erythematous to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 129, a laboratory work-up showed Grade 2 aspartate aminotransferase increased (non-serious, related; AST 102 U/L) and Grade 2 alanine aminotransferase increased (non-serious, unrelated; ALT 127 U/L). The patient received treatment with *Cynara cardunculus* extract, arginine citrate/betaine/betaine hydrochloride and phospholipids. On Study Day 148, the events of AST and ALT increased were considered resolved.

Event 2: Aspartate aminotransferase increased (High level of AST)
Event 3: Alanine aminotransferase increased (High level of ALT)

Prior to the events of aspartate aminotransferase increased and alanine aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 178 and ipatasertib (200 mg) on Study Day 184.

On Study Day 185, a laboratory work-up showed non-serious Grade 2 aspartate aminotransferase increased (AST 95 U/L) and Grade 2 alanine aminotransferase increased (ALT 96 U/L). The patient received treatment with *Cynara cardunculus* extract, arginine citrate/betaine/betaine hydrochloride and phospholipids for the events of AST and ALT increased. On Study Day 192, the events of ALT and AST increased worsened to Grade 3. On Study Day 199, the event of ALT increased and AST increased improved to Grade 2. On Study Day 207, the events of AST and ALT increased were considered as resolved.

Due to the events of AST and ALT increased, study treatment with paclitaxel (Cycle 7 Day 1 and Day 8) was interrupted and the next dose was administered on Study Day 207.

Due to the event of AST increased, there was no change in study treatment with ipatasertib; however, due to the event of ALT increased, ipatasertib was permanently discontinued with the last dose administered on Study Day 191.

The Investigator considered AST increased to be unrelated to ipatasertib and related to paclitaxel and concurrent illness.

The Investigator considered ALT increased to be unrelated to paclitaxel and related to ipatasertib and disease under study.

Relevant laboratory work-up:

Study Day	**AST** Normal range: 8-33 U/L	**ALT** Normal range: 4-36 U/L	**Total bilirubin** Normal range: 4.27-20.52 μmol/L	**ALP** Normal range: 42-98 U/L
Screening	104	52	13.2	227.3
129	102	127	13	187.7
135	114	162	14.8	225.9
143	93	127	11.7	301
148	74	66	12.4	268
185	95	96	12.8	195
192	192	196	13	253
199	101	110	11.4	270.9
207	88	73	12	290.4

On Study Day 225, radiographic response assessment showed disease progression.

On Study Day 246, study treatment with paclitaxel was permanently discontinued due to disease progression with the last dose administered on Study Day 221. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Doxorubicin	260	401
Eribulin	465	523
Tamoxifen	550	708
Fulvestrant	709	Ongoing

On Study Day 991, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious/Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Diarrhea	2	Non-serious	8	84	Related	Unrelated

Event	Most extreme grade	Serious/Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Fatigue	2	Non-serious	20	39	Related	Unrelated
Alopecia	2	Non-serious	23	211	Unrelated	Related
Anemia	2	Non-serious	64	135	Related	Related
Back pain	1	Non-serious	66	66	Unrelated	Unrelated
Pain	1	Non-serious	94	121	Unrelated	Unrelated
Spinal pain	1	Non-serious	122	198	Unrelated	Unrelated
Amylase increased	2	Non-serious	129	135	Unrelated	Unrelated
Blood cholesterol increased	2	Non-serious	192	199	Related	Unrelated
Anemia	2	Non-serious	221	233	Unrelated	Related

Study Number/CRTN:	CO40016/304789	Patient number	2101
Demographics:	73-year-old Black or African American female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Dizziness AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with tubular, well differentiated, ER/PR positive and HER2-negative left breast cancer (T3N2M1) on Study Day −109.

On Study Day −11, the metastatic tissue showed ER positive, PR unknown and HER2-negative disease. At screening, sites of disease involvement included lymph nodes (right upper paratracheal and left axilla), pleura (left superior lobe and left pulmonary base), bone, and lung (left medial lobe), and left breast (junction of internal quadrants). The patient was assessed by the Investigator to have visceral crisis.

No past cancer treatment was reported.

The patient′s medical history included cholecystitis acute. Concurrent conditions included hypertension and anemia.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included amlodipine and furosemide.

Event: Dizziness

Prior to the event of dizziness, the most recent dose of paclitaxel was administered on Study Day 772 and ipatasertib (400 mg) on Study Day 904.

On Study Day 907, the patient experienced non-serious Grade 2 dizziness. No treatment was reported for this event. The event of dizziness remained unresolved at the time of study discontinuation.

Due to this event, there was no change in study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 772.

The Investigator considered dizziness, to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 1234, a radiographic response assessment showed disease progression with new lesion in bilateral bone.

On Study Day 1256, the patient was diagnosed with symptomatic deterioration due to bone pain.

On Study Day 1285, study treatment with ipatasertib and study was permanently discontinued due to disease progression with the last dose of ipatasertib administered on Study Day 1162.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Headache	1	Non-serious	6	6	Related	Related
Alopecia	1	Non-serious	21	941	Related	Related
Diarrhea	2	Non-serious	38	44	Related	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	2	Non-serious	63	63	Related	Related
Diarrhea	2	Non-serious	66	72	Related	Related
Bone pain	2	Non-serious	71	71	Unrelated	Unrelated
Paraesthesia	1	Non-serious	73	207	Related	Related
Diarrhea	2	Non-serious	124	135	Related	Related
Anemia	2	Non-serious	144	Unresolved	Related	Related
Neck pain	1	Non-serious	145	173	Unrelated	Unrelated
Vomiting	1	Non-serious	150	152	Related	Related
Diarrhea	1	Non-serious	152	173	Related	Related
Diarrhea	2	Non-serious	179	180	Related	Related
Hypernatremia	1	Non-serious	200	207	Related	Related
Edema peripheral	1	Non-serious	200	207	Related	Related
Edema peripheral	1	Non-serious	243	269	Related	Related
Peripheral sensory neuropathy	2	Non-serious	290	301	Related	Related
Nail discoloration	2	Non-serious	294	941	Related	Related
Rhinitis	1	Non-serious	296	393	Unrelated	Unrelated
Oropharyngeal pain	1	Non-serious	316	336	Unrelated	Unrelated
Cough	1	Non-serious	316	350	Unrelated	Unrelated
Myalgia	1	Non-serious	316	336	Unrelated	Unrelated
Peripheral sensory neuropathy	2	Non-serious	341	Unresolved	Related	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Cough	1	Non-serious	350	377	Unrelated	Unrelated
Lacrimation increased	2	Non-serious	372	408	Related	Related
Visual acuity reduced	2	Non-serious	372	1077	Related	Related
Dry eye	1	Non-serious	408	485	Related	Related
Edema peripheral	1	Non-serious	432	Unresolved	Unrelated	Unrelated
Hypotension	1	Non-serious	435	441	Unrelated	Unrelated
Back pain	1	Non-serious	451	Unresolved	Related	Related
Pain in extremity	2	Non-serious	473	Unresolved	Related	Related
Peripheral motor neuropathy	2	Non-serious	494	Unresolved	Unrelated	Related
Lacrimation increased	2	Non-serious	494	1077	Related	Related
Headache	1	Non-serious	533	546	Related	Related
Paronychia	2	Non-serious	535	716	Related	Related
Cough	1	Non-serious	554	569	Related	Related
Diarrhea	1	Non-serious	588	589	Related	Related
Onychomadesis	1	Non-serious	631	884	Related	Related
Anemia	1	Non-serious	667	912	Related	Related
Disturbance in attention	1	Non-serious	707	Unresolved	Related	Related
Cataract	2	Non-serious	738	1077	Related	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Extrasystoles	2	Non-serious	800	884	Related	Related
Insomnia	2	Non-serious	950	Unresolved	Related	Unrelated
Anal hemorrhage	2	Non-serious	955	Unresolved	Related	Unrelated

Study Number/CRTN:	CO40016/304195	Patient number	2107
Demographics:	70-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Categories:	Cerebrovascular accident SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/305252	Patient number	2116
Demographics:	78-year-old female (Race unknown)		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		
Event 2 (PT) Categories:	Diarrhea SAE, AESI: Grade $\geq$ 3 diarrhea		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304777	Patient number	2121
Demographics:	71-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative metastatic right breast cancer (T2N2aM1) on Study Day –46.

At screening, sites of disease involvement included bone (bilateral, multiple metastatic lesions), chest (bilateral cardial effusion), lung (bilateral, metastatic lesions), right breast and right axillary lymph node. The patient was assessed by the Investigator to have visceral crisis.

No past cancer treatment was reported.

No medical or surgical history and concurrent condition was reported.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included denosumab.

Event: Peripheral sensory neuropathy

Prior to the event of peripheral sensory neuropathy, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 36.

On Study Day 36, the patient was diagnosed with non-serious Grade 2 (initial intensity: Grade 1) peripheral sensory neuropathy (presenting signs and symptoms not reported). Reportedly, the event was considered as local infusion site reaction. No treatment was administered for this event. The event of peripheral sensory neuropathy remained unresolved at the time of patient's death (see narrative below).

Due to the event of peripheral sensory neuropathy, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 119.

The Investigator considered peripheral sensory neuropathy to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 140, study treatment with ipatasertib was permanently discontinued as per physician′s decision (as paclitaxel was discontinued and the ipatasertib was blind treatment it means subject had risk without treatment) with the last dose administered on Study Day 132. The patient entered into long-term follow-up.

On Study Day 336, a radiographic response assessment showed disease progression.

On Study Day 338, a repeat radiographic response assessment showed disease progression with new lesions in brain (bilateral cerebellar hemispheres with leptomeningeal carcinomatosis along the fissure at the superior aspect).

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Cyclophosphamide and epirubicin	140	203
Cyclophosphamide and liposomal doxorubicin	231	322
Radiotherapy to whole brain (total dose: 3000 cGy, 12 fraction)	354	373

On Study Day 505, the patient died due to disease progression. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious/ non-serious**	**Onset Day**	**Resolution Day/ Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Mouth ulceration	2	Non-serious	93	Unresolved	Unrelated	Unrelated
Chest discomfort	2	Non-serious	93	Unresolved	Unrelated	Unrelated
Medication error	1	Non-serious	112	132	Unrelated	Unrelated
Arthralgia	2	Non-serious	133	Unresolved	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305633	Patient number	2122
Demographics:	70-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Categories:	COVID-19 SAE, AE leading to study treatment discontinuation, COVID-19 SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304623	Patient number	2126
Demographics:	72-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade $\geq$ 3 diarrhea		
Event 2 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative right breast cancer (T4bN1M0), approximately 5 years prior to study entry.

On Study Day –46, the patient was diagnosed with metastatic disease (PR receptor status unknown, ER and HER2 status was not evaluated in metastatic tissue). At screening, sites of disease involvement included lung (right lung hilus and segment 3 of left lung), multiple lesions in bone and lymph nodes (midline of para-trachealis on mediastinum and liver hilus). The patient was assessed by the Investigator to have visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neo-adjuvant	Doxorubicin, cyclophosphamide and paclitaxel	Approximately 5 years prior to study entry	Approximately 5 years prior to study entry
Surgery	Diagnostic	Right axillary lymph node dissection	Approximately 4 years 9 months prior to study entry	NA
Surgery	Curative	Right partial mastectomy and right axillary lymph node dissection	Approximately 4 years 9 months prior to study entry	NA
Cancer therapy	Adjuvant	Tamoxifen	Approximately 4 years 8 months prior to study entry	Approximately 4 years 4 months prior to study entry
Radiotherapy	Adjuvant	Breast (boost) (total dose: 10 cGy; 25 fractions)	Approximately 4 years 4 months prior to study entry	Approximately 4 years 3 months prior to study entry
Radiotherapy	Adjuvant	Breast (total dose: 50 cGy; 25 fractions)	Approximately 4 years 4 months prior to study entry	Approximately 4 years 2 months prior to study entry
Cancer therapy	Adjuvant	Anastrozole	Approximately 4 years 3 months prior to study entry	−54
Cancer therapy	Adjuvant	Anastrozole	−448	−54

The patient's medical history included nephritis. Other surgical history included tooth extraction, cholecystectomy and carpal tunnel decompression. Concurrent conditions included insomnia, neuropathy peripheral, arthralgia, cough, stress urinary incontinence, liver disorder, gastric ulcer, dyspnea exertional and rosacea.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. On the same day (Study Day 1), she received loperamide prophylactically (total daily dose: 2 mg).

Concomitant medications ongoing at Study Day 1 included zolpidem, calcium/cholecalciferol and magnesium lactate/magnesium pidolate/pyridoxine.

The patient experienced Grade 2 diarrhea (non-serious, related to ipatasertib) on Study Day 9 for which she received treatment with loperamide.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea prophylaxis	2	PO	1	1
Diarrhea	2	PO	9	10

On Study Day 50, the patient was diagnosed with Grade 1 peripheral neuropathy in the upper extremity (presenting signs and symptoms not reported, non-serious, related to paclitaxel). On Study Day 71, she started treatment with curcumin/lecithin/*Mangifera indica*/*Piper nigrum*/pyridoxine /resveratrol/riboflavin. On Study Day 127, the event of peripheral neuropathy in the upper extremity worsened to Grade 2.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 148 and ipatasertib (400 mg) on Study Day 151.

On Study Day 152, the patient experienced non-serious Grade 3 diarrhea. No diagnostic test was performed. She received treatment with activated charcoal. On the same day (Study Day 152), the event of diarrhea was considered resolved.

There was no change in the study treatment due to the event of diarrhea.

The Investigator considered diarrhea to be related to paclitaxel and unrelated to ipatasertib.

Event 2: Neuropathy peripheral (Peripheral neuropathy of the lower extremity)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel was administered on Study Day 183 and ipatasertib (400 mg) on Study Day 189.

On Study Day 198, the patient was diagnosed with non-serious Grade 2 neuropathy peripheral of the lower extremity (presenting signs and symptoms not reported). Treatment with curcumin/lecithin/*Mangifera indica/Piper nigrum*/pyridoxine /resveratrol/riboflavin was maintained for neuropathy peripheral. On Study Day 312, the events of neuropathy peripheral in upper and lower extremity were considered as resolved.

Due to the event of neuropathy peripheral (lower extremity), there was no change in the study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 267.

The Investigator considered neuropathy peripheral to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 331, a radiographic response assessment showed disease progression with new lesions in bone (6^{th} rib, TH 4 and manubrium of sternum).

On Study Day 337, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 331. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Fulvestrant	365	Ongoing

On Study Day 1123, the patient was permanently discontinued from the study as LTFU terminated by Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Headache	1	Non-serious	1	1	Unrelated	Related
Flatulence	1	Non-serious	1	8	Unrelated	Unrelated
Arthralgia	2	Non-serious	3	Resolving	Unrelated	Unrelated
Pollakiuria	1	Non-serious	5	6	Unrelated	Unrelated
Rash	1	Non-serious	11	25	Unrelated	Unrelated
Neutropenia	2	Non-serious	15	28	Unrelated	Related
Fatigue	1	Non-serious	15	71	Unrelated	Related
Hemoptysis	1	Non-serious	25	25	Unrelated	Unrelated
Visual Impairment	1	Non-serious	25	Resolving	Unrelated	Unrelated
Alopecia	1	Non-serious	29	407	Unrelated	Related
Pyrexia	1	Non-serious	30	32	Unrelated	Unrelated
Hemoptysis	1	Non-serious	32	35	Unrelated	Unrelated
Nausea	1	Non-serious	54	56	Unrelated	Unrelated
Anemia	2	Non-serious	57	Resolving	Unrelated	Related
Rash	1	Non-serious	58	133	Related	Related
Hemoptysis	1	Non-serious	70	206	Unrelated	Unrelated
Fatigue	2	Non-serious	72	434	Unrelated	Related
Arthralgia	1	Non-serious	89	131	Unrelated	Unrelated
Dyspnoea	1	Non-serious	92	Resolving	Unrelated	Unrelated
Abdominal pain upper	1	Non-serious	99	Resolving	Unrelated	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Weight decreased	1	Non-serious	99	141	Unrelated	Unrelated
Vomiting	1	Non-serious	114	114	Unrelated	Related
Pain in extremity	1	Non-serious	130	336	Unrelated	Unrelated
Rhinitis	1	Non-serious	149	343	Unrelated	Related
Back Pain	2	Non-serious	173	174	Unrelated	Unrelated
Back Pain	1	Non-serious	175	190	Unrelated	Unrelated
Nasopharyngitis	2	Non-serious	185	199	Unrelated	Unrelated
Edema peripheral	1	Non-serious	220	307	Unrelated	Unrelated
Dyspepsia	1	Non-serious	227	307	Unrelated	Related
Neutropenia	2	Non-serious	239	253	Unrelated	Related
Abdominal pain upper	1	Non-serious	248	435	Unrelated	Unrelated
Diarrhea	1	Non-serious	270	271	Related	Unrelated
Weight decreased	1	Non-serious	310	Resolving	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304880	Patient number	2131
Demographics:	61-year-old Asian female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Alanine aminotransferase increased AESI: Grade $\geq$ 3 hepatotoxicity		
Event 2 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was diagnosed with ductal, well differentiated, ER/PR positive and HER2 negative, left breast cancer (T4dN3M1) on Study Day −607.

On Study Day -574, the metastatic tissue was ER/PR positive and HER2 receptor equivocal. At screening, sites of disease involvement included bone (multiple metastasis) and left breast. The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Metastatic	Letrozole	−572	−322
Cancer therapy	Metastatic	Tamoxifen	−152	−40

The patient′s medical history included herpes zoster. No surgical history was reported. Concurrent conditions included alanine aminotransferase increased, aspartate aminotransferase increased, hepatic steatosis, lymphedema, left breast injury, breast pain, hypertension, blood cholesterol increased and hyperglycemia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included amlodipine, amlodipine/hydrochlorothiazide/olmesartan medoxomil and acetylsalicylic acid.

Event 1: Alanine aminotransferase increased

On Study Day 1, a laboratory work-up revealed ALT 172 U/L (normal range: 5-46 U/L).

Prior to the event of Grade 3 alanine aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 7.

On Study Day 8, a laboratory work-up revealed ALT 233 U/L (normal range: 5-46 U/L) and the patient was reported with worsening of pre-existing condition of alanine aminotransferase increased to Grade 3 (non-serious). The Investigator considered the event as non-clinically significant. No treatment was given for this event. On Study Day 14, the event of Grade 3 ALT increased was considered as resolved (ALT value on Study Day 15 was 196 U/L).

Relevant laboratory work-up:

Study Day	AST Normal range: 13-34 U/L	ALT Normal range: 5-46 U/L	Total bilirubin Normal range: 0.4-1.5 mg/dL	ALP Normal range: 50-155 U/L
Screening	165	100	0.4	105
1	117	172	0.4	115
8	141	233	0.3	96

Study Day	AST Normal range: 13-34 U/L	ALT Normal range: 5-46 U/L	Total bilirubin Normal range: 0.4-1.5 mg/dL	ALP Normal range: 50-155 U/L
15	92	196	0.3	103
29	77	140	0.3	128
35	79	164	0.3	112
44	37	103	0.4	87

There was no change in the study treatment due to this event.

The Investigator considered alanine aminotransferase increased to be unrelated to ipatasertib and paclitaxel and related to concurrent illness.

Event 2: Neuropathy peripheral (Peripheral neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 29.

On Study Day 30, the patient was diagnosed with Grade 1 neuropathy peripheral (non-serious, presenting signs and symptoms not provided). She was started on treatment with pregabalin; however, on Study Day 85, the event of neuropathy peripheral worsened to Grade 2. On Study Day 128, the event of neuropathy peripheral further worsened to Grade 3. Treatment with pregabalin was maintained and on Study Day 196, the event of neuropathy peripheral improved to Grade 2.

Due to the event neuropathy peripheral, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 120.

The Investigator considered neuropathy peripheral to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 330, radiographic response assessment showed disease progression with new lesion in the liver (segment 5).

On Study Day 338, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 300. The patient entered long-term follow-up.

On Study Day 441, the event of neuropathy peripheral was considered as resolved.

The patient received follow-up anti-cancer therap as listed in table below:

Treatments	Start Day	Stop Day
Exemestane and everolimus	350	427

Radiotherapy to left chest wall, skin and left breast (dose: 5100 cGy, 15 fractions)	393	413
Radiotherapy to right pelvic bone L5 (dose: 2000 cGy, 7 fractions)	457	463
Capecitabine	497	–

On Study Day 882, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious/ Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Dyspepsia	1	Non-serious	2	60	Unrelated	Related
Constipation	1	Non-serious	3	37	Unrelated	Unrelated
Neutrophil count decreased	3	Non-serious	8	28	Unrelated	Related
Nausea	1	Non-serious	30	350	Unrelated	Related
Diarrhea	1	Non-serious	38	55	Related	Unrelated
Epistaxis	1	Non-serious	51	51	Unrelated	Unrelated
Urticaria	1	Non-serious	53	441	Unrelated	Related
Pyrexia	1	Non-serious	56	56	Unrelated	Unrelated
Rash	1	Non-serious	56	92	Unrelated	Related
Type 2 diabetes mellitus	1	Non-serious	63	Unresolved	Related	Unrelated
Amnesia	1	Non-serious	63	441	Unrelated	Unrelated
Edema	1	Non-serious	85	155	Unrelated	Related
Dizziness	1	Non-serious	86	149	Unrelated	Unrelated
Neutrophil count decreased	2	Non-serious	114	120	Unrelated	Related
Neutrophil count decreased	2	Non-serious	134	141	Unrelated	Related
Hypertriglyceridemia	2	Non-serious	141	309	Unrelated	Unrelated
Diarrhea	1	Non-serious	190	350	Related	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Abdominal pain	1	Non-serious	253	441	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305247	Patient number	2133
Demographics:	72-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Category:	Alanine aminotransferase increased AESI: Grade $\geq$ 3 hepatotoxicity		
Event 2 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative right breast cancer (T1N0MX), approximately 11 years prior to study entry.

On Study Day −729, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included lung (right and left upper lobe, multiple metastatic lesions) and bone (multiple metastatic lesions). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right breast lumpectomy	Approximately 11 years prior to study entry	NA
Cancer therapy	Adjuvant	Doxorubicin, fluorouracil, cyclophosphamide	Approximately 11 years prior to study entry	Approximately 10 years prior to study entry
Radiotherapy	Adjuvant	Breast (loco regional, dose and fractions unknown)	Approximately 10 years prior to study entry	Approximately 10 years prior to study entry
Cancer therapy	Adjuvant	Docetaxel	Approximately 10 years prior to study entry	Approximately 10 years prior to study entry
Cancer therapy	Adjuvant	Letrozole	Approximately 10 years prior to study entry	Approximately 5 years prior to study entry
Radiotherapy	Metastatic	Bone (sacrum; dose: 3000 cGy, 10 fractions)	−719	−702
Cancer therapy	Metastatic	Tamoxifen	−714	−666
Radiotherapy	Metastatic	Bone (sacrum; dose: 3000 cGy, 10 fractions)	−694	−679
Cancer therapy	Metastatic	Fulvestrant	−665	−218
Cancer therapy	Metastatic	Everolimus and exemestane	−218	−23

The patient′s medical history included uterine leiomyoma, scoliosis and tendon injury. Other surgical history included hysterectomy. Concurrent conditions included peripheral sensory neuropathy, anxiety, insomnia, arthralgia, diarrhea, back pain, fatigue, rhinitis allergic, glaucoma, cataract, drug intolerance, drug intolerance and thrombosis.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included bimatoprost/timolol, brinzolamide/timolol, paracetamol, denosumab, calcium carbonate/cholecalciferol, lorazepam, carbomer, indomethacin and tinzaparin.

Event 1: Alanine aminotransferase increased

Prior to the event of alanine aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 5.

On Study Day 6, the patient was noted with non-serious Grade 3 alanine aminotransferase increased (ALT 269 U/L; normal range: 7-33 U/L). No treatment was given for this event. On Study Day 14, the event of ALT increased improved to Grade 2. On Study Day 21, the event of ALT increased further improved to Grade 1. Relevant laboratory values are given in the table below. On Study Day 33, the event of alanine aminotransferase increased was considered resolved.

Relevant laboratory work-up:

Study Day	**AST** Normal range: 8-33 U/L	**ALT** Normal range: 4-36 U/L	**Total Bilirubin** Normal range: 2-21 μmol/L	**ALP** Normal range: 35-104 U/L
Screening	19	44	7.9	79
6	88[a]	269[b]	10.8[c]	160[d]
13	26	108	6.5	114
20	19	76	6.8	104
23	21	64	9	95
26	11	40	9.5	95
33	9	22	7.2	79

[a]normal range: 7-32 U/L, [b]normal range: 7-33 U/L, [c]normal range: 0-15 μmol/L, [d]normal range: 35-105 U/L

Due to this event, study treatment with ipatasertib was interrupted on Study Day 8 and Cycle 1 Day 8 dose of paclitaxel was not administered. The next dose of paclitaxel and ipatasertib (at a reduced dose of 300 mg) was administered on Study Day 21.

The Investigator considered alanine aminotransferase increased, to be related to ipatasertib and paclitaxel.

Event 2: Peripheral sensory neuropathy (peripheral sensitive neuropathy)

Prior to the event of peripheral sensory neuropathy, the most recent dose of paclitaxel was administered on Study Day 168 and ipatasertib (300 mg) on Study Day 173.

On Study Day 174, the patient was diagnosed with worsening of her pre-existing condition of peripheral sensory neuropathy to non-serious Grade 3 (presenting signs and symptoms were not reported). On Study Day 183, she experienced Grade 1 pain in extremity (left leg, non-serious, related to paclitaxel). No treatment was given for these events.

Due to the event of peripheral sensory neuropathy, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 168.

On Study Day 297, the event of peripheral sensory neuropathy improved to Grade 2. On Study Day 363, the event of pain in extremity was considered resolved. The event of peripheral sensory neuropathy remained unresolved at the time of patient's death (see narrative below).

The Investigator considered peripheral sensory neuropathy to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 334, a radiographic response assessment showed disease progression with new lesions in liver (multiple).

On Study Day 335, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 328. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatment	Start Day	Stop Day
Capecitabine	347	474
Abemaciclib and fulvestrant	482	566
Eribulin	585	697
Cyclophosphamide	707	806
Radiotherapy to panencephalic brain (dose: 3750 cGy, 15 fractions)	770	790

On Study Day 877, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ non-serious	Onset Day	Resolution Day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Neutropenia	2	Non-serious	13	20	Unrelated	Related
Gastroesophageal reflux disease	1	Non-serious	22	24	Unrelated	Unrelated
Neutrophil count decreased	2	Non-serious	33	47	Related	Related
Gastroesophageal reflux disease	1	Non-serious	43	100	Unrelated	Unrelated
Rhinitis	2	Non-serious	49	102	Unrelated	Unrelated
Nasal congestion	2	Non-serious	56	111	Unrelated	Unrelated

Event	Most extreme grade	Serious/ non-serious	Onset Day	Resolution Day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Erythema	1	Non-serious	56	90	Unrelated	Unrelated
Epistaxis	1	Non-serious	57	120	Related	Related
Fatigue	2	Non-serious	63	67	Related	Related
Epistaxis	1	Non-serious	148	183	Related	Related
Arthralgia	1	Non-serious	156	183	Unrelated	Unrelated
Onychomadesis	2	Non-serious	168	296	Unrelated	Related
Edema peripheral	1	Non-serious	183	296	Unrelated	Related
Headache	1	Non-serious	183	214	Unrelated	Unrelated
Headache	1	Non-serious	240	296	Unrelated	NA
Back pain	1	Non-serious	240	363	Unrelated	NA
Neck pain	1	Non-serious	268	Unresolved	Unrelated	NA
Arthralgia	1	Non-serious	268	363	Unrelated	NA
Constipation	1	Non-serious	297	313	Unrelated	Unrelated
Nail disorder	1	Non-serious	297	363	Unrelated	Related
Orthostatic hypotension	1	Non-serious	298	363	Unrelated	Unrelated
Bone pain	1	Non-serious	298	304	Unrelated	Unrelated
Headache	1	Non-serious	318	363	Unrelated	NA

Study Number/CRTN:	CO40016/304786	Patient number	2136
Demographics:	48-year-old White male		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Anxiety SAE		
Event 2 (PT) Category:	Alanine aminotransferase increased AESI: Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Category:	Nausea AE leading to study treatment discontinuation		
Event 4 (PT) Category:	Asthenia AE leading to study treatment discontinuation		
Event 5 (PT) Category:	Fatigue AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/305629	Patient number	2139
Demographics:	39-year-old female (race unknown)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Hypertransaminasemia AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with poorly differentiated, ER/PR positive and HER 2 negative left breast cancer (T4cN2aM0; histological subtype: not otherwise specified) on Study Day −253.

On Study Day −58, the patient was diagnosed with locally advanced unresectable disease with ER/PR positive and HER2 negative disease in recurrent/metastatic tissue. At screening, sites of disease involvement included solid lesion in the upper external quadrant of the left breast, left axillary adenopathy and neck (ganglion with a fatty hilum of 1.3×1.1 cm in the right IB group).

No past cancer treatments were reported.

No medical or surgical history and concurrent conditions were reported.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing on Study Day 1 were reported.

Event: Hypertransaminasemia

Prior to the event of hypertransaminasemia, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 30 and Study Day 34, respectively.

On Study Day 35, laboratory work-up showed ALT 123 U/L (normal range: 6-40 U/L) and AST 144 U/L (normal range: 9-37 U/L). The patient was diagnosed with non-serious Grade 2 hypertransaminasemia. No treatment was given for this event. On Study Day 150, the event of hypertransaminasemia worsened to Grade 3.

Relevant laboratory work-up:

Study Day	**AST** Normal range: 9-37 U/L	**ALT** Normal range: 6-40 U/L	**Total bilirubin** Normal range: 0.1-1 mg/dL	**ALP** Normal range: 35-104 U/L
Screening	64	67	0.48	47
35	144	123	0.66	59
41	132	155	0.48	65
57	110	95	0.34	67
65	136	123	0.58	61
72	125	121	0.47	58
84	138	92	0.33	58
120	140	126	0.44	66
148	178	163	0.25	69
156	234	166	0.54	68
178	150	123	0.33	68

Due to the event of hypertransaminasemia, study treatment with paclitaxel and ipatasertib was permanently discontinued on Study Day 178 with the last dose of paclitaxel administered on Study Day 136 and ipatasertib on Study Day 142. The patient entered into long-term follow up.

The Investigator considered hypertransaminasemia, to be related to ipatasertib and unrelated to paclitaxel.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Surgery (left breast)	169	NA
Exemestane and leuprorelin	174	Ongoing
Radiotherapy to left breast (total dose: 50 cGy, 25 fractions)	259	291

On Study Day 381, the event of hypertransaminasemia was considered resolved.

On Study Day 1203, the patient was permanently discontinued from the study as the LTFU was terminated by Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Myalgia	2	Non-serious	4	15	Unrelated	Related
Diarrhea	1	Non-serious	5	25	Related	Unrelated
Nausea	2	Non-serious	8	28	Unrelated	Related
Neutropenia	1	Non-serious	14	28	Unrelated	Related
Hyperglycemia	1	Non-serious	14	14	Related	Unrelated
Influenza	1	Non-serious	35	42	Unrelated	Unrelated
Alopecia	2	Non-serious	36	244	Unrelated	Related
Diarrhea	1	Non-serious	94	98	Related	Unrelated
Neuropathy peripheral	1	Non-serious	103	Unresolved	Unrelated	Related

Study Number/CRTN:	CO40016/307260	Patient number	2142
Demographics:	74-year-old Asian female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Decreased appetite SAE		
Event 3 (PT) Category:	Erythema multiforme SAE		
Event 4 (PT) Category:	Decreased appetite SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304776	Patient number	2145
Demographics:	52-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER positive/PR negative and HER 2 positive right breast cancer (T1N1M0) (histological grade unknown), approximately 13 years prior to study entry followed by modified right radical mastectomy.

On Study Day −913, the patient was diagnosed with metastatic disease with ER/PR positive and HER 2 negative in metastatic tissue. At screening, sites of disease involvement included right lung (mediastinum and subcarinal), small pericardial effusion in mediastinum, chest (small left pleural effusion) and bone (osteolytic focus at the T 11 and distal sternum). The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Epirubicin, cyclophosphamide and fluorouracil	Approximately 13 years prior to study entry	Approximately 12 years prior to study entry
Cancer therapy	Adjuvant	Docetaxel	Approximately 12 years prior to study entry	Approximately 12 years prior to study entry
Surgery	Curative	Right partial mastectomy and right lymph node surgery	−882	NA
Cancer therapy	Metastatic	Tamoxifen	−872	−98
Radiotherapy	Metastatic	Right breast chest wall and supraclavicular region (dose: 4400 cGy, 22 fractions)	−827	−798
Cancer therapy	Metastatic	Letrozole and goserelin	−105	−18

The patient's medical history included cholelithiasis and insomnia. Surgical history included central venous catheterization. Concurrent condition included cough.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 was reported.

Event: Neuropathy peripheral (Neuropathy on both hands)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel was administered on Study Day 106 and ipatasertib (400 mg) on Study Day 112.

On Study Day 115, the patient was diagnosed with non-serious Grade 1 neuropathy peripheral of both hands (presenting sign and symptoms not reported). No treatment was given for this event. On Study Day 165, the event of neuropathy peripheral worsened to Grade 2. On Study Day 307, the event of neuropathy peripheral improved to Grade 1. The event of neuropathy peripheral remained unresolved at the time of study discontinuation.

Due to the event of neuropathy peripheral, study treatment with ipatasertib was interrupted on Study Day 172 and the next dose was administered in Study Day 179; however, study treatment with paclitaxel was permanently discontinued with the last dose administered on Study Day 158.

The Investigator considered neuropathy peripheral, to be unrelated to ipatasertib and related to paclitaxel and disease under study.

On Study Day 392, a radiographic response assessment showed disease progression with new lesions in bilateral lung and liver (multiple bilateral hepatic tumor).

On Study Day 396, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 360. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Vinorelbine and capecitabine	396	545
Bevacizumab, cisplatin and etoposide	568	–
Radiotherapy to whole brain (dose: 3000 cGy, 10 fractions)	606	617

On Study Day 1088, the patient was permanently discontinued from the study as LTFU terminated by Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ non-serious	Onset Day	Resolution Day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nausea	1	Non-serious	32	Unresolved	Unrelated	Related
Constipation	1	Non-serious	37	58	Unrelated	Unrelated
Chest discomfort	1	Non-serious	101	Unresolved	Unrelated	Unrelated
Rash	1	Non-serious	128	Unresolved	Unrelated	Related

Study Number/CRTN:	CO40016/304330	Patient number	2147
Demographics:	77-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Category:	Flushing AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Abdominal discomfort AE leading to study treatment discontinuation		
Event 3 (PT) Category:	Dyspnea AE leading to study treatment discontinuation		

The patient was randomized on Study Day −3.

The patient was initially diagnosed with ER/PR positive left breast cancer (TXN1M0; histological subtype not reported, histological grade unknown and HER2 status not assessed), approximately 30 years prior to study entry, followed by left radical mastectomy.

On Study Day −101, the patient was diagnosed with metastatic disease, with ER positive/ PR negative and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included liver (segment II and V) and left supraclavicular lymph node.

Past cancer treatment is listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Cyclophosphamide, methotrexate and fluorouracil	Approximately 30 years prior to study entry	Approximately 30 years prior to study entry

No medical history was reported. Other surgical history included hysterosalpingo-oophorectomy. Concurrent conditions included hypercholesterolemia and hypertension.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included ramipril, bisoprolol and rosuvastatin.

Event 1: Flushing (flushing of face and upper chest)
Event 2: Abdominal discomfort
Event 3: Dyspnea (mild dyspnea)

Prior to the events of flushing, abdominal discomfort and dyspnea, the most recent dose of ipatasertib (400 mg) was administered on Study Day 1.

On the same day (Study Day 1), scheduled Cycle 1 Day 1 infusion of paclitaxel was started. Prior to the paclitaxel infusion her vitals showed body temperature 36°C, pulse 70 beats/min, respiratory rate 18 breaths/min and blood pressure 120/80 mmHg. Later, during the paclitaxel infusion, the patient experienced non-serious Grade 2 flushing (face and upper chest), abdominal discomfort and dyspnea. She received treatment with chlorphenamine and hydrocortisone for these events. On the same day (Study Day 1), the events of flushing, abdominal discomfort and dyspnea were considered resolved.

Due to the events of flushing, abdominal discomfort and dyspnea, study treatment with ipatasertib and paclitaxel was permanently discontinued with the last dose administered on Study Day 1. The patient entered into long-term follow-up.

The Investigator considered flushing, abdominal discomfort and dyspnea to be unrelated to ipatasertib and related to paclitaxel.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatment	Start Day	Stop Day
Paclitaxel albumin	11	165

On Study Day 182, radiographic response assessment showed disease progression with new lesions in liver (segment VI and VIII).

The patient further received follow-up anti-cancer therapies with:

Treatments	Start Day	Stop Day
Pegylated liposomal doxorubicin	193	193
Eribulin	195	441
Capecitabine	484	–

On Study Day 1085, the patient was permanently discontinued from the study as LTFU was terminated by Sponsor.

No other AE were experienced by the patient during the study.

Study Number/CRTN:	CO40016/304880	Patient number	2148
Demographics:	74-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Categories:	Diarrhea SAE, AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Febrile neutropenia AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304622	Patient number	2150
Demographics:	76-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Categories:	Neutropenia SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/305252	Patient number	2152
Demographics:	69-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 3 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 4 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 5 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was diagnosed with tubular, poorly differentiated, ER/PR positive and HER2 negative metastatic right breast cancer (TXNXMX), approximately 4 years 4 months prior to study entry.

At screening, sites of disease involvement included lymph nodes (right adenopathy axillary and left adenopathy), skin (right cutaneous lesion), right breast and bone (right iliac wing). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	**Therapy Setting/Intent**	**Treatments details**	**Start Day**	**Stop Day**
Cancer therapy	Metastatic	Letrozole and denosumab	Approximately 3 years 7 months prior to study entry	−905
Radiotherapy	Metastatic	Right breast (20 cGy, 5 fractions)	Approximately 2 years 10 months prior to study entry	Approximately 2 years 10 months prior to study entry
Cancer therapy	Metastatic	Fulvestrant and denosumab	−877	−786

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Metastatic	Everolimus and exemestane	−665	−380
Cancer therapy	Metastatic	Palbociclib and fulvestrant	−296	−79

The patient′s medical history included inguinal hernia. Surgical history included hysterectomy. Concurrent conditions included hypertension, dyslipidemia, insomnia, and bone pain.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. On the same day (Study Day 1), she started receiving prophylactic loperamide (total daily dose: 2 mg) for diarrhea.

Concomitant medications ongoing at Study Day 1 included zopiclone, perindopril, lercanidipine, fluvastatin and atenolol.

Prior to onset of Grade 3 diarrhea (onset: Study Day 61), the patient experienced multiple non-serious events of diarrhea detailed in the table below. Treatment included loperamide (details reported in table below).

Most extreme Grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Action taken (Ipatasertib)	Action taken (Paclitaxel)
2	7	17	Related	Unrelated	Drug interrupted on Study Day 16 resumed on Study Day 29 at a reduced dose of 300 mg	None
1	33	33	Related	Unrelated	None	None
1	40	40	Related	Unrelated	None	None
2	43	45	Related	Related	None	None

Event 1: Neuropathy peripheral (neuropathy)

Prior to the event of peripheral neuropathy, the most recent dose of paclitaxel and ipatasertib (300 mg) was administered on Study Day 43.

On Study Day 44, the patient was diagnosed with Grade 2 (initial intensity) neuropathy peripheral (presenting symptoms not reported). No treatment was reported for this event. On Study Day 64, neuropathy peripheral improved to Grade 1. On Study Day 127, neuropathy peripheral worsened to Grade 2 which further worsened to Grade 3 on Study Day 197. On Study Day 405, the event of neuropathy peripheral was considered resolved.

Due to the event of neuropathy peripheral, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 183.

The Investigator considered neuropathy peripheral to be unrelated to ipatasertib and related to paclitaxel.

Event 2: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 57 and ipatasertib (300 mg) on Study Day 60.

On Study Day 61, the patient experienced non-serious Grade 2 diarrhea. On Study Day 62, she started receiving loperamide (total daily dose: 4 mg) and racecadotril. On Study Day 69, the event of diarrhea worsened to Grade 3. Loperamide dose was increased to 8 mg. On Study Day 76, the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea prophylaxis	2	PO	1	6
Diarrhea	4	PO	7	7
Diarrhea	6	PO	8	8
Diarrhea	8	PO	9	9
Diarrhea	10	PO	10	10
Diarrhea	6	PO	11	11
Diarrhea	2	PO	12	12
Diarrhea	10	PO	13	13
Diarrhea	8	PO	14	16
Diarrhea	4	PO	29	30
Diarrhea	6	PO	31	31
Diarrhea	4	PO	32	32
Diarrhea	4	PO	35	35
Diarrhea	4	PO	40	43
Diarrhea	10	PO	44	44
Diarrhea	4	PO	45	45
Diarrhea	6	PO	46	48
Diarrhea	4	PO	62	67
Diarrhea	6	PO	68	68
Diarrhea	8	PO	69	69
Diarrhea	4	PO	70	70
Diarrhea	4	PO	73	73
Diarrhea	8	PO	74	74
Diarrhea	6	PO	75	75

There was no change in study treatment due to the event of diarrhea.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

Prior to onset of Grade 3 diarrhea (onset day: Study Day 128), the patient experienced multiple non-serious events of diarrhea detailed in the table below. Treatment included loperamide (details reported in table below).

Most extreme Grade	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**	**Action taken** (Ipatasertib)	**Action taken** (Paclitaxel)
1	91	91	Related	Related	None	None
2	96	118	Related	Unrelated	None	None
1	121	121	Related	Unrelated	None	None

Event 3: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel and ipatasertib (300 mg) was administered on Study Day 127.

On Study Day 128, the patient experienced non-serious Grade 2 diarrhea. She received treatment with loperamide (details in the table below). On Study Day 143, diarrhea improved to Grade 1. On Study Day 157, the event of diarrhea worsened to Grade 3. Loperamide dose was increased to 12 mg. On Study Day 162, the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	**Total daily dose (Units: mg)**	**Route**	**Start day**	**Stop day**
Diarrhea	6	PO	96	97
Diarrhea	6	PO	99	103
Diarrhea	6	PO	105	105
Diarrhea	6	PO	118	118
Diarrhea	8	PO	121	121
Diarrhea	4	PO	127	127
Diarrhea	16	PO	129	129
Diarrhea	8	PO	131	131
Diarrhea	4	PO	132	132
Diarrhea	6	PO	133	134
Diarrhea	6	PO	143	143
Diarrhea	6	PO	146	146
Diarrhea	4	PO	148	148
Diarrhea	4	PO	152	152
Diarrhea	4	PO	155	155
Diarrhea	8	PO	157	159
Diarrhea	12	PO	160	160
Diarrhea	16	PO	161	161

There was no change in study treatment due to the event of diarrhea.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

Event 4: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel and ipatasertib (300 mg) was administered on Study Day 183.

On Study Day 184, the patient experienced non-serious Grade 2 diarrhea. She received treatment with loperamide (details in the table below). On Study Day 187, the event of diarrhea worsened to Grade 3. Loperamide dose was increased to 8 mg following which diarrhea improved to Grade 2 on Study Day 188. On Study Day 189, the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	172	172
Diarrhea	4	PO	179	179
Diarrhea	4	PO	181	181
Diarrhea	4	PO	183	183
Diarrhea	6	PO	184	184
Diarrhea	4	PO	185	185
Diarrhea	8	PO	187	187
Diarrhea	6	PO	188	189

There was no change in study treatment due to the event of diarrhea.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 197, the patient experienced Grade 1 dehydration and Grade 2 weight decreased (both non-serious, unrelated). She received dietary supplements for weight decreased; however, no treatment was reported for dehydration.

Event 5: Diarrhea

Prior to the event of diarrhea, the most recent dose of ipatasertib (300 mg) was administered on Study Day 201; study treatment with paclitaxel had already been discontinued.

On Study Day 202, the patient experienced non-serious Grade 3 diarrhea. She received treatment with loperamide (details in the table above). On Study Day 209, the event of diarrhea was considered resolved. On Study Day 229, the event of dehydration was considered resolved. On Study Day 317, the event of weight decreased was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	6	PO	197	202

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	203	203
Diarrhea	6	PO	204	204
Diarrhea	4	PO	205	206

Due to the event of diarrhea, ipatasertib was interrupted on Study Day 202.

On Study Day 217, a radiographic response assessment showed disease progression with new lesions in bone (inter-trochanteric massif), kidney (right ureter) and skin (breast). Subsequently, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 201. The patient entered into long-term follow-up.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Cyclophosphamide and epirubicin	260	524
Capecitabine	587	671
Eribulin	699	790
Cyclophosphamide and epirubicin	804	888
Cyclophosphamide	918	Ongoing

On Study Day 1058, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Hypercalcemia	1	Non-serious	5	83	Unrelated	Unrelated
Hypercalcemia	1	Non-serious	166	314	Unrelated	Unrelated
Cystitis	2	Non-serious	169	174	Unrelated	Unrelated
Hypotension	1	Non-serious	175	197	Unrelated	Unrelated
Asthenia	1	Non-serious	177	314	Related	Related
Anemia	2	Non-serious	181	314	Related	Related
Neutropenia	1	Non-serious	181	195	Related	Related
Lymphopenia	1	Non-serious	181	195	Related	Related
Blood creatinine increased	1	Non-serious	195	209	Unrelated	Unrelated
Blood albumin decreased	1	Non-serious	195	246	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304929	Patient number	2157
Demographics:	56-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day −2.

The patient was initially diagnosed with lobular, moderately differentiated, ER/PR positive and HER2 negative left breast cancer (TXNXM1), on Study Day −184.

On Study Day -169, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included bone (cervical, thoracic, lumbar spine, clavicle, sternum, ribs, pelvis and femur) and left breast (from nipple 1 o′clock: 6 cm and 3 o′clock: 4 cm). The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatment is listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Chemotherapy	Metastatic	Letrozole and ribociclib	−173	−21

No medical or surgical history was reported. Concurrent conditions included hypertension, hepatic steatosis, hypercholesterolemia, goiter and pain in extremity (left arm).

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included hydrochlorothiazide/irbesartan and fish oil.

Event: Neuropathy peripheral [Neuropathy (bilateral hands and feet)]

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 57.

On Study Day 58, the patient was diagnosed with non-serious Grade 1 neuropathy peripheral of bilateral hands and feet (presenting signs and symptoms were not reported). No treatment was reported for this event. On Study Day 223, the event of neuropathy peripheral worsened to

Grade 2. On Study Day 309, the event improved to Grade 1. The event of neuropathy peripheral remained unresolved at the time of the study discontinuation.

Due to the event of neuropathy peripheral, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 267.

The Investigator considered neuropathy peripheral, to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 443, symptomatic deterioration assessment showed increase in non-mass vascularity in the lower central left breast and in the upper quadrant region of uncertain significance with respect to treated malignancy.

On Study Day 477, study treatment with ipatasertib was permanently discontinued due to symptomatic deterioration with the last dose administered on Study Day 469. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Surgery of bilateral breast	482	–
Tamoxifen and denosumab	503	–
Radiotherapy to left chest wall, internal mammary chain, supraclavicular fossa and axilla (dose: 40 cGy, 15 fractions)	524	546

On Study Day 1135, the patient was permanently discontinued from the study as LTFU was terminated by Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Fatigue	1	Non-serious	1	Unresolved	Unrelated	Related
Constipation	1	Non-serious	4	Unresolved	Unrelated	Unrelated
Furuncle	1	Non-serious	6	10	Unrelated	Unrelated
Alopecia	2	Non-serious	11	Unresolved	Unrelated	Related
Diarrhea	1	Non-serious	12	Unresolved	Unrelated	Related
Vomiting	1	Non-serious	57	57	Unrelated	Related
Upper respiratory tract infection	2	Non-serious	61	76	Unrelated	Related
Nausea	2	Non-serious	67	341	Related	Unrelated
Mouth ulceration	1	Non-serious	76	80	Unrelated	Related

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Influenza like illness	1	Non-serious	170	346	Unrelated	Unrelated
Epistaxis	1	Non-serious	179	190	Unrelated	Related
Mouth ulceration	1	Non-serious	229	234	Unrelated	Related
Nail infection	1	Non-serious	235	239	Unrelated	Related
Rash	1	Non-serious	305	311	Unrelated	Related
Rash	1	Non-serious	332	376	Unrelated	Related

Study Number/CRTN:	CO40016/305637	Patient number	2161
Demographics:	59-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Neutropenia SAE		
Event 2 (PT) Categories:	Febrile neutropenia Death due to AE, SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.1; Narratives for patients who died due to adverse event(s).

Study Number/CRTN:	CO40016/305245	Patient number	2166
Demographics:	70-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Scleroderma AE leading to study treatment discontinuation		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative left breast cancer (T1cN2aM0), approximately 14 years prior to study entry.

On Study Day −7, the patient was diagnosed with metastatic disease with ER/PR negative and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included pancreas (pancreatic tail and body) and bone (cranial calvaria, sternum, right scapula, clavicle, bilateral rib cage, lumbar and sacrum cervical dorsum, sacroiliac joint, proximal third of femur and bilateral distal femoral diaphysis).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left lumpectomy	Approximately 13 years prior to study entry	N/A
Chemotherapy	Adjuvant	Didecyldimethyl-ammonium and paclitaxel	Approximately 13 years prior to study entry	Approximately 8 years prior to study entry
Radiotherapy	Adjuvant	Breast (thoracic wall, ganglionar axillo-supraclavicular chain; 5040 cGy, 28 fractions)	Approximately 13 years prior to study entry	Approximately 13 years prior to study entry

No medical or surgical history was reported. Concurrent condition included anxiety, dyslipidemia, hypothyroidism, hypertension, blood alkaline phosphatase increased, amylase increased, and blood triglycerides increased.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included calcium carbonate/cholecalciferol, omeprazole, simvastatin, alprazolam, enalapril, levothyroxine and calcifediol.

Event: Scleroderma (Scleroderma in hands)

Prior to the event of scleroderma, the most recent dose of paclitaxel was administered on Study Day 126 and ipatasertib (400 mg) on Study Day 129.

On Study Day 130, the patient was diagnosed with non-serious Grade 2 scleroderma on hands (presenting signs and symptoms not reported). On Study Day 154, she was noted with Grade 2 edema peripheral on hands (non-serious, related to paclitaxel). No treatment was administered for these events.

On Study Day 168, dose of paclitaxel was reduced to 65 mg/m^2 due to the event of edema peripheral. On Study Day 196, the event of edema peripheral improved to Grade 1. The event of scleroderma remained unresolved and edema peripheral was resolving at the time of patient′s death (see narrative below).

Due to the event of scleroderma, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 244.

The Investigator considered scleroderma to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 651, a radiographic response assessment showed disease progression with new lesions in skin (right cervical lesion).

On Study Day 665, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 643. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Gen 1046	678	780
Cyclophosphamide and doxorubicin	903	903

On Study Day 920, the patient died due to disease progression. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ non-serious	Onset Day	Resolution Day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Blood triglycerides increased	2	Non-serious	6	Unresolved	Unrelated	Unrelated
Blood glucose increased	1	Non-serious	6	26	Related	Unrelated
Diarrhea	2	Non-serious	7	22	Related	Related
Gamma-glutamyl transferase increased	1	Non-serious	27	40	Unrelated	Unrelated
Alopecia	2	Non-serious	28	Unresolved	Unrelated	Related
Diarrhea	1	Non-serious	33	33	Related	Related
Diarrhea	2	Non-serious	36	51	Related	Unrelated

Event	Most extreme grade	Serious/ non-serious	Onset Day	Resolution Day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Hemoglobin decreased	1	Non-serious	55	313	Related	Related
Diarrhea	2	Non-serious	56	Unresolved	Related	Unrelated
Upper respiratory tract infection	2	Non-serious	93	98	Unrelated	Unrelated
Asthenia	1	Non-serious	238	343	Unrelated	Related
Alanine aminotransferase increased	1	Non-serious	370	566	Related	Related
Gamma-glutamyl transferase increased	1	Non-serious	370	594	Related	Related
Aspartate aminotransferase increased	1	Non-serious	398	566	Related	Related
Hemoglobin decreased	1	Non-serious	426	594	Related	Related
Anxiety	2	Non-serious	567	Unresolved	Unrelated	Unrelated
Hemoglobin decreased	1	Non-serious	650	Unresolved	Related	Related
Gamma-glutamyl transferase increased	1	Non-serious	650	Unresolved	Related	Related
Blood triglycerides increased	2	Non-serious	650	Unresolved	Related	Related

Study Number/CRTN:	CO40016/304332	Patient number	2167
Demographics:	66-year-old White female		
Study treatment/ Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Diarrhea AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was diagnosed with ductal, moderately differentiated, ER positive/PR negative and HER2 negative left breast cancer (T4N1M1) on Study Day −30 following left breast biopsy.

At screening, sites of disease involvement included left breast and lymph nodes (left axillary, left upper clavicular, sub-clavicular, left interpectoral and mediastinal) and bilateral lungs. The patient was assessed by the Investigator to have visceral crisis.

No past cancer treatments were reported.

The patient′s medical history included cerebral ischemia. No surgical history was reported. Concurrent conditions included hypertension, hypertensive cerebrovascular disease, renal cyst, myocardial ischemia, arteriosclerosis coronary artery and hypercholesterolemia.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. On the same day, she also started prophylactic loperamide (total daily dose: 2 mg) for diarrhea.

Concomitant medication ongoing at Study Day 1 included atenolol/chlortalidone/nifedipine.

Prior to onset of the event of diarrhea that led discontinuation of ipatasertib, the patient experienced multiple non-serious events of diarrhea detailed in the table below. Treatment included loperamide (details reported in table below).

Most extreme Grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Action taken (Ipatasertib)	Action taken (Paclitaxel)
2	9	10	Related	Unrelated	None	None
2	12	14	Related	Unrelated	Dose reduced to 300 mg on Study Day 15	None
2	16	23	Related	Unrelated	Dose further reduced to 200 mg on Study Day 29	None
1	41	42	Related	Unrelated	None	None

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 36 and ipatasertib (200 mg) on Study Day 43.

On Study Day 44, the patient experienced non-serious Grade 2 diarrhea. She received treatment with loperamide (details reported in table below). On Study Day 46, diarrhea improved to Grade 1. On Study Day 50, the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of diarrhea	2	PO	1	2
Prophylaxis of diarrhea	2	PO	4	4
Prophylaxis of diarrhea	2	PO	7	8
Diarrhea	4	PO	9	10
Prophylaxis of diarrhea	2	PO	11	11
Diarrhea	4	PO	12	14
Prophylaxis of diarrhea	2	PO	15	15
Diarrhea	6	PO	16	16
Diarrhea	12	PO	17	17
Diarrhea	8	PO	18	22
Diarrhea	4	PO	23	23
Prophylaxis of diarrhea	6	PO	24	24
Prophylaxis of diarrhea	2	PO	25	40
Diarrhea	4	PO	41	42
Prophylaxis of diarrhea	2	PO	43	43
Diarrhea	8	PO	44	44
Diarrhea	10	PO	45	45
Diarrhea	4	PO	46	47
Diarrhea	6	PO	48	48
Diarrhea	4	PO	49	49
Diarrhea	2	PO	50	50
Prophylaxis of diarrhea	2	PO	51	56

Due to the event of diarrhea, there was no change in study treatment with paclitaxel; however, ipatasertib was permanently discontinued with the last dose administered on Study Day 49.

The Investigator considered diarrhea to be unrelated to paclitaxel and related to ipatasertib.

On Study Day 176, a radiographic response assessment showed disease progression with progression of non-target lesions.

On Study Day 191, study treatment with paclitaxel was permanently discontinued due to disease progression with the last dose administered on Study Day 170. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Exemestane	191	460
Capecitabine	461	660

On Study Day 679, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/Non-serious	Onset day	Resolution day/Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	1	Non-serious	3	3	Unrelated	Unrelated
Bone pain	2	Non-serious	4	5	Unrelated	Related
Constipation	1	Non-serious	5	6	Unrelated	Unrelated
Neutropenia	2	Non-serious	15	29	Unrelated	Related
Alopecia	2	Non-serious	35	155	Unrelated	Related
Neutropenia	2	Non-serious	43	55	Unrelated	Related
Anemia	2	Non-serious	55	114	Unrelated	Related
Arthritis	2	Non-serious	92	95	NA	Unrelated
Anemia	2	Non-serious	121	142	Unrelated	Related
Neutropenia	3	Non-serious	128	142	Unrelated	Related

Study Number/CRTN:	CO40016/305300	Patient number	2169
Demographics:	72-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Diarrhea AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR positive and HER2 negative left breast cancer (T2N1M0), approximately 5 years 2 months prior to study entry following left breast lumpectomy and surgery of lymph nodes.

On Study Day −241, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative in metastatic tissue following surgery of lymph nodes. At screening, sites of disease involvement included lung (bilateral including left subpleural anterior segment), liver (segments V, VI and VII) and lymph nodes (bilateral axillary supraclavicular, mediastinal adenopathy. The patient was assessed by the Investigator to have visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Adjuvant	Breast (dose unknown)	Approximately 5 years 6 months prior to study entry	Not reported
Cancer therapy	Adjuvant	Docetaxel and cyclophosphamide	Approximately 5 years prior to study entry	Approximately 4 years 8 months prior to study entry
Cancer therapy	Adjuvant	Anastrozole	Approximately 4 years 7 months prior to study entry	−220
Cancer therapy	Metastatic	Palbociclib and fulvestrant	−216	−100
Cancer therapy	Metastatic	Alpelisib and letrozole	−70	−41

The patient′s medical history included nodular vasculitis and pulmonary embolism. Surgical history included varicose vein operation, uterine polypectomy, cholecystectomy and appendicectomy. Concurrent conditions included dyslipidemia, hypertension, varicose vein, neuralgia, contrast media allergy, hepatic pain and pain in extremity (upper left).

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. On the same day, she received loperamide (total daily dose: 4 mg) for diarrhea.

Concomitant medications ongoing at Study Day 1 included zolpidem, rabeprazole, hydrochlorothiazide and pregabalin.

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 2.

On Study Day 3, the patient experienced non-serious Grade 2 diarrhea and Grade 2 asthenia (non-serious, unrelated). She received loperamide (total daily dose: 10 mg on Study Day 3-4) for diarrhea. No treatment was given for asthenia. On Study Day 27, the event of asthenia was considered resolved. The patient further received treatment with *Saccharomyces boulardii* and pancreatin for diarrhea. On Study Day 41, the event of diarrhea improved to Grade 1. On Study Day 54, the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	Oral	1	1
Diarrhea	6	Oral	2	2
Diarrhea	10	Oral	3	4
Diarrhea	12	Oral	5	5

Due to the event of diarrhea, study treatment with paclitaxel was interrupted at Cycle 1 Day 8 and the next dose was given on Study Day 15; however, ipatasertib was permanently discontinued with the last dose administered on Study Day 3.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 51, a radiographic response assessment showed disease progression. On the same day (Study Day 51), study treatment with paclitaxel was permanently discontinued due to disease progression with the last dose administered on Study Day 42. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Liposomal doxorubicin	86	Ongoing

On Study Day 209, the patient was lost to follow-up.

Other AE experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Neutropenia	1	Non-serious	27	53	Unrelated	Related

Study Number/CRTN:	CO40016/306642	Patient number	2176
Demographics:	44-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Categories:	Rash AE leading to study treatment discontinuation, AESI: Grade $\geq$ 3 rash		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR positive and HER2 negative left breast cancer (T2N0M0) on Study Day -959.

On Study Day -27, the patient was diagnosed with metastatic disease with ER positive, PR negative and HER2 negative disease in metastatic tissue. At screening sites of disease involvement liver (right side). The patient was assessed by the Investigator to have visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neo-adjuvant	Epirubicin, cyclophosphamide and docetaxel	–933	-814
Surgery	Curative	Left breast lumpectomy and left axillary lymph node sampling	-793	NA
Radiotherapy	Adjuvant	Left breast (total dose: 5000 cGy; 25 fractions) and tumor bed (total dose: 1000 cGy; 5 fractions)	-764	-717
Cancer therapy	Adjuvant	Tamoxifen	-708	-66

No medical or other surgical history was reported. Concurrent condition included glucose-6-phosphate dehydrogenase deficiency.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medication ongoing at Study Day 1 was reported.

Prior to the event of Grade 3 rash that led to paclitaxel discontinuation, the patient was noted with multiple events of non-serious rash and pruritus (please refer to table below for details). She received treatment with levocetirizine and betamethasone/fusidic acid. No action was taken with study treatments due to these events.

Event	Most extreme grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Pruritus (hands)	1	9	39	Related	Related
Rash	1	9	39	Unrelated	Related

Event	Most extreme grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Rash	2	40	51	Unrelated	Related
Pruritus (hands)	2	40	51	Related	Related
Rash	1	51	126	Related	Related
Pruritus (hands)	1	51	62	Unrelated	Related
Pruritus	2	58	61	Related	Related
Pruritus (hands)	1	86	89	Related	Related

Event: Rash

Prior to the event of Grade 3 rash, the most recent dose of paclitaxel and ipatasertib (300 mg) was administered on Study Day 126.

On Study Day 127, the ongoing Grade 1 event of rash worsened to Grade 3. Treatment with levocetirizine and betamethasone /fusidic acid was maintained.

Due to the event of rash, there was no change in treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 126.

On Study Day 132, rash improved to Grade 2. On Study Day 152, rash further improved to Grade 1. On Study Day 197, the event of rash was considered as resolved.

The Investigator considered Grade 3 rash to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 225, radiographic response assessment showed disease progression with new lesion in the liver.

On the same day (Study Day 225), study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 217. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Letrozole and ribociclib	226	311
Capecitabine	325	596
Vinorelbine and carboplatin	604	730
Gemcitabine	765	814
Exemestane and everolimus	828	916

On Study Day 943, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	1	Non-serious	3	5	Unrelated	Unrelated
Diarrhea	2	Non-serious	6	6	Related	Unrelated
Diarrhea	1	Non-serious	8	8	Related	Unrelated
Neutropenia	2	Non-serious	8	15	Related	Unrelated
Diarrhea	1	Non-serious	9	10	Related	Unrelated
Nausea	1	Non-serious	9	58	Related	Unrelated
Diarrhea	1	Non-serious	12	14	Related	Unrelated
Diarrhea	1	Non-serious	16	25	Related	Unrelated
Diarrhea	1	Non-serious	31	31	Related	Unrelated
Diarrhea	1	Non-serious	33	37	Related	Unrelated
Diarrhea	1	Non-serious	39	43	Related	Unrelated
Neutropenia	3	Non-serious	43	57	Related	Related
Diarrhea	1	Non-serious	46	46	Related	Unrelated
Pneumonitis	1	Non-serious	55	113	Unrelated	Related
Diarrhea	1	Non-serious	62	62	Related	Unrelated
Diarrhea	1	Non-serious	68	68	Related	Unrelated
Pyrexia	1	Non-serious	68	75	Unrelated	Unrelated
Headache	1	Non-serious	68	75	Unrelated	Related
Diarrhea	1	Non-serious	70	71	Related	Unrelated
Neutropenia	3	Non-serious	71	78	Related	Related
Vaginal infection	1	Non-serious	76	80	Unrelated	Unrelated
Anemia	2	Non-serious	78	197	Related	Related
Hemorrhoids	1	Non-serious	82	83	Unrelated	Related

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nausea	1	Non-serious	84	84	Related	Related
Otitis media acute	2	Non-serious	94	100	Unrelated	Unrelated
Diarrhea	1	Non-serious	108	108	Related	Unrelated
Diarrhea	1	Non-serious	110	110	Related	Unrelated
Diarrhea	1	Non-serious	121	121	Related	Related
Hypoesthesia	1	Non-serious	121	Resolving	Unrelated	Related
Diarrhea	1	Non-serious	124	124	Related	Related
Diarrhea	1	Non-serious	129	129	Related	Related
Diarrhea	2	Non-serious	130	132	Related	Related
Edema peripheral	1	Non-serious	143	197	Unrelated	Unrelated
Diarrhea	1	Non-serious	157	157	Related	Unrelated
Abdominal pain	1	Non-serious	166	166	Unrelated	Unrelated
Diarrhea	2	Non-serious	168	170	Related	NA
Diarrhea	1	Non-serious	174	177	Related	NA
Diarrhea	1	Non-serious	183	183	Related	NA
Diarrhea	2	Non-serious	184	189	Related	NA
Diarrhea	1	Non-serious	191	197	Related	NA
Diarrhea	2	Non-serious	200	206	Related	NA
Ear Pain	1	Non-serious	201	202	Unrelated	NA
Chest pain	1	Non-serious	204	204	Unrelated	NA
Diarrhea	1	Non-serious	209	213	Related	NA
Diarrhea	1	Non-serious	215	216	Related	NA
Diarrhea	1	Non-serious	219	224	Related	NA

Study Number/CRTN:	CO40016/304195	Patient number	2180
Demographics:	57-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		
Additional category:	Death due to disease progression		

A narrative for this patient is available under Section 1.2; Narratives for patients who died due to disease progression.

Study Number/CRTN:	CO40016/304641	Patient number	2181
Demographics:	65-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Polyneuropathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR positive and HER 2 negative left breast cancer (T2N2M1) on Study Day −95.

On Study Day −47, the patient was diagnosed with metastatic disease with ER/PR positive and HER 2 negative disease in metastatic tissue. At screening, sites of disease involvement included latero-superior region of left breast and midline mediastinum (in front of tracheal bifurcation). The patient was assessed by the Investigator to have visceral crisis.

No past cancer treatments were reported.

No medical history was reported. The patient′s surgical history included tonsillectomy and adnexectomy. Concurrent condition included hypertonia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included bisoprolol, hydrochlorothiazide/losartan and losartan.

Event: Polyneuropathy (Polyneuropathia)

Prior to the event of polyneuropathy, the most recent dose of paclitaxel was administered on Study Day 155 and ipatasertib (400 mg) on Study Day 162.

On Study Day 163, the patient was diagnosed with non-serious Grade 2 polyneuropathy (presenting signs and symptoms not reported). No treatment was given for this event. On Study Day 232, the event of polyneuropathy worsened to Grade 3 and remained unresolved at the time of study discontinuation.

Due to the event of polyneuropathy, there was no change in the study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose administered on Study Day 225.

The Investigator considered polyneuropathy to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 1177, study treatment with ipatasertib was permanently discontinued as per the physician′s decision (patient to enter post trial access program) with the last dose administered on Study Day 1171.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious / non-serious**	**Onset Day**	**Resolution Day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Hyperchlorhydria	2	Non-serious	8	Unresolved	Related	Unrelated
Lipase increased	3	Non-serious	142	281	Unrelated	Unrelated
Diarrhea	2	Non-serious	232	260	Related	Unrelated
Low density lipoprotein increased	1	Non-serious	393	Unresolved	Unrelated	Unrelated
Diarrhea	2	Non-serious	564	575	Related	NA
Diarrhea	1	Non-serious	595	595	Related	NA
Incorrect dose administered	1	Non-serious	607	609	NA	NA
Spinal pain	1	Non-serious	674	Unresolved	Unrelated	NA
Diarrhea	1	Non-serious	730	733	Related	Unrelated

Study Number/CRTN:	CO40016/304627	Patient number	2185
Demographics:	78-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, well differentiated, ER/PR negative, left breast cancer (T1N1aM0; HER2 receptor status was not assessed), approximately 36 years prior to study entry following left modified radical mastectomy.

The patient was diagnosed with metastatic disease, approximately 12 years prior to study entry, with ER/PR positive and HER2 negative in metastatic tissue. At screening, sites of disease involvement included liver (multiple lesions in segment IV, V and VI), bone (multiple) and left pleural effusion. The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Cyclophosphamide, fluorouracil and methotrexate	Approximately 36 years prior to study entry	Approximately 36 years prior to study entry
Cancer therapy	Metastatic	Letrozole	Approximately 12 years prior to study entry	Approximately 7 years prior to study entry
Radiotherapy	Metastatic	Bone (lumbar spine; 2000 cGy, 5 fractions)	Approximately 12 years prior to study entry	Approximately 12 years prior to study entry
Cancer therapy	Metastatic	Tamoxifen	Approximately 7 years prior to study entry	Approximately 2 years 8 months prior to study entry
Cancer therapy	Metastatic	Exemestane	Approximately 2 years 8 months prior to study entry	–524
Cancer therapy	Metastatic	Fulvestrant	–516	–404
Cancer therapy	Metastatic	Everolimus and exemestane	–383	–48

No medical or other surgical history was reported. Concurrent condition included hypertension.

At screening, the patient’s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. On the same day (Study Day 1), she received loperamide prophylactically (total daily dose: 2 mg) for diarrhea.

Concomitant medications ongoing at Study Day 1 included losartan and cholecalciferol.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 6.

On Study Day 7, the patient experienced non-serious Grade 2 (initial intensity) diarrhea. On Study Day 11, diarrhea worsened to most extreme Grade 3 severity. Grade changes for diarrhea and loperamide treatment details are reported in the table below. On Study Day 80, the event of diarrhea was considered resolved.

Grade changes for diarrhea:

Study Day	Grade changes for diarrhea
8	2
9	1
11	3
17	2
18	1
57	2
58	1
78	2
79	1

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea prophylaxis	2	PO	1	1
Diarrhea	4	PO	2	7
Diarrhea	12	PO	8	18
Diarrhea	4	PO	37	44
Diarrhea	4	PO	51	58

Due to the event of diarrhea, there was no change in study treatment with paclitaxel; however, ipatasertib was interrupted on Study Day 16 and resumed at a reduced dose of 300 mg on Study Day 30.

The Investigator considered diarrhea to be related ipatasertib and unrelated to paclitaxel.

After the resolution Grade 3 diarrhea, the patient experienced multiple non-serious Grade 2 events of diarrhea detailed in the table below. Treatment included loperamide (details reported in table below).

Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Action taken (Ipatasertib)	Action taken (Paclitaxel)
103	127	Unrelated	Unrelated	None	None
131	155	Related	Unrelated	None	None
157	169	Related	Unrelated	None	None

Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Action taken (Ipatasertib)	Action taken (Paclitaxel)
178	198	Related	Unrelated	None	NA
206	222	Related	Unrelated	None	None
241	241	Related	NA	None	NA
245	246	Related	NA	None	NA
251	252	Related	NA	None	NA
254	254	Related	NA	None	NA

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	8	PO	101	105
Diarrhea	4	PO	131	133
Diarrhea	4	PO	135	141
Diarrhea	4	PO	155	155
Diarrhea	2	PO	159	159
Diarrhea	4	PO	160	160
Diarrhea	2	PO	161	162
Diarrhea	2	PO	166	166
Diarrhea	2	PO	168	169
Diarrhea	2	PO	178	178
Diarrhea prophylaxis	2	PO	179	179
Diarrhea	2	PO	188	188
Diarrhea	2	PO	193	193
Diarrhea	4	PO	241	241
Diarrhea	2	PO	245	246
Diarrhea	2	PO	251	252
Diarrhea	2	PO	254	254

Event 2: Peripheral sensory neuropathy

Prior to the event of peripheral sensory neuropathy, the most recent dose of paclitaxel and ipatasertib (300 mg) was administered on Study Day 156.

On Study Day 157, the patient was diagnosed with Grade 1 (initial intensity) peripheral sensory neuropathy (presenting symptoms not reported). On Study Day 177, the event of peripheral sensory neuropathy worsened to Grade 2. No treatment was administered for the event. The event of peripheral sensory neuropathy remained unresolved at the time of study discontinuation.

Due to the event of peripheral sensory neuropathy, there was no change in study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 163.

The Investigator considered peripheral sensory neuropathy to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 345, a radiographic response assessment showed disease progression with new lesions in liver (multiple).

On Study Day 352, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 338. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Ribociclib and letrozole	352	801
Capecitabine	806	985
Megestrol	990	–

On Study Day 1009, the patient was permanently discontinued from the study as LTFU was terminated by Sponsor.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious/ Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Fatigue	1	Non-serious	5	30	Related	Related
Decreased appetite	1	Non-serious	5	72	Related	Unrelated
Nasopharyngitis	1	Non-serious	24	28	Unrelated	Unrelated
Infusion site extravasation	2	Non-serious	30	30	Unrelated	Related
Neutrophil count decreased	3	Non-serious	44	51	Unrelated	Related
Neutrophil count decreased	1	Non-serious	79	93	Unrelated	Related
Vomiting	1	Non-serious	102	102	Unrelated	Unrelated
Bone pain	1	Non-serious	102	102	Unrelated	Unrelated
Decreased appetite	1	Non-serious	150	165	Related	Unrelated
Dysgeusia	1	Non-serious	150	Unresolved	Related	Unrelated
Edema peripheral	1	Non-serious	165	167	Unrelated	Unrelated

Study Number/CRTN:	CO40016/306252	Patient number	2189
Demographics:	49-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade $\geq$ 3 diarrhea		
Event 2 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER positive/PR negative and HER 2-negative left breast cancer (T3N2M0), approximately 10 years prior to study entry.

On Study Day −180, the patient was diagnosed with metastatic disease with ER positive/PR negative and HER 2-negative disease in metastatic tissue. At screening, sites of disease involvement in left lung, bone (axial and appendicular skeleton) and mediastinum lymph node. The patient was assessed by the investigator to have visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	**Therapy Setting/Intent**	**Treatments details**	**Start Day**	**Stop Day**
Cancer therapy	Neo-adjuvant	Epirubicin, cyclophosphamide and docetaxel	Approximately 10 years prior to study entry	Approximately 10 years prior to study entry
Surgery	Curative	Left modified radical mastectomy	Approximately 10 years prior to study entry	NA
Radiotherapy	Adjuvant	Breast (left chest wall; dose: 50 cGy 25 fractions)	Approximately 10 years prior to study entry	Approximately 9 years prior to study entry

No medical or surgical history was reported. Concurrent condition included hypertension.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included telmisartan. She also received prophylactic loperamide (4 mg, PO) for diarrhea on Study Days 1-4.

On Study Day 32, the patient experienced Grade 1 diarrhea (non-serious, related to ipatasertib). On Study Day 40, the event of diarrhea worsened to Grade 2. She received treatment with loperamide (details reported in the table below). On Study Day 54, the event of diarrhea was considered resolved.

Event 1: Diarrhea (Grade 3)

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 94 and ipatasertib (300 mg) on Study Day 98.

On Study Day 99, the patient experienced non-serious Grade 3 acute diarrhea (13 evacuations). On Study Day 100, laboratory work-up showed sodium 139 mEq/L (normal range: 136-145 mEq/L), potassium 4.9 mEq/L (normal range: 3.5-5.1 mEq/L) and creatinine was 3.20 mg/dL (normal range: 0.5-1.2 mg/dL). Reportedly, increased creatinine was considered due to dehydration caused by diarrhea. She was given dietary advice and treatment with loperamide, ciprofloxacin, IV fluids and racecadotril. Later, on the same day (Study Day 100), the event of diarrhea improved to Grade 2. On Study Day 102, the event further improved to Grade 1. On the following day (Study Day 103), the event of diarrhea was considered resolved.

Loperamide details

Indication	Loperamide Dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	32	98
Diarrhea	8	PO	99	100

Relevant laboratory work-up:

Study Day	Creatinine Normal range: 0.5-1.2 mg/dL
Screening	0.74
100	3.2
101	1.47

Due to the event of diarrhea, Cycle 4 Day 15 dose of paclitaxel was interrupted and treatment with ipatasertib was interrupted on Study Day 107. The next dose of paclitaxel (at a reduced dose of 65 mg) and ipatasertib (at a reduced dose of 200 mg) was given on Study Day 114.

The Investigator considered diarrhea, to be related to ipatasertib and paclitaxel.

On Study Day 122, the patient experienced Grade 1 diarrhea (non-serious, related to ipatasertib). No treatment was given for this event. On Study Day 152, the event of diarrhea was considered resolved.

Event 2: Peripheral sensory neuropathy

Prior to the event of peripheral sensory neuropathy, the most recent dose of paclitaxel was administered on Study Day 156 and ipatasertib (200 mg) on Study Day 157.

On Study Day 158, the patient was diagnosed with non-serious Grade 2 peripheral sensory neuropathy (presenting signs and symptoms not reported). No treatment was given for this event. On Study Day 165, the event of peripheral sensory neuropathy was considered resolved.

Due to the event of peripheral sensory neuropathy, there was no change in the study treatment with ipatasertib; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 156.

The Investigator considered peripheral sensory neuropathy to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 622, a radiographic response assessment showed disease progression.

On Study Day 624, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose given on Study Day 614. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Palbociclib and fulvestrant	679	Ongoing

On Study Day 992, the patient was permanently discontinued from the study as LTFU was terminated by Sponsor.

Other event experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	1	Non-serious	2	5	Unrelated	Unrelated
Peripheral sensory neuropathy	2	Non-serious	445	483	Related	NA

Study Number/CRTN:	CO40016/306642	Patient number	2191
Demographics:	57-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, well differentiated, ER positive, PR negative and HER2-negative left breast cancer (T1bN0M0) approximately 4 years and 9 months prior to study entry.

On Study Day −26, the patient was diagnosed with metastatic disease with ER positive, PR negative and HER2-negative disease in metastatic tissue. At screening, sites of disease involvement included liver. The patient was assessed by the Investigator to have visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right radical mastectomy	Approximately 4 years and 9 months prior to study entry	NA
Cancer therapy	Adjuvant	Letrozole	Approximately 4 years and 8 months prior to study entry	−607
Cancer therapy	Neo-adjuvant	Cyclophosphamide, docetaxel, and epirubicin (4 cycles each)	−595	−448
Surgery	Curative	Right axillary lymph node dissection	−406	NA
Radiotherapy	Adjuvant	Axillary and supraclavicular lymph nodes (dose: 50 cGy, 25 fractions)	−364	−330
Cancer therapy	Adjuvant	Tamoxifen	−328	−26

The patient's medical history included hyperlipidemia. No surgical history was reported. Concurrent condition included multiple sclerosis.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 was reported.

Event: Neuropathy peripheral (Peripheral neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel and ipatasertib was administered (400 mg) on Study Day 169.

On Study Day 170, the patient was diagnosed with non-serious Grade 1 neuropathy peripheral (presenting signs and symptoms not reported). On Study Day 232, the event of neuropathy peripheral worsened to Grade 3. No treatment was reported for this event. On Study Day 288, the event of neuropathy peripheral improved to Grade 2. The event of neuropathy peripheral remained unresolved at the time of study discontinuation.

Due to this event, there was no change in study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 232.

The Investigator considered neuropathy peripheral, to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 394, a radiographic response assessment showed disease progression with new lesion in liver.

On Study Day 395, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose of ipatasertib administered on Study Day 395. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Fulvestrant and palbociclib	421	499
Capecitabine	515	Ongoing

On Study Day 987, the patient was discontinued from the study as long term follow-up was terminated by Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Sinus tachycardia	2	Non-serious	1	36	Unrelated	Unrelated
Diarrhea	1	Non-serious	2	7	Related	Unrelated
Diarrhea	1	Non-serious	9	15	Related	Unrelated
Diarrhea	2	Non-serious	17	23	Related	Unrelated
Diarrhea	1	Non-serious	25	25	Related	Unrelated
Diarrhea	1	Non-serious	28	28	Related	Unrelated
Flushing	1	Non-serious	30	30	Unrelated	Related
Diarrhea	1	Non-serious	31	34	Related	Unrelated
Constipation	1	Non-serious	35	36	Unrelated	Unrelated
Sinus tachycardia	1	Non-serious	36	71	Unrelated	Unrelated
Diarrhea	1	Non-serious	37	39	Related	Unrelated
Diarrhea	1	Non-serious	41	42	Related	Unrelated
Diarrhea	2	Non-serious	44	49	Related	Unrelated
Fatigue	1	Non-serious	45	Unresolved	Related	Unrelated
Diarrhea	1	Non-serious	58	62	Related	Unrelated
Neutropenia	2	Non-serious	64	71	Unrelated	Related
Diarrhea	2	Non-serious	65	86	Related	Unrelated
Constipation	1	Non-serious	87	88	Unrelated	Unrelated
Diarrhea	1	Non-serious	89	91	Related	Unrelated
Diarrhea	1	Non-serious	95	107	Related	Unrelated
Diarrhea	1	Non-serious	113	113	Related	Unrelated
Diarrhea	1	Non-serious	117	135	Related	Unrelated
Diarrhea	1	Non-serious	138	138	Related	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Rash	1	Non-serious	138	144	Unrelated	Unrelated
Diarrhea	1	Non-serious	142	148	Related	Unrelated
Diarrhea	1	Non-serious	150	165	Related	Unrelated
Diarrhea	1	Non-serious	167	167	Related	Unrelated
Diarrhea	1	Non-serious	169	172	Related	Unrelated
Diarrhea	1	Non-serious	175	176	Related	Unrelated
Diarrhea	1	Non-serious	178	180	Related	Unrelated
Diarrhea	2	Non-serious	183	195	Related	Unrelated
Diarrhea	1	Non-serious	199	200	Related	Unrelated
Diarrhea	1	Non-serious	206	209	Related	Unrelated
Diarrhea	1	Non-serious	213	213	Related	Unrelated
Diarrhea	1	Non-serious	215	218	Related	Unrelated
Onycholysis	1	Non-serious	226	344	Unrelated	Related
Diarrhea	1	Non-serious	232	232	Related	Unrelated
Diarrhea	1	Non-serious	238	239	Related	Unrelated
Arthralgia	1	Non-serious	241	738	Unrelated	Not Applicable
Constipation	1	Non-serious	323	671	Unrelated	Not Applicable

Study Number/CRTN:	CO40016/306642	Patient number	2192

Demographics:	53-year-old White female
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)
Cohort:	Cohort B
Event (PT) Categories:	Febrile neutropenia SAE, AE leading to study treatment discontinuation
Additional category:	Death due to disease progression

A narrative for this patient is available under Section 1.2; Narratives for patients who died due to disease progression.

Study Number/CRTN:	CO40016/305252	Patient number	2195
Demographics:	68-year-old female (race unknown)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Neutropenia AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was diagnosed with tubular ER/PR positive, and HER2-negative metastatic left breast cancer (histopathology unknown) (TXNXM1) approximately 5 years and 9 months prior to study entry.

At screening, sites of disease involvement included bone and liver. The patient was assessed by the Investigator to have endocrine resistant.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Metastatic	Letrozole and denosumab	Approximately 5 years and 8 months prior to study entry	Approximately 3 years and 10 months prior to study entry
Cancer therapy	Metastatic	Abemaciclib and fulvestrant (32 cycles each)	Approximately 3 years and 9 months prior to study entry	–546
Cancer therapy	Metastatic	Everolimus and exemestane (16 cycles each)	–511	–98

No medical/surgical history was reported. The patient′s concurrent conditions included hypertension and hypercholesterolemia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included heparin, bisoprolol/hydrochlorothiazide, nifedipine, urapidil, and *Ginkgo biloba*/heptaminol/troxerutin.

Event: Neutropenia

Prior to the event of neutropenia, the most recent dose of paclitaxel was administered on Study Day 323 and ipatasertib (400 mg) on Study Day 329.

On Study Day 335, a laboratory work-up showed WBC count 3.5×10^9/L (normal range: $3.8\text{-}9.8 \times 10^9$/L) and neutrophil count 1.48×10^9/L (normal range: $1.7\text{-}5.8 \times 10^9$/L). The patient was diagnosed with non-serious Grade 2 neutropenia. No treatment was given for the event. On Study Day 363, the event of neutropenia was considered resolved.

Due to this event, there was no change in study treatment with ipatasertib; however, study treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 323.

Relevant lab values are listed in the table below:

Study Day	WBC count (normal range: $3.8\text{-}9.8 \times 10^9$/L)	Neutrophil count (normal range: $1.7\text{-}5.8 \times 10^9$/L
Screening	6.2	3.99
335	3.5	1.48
363	4.6	2.55

The Investigator considered neutropenia, to be unrelated to ipatasertib and related to paclitaxel.

On Study Day 393, a radiographic response assessment showed disease progression with new lesion in liver and lung (infra-centric lymph node).

On Study Day 407, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose of ipatasertib administered on Study Day 385. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Epirubicin and cyclophosphamide	407	Ongoing

On Study Day 494, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	4	393	Related	Unrelated
Asthenia	1	Non-serious	9	22	Unrelated	Related
Neutropenia	2	Non-serious	13	20	Unrelated	Related
Neutropenia	2	Non-serious	41	55	Unrelated	Related
Anemia	2	Non-serious	41	Unresolved	Related	Related
Neuropathy peripheral	1	Non-serious	64	112	Unrelated	Related
Cough	1	Non-serious	105	126	Unrelated	Unrelated
Neutropenia	2	Non-serious	125	139	Unrelated	Related
Neuropathy peripheral	2	Non-serious	128	Unresolved	Unrelated	Related
Neuropathy peripheral	1	Non-serious	128	Unresolved	Unrelated	Related
Nail toxicity	1	Non-serious	147	183	Unrelated	Related
Hypercholesterolemia	1	Non-serious	209	Unresolved	Unrelated	Unrelated
Nausea	1	Non-serious	224	253	Related	Unrelated
Neutropenia	2	Non-serious	237	251	Unrelated	Related
Muscular weakness	1	Non-serious	253	259	Unrelated	Unrelated
Nail toxicity	1	Non-serious	295	309	Unrelated	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Asthenia	1	Non-serious	295	Unresolved	Unrelated	Related

Study Number/CRTN:	CO40016/318262	Patient number	2198
Demographics:	44-year-old Asian female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Neutrophil count decreased AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER/PR positive and HER2 negative right breast cancer (T2N1miMX; histological grade unknown), approximately 4 years 11 months prior to study entry.

On Study Day -977, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included liver and bone (sternum). The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right partial mastectomy	Approximately 4 years 11 months prior to study entry	NA
Cancer therapy	Adjuvant	Cyclophosphamide and doxorubicin	Approximately 4 years 10 months prior to study entry	Approximately 4 years 9 months prior to study entry
Cancer therapy	Adjuvant	Tamoxifen and goserelin	Approximately 4 years 3 months prior to study entry	–973
Cancer therapy	Metastatic	Palbociclib, exemestane and leuprorelin	–949	–312

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Metastatic	Breast (rib cage and chest wall) (total dose: 4500 cGy; 14 fractions)	−301	−277
Cancer therapy	Metastatic	Palbociclib and letrozole	−245	−166
Cancer therapy	Metastatic	Alpelisib and fulvestrant	−140	−29

No medical and other surgical history was reported. Concurrent conditions included insomnia, arthralgia (shoulder), musculoskeletal chest pain (ribs).

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 doxepin.

Prior to the event of neutrophil count decreased that led to paclitaxel discontinuation, the patient was noted with multiple non-serious events of neutrophil count decreased (please refer to table below for details). She received treatment with filgrastim for Grade 3 events of neutrophil count decreased, however, no treatment was reported for Grade 2 neutrophil count decreased.

Most extreme grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Action taken (Ipatasertib)	Action taken (Paclitaxel)
3	8	11	Unrelated	Related	Drug interrupted from Study Day 8 to Study Day 10	None
3	18	22	Unrelated	Related	Drug interrupted from Study Day 18 to Study Day 21 and resumed on Study Day 22 at reduced dose of 300 mg	Cycle 1 Day 15 dose delayed and administered Study Day 22 at reduced dose of 65 mg/m^2
2	29	32	Unrelated	Related	None	Cycle 2 Day 1 given on

Most extreme grade	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Action taken (Ipatasertib)	Action taken (Paclitaxel)
						Study Day 33 at reduced dose of 65 mg/m^2

Event: Neutrophil count decreased

Prior to the event of neutrophil count decreased, the most recent dose of paclitaxel was administered on Study Day 40 and ipatasertib (300 mg) on Study Day 45.

On Study Day 46, a laboratory work-up showed WBC count 2.08 x 10^9/L (normal range: 3.15-8.63 x 10^9/L) and neutrophils 27.9% (normal range: 40.6-73.5%; 0.58 x 10^9/L). The patient was noted with non-serious Grade 3 neutrophil count decreased. No treatment was reported for the event. On Study Day 50, the event of neutrophil count decreased was considered resolved.

Relevant laboratory work-up:

Study Day	WBC count Normal range: 3.15-8.63 $\times$ 10^9/L	Neutrophils Normal range: 40.6-73.5%
Screening	7.97	76.3
8	2.07	29.5
11	11.58	80.4
18	2.27	38.4
22	7.59	80.2
29	2.46	41.5
32	3.77	43.7
40	16.47	82.4
46	2.08	27.9
50	5.27	66.6
57	3.7	61.3
68	4.79	85.4

Due to the event of neutrophil count decreased, study treatment with ipatasertib was interrupted on Study Day 46 and resumed on Study Day 50 at a reduced dose of 200 mg, however, paclitaxel was permanently discontinued with the last dose administered on Study Day 40.

The Investigator considered neutrophil count decreased to be related to paclitaxel and ipatasertib.

On Study Day 64, the patient was noted to have Grade 2 neutrophil count decreased (non-serious, related to ipatasertib). On Study Day 68, the event of neutrophil count decreased was considered as resolved without any treatment.

On Study Day 85, a radiographic response assessment showed disease progression.

On Study Day 92, study treatment with ipatasertib was permanently discontinued due to disease progression with the last dose administered on Study Day 77. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Paclitaxel and carboplatin	92	Ongoing
Radiotherapy to bone (L1-L3) (total dose: 2000 cGy; 5 fractions)	277	283

On Study Day 435, the patient was lost to follow-up.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Fatigue	1	Non-serious	2	126	Unrelated	Related
Peripheral sensory neuropathy	1	Non-serious	3	Unresolved	Unrelated	Related
Alopecia	1	Non-serious	4	13	Unrelated	Related
Diarrhea	1	Non-serious	8	77	Related	Unrelated
Arthralgia	2	Non-serious	8	126	Unrelated	NA
Abdominal pain upper	2	Non-serious	8	126	Unrelated	NA
Pruritus	1	Non-serious	12	35	Unrelated	Related
Alopecia	2	Non-serious	14	Unresolved	Unrelated	Related
Pain of skin	1	Non-serious	14	35	Unrelated	Related
Upper respiratory tract infection	2	Non-serious	26	35	Unrelated	Unrelated
Vomiting	1	Non-serious	85	85	Unrelated	NA
Constipation	1	Non-serious	89	Unresolved	Unrelated	NA
Abdominal pain	2	Non-serious	89	91	Unrelated	NA

Study Number/CRTN:	CO40016/305649	Patient number	2208
Demographics:	58-year-old female (race unknown)		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Pleural effusion SAE		
Event 2 (PT) Category:	Lower respiratory tract infection SAE		
Event 3 (PT) Categories:	Pneumonia Death due to AE, SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.1; Narratives for patients who died due to adverse event(s).

1.5 NARRATIVES FOR PATIENTS WHO BECAME PREGNANT WHILE IN THE STUDY

No patient became pregnant while in the study.

1.6 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥ 3 HYPERGLYCEMIA

Study Number/CRTN:	CO40016/305629	Patient number	2008
Demographics:	76-year-old American Indian or Alaska native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Categories:	Diarrhea SAE, AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Categories:	Hyperglycemia SAE, AE leading to study treatment discontinuation, AESI: Grade ≥ 3 hyperglycemia		
Event 3 (PT) Category:	Dehydration SAE		
Event 4 (PT) Category:	Hypoglycemia SAE		
Event 5 (PT) Categories:	Respiratory distress Death due to AE, SAE		

A narrative for this patient is available under Section 1.1; Narratives for patients who died due to adverse event(s).

Study Number/CRTN:	CO40016/305386	Patient number	2032
Demographics:	51-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Hyperglycemia AESI: Grade ≥ 3 hyperglycemia		
Event 2 (PT) Categories:	Hyperglycemia AE leading to study treatment discontinuation, AESI: Grade ≥ 3 hyperglycemia		
Event 3 (PT) Category:	Deep vein thrombosis SAE		

Event 4 (PT) Category:	Extravasation SAE

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/307257	Patient number	2079
Demographics:	62-year-old Asian female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Hyperglycemia AESI: Grade $\geq$ 3 hyperglycemia		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER positive, PR negative and HER2 negative right breast cancer (T2N2aM0), approximately 6 years prior to study entry.

On Study Day -55, the patient was diagnosed with metastatic disease (ER and PR status was unknown and HER2 status was not assessed in metastatic tissue). At screening sites of disease involvement included liver (S8) and bone (left shoulder blade). The patient was assessed by the Investigator to have visceral crisis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right partial mastectomy and right axillary lymph node dissection	Approximately 6 years prior to study entry	NA
Cancer therapy	Adjuvant	Docetaxel and cyclophosphamide	Approximately 5 years prior to study entry	Approximately 5 years and 4 months prior to study entry
Cancer therapy	Adjuvant	Letrozole	Approximately 5 years and 3 months prior to study entry	–42

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Adjuvant	Right breast (dose: 60 cGy; 30 fractions) and right supraclavicular lymph nodes (dose: 50 cGy; 25 fractions)	Approximately 5 years and 2 months prior to study entry	Approximately 5 years and 1 month prior to study entry

The patient's medical history included atrial septal defect. No other surgical history and concurrent condition was reported.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medication ongoing at Study Day 1 was reported.

On Study Day 60, a laboratory work-up revealed Grade 2 glycosylated hemoglobin increased (HbA1c 7.4%; normal range: 4.6-6.2%; non-serious, related). No treatment was reported for this event; however, Cycle 3 Day 1 dose of paclitaxel was interrupted and ipatasertib was interrupted from Study Day 60. The next dose of ipatasertib and paclitaxel (Cycle 3 Day 8) was given on Study Day 67.

Event: Hyperglycemia (Postprandial hyperglycemia)

Prior to the event of hyperglycemia, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 67.

On the same day (Study Day 67), within 24 hours after the end of paclitaxel infusion, a laboratory work-up showed non-serious Grade 3 postprandial hyperglycemia (glucose level not provided for this date). The patient received treatment with metformin, teneligliptin, miglitol and repaglinide (for treatment details please refer to table below). Relevant laboratory work-up has been reported in the table below. On Study Day 141, the event of glycosylated hemoglobin increased was considered as resolved; however, the event of hyperglycemia improved to Grade 1 and on Study Day 624, the event of hyperglycemia was considered resolved.

Hyperglycemia treatment details:

Treatment	Indication	Dose (Units: mg)	Route	Frequency	Start day	Stop day
Metformin	Postprandial hyperglycemia	250	PO	BID	92	95
Teneligliptin	Postprandial hyperglycemia	20	PO	QD	106	128
Miglitol	Postprandial hyperglycemia	50	PO	QD	120	128

Treatment	Indication	Dose (Units: mg)	Route	Frequency	Start day	Stop day
Repaglinide	Postprandial hyperglycemia	0.5	PO	PRN	151	331
Teneligliptin	Postprandial hyperglycemia	20	PO	PRN	158	173

Relevant laboratory work-up:

Study Day	Glucose (fasting) Normal range: 70-110 mg/dL	HbA1c Normal range: 4.6-6.2%
Screening	105	6.2
60	101	7.4
74	104	—
85	99	—
99	97	—
106	96	—
113	94	—
141	100	6.1
172	99	—
197	94	—
225	106	6.3
253	100	—
281	108	—
309	103*	6.5
344	105*	6.7

*Normal range: 70-109 mg/dL

Due to the event of hyperglycemia, there was no change in study treatment with paclitaxel; however, ipatasertib was interrupted on Study Day 74 and resumed at a reduced dose of 300 mg on Study Day 92.

The Investigator considered hyperglycemia to be related to ipatasertib, paclitaxel and concomitant medication.

On Study Day 330, a radiographic response assessment showed disease progression.

On Study Day 336, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and ipatasertib given on Study Day 330 and Study Day 336, respectively. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Eribulin mesylate	344	526
Capecitabine	541	729
Anastrozole (3 cycles) and abemaciclib (2 cycles)	737	792
Bevacizumab and paclitaxel (7 cycles each)	799	981
Vinorelbine (3 cycles)	995	1037
Epirubicin and cyclophosphamide (3 cycles each)	1051	1093
Everolimus and exemestane (3 cycles each)	1114	1176
Gimeracil/oteracil potassium/tegafur	1177	Ongoing

On Study Day 1219, the patient was permanently discontinued from the study as per the physician's decision (LTFU terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Constipation	1	Non-serious	1	4	Unrelated	Unrelated
Diarrhea	2	Non-serious	10	70	Related	Related
Stomatitis	1	Non-serious	22	29	Related	Related
Alopecia	2	Non-serious	29	Unresolved	Related	Related
Vomiting	1	Non-serious	36	36	Related	Unrelated
Neutrophil count decreased	2	Non-serious	43	50	Related	Related
Nausea	1	Non-serious	50	99	Related	Related
Anemia	2	Non-serious	60	449	Related	Related
Neutrophil count decreased	2	Non-serious	99	106	Related	Related
Rash	1	Non-serious	127	288	Unrelated	Unrelated
Accidental overdose	N/A	Non-serious	134	134	N/A	N/A

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Neuropathy peripheral	1	Non-serious	202	Unresolved	Unrelated	Related
Bronchitis	2	Non-serious	281	295	Related	Related
Bronchitis	2	Non-serious	307	316	Related	Related

1.7 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥ 3 DIARRHEA

Study Number/CRTN:	CO40016/305629	Patient number	2008
Demographics:	76-year-old American Indian or Alaska native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Categories:	Diarrhea SAE, AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Categories:	Hyperglycemia SAE, AE leading to study treatment discontinuation, AESI: Grade ≥ 3 hyperglycemia		
Event 3 (PT) Category:	Dehydration SAE		
Event 4 (PT) Category:	Hypoglycemia SAE		
Event 5 (PT) Categories:	Respiratory distress Death due to AE, SAE		

A narrative for this patient is available under Section 1.1; Narratives for patients who died due to adverse event(s).

Study Number/CRTN:	CO40016/304203	Patient number	2028
Demographics:	52-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 day cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 day cycle)		
Cohort	Cohort B		
Event (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		

The patient was randomized on Study Day -3.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative left breast cancer (T2N0M0), approximately 4 years 10 months prior to study entry.

On Study Day -825, the patient was diagnosed with metastatic disease with ER positive, PR negative and HER2 negative disease in metastatic tissue. At screening sites of disease involvement included liver (right hepatic lobe and adjacent to gall bladder fossa) and bone (multiple locations: sacrum, lumbar spine, lower thoracic spine, bilateral clavicles). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left radical mastectomy	Approximately 4 years 10 months prior to study entry	NA
Cancer therapy	Adjuvant	Doxorubicin, Cyclophosphamide, and tamoxifen	Approximately 4 years 6 months prior to study entry	Approximately 4 years prior to study entry
Cancer therapy	Adjuvant	Tamoxifen	Approximately 4 years prior to study entry	-836
Chemotherapy	Adjuvant	Paclitaxel	Approximately 4 years prior to study entry	Approximately 4 years prior to study entry
Cancer therapy	Metastatic	Letrozole and palbociclib	-805	-258
Radiotherapy	Metastatic	Bone (T11-L1) (dose: 3000 cGy, 10 fractions)	-693	-682

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Metastatic	Fulvestrant and palbociclib	-227	-31

No medical history was reported. Other surgical history included thyroidectomy, hysterectomy, appendicectomy and cholecystectomy. Concurrent conditions included hypothyroidism, edema peripheral (bilateral legs), dyspepsia, arthralgia, anxiety, depression, contusion, hot flush, insomnia, bone pain, constipation, abdominal distension, headache, dyspnea, myalgia, rash, anemia, hyperglycemia, aspartate aminotransferase increased, paresthesia (left breast), hypertriglyceridemia, disturbance in attention, neuropathy peripheral and fatigue.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included diclofenac, clonazepam, venlafaxine, eszopiclone, furosemide, calcium carbonate, levothyroxine, omeprazole, senna and docusate.

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 4.

On Study Day 5, the patient experienced non-serious Grade 1 diarrhea. She received treatment with loperamide (details reported in table below). On Study Day 46, diarrhea worsened to Grade 3. She experienced >10 episodes of diarrhea per day until Study Day 57. It was reported that during this time she continued to take 2-4 mg loperamide daily, despite instructions to increase the dose of loperamide. She also received dietary and hydration advice. On the same day (Study Day 57), diarrhea was reported to have improved to Grade 1. On Study Day 58, the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of diarrhea	2	PO	1	1
Diarrhea	2	PO	19	19
Diarrhea	12	PO	41	41
Diarrhea	2	PO	45	46
Diarrhea	8	PO	47	51
Diarrhea	2	PO	52	53
Diarrhea	4	PO	54	55

Due to the event of diarrhea, study treatment with ipatasertib was interrupted on Study Day 59 and Cycle 3 Day 1 dose of paclitaxel was not administered. The next dose of ipatasertib at a reduced dose of 300 mg and paclitaxel was given on Study Day 65.

The Investigator considered diarrhea, to be related to ipatasertib and paclitaxel.

On Study Day 164, radiographic response assessment showed disease progression.

On Study Day 171, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 150 and ipatasertib on Study Day 163. The patient entered into long-term follow-up phase.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine	185	590
Eribulin, trastuzumab and pertuzumab	614	1090
Trastuzumab	1111	Ongoing

On Study Day 1314, the patient was discontinued from the study as per physician's decision (study was terminated by the Sponsor).

Other AEs experienced by patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Nausea	2	Non-serious	5	143	Related	Related
Vomiting	1	Non-serious	5	143	Related	Related
Nasal congestion	2	Non-serious	5	65	Unrelated	Unrelated
Upper-airway cough syndrome	1	Non-serious	5	59	Unrelated	Unrelated
Chills	1	Non-serious	5	59	Unrelated	Related
Paranasal sinus discomfort	1	Non-serious	5	59	Unrelated	Unrelated
Oropharyngeal pain	1	Non-serious	5	59	Unrelated	Unrelated
Dizziness	2	Non-serious	5	Unresolved	Unrelated	Related
Pain in jaw	1	Non-serious	6	7	Unrelated	Unrelated

Event	Most extreme grade	Serious / non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Alanine aminotransferase increased	1	Non-serious	8	15	Unrelated	Related
Aspartate aminotransferase increased	1	Non-serious	15	31	Unrelated	Related
Anemia	2	Non-serious	31	255	Unrelated	Related
Back pain	1	Non-serious	33	45	Unrelated	Unrelated
Hyperglycemia	1	Non-serious	38	178	Related	Unrelated
Blood alkaline phosphatase increased	1	Non-serious	38	45	Unrelated	Related
Alopecia	2	Non-serious	38	283	Unrelated	Related
Upper respiratory tract infection	2	Non-serious	42	59	Unrelated	Unrelated
Blood alkaline phosphatase increased	1	Non-serious	59	73	Unrelated	Related
Blood cholesterol increased	1	Non-serious	59	Unresolved	Unrelated	Unrelated
Constipation	1	Non-serious	62	101	Unrelated	Unrelated
Rash	1	Non-serious	75	94	Related	Related
Hypocalcemia	2	Non-serious	87	157	Unrelated	Unrelated
Hypophosphatasemia	2	Non-serious	101	122	Unrelated	Related
Nail discoloration	1	Non-serious	101	283	Unrelated	Related
Sinusitis	2	Non-serious	103	110	Unrelated	Unrelated
Fatigue	2	Non-serious	126	Unresolved	Unrelated	Related
Sinus pain	2	Non-serious	126	129	Unrelated	Unrelated
Nasal congestion	2	Non-serious	138	227	Unrelated	Related
Upper respiratory tract infection	2	Non-serious	138	157	Unrelated	Related

Event	Most extreme grade	Serious / non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Dyspnea	2	Non-serious	143	227	Unrelated	Related
Neuropathy peripheral	3	Non-serious	143	Unresolved	Unrelated	Related
Edema peripheral	2	Non-serious	151	Unresolved	Unrelated	Related
Foot fracture	2	Non-serious	173	283	Unrelated	Unrelated
Upper respiratory tract infection	2	Non-serious	174	283	Unrelated	Related

Study Number/CRTN:	CO40016/305631	Patient number	2046
Demographics:	73-year-old female (race unknown)		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade ≥ 3 Diarrhea		
Event 2 (PT) Categories:	Diarrhea AE leading to study treatment discontinuation, AESI: Grade ≥ 3 Diarrhea		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/304191	Patient number	2051
Demographics:	68-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 2 (PT)	Peripheral sensory neuropathy		

Category:	AE leading to study treatment discontinuation

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/304623	Patient number	2062
Demographics:	43-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Diarrhea AESI: Grade $\geq$ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with lobular, well differentiated, ER/PR positive and HER2 negative right breast cancer (T3N2aM0), approximately 7 years prior to study entry.

On Study Day –905, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative disease in metastatic tissue. At screening sites of disease involvement included liver (L1 and left lobe subcapsular), bone (multiple) and right ovary. The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	**Therapy Setting/Intent**	**Treatments details**	**Start Day**	**Stop Day**
Surgery	Curative	Right modified radical mastectomy	Approximately 7 years prior to study entry	NA
Cancer therapy	Adjuvant	Doxorubicin, cyclophosphamide and paclitaxel	Approximately 7 years prior to study entry	Approximately 7 years prior to study entry
Cancer therapy	Adjuvant	Tamoxifen	Approximately 7 years prior to study entry	Approximately 2 years 5 months prior to study entry

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Adjuvant	Right chest wall, sub-clavicular area, supraclavicular area, right axilla (50 cGy, 25 fractions)	Approximately 6 years prior to study entry	Approximately 6 years prior to study entry
Cancer therapy	Metastatic	Fulvestrant	−842	−794
Cancer therapy	Metastatic	Letrozole	−758	−300
Cancer therapy	Metastatic	Exemestane and Everolimus	−299	−40

The patient′s medical history included humerus fracture. Other surgical history included hysterectomy, bilateral salpingo-oophorectomy and appendicectomy. Concurrent conditions included liver disorder and anemia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. On the same day (Study Day 1), she also received loperamide (total daily dose: 4 mg) prophylactically for diarrhea.

Concomitant medications ongoing at Study Day 1 included calcium/cholecalciferol and denosumab.

The patient experienced Grade 2 diarrhea (non-serious, related to ipatasertib) from Study Day 51 to Study Day 52 and Grade 2 proctalgia (non-serious, unrelated) from Study Day 51 to Study Day 53. She received treatment with diosmectite and loperamide (total daily dose: 4 mg) for diarrhea and *Quercus spp*. bark extract for proctalgia.

On Study Day 61, the patient experienced Grade 1 diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide (total daily dose: 2 mg) and diarrhea was considered resolved. On Study Day 64, dose of loperamide increased to 4 mg.

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 66.

On Study Day 67, the patient experienced non-serious Grade 2 (initial intensity) diarrhea. On Study Day 70, dose of loperamide was further increased to 6 mg and she also received diosmectite for diarrhea. On Study Day 79, the event of diarrhea worsened to Grade 3.

Loperamide dose was increased to 8 mg (details reported in table below). On the same day (Study Day 79), the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Prophylaxis of diarrhea	4	PO	1	1
Diarrhea	2	PO	2	6
Diarrhea	4	PO	7	21
Diarrhea	4	PO	30	36
Diarrhea	2	PO	30	30
Diarrhea	4	PO	31	36
Diarrhea	2	PO	37	42
Diarrhea	4	PO	43	43
Diarrhea	2	PO	44	45
Diarrhea	4	PO	46	46
Diarrhea	2	PO	47	49
Diarrhea	4	PO	50	54
Diarrhea	2	PO	61	63
Diarrhea	4	PO	64	69
Diarrhea	6	PO	70	74
Diarrhea	4	PO	75	75
Diarrhea	6	PO	76	76
Diarrhea	4	PO	77	78
Diarrhea	8	PO	79	79
Diarrhea	4	PO	87	92
Diarrhea	2	PO	93	99
Diarrhea	4	PO	100	100
Diarrhea	2	PO	101	103
Diarrhea	4	PO	104	106
Diarrhea	2	PO	115	115
Diarrhea	2	PO	124	128
Diarrhea	2	PO	158	158

Due to the event of diarrhea, there was no change in study treatment with paclitaxel; however, ipatasertib dose was reduced to 300 mg on Study Day 86.

The Investigator considered diarrhea to be unrelated to paclitaxel and related to ipatasertib.

Study treatment with paclitaxel first interrupted and then permanently discontinued as per patient′s wish. The last dose of paclitaxel was administered on Study Day 212.

On Study Day 274, a radiographic response assessment showed disease progression.

On Study Day 289, study treatment with ipatasertib was permanently discontinued due to disease progression. The patient received the last dose of ipatasertib on Study Day 288. She entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Investigational drug (SAR439859)	316	372
Radiotherapy to brain (30 cGy, 10 fractions)	462	476

On Study Day 472, the patient withdrew consent from study.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Drug hypersensitivity	1	Non-serious	15	15	Unrelated	Related
Alopecia	1	Non-serious	22	289	Unrelated	Related
Fatigue	1	Non-serious	53	Resolving	Unrelated	Unrelated
Back pain	1	Non-serious	138	144	Unrelated	Unrelated
Back pain	1	Non-serious	168	171	Unrelated	Unrelated
Influenza like illness	1	Non-serious	176	181	Unrelated	Unrelated
Back pain	1	Non-serious	196	197	Unrelated	Unrelated
Nausea	1	Non-serious	197	198	Unrelated	Unrelated
Pain in extremity	1	Non-serious	199	201	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Proctalgia	1	Non-serious	212	242	Unrelated	Unrelated
Paresthesia	2	Non-serious	214	Unresolved	Unrelated	Related
Influenza	2	Non-serious	233	242	Unrelated	Unrelated
Lipase increased	4	Non-serious	241	323	Related	Related
Amylase increased	2	Non-serious	241	313	Related	Related

Study Number/CRTN:	CO40016/304335	Patient number	2092
Demographics:	37-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Abdominal pain SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/307256	Patient number	2102
Demographics:	39-year-old Asian female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Additional category:	Death due to disease progression		

A narrative for this patient is available under Section 1.2; Narratives for patients who died due to disease progression.

Study Number/CRTN:	CO40016/305252	Patient number	2116
Demographics:	78-year-old female (Race unknown)		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		
Event 2 (PT) Categories:	Diarrhea SAE, AESI: Grade ≥ 3 diarrhea		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304622	Patient number	2118
Demographics:	65-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Diarrhea AESI: Grade $\geq$ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive, and HER2 negative right breast cancer (T2N1M0), approximately 7 years prior to study entry following right partial mastectomy.

On Study Day -327, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included chest wall, lung (bilateral lower lobe and parenchyma), lymph node (hilum of the right lung, retroperitoneum, and mediastinum: right paratracheal), soft tissue (4th right rib) and bone (right humerus). The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Cyclophosphamide and doxorubicin	Approximately 7 years prior to study entry	Approximately 6 years prior to study entry
Cancer therapy	Adjuvant	Paclitaxel	Approximately 6 years prior to study entry	Approximately 6 years prior to study entry
Cancer therapy	Adjuvant	Letrozole	Approximately 6 years prior to study entry	−460
Radiotherapy	Adjuvant	Right breast and lymph nodes (5000 cGy; 25 fractions)	Approximately 6 years prior to study entry	Approximately 6 years prior to study entry
Cancer therapy	Metastatic	Fulvestrant	Approximately 9 months prior to study entry	−54
Surgery	Curative	Right breast axillary dissection	−241	NA

No medical history was reported. Other surgical history included arthroscopy and hysterectomy. Concurrent conditions included hypertension, osteoporosis, neuropathy peripheral, pain in extremity, and edema peripheral.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. On the same day (Study Day 1), she started receiving loperamide (total daily dose: 4 mg) for diarrhea.

Concomitant medications ongoing at Study Day 1 included calcium carbonate/cholecalciferol, cholecalciferol, nebivolol, gabapentin, paracetamol/tramadol, ibuprofen, *Aesculus hippocastanum* extract, zoledronic acid, and omeprazole.

On Study Day 10, the patient experienced Grade 1 diarrhea (non-serious, related to ipatasertib). On Study Day 13, diarrhea worsened to Grade 2 and loperamide dose was increased to 12 mg (for detailed dosing please refer to table below). She also received treatment with atropine sulfate/diphenoxylate and codeine. On Study Day 16, diarrhea improved to Grade 1. On Study Day 24, the event of diarrhea was considered resolved. On Study Day 26, loperamide was stopped.

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 36.

On Study Day 37, the patient experienced non-serious Grade 2 (initial intensity) diarrhea. Treatment with atropine sulfate/diphenoxylate and codeine was maintained. On Study Day 38, diarrhea improved to Grade 1. On Study Day 128, the event of diarrhea worsened to Grade 3 (most extreme intensity). Grade changes details during the course of the event are reported in the table below. On Study Day 148, she was again started on loperamide (for detailed dosing please refer to table below). On Study Day 445, the event of diarrhea was considered resolved.

Grade change details for diarrhea:

Study Day	Grade changes for diarrhea
13	2
16	1
38	1
50	2
51	1
66	2
67	1
68	2
70	1
73	2

Study Day	Grade changes for diarrhea
74	1
76	2
77	1
78	2
79	1
97	2
100	1
103	2
105	1
128	3
129	1
132	3
133	2
136	3
138	2
140	1
141	3
142	1
157	2
158	1
195	2
196	1
226	2
227	1
229	2
230	1
231	2
232	1
242	2
243	1
244	2
245	1
249	2
250	1
259	2
260	1
276	2
277	1
286	2
287	1
305	2
307	1
340	2
341	1
388	2
389	1

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	1	12
Diarrhea	12	PO	13	13
Diarrhea	6	PO	14	14
Diarrhea	4	PO	15	26
Diarrhea	4	PO	148	156
Diarrhea	10	PO	157	157
Diarrhea	6	PO	158	159
Diarrhea	8	PO	160	160
Diarrhea	4	PO	161	161
Diarrhea	8	PO	162	162
Diarrhea	4	PO	163	169
Diarrhea	4	PO	183	195
Diarrhea	6	PO	196	196
Diarrhea	4	PO	197	203
Diarrhea	2	PO	204	204
Diarrhea	4	PO	211	223
Diarrhea	6	PO	224	226
Diarrhea	4	PO	227	228
Diarrhea	6	PO	229	229
Diarrhea	4	PO	230	231
Diarrhea	2	PO	232	232
Diarrhea	4	PO	239	245
Diarrhea	6	PO	246	246
Diarrhea	4	PO	247	247
Diarrhea	6	PO	248	248
Diarrhea	4	PO	249	252
Diarrhea	6	PO	253	253
Diarrhea	4	PO	254	259
Diarrhea	2	PO	260	260
Diarrhea	4	PO	267	280
Diarrhea	6	PO	281	281
Diarrhea	4	PO	282	287
Diarrhea	2	PO	288	288
Diarrhea	4	PO	295	301
Diarrhea	8	PO	302	302
Diarrhea	4	PO	303	308
Diarrhea	6	PO	309	309
Diarrhea	4	PO	310	315
Diarrhea	2	PO	317	317
Diarrhea	4	PO	323	325
Diarrhea	4	PO	327	329
Diarrhea	6	PO	330	330
Diarrhea	4	PO	331	333
Diarrhea	6	PO	334	334
Diarrhea	4	PO	335	336
Diarrhea	6	PO	337	337
Diarrhea	4	PO	338	344
Diarrhea	4	PO	351	357
Diarrhea	6	PO	358	358

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	359	360
Diarrhea	6	PO	361	361
Diarrhea	4	PO	362	364
Diarrhea	6	PO	365	365
Diarrhea	4	PO	366	372
Diarrhea	2	PO	373	374
Diarrhea	4	PO	379	385
Diarrhea	6	PO	386	386
Diarrhea	4	PO	387	393
Diarrhea	6	PO	394	394
Diarrhea	4	PO	395	399
Diarrhea	2	PO	400	400
Diarrhea	4	PO	407	427
Diarrhea	2	PO	428	428
Diarrhea	2	PO	432	432
Diarrhea	4	PO	435	435
Diarrhea	2	PO	436	436

There was no change in study treatment due to the event of diarrhea.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 436, a radiographic response assessment showed disease progression with new lesions in brain (bilateral choroid plexus, right occipital and left parietal).

On Study Day 464, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 421 and ipatasertib on Study Day 436. The patient entered into the long-term follow-up.

On Study Day 480, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Pyrexia	2	Non-serious	4	7	Unrelated	Unrelated
Pain in extremity	2	Non-serious	4	8	Unrelated	Unrelated
Aphthous ulcer	1	Non-serious	7	10	Unrelated	Related
Nausea	2	Non-serious	10	11	Related	Unrelated
Pyrexia	2	Non-serious	10	14	Unrelated	Unrelated
Face edema	1	Non-serious	23	27	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Rash pruritic	1	Non-serious	24	27	Unrelated	Unrelated
Cataract	2	Non-serious	61	115	Unrelated	Unrelated
Nausea	2	Non-serious	66	67	Related	Unrelated
Neutropenia	2	Non-serious	82	87	Unrelated	Related
Neuropathy peripheral	2	Non-serious	114	Resolving	Unrelated	Related
Onycholysis	1	Non-serious	114	Resolving	Unrelated	Related
Urinary tract infection	2	Non-serious	142	147	Unrelated	Unrelated
Palmar-plantar erythrodysesthesia syndrome	1	Non-serious	143	445	Related	Unrelated
Neutropenia	2	Non-serious	176	183	Unrelated	Related
Pain in extremity	1	Non-serious	177	186	Unrelated	Unrelated
Hemoptysis	2	Non-serious	208	208	Unrelated	Unrelated
Hemoptysis	1	Non-serious	209	262	Unrelated	Unrelated
Pharyngitis	2	Non-serious	234	239	Unrelated	Unrelated
Anemia	2	Non-serious	267	294	Unrelated	Related
Hemoptysis	1	Non-serious	280	295	Unrelated	Unrelated
Cough	1	Non-serious	320	Resolving	Unrelated	Unrelated
Cystitis	2	Non-serious	326	336	Unrelated	Unrelated
Musculoskeletal pain	1	Non-serious	327	333	Unrelated	Unrelated
Bronchitis	1	Non-serious	388	404	Unrelated	Unrelated
Anemia	2	Non-serious	435	464	Unrelated	Related

Study Number/CRTN:	CO40016/304623	Patient number	2126
Demographics:	72-year-old White female		

Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)
Cohort:	Cohort B
Event 1 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea
Event 2 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/304880	Patient number	2148
Demographics:	74-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Categories:	Diarrhea SAE, AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Febrile neutropenia AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/305252	Patient number	2152
Demographics:	69-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 3 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 4 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 5 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/304634	Patient number	2175
Demographics:	55-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative right breast cancer (T1cN0M0), approximately 9 years prior to study entry following right lumpectomy.

On Study Day −763, the patient was diagnosed with metastatic disease (ER and PR status were unknown and HER2 status was not assessed) in metastatic tissue. At screening, site of disease

involvement included lung (segment 7), liver (whole liver) and bone (right acetabulum of the hip joint). The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Docetaxel and Cyclophosphamide	Approximately 8 years prior to study entry	Approximately 8 years prior to study entry
Cancer therapy	Adjuvant	Tamoxifen	Approximately 8 years prior to study entry	Approximately 2 years prior to study entry
Radiotherapy	Adjuvant	Right breast (total dose: 4250 cGy; 17 fractions)	Approximately 8 years prior to study entry	Approximately 8 years prior to study entry
Radiotherapy	Adjuvant	Boost (total dose: 1000 cGy; 4 fractions)	Approximately 8 years prior to study entry	Approximately 8 years prior to study entry
Radiotherapy	Metastatic	Bone (right hip) (total dose: 3000 cGy; 10 fractions)	−752	−742
Cancer therapy	Metastatic	Fulvestrant	−744	−625
Cancer therapy	Metastatic	Letrozole	−597	−506
Radiotherapy	Metastatic	Bone (C6 and TH5) (total dose: 2000 cGy; 5 fractions)	−511	−506
Cancer therapy	Metastatic	Radium 223 dichloride	−484	−343
Cancer therapy	Metastatic	Exemestane and Everolimus	−484	−91
Radiotherapy	Metastatic	Liver (total dose: 50 cGy; 10 fractions)	−57	−49

No medical or other surgical history was reported. Concurrent conditions included bone pain and asthenia.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel. She received loperamide prophylactically from Study Day 1 to Study Day 28 (total daily dose: 4 mg).

Concomitant medications ongoing at Study Day 1 included zoledronic acid and nimesulide.

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 36 and ipatasertib (400 mg) on Study Day 38.

On Study Day 39, the patient experienced non-serious Grade 2 diarrhea. She received treatment with loperamide (8 mg). The following day (Study Day 40), diarrhea worsened to Grade 3. Reportedly, dietary etiologies and infections were ruled out (details not provided). She received treatment with loperamide (16 mg), diosmectite and intravenous hydration with glucose and unspecified electrolytes. She was also given dietary advice. On Study Day 41, diarrhea improved to Grade 2. On Study Day 44, the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea prophylaxis	4	PO	1	28
Diarrhea	8	PO	39	39
Diarrhea	16	PO	40	40
Diarrhea	10	PO	41	41
Diarrhea	8	PO	42	43
Diarrhea	4	PO	44	44

Due to the event of diarrhea, there was no change in study treatment with paclitaxel; however, study treatment with ipatasertib was interrupted on Study Day 42 and thereafter permanently discontinued due to disease progression (see narrative below).

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 54, a radiographic response assessment showed disease progression with new lesions in bone (right acetabulum of the hip joint).

On Study Day 57, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 36 and ipatasertib on Study Day 41. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Paclitaxel	57	256
Doxorubicin	284	543
Capecitabine	564	753
Letrozole	760	Ongoing
Alpelisib	781	816
Cyclophosphamide	837	Ongoing

On Study Day 864, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Neutropenia	4	Non-serious	8	22	Unrelated	Related
Anemia	2	Non-serious	8	Unresolved	Unrelated	Related
Thrombocytopenia	1	Non-serious	29	36	Unrelated	Related
Neutropenia	3	Non-serious	42	57	Unrelated	Related

Study Number/CRTN:	CO40016/304627	Patient number	2185
Demographics:	78-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/306252	Patient number	2189
Demographics:	49-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/318833	Patient number	2199
Demographics:	59-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Category:	Diarrhea AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Chronic gastritis SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/305629	Patient number	2201
Demographics:	68-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Categories:	Diarrhea SAE, AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Categories:	Diarrhea SAE, AESI: Grade ≥ 3 diarrhea		
Event 3 (PT) Categories:	Enterocolitis SAE, AESI: Grade ≥ 2 enterocolitis/colitis		
Event 4 (PT) Category:	Intestinal obstruction SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

1.8 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥ 2 COLITIS/ ENTEROCOLITIS

Study Number/CRTN:	CO40016/305629	Patient number	2201
Demographics:	68-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Categories:	Diarrhea SAE, AESI: Grade ≥ 3 diarrhea		
Event 2 (PT) Categories:	Diarrhea SAE, AESI: Grade ≥ 3 diarrhea		
Event 3 (PT) Categories:	Enterocolitis SAE, AESI: Grade ≥ 2 enterocolitis/colitis		
Event 4 (PT) Category:	Intestinal obstruction SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

1.9 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥ 3 RASH

Study Number/CRTN:	CO40016/307263	Patient number	2038
Demographics:	69-year-old Asian female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 day cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 day cycle)		
Cohort	Cohort B		
Event (PT) Category:	Drug eruption AESI: Grade ≥ 3 rash		

The patient was randomized on Study Day -1.

The patient was diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 negative locally advanced unresectable metastatic left breast cancer (T4cN1M1), on Study Day -72.

At screening sites of disease involvement included bone, lymph nodes (left axillary), and left breast

No past cancer treatment was reported.

No medical/surgical history was reported. The patient's concurrent conditions included cancer pain, and skin ulcer.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included guaiazulene and metronidazole.

Event: Drug eruption (Severe drug eruption)

Prior to the event of drug eruption, the most recent dose of paclitaxel was administered on Study Day 232 and ipatasertib (400 mg) on Study Day 238.

On Study Day 239, the patient was noted with severe non-serious Grade 2 drug eruption (site and presenting symptoms not reported). She received treatment with betamethasone, hydrocortisone, oxytetracycline, nadifloxacin, and prednisolone. On Study Day 701, the event of drug eruption worsened to Grade 3. She received further treatment with diflucortolone. On Study Day 827, the event of drug eruption improved to Grade 2. On Study Day 841, the event of drug eruption was considered resolved.

Due to the event of drug eruption, there was no change in the study treatment with paclitaxel; however, treatment with ipatasertib was interrupted on Study Day 652 and the next dose was given on Study Day 673.

The Investigator considered drug eruption, to be related to ipatasertib and other cause (unspecified) and unrelated to paclitaxel.

On Study Day 784, radiographic response assessment showed disease progression with new lesions in liver (S7).

On Study Day 777, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 771 and ipatasertib on Study Day 777. The patient entered into long-term follow-up phase.

On Study Day 841, the patient was lost to follow-up.

Other AEs experienced by patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Diarrhea	2	Non-serious	5	799	Related	Unrelated
Vomiting	2	Non-serious	14	799	Unrelated	Unrelated
Decreased appetite	2	Non-serious	15	799	Unrelated	Unrelated
Urticaria	1	Non-serious	26	36	Unrelated	Unrelated
Hypophosphatasemia	1	Non-serious	36	799	Unrelated	Unrelated
Hyperglycemia	2	Non-serious	48	422	Unrelated	Related
Pyrexia	1	Non-serious	48	49	Unrelated	Unrelated
Contrast media allergy	1	Non-serious	55	55	Unrelated	Unrelated
Pneumonitis	1	Non-serious	55	784	Related	Related
Urticaria	2	Non-serious	107	113	Unrelated	Unrelated
Dermatitis contact	2	Non-serious	141	Unresolved	Unrelated	Unrelated
Nasopharyngitis	1	Non-serious	455	463	Unrelated	Unrelated
Product dose omission issue	—	Non-serious	526	528	—	—
Folliculitis	2	Non-serious	573	617	Unrelated	Unrelated
Contusion	1	Non-serious	780	799	Not Applicable	Not Applicable

Study Number/CRTN:	CO40016/307260	Patient number	2071
Demographics:	46-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Category:	Rash maculo-papular Grade ≥ 3 rash		

The patient was randomized on Study Day 1.

The patient was diagnosed with ductal, moderately differentiated, ER/PR positive and HER 2-negative metastatic left breast cancer (T2N1M1) on Study Day −705 following left breast biopsy.

At screening, sites of disease involvement included bone (multiple bone metastasis) and liver (right and left lobes). The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Metastatic	Goserelin and tamoxifen	−658	−351
Surgery	Curative	Left partial mastectomy	−531	NA
Cancer therapy	Metastatic	Goserelin and anastrozole	−350	−295
Cancer therapy	Metastatic	Goserelin, exemestane and histone deacetylase unspecified	−294	−183
Cancer therapy	Metastatic	Goserelin, palbociclib and fulvestrant	−182	−36

No medical or surgical history was reported. Concurrent conditions included hyperuricemia, hepatic function abnormal and hypertension.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

Event: Rash maculo-papular

Prior to the event of rash maculo-papular, the most recent dose of paclitaxel was administered on Study Day 8 and ipatasertib (400 mg) on Study Day 14. From Study Day 15, study treatment with ipatasertib was interrupted due to an event of Grade 2 neutrophil count decreased (non-serious, related).

On Study Day 16, the patient experienced non-serious Grade 1 itchy rash maculo-papular which gradually diffused and worsened to Grade 3 on Study Day 19. She was started on treatment with prednisolone, clemastine and betamethasone/dexchlorpheniramine maleate. On Study Day 29, the event of rash maculo-papular improved to Grade 2; however, itchiness and redness continued. Grade changes during the course of the event are reported in the table

below. She further received treatment with fexofenadine and betamethasone valerate. The event of rash maculo-papular remained unresolved at the time of study discontinuation.

Study Day	Grade changes for rash
19	3
29	2
36	1
77	2
85	1
161	2
166	1

Due to this event, there was no change in study treatment with paclitaxel; however, dose of ipatasertib was reduced to 300 mg from Study Day 36.

The Investigator considered rash maculo-papular, to be related to ipatasertib and unrelated to paclitaxel.

On Study Day 947, a radiographic response assessment showed disease progression. Subsequently, study treatment was permanently discontinued with the last dose of paclitaxel and ipatasertib given on Study Day 939 and Study Day 952, respectively. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatment	**Start Day**	**Stop Day**
Epirubicin (10 cycles) and cyclophosphamide (8 cycles)	966	Ongoing

On Study Day 1198, the patient was permanently discontinued from the study as per the physician's decision (LTFU terminated by Sponsor).

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious / non-serious**	**Onset Day**	**Resolution Day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**
Stomatitis	1	Non-serious	3	15	Related	Related
Constipation	1	Non-serious	3	4	Unrelated	Related
Arthralgia	2	Non-serious	4	23	Related	Related
Pyrexia	1	Non-serious	4	4	Related	Related
Diarrhea	1	Non-serious	7	23	Related	Unrelated
Malaise	1	Non-serious	10	13	Related	Related
Decreased appetite	1	Non-serious	10	13	Related	Related
Neutrophil count decreased	2	Non-serious	15	99	Related	Related
Diarrhea	2	Non-serious	53	966	Related	Unrelated
Arthralgia	1	Non-serious	53	92	Related	Related
Nausea	1	Non-serious	58	80	Related	Related

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Malaise	1	Non-serious	87	88	Related	Related
Nausea	1	Non-serious	87	127	Related	Related
Nasopharyngitis	1	Non-serious	96	113	Unrelated	Unrelated
Oropharyngeal pain	1	Non-serious	116	117	Unrelated	Unrelated
Stomatitis	1	Non-serious	132	137	Related	Related
Nausea	1	Non-serious	143	422	Related	Related
Oropharyngeal pain	1	Non-serious	144	145	Unrelated	Unrelated
Arthralgia	1	Non-serious	175	Unresolved	Unrelated	Unrelated
Epistaxis	1	Non-serious	197	330	Unrelated	Related
Stomatitis	1	Non-serious	197	204	Related	Related
Stomatitis	1	Non-serious	238	243	Related	Related
Treatment non-compliance	Not reported	Not reported	256	256	Not reported	Not reported
Nail discoloration	1	Non-serious	267	Unresolved	Related	Related
Nail Ridging	1	Non-serious	267	Unresolved	Related	Related
Treatment non-compliance	Not reported	Not reported	306	306	Not reported	Not reported
Epistaxis	1	Non-serious	334	335	Unrelated	Unrelated
White blood cell count decreased	2	Non-serious	344	435	Unrelated	Related
Mucosal inflammation	1	Non-serious	354	423	Related	Related
Neutrophil count decreased	3	Non-serious	365	435	Related	Unrelated
Nasopharyngitis	2	Non-serious	430	442	Related	Related
Neutrophil count decreased	1	Non-serious	449	505	Related	Related
Contusion	2	Non-serious	484	966	Unrelated	Unrelated
Stomatitis	1	Non-serious	488	Unresolved	Related	Related
Dysgeusia	1	Non-serious	519	966	Unrelated	Related
White blood cell count decreased	2	Non-serious	533	841	Unrelated	Related
Abdominal pain	2	Non-serious	563	564	Unrelated	Unrelated
Cystitis	2	Non-serious	565	569	Unrelated	Related
Abdominal pain	1	Non-serious	589	590	Unrelated	Unrelated
Neutrophil count decreased	1	Non-serious	589	841	Unrelated	Related
Oropharyngeal pain	1	Non-serious	661	662	Unrelated	Unrelated
Anemia	1	Non-serious	672	785	Related	Related
Headache	1	Non-serious	674	675	Unrelated	Related
Fatigue	1	Non-serious	674	Unresolved	Unrelated	Related
White blood cell count decreased	1	Non-serious	869	966	Unrelated	Related
Neutrophil count decreased	1	Non-serious	869	897	Unrelated	Related
Neutrophil count decreased	1	Non-serious	925	966	Unrelated	Related

Study Number/CRTN:	CO40016/304332	Patient number	2098
Demographics:	57-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Rash erythematous AESI: Grade ≥ 3 rash		
Event 2 (PT) Category:	Aspartate aminotransferase increased AESI: Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Categories:	Alanine aminotransferase increased AE leading to study treatment discontinuation, AESI: Grade ≥ 3 hepatotoxicity		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/304640	Patient number	2135
Demographics:	59-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Rash AESI: Grade ≥ 3 rash		
Event 2 (PT) Category:	Dyspnea SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/305639	Patient number	2173
Demographics:	61-year-old Asian female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Rash maculo-papular AESI: Grade ≥ 3 rash		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR positive and HER2 receptor equivocal, left breast cancer (T1cNxM0), approximately 7 years prior to study entry.

On Study Day -905, the patient was diagnosed with metastatic disease with ER/PR positive and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included liver, bone and chest (right pleural effusion). The patient was assessed by the Investigator to have endocrine resistant disease.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left lumpectomy	Approximately 7 years prior to study entry	NA
Radiotherapy	Adjuvant	Left breast (total dose unknown; 37 fractions)	Approximately 7 years prior to study entry	Approximately 7 years prior to study entry
Cancer therapy	Adjuvant	Anastrozole	Approximately 7 years prior to study entry	-987
Cancer therapy	Metastatic	Palbociclib and letrozole	-896	-196
Cancer therapy	Metastatic	Palbociclib and fulvestrant	-196	-104
Cancer therapy	Metastatic	Exemestane and everolimus	-104	-43

The patient′s medical history included pneumonitis. No other surgical history was reported. Concurrent conditions included hypertension, post menopause, dyspepsia, rhinitis allergic, metastasis to bone, arthralgia (right shoulder) and right pleural effusion.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included calcium carbonate/cholecalciferol, esomeprazole, hydrochlorothiazide/lisinopril and denosumab.

Event: Rash maculo-papular

Prior to the event of rash maculo-papular, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 14.

On Study Day 15, the patient experienced non-serious Grade 3 maculo-papular rash. She had received two injections of filgrastim on Study Day 15 and Study Day 16 for neutrophil count decreased (for details please refer to other AEs table below) and the investigator felt that possibility of relationship of rash to filgrastim could not be ruled out. The investigator classified the eruption as generalized morbilliform (exanthematous; maculopapular) drug eruption. It was considered as minor non-exfoliative and non-ulcerative rash.

On Study Day 18, a biopsy performed to exclude other possibilities revealed superficial perivascular infiltrate containing numerous eosinophils and foci of subtle interface changes. All these features were entirely consistent with drug eruption secondary to ATK inhibitor (ipatasertib). However, filgrastim was not excluded as the cause of the event but was less likely related. She received treatment with triamcinolone for symptomatic relief of her minor pruritus and methylprednisolone (treatment details reported in table below). On Study Day 42, rash maculo-papular improved to Grade 1. On Study Day 56, the event of rash maculo-papular was considered as resolved.

On the same day (Study Day 56), radiographic response assessment showed disease progression. However, the patient continued to receive the study treatment as per the physician′s decision since the patient had received few doses of study treatment and measurements of the lesions were not available. Also, it was concluded that the patient was deriving benefit from the treatment.

Rash maculo-papular treatment details:

Treatment	Indication	Dose (Units: mg)	Route	Frequency	Start day	Stop day
Triamcinolone	Rash maculo-papular	0.1*	TO	BID	18	Ongoing
Methylprednisolone	Rash maculo-papular	4	PO	QID	21	22
Methylprednisolone	Rash maculo-papular	4	PO	Q3D	23	24
Methylprednisolone	Rash maculo-papular	4	PO	BID	25	26
Methylprednisolone	Rash maculo-papular	4	PO	QD	27	28

*Units: %

Due to the event of rash maculo-papular, Cycle 2 Day 1 dose of paclitaxel was interrupted, and ipatasertib was interrupted from Study Day 18. The next dose of paclitaxel was administered on Study Day 35 and ipatasertib on Study Day 42 at a reduced dose of 300 mg.

The Investigator considered rash maculo-papular to be related to ipatasertib and paclitaxel.

On Study Day 84, a repeat response assessment showed disease progression.

On Study Day 98, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 91 and ipatasertib on Study Day 97. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine	98	203

On Study Day 401, the patient died due to disease progression. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Fatigue	1	Non-serious	2	Unresolved	Related	Related
Dry mouth	1	Non-serious	3	Unresolved	Related	Unrelated
Flatulence	1	Non-serious	3	Unresolved	Unrelated	Unrelated
Neutrophil count decreased	2	Non-serious	14	28	Related	Related
Peripheral motor neuropathy	1	Non-serious	61	Unresolved	Unrelated	Related
Diarrhea	1	Non-serious	74	75	Related	Related
Diarrhea	1	Non-serious	85	Unresolved	Related	Related
Hypokalemia	1	Non-serious	98	Unresolved	Unrelated	Unrelated

Study Number/CRTN:	CO40016/306642	Patient number	2176
Demographics:	44-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Categories:	Rash AE leading to study treatment discontinuation, AESI: Grade ≥ 3 rash		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

1.10 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥ 2 PNEUMONITIS

Study Number/CRTN:	CO40016/305631	Patient number	2029
Demographics:	50-year-old female (race unknown)		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Categories:	Pneumonitis SAE, AE leading to study treatment discontinuation, AESI: Grade ≥ 2 Pneumonitis		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

Study Number/CRTN:	CO40016/304640	Patient number	2120
Demographics:	63-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Categories:	Pneumonitis SAE, Grade ≥ 3 pneumonitis		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

1.11 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥ 3 HEPATOTOXICITY

Study Number/CRTN:	CO40016/304193	Patient number	2005
Demographics:	62-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Alanine aminotransferase increased AESI: Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Category:	Aspartate aminotransferase increased AESI: Grade ≥ 3 hepatotoxicity		
Additional category:	Death due to disease progression		

A narrative for this patient is available under Section 1.2; Narratives for patients who died due to disease progression.

Study Number/CRTN:	C040016/305626	Patient number	2048
Demographics:	57-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		

Cohort	Cohort B
Event (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity

The patient was randomized on Study Day 1.

The patient was initially diagnosed with poorly differentiated, ER positive/PR positive and HER 2-receptor negative, right breast cancer (T4N2M0; histological subtype: not otherwise specified) on Study Day −84.

On Study Day −31, the patient was diagnosed with locally recurrent disease with ER/PR positive and HER2 negative disease in recurrent/metastatic tissue. At screening, sites of disease involvement included right breast (retro areolar lesion and anterior antero-lesion in glandular tissue) and right axillary adenopathy.

No past cancer treatment was reported.

No medical history was reported. The patient′s other surgical history included hysterectomy, cholecystectomy, benign breast lump removal and breast operation (duct excision). Concurrent conditions included hypertriglyceridemia.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 were reported.

Event Alanine aminotransferase increased

Prior to the event of alanine aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 1 and ipatasertib on Study Day 6.

On Study Day 7, a laboratory work-up showed ALT 226 U/L (normal range: 6-30 U/L) and AST 105 U/L (normal range: 9-31 U/L) and the patient was noted with non-serious Grade 3 alanine aminotransferase increased and Grade 2 aspartate aminotransferase increased (non-serious, unrelated). It was reported that the event was caused by guanabana leaves infusion which the patient took even though she was instructed not to take the infusion. No treatment was given for these events. On Study Day 28, the event of aspartate aminotransferase increased was considered resolved. On Study Day 35, the event of alanine aminotransferase increased was considered resolved.

Relevant laboratory work-up:

Study Day	**AST** Normal range: 9-31 U/L	**ALT** Normal range: 6-30 U/L	**Total bilirubin** Normal range: 0.1-1 mg/dL	**ALP** Normal range: 35-104 U/L
Screening	18	20	0.64	134
7	105	226	1.32	186
14	50	119	1.15	216
28	21	40	0.67	191
35	14	21	0.72	156

There was no change in study treatment due to the event of alanine aminotransferase increased.

The Investigator considered alanine aminotransferase increased, to be unrelated to ipatasertib and paclitaxel and related to other causes.

On Study Day 371, study treatment was permanently discontinued as per physician decision (the principal investigator decided to discontinue the patient due to the need for surgery) with the last dose of paclitaxel given on Study Day 354 and ipatasertib on Study Day 361. The patient entered into long-term follow up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
″Other″ surgery of right breast	386	NA
Doxorubicin and cyclophosphamide	466	539
Anastrozole	582	Ongoing
Radiotherapy to breast and rib grid (dose: 5000 cGy and 25 fractions)	639	672

On Study Day 1187, the patient was lost to follow-up.

Other AEs experienced by the patient during the study:

Event	Most extreme Grade	Serious/ Non-Serious	Onset Day	Resolution Day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Hypertriglyceridemia	3	Non-serious	56	168	Unrelated	Unrelated
Paresthesia	1	Non-serious	78	Unresolved	Unrelated	Related
Dysuria	1	Non-serious	82	84	Unrelated	Unrelated
Nausea	1	Non-serious	121	121	Unrelated	Related
Dyslipidemia	2	Non-serious	130	Unresolved	Unrelated	Unrelated
Nausea	1	Non-serious	179	179	Unrelated	Related
Urinary tract infection	2	Non-serious	232	237	Unrelated	Unrelated
Bronchitis	2	Non-serious	291	305	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304335	Patient number	2064
Demographics:	48-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Category:	Anemia AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Gamma-glutamyl transferase increased Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Category:	Leukopenia AE leading to study treatment discontinuation		
Event 4 (PT) Category:	Neutropenia AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/304879	Patient number	2074
Demographics:	47-year-old Asian female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event (PT) Category:	Alanine aminotransferase increased AESI: Grade $\geq$ 3 hepatotoxicity		

The patient was randomized on Study Day 1.

The patient was diagnosed with ductal, ER/PR positive, HER2 negative, metastatic left breast cancer (T2N2M1; histological grade unknown) on Study Day −665.

At screening sites of disease involvement included liver (right S8 metastasis and multiple), bone (multiple) and chest wall nodule. The patient was assessed by the Investigator to have endocrine resistance.

Past cancer treatment is listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Metastatic	Palbociclib, exemestane and leuprorelin	−632	−38

No medical or surgical history was reported. Concurrent conditions included Grade 1 alanine aminotransferase increased and Grade 1 aspartate aminotransferase increased.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included zoledronic acid.

Event: Alanine aminotransferase increased (ALT increased)

Prior to the event of alanine aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 15 and ipatasertib (400 mg) on Study Day 21.

On Study Day 29, a laboratory work-up showed worsening of pre-existing aspartate aminotransferase increased (non-serious, related) and alanine aminotransferase increased to Grade 2 (non-serious) with AST 130 U/L and ALT 156 U/L. On Study Day 36, the event of alanine aminotransferase increased further worsened to Grade 3 (ALT 291 U/L). She received

treatment with *Silybum marianum*, ursodeoxycholic acid and calcium pantothenate/cyanocobalamin/folic acid/nicotinamide/pyridoxine hydrochloride/riboflavin/thiamine mononitrate/zinc oxide. On Study Day 43, the events of alanine aminotransferase increased and aspartate aminotransferase increased were considered resolved.

Due to the event of alanine aminotransferase increased, study treatment with ipatasertib was interrupted on Study Day 29 and Cycle 2 Day 1 and Cycle 2 Day 8 doses of paclitaxel were not administered. The next dose of paclitaxel and ipatasertib was given on Study Day 43.

The Investigator considered alanine aminotransferase increased, to be related to ipatasertib and paclitaxel.

The patient was noted with another episode of Grade 2 alanine aminotransferase increased (non-serious, related to ipatasertib) from Study Day 57 to Study Day 71. Relevant laboratory work-up reported in the table below. Treatment with *Silybum marianum*, ursodeoxycholic acid and calcium pantothenate/ cyanocobalamin/ folic acid/ nicotinamide/ pyridoxine hydrochloride/ riboflavin/ thiamine mononitrate/ zinc oxide was maintained.

Relevant laboratory work-up:

Study Day	**AST** Normal range: 1-40 U/L	**ALT** Normal range: 1-40 U/L	**Bilirubin** Normal range: 0.2-1.2 mg/dL	**ALP** Normal range: 30-115 U/L
Screening	71	76	0.6	181
29	130	156	0.6	249
36	170	291	0.6	328
43	61	115	0.7	345
57	93	143	0.4	256
71	56	93	0.4	229

On Study Day 274, a radiographic response assessment showed disease progression with progression of non-target lesions. On Study Day 278, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and ipatasertib given on Study Day 265 and Study Day 271, respectively. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	**Start Day**	**Stop Day**
Fulvestrant	278	307
Doxorubicin and Cyclophosphamide	335	356
Vinorelbine and capecitabine	424	Ongoing

On Study Day 524, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)
Pruritus	1	Non-serious	2	13	Related	Unrelated
Constipation	1	Non-serious	6	9	Unrelated	Unrelated
Aphthous ulcer	1	Non-serious	8	56	Related	Unrelated
Rash	2	Non-serious	8	56	Related	Unrelated
Pruritus	1	Non-serious	15	56	Related	Unrelated
Edema	1	Non-serious	25	56	Related	Unrelated
Alopecia	1	Non-serious	37	Unresolved	Related	Related
Neuropathy peripheral	2	Non-serious	118	Unresolved	Unrelated	Related
Edema	1	Non-serious	190	Unresolved	Related	Unrelated
Diarrhea	1	Non-serious	237	277	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304332	Patient number	2098
Demographics:	57-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Rash erythematous AESI: Grade ≥ 3 rash		
Event 2 (PT) Category:	Aspartate aminotransferase increased AESI: Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Categories:	Alanine aminotransferase increased AE leading to study treatment discontinuation, AESI: Grade ≥ 3 hepatotoxicity		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/304880	Patient number	2131
Demographics:	61-year-old Asian female		

Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)
Cohort:	Cohort B
Event 1 (PT) Category:	Alanine aminotransferase increased AESI: Grade ≥ 3 hepatotoxicity
Event 2 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/305247	Patient number	2133
Demographics:	72-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event 1 (PT) Category:	Alanine aminotransferase increased AESI: Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		

A narrative for this patient is available under Section 1.4; Narratives for patients who experienced adverse events leading to study treatment discontinuation.

Study Number/CRTN:	CO40016/304786	Patient number	2136
Demographics:	48-year-old White male		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort:	Cohort B		
Event 1 (PT) Category:	Anxiety SAE		
Event 2 (PT) Category:	Alanine aminotransferase increased AESI: Grade ≥ 3 hepatotoxicity		

Event 3 (PT) Category:	Nausea AE leading to study treatment discontinuation
Event 4 (PT) Category:	Asthenia AE leading to study treatment discontinuation
Event 5 (PT) Category:	Fatigue AE leading to study treatment discontinuation

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

1.12 NARRATIVES FOR PATIENTS WHO EXPERIENCED POTENTIAL DRUG-INDUCED LIVER INJURY AS DEFINED BY HY'S LAW

No patient experienced potential drug-induced liver injury as defined by Hy's law while in the study.

1.13 NARRATIVES FOR PATIENTS WHO EXPERIENCED SUSPECTED TRANSMISSION OF AN INFECTIOUS AGENT BY THE STUDY DRUG

No patient experienced suspected transmission of an infectious agent by the study drug while in the study.

1.14 NARRATIVES FOR PATIENTS WHO EXPERIENCED COVID-19 SAE

Study Number/CRTN:	CO40016/305633	Patient number	2122
Demographics:	70-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle)		
Cohort	Cohort B		
Event (PT) Categories:	COVID-19 SAE, AE leading to study treatment discontinuation, COVID-19 SAE		

A narrative for this patient is available under Section 1.3; Narratives for patients who experienced serious adverse event(s).

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1. NARRATIVES

1.1 NARRATIVES FOR THE PATIENT WHO DIED DUE TO AN ADVERSE EVENT(S)

Study Number/CRTN:	CO40016/305639	Patient number	3016
Demographics:	62-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Peripheral motor neuropathy AE leading to study treatment discontinuation		
Event 3 (PT) Category:	Fatigue AE leading to study treatment discontinuation		
Event 4 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 5 (PT) Categories:	Cardiac arrest Deaths due to adverse event, SAE		

The patient was randomized on Study Day – 1.

The patient was initially diagnosed with ductal, ER negative, PR positive and HER2 negative, left breast cancer (T1N0M0, histological grade unknown) approximately 4 years and 5 months prior to study entry.

On Study Day – 56, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative in metastatic tissue. At screening sites of disease involvement included lymph nodes (port hepatis node and other adenopathy/periaortic).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Simple Mastectomy of bilateral breast	Approximately 4 years and 4 months prior to study entry	NA

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	'Other' surgery of left lymph node	-862	NA
Cancer therapy	Adjuvant	Paclitaxel	-850	-721
Radiotherapy	Adjuvant	Left chest wall and superior vena cava fossa/axilla (dose: 5000 cGy and 25 fractions) and breast mastectomy scar (boost) (dose: 1000 cGy and 5 fractions)	-744	-703

The patient's medical history included basal cell carcinoma. Surgical history included appendicectomy, cholecystectomy and hysterectomy. Concurrent conditions included insomnia, hypertension, anxiety, gastroesophageal reflux disease, macular degeneration, asthma, and hyperglycemia.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab. On the same day (Study Day 1), the patient received loperamide prophylactically (total daily dose: 4 mg).

Concomitant medications ongoing at Study Day 1 included nadolol, hydrochlorothiazide/triamterene, lisinopril, salbutamol, escitalopram oxalate, cetirizine hydrochloride, lorazepam and loratadine.

On Study Day 4, the patient experienced Grade 1 diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide (details in the table below). The event of diarrhea was considered resolved on the same day.

On Study Day 6, the patient experienced Grade 2 diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide (details in the table below) and atropine sulfate/diphenoxylate hydrochloride. On Study Day 10, the event of diarrhea was considered resolved.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of atezolizumab was administered on Study Day 1, paclitaxel on Study Day 8 and ipatasertib (400 mg) on Study Day 10.

On Study Day 11, the patient experienced non-serious Grade 3 diarrhea. No diagnostic test was performed. It was reported that the patient was not taking treatment with atropine

sulfate/diphenoxylate hydrochloride properly and was re-educated to continue the treatment with atropine sulfate/diphenoxylate hydrochloride. She experienced 7-8 bowel movements during the event. On Study Day 13, the event of diarrhea was considered resolved.

There was no change in study treatment due to the event of diarrhea.

The Investigator considered diarrhea, to be related to ipatasertib, paclitaxel and atezolizumab.

Loperamide details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	1	1
Diarrhea	2	PO	3	3
Diarrhea	4	PO	4	4
Diarrhea	2	PO	5	6
Diarrhea	4	PO	7	8
Diarrhea	2	PO	9	10

On Study Day 14, the patient experienced 5-6 bowel movements and was noted with Grade 2 diarrhea (non-serious, related to ipatasertib). She received treatment with atropine sulfate/diphenoxylate hydrochloride for the event. On Study Day 29, it was reported that she did not have any further episodes of diarrhea and it was considered resolved.

Event 2: Peripheral motor neuropathy

Prior to the event of peripheral motor neuropathy, the most recent dose of atezolizumab was administered on Study Day 29, paclitaxel and ipatasertib (400 mg) on Study Day 36.

On Study Day 37, the patient was noted with non-serious Grade 1 peripheral motor neuropathy (presenting signs and symptoms not reported). She received treatment with gabapentin for the event of peripheral motor neuropathy. The event of peripheral motor neuropathy remained unresolved at the time of patient's death (see narrative below).

The Investigator considered peripheral motor neuropathy, to be unrelated to ipatasertib and atezolizumab and related to paclitaxel and other cause (unspecified).

Event 3: Fatigue

Prior to the event of fatigue, the most recent dose of atezolizumab was administered on Study Day 85, paclitaxel and ipatasertib (400 mg) on Study Day 92.

On Study Day 93, the patient experienced non-serious Grade 1 fatigue. She received treatment with ferric carboxymaltose for the event of fatigue. The event of fatigue remained unresolved at the time of patient's death (see narrative below).

The Investigator considered fatigue, to be unrelated to atezolizumab and related to paclitaxel, ipatasertib and other cause (unspecified).

Due to the events of peripheral motor neuropathy and fatigue, there was no change in study treatment with ipatasertib and atezolizumab, however, study treatment with paclitaxel was permanently discontinued with last dose administered on Study Day 113.

Event 4: Aspartate aminotransferase increased (AST increase)

Prior to the event of aspartate aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 113, atezolizumab on Study Day 183 and ipatasertib (400 mg) on Study Day 189.

On Study Day 169, the patient was noted with Grade 1 aspartate aminotransferase increased (AST: 64 U/L, normal range: 15-46 U/L) and Grade 2 blood lactate dehydrogenase increased (LDH: 746 U/L, normal range: 313-618 U/L) (both non-serious, unrelated). No treatment was administered for the events.

On the same day (Study Day 169), a CT of chest, abdomen and pelvis showed interval enlargement of portacaval and gastric hepatic ligament nodes with heterogeneity of hepatic enhancement. Non-specific hepatitis, reactive nodes and disease progression were suspected as the reason for this appearance.

On Study Day 170, an MRI of abdomen showed abnormal appearance of the liver with differential metastatic disease, drug induced hepatotoxicity or possibly and atypical appearance of untreated metastatic disease.

On Study Day 183, the patient was noted with Grade 1 alanine aminotransferase increased (ALT: 49 U/L, normal range: 11-66 U/L) and Grade 1 blood alkaline phosphatase increased (ALP: 142 U/L, normal range: 38-126 U/L) (both non-serious, unrelated). No treatment was administered for the events.

On Study Day 194, the event of aspartate aminotransferase increased was considered resolved.

On Study Day 195, the patient was noted with Grade 2 aspartate aminotransferase increased (AST value not reported) (non-serious, unrelated). No treatment was administered for the event.

On Study Day 196, abdominal ultrasound showed enlarged liver with pronounced parenchymal heterogeneity with no clearly definable focal hepatic mass identified. The abnormal appearance

of the liver was nonspecific with differential considerations including neoplastic and non-neoplastic processes indicated in prior MRI. It showed enlarged gastro hepatic/porta hepatis lymph nodes. Liver biopsy and CT scan were recommended.

On Study Day 204, the patient was noted with Grade 1 blood bilirubin increased (bilirubin: 1.50 mg/dL, normal range: 0.2-1.3 mg/dL) (non-serious, unrelated). No treatment was administered for the event. On Study Day 205, the event of blood bilirubin increased was considered resolved.

On Study Day 209, the event of aspartate aminotransferase increased was considered resolved.

On Study Day 210, the patient′s laboratory work-up showed: AST: 256 U/L (normal range: 15-46 U/L) and bilirubin: 2.30 mg/dL (normal range: 0.2-1.3 mg/dL), leading to diagnosis of non-serious Grade 3 aspartate aminotransferase increased and Grade 2 blood bilirubin increased (non-serious, unrelated). Relevant laboratory work-up throughout the event was not reported. No treatment was administered for the events. The event of aspartate aminotransferase increased was resolving and blood bilirubin increased blood lactate dehydrogenase increased, alanine aminotransferase increased, and blood alkaline phosphatase increased remained unresolved at the time of patient′s death (see narrative below).

Due to the event of aspartate aminotransferase increased, study treatment with atezolizumab was interrupted on Study Day 183, ipatasertib was interrupted on Study Day 189, and was never resumed later (see narrative below)

The Investigator considered aspartate aminotransferase increased, to be unrelated to ipatasertib and atezolizumab and related to other cause (unspecified) (causality relation with paclitaxel was NA).

On Study Day 212, an echocardiogram showed severe pulmonary hypertension, Left ventricular ejection fraction (LVEF): 67%, no left ventricular hypertrophy, mild diastolic dysfunction, severe pulmonary hypertension, right ventricular systolic pressure (RVSP): 81 mmHg, no pericardial effusion, no aortic dilatation, mild right atrial and right ventricular enlargement.

Event 5: Cardiac arrest

Prior to the event of cardiac arrest, the most recent dose of paclitaxel was administered on Study Day 113, atezolizumab on Study Day 183 and ipatasertib (400 mg) on Study Day 189. It was also the last dose prior to death.

On Study Day 215, the patient experienced respiratory distress, lost consciousness and hospitalized for life-threatening cardiac arrest. A chest compression was given and after 30 minutes of resuscitation the patient returned with spontaneous circulation. Chest X-ray showed cardiomegaly, diffuse bilateral airway disease, greater on left side than on right with a

suspected effusion layering out posteriorly on the left and no pneumothorax. Changes noted in lung were suspected due to progression and not considered as inflammatory changes. Relevant vital signs were not reported. Laboratory work-up showed troponin was elevated at: 0.251 ng/mL (normal value: $<$0.045 ng/mL), lactic acid: 14.1 mmol/L (normal range: 0.4-2.0 mmol/L), pH arterial: 7.21 (normal range: 7.34-7.45), pCO_2 arterial: 56 mmHg (normal range: 35-45 mmHg), pO_2 arterial: 113 mmHg (72-84 mmHg), lactate arterial: 17.0 mmoL (normal range: $<$2.00), base excess arterial: 6.2 mmol/L (normal range: 2-2 mmol/L), glucose: 69 mg/dL (70-110 mg/dL), blood urea nitrogen: 69 mg/dL (normal range: 7-18 mg/dL), carbon dioxide: 11 mmol/L (normal range: 21-32 mmol/L), potassium: 5.4 mmol/L (normal range: 3.5-5.0 mmol/L) and creatinine: 1.50 mg/dL (normal range: 0.60-1.30 mmol/L). An ECG showed atrial fibrillation with a competing junctional pacemaker and right bundle branch block. She received treatment with epinephrine, amiodarone, atropine, dobutamine, magnesium sulfate and sodium bicarbonate for the event of cardiac arrest. A few minutes later, she was reported to have lost pulse again due to which code was called and advanced cardiovascular life support (ACLS) was initiated. After another 30 minutes of resuscitation, no pulse was noted, and family decided to withdraw from any cardio resuscitative efforts. She remained pulseless. At 10:52 hours, the patient was pronounced dead. It was unknown whether an autopsy was performed or not.

There was no change in study treatment due to the event of cardiac arrest (action taken with paclitaxel was NA).

The Investigator considered cardiac arrest, to be unrelated to ipatasertib, paclitaxel and atezolizumab and related to disease under study.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Gingival pain	1	Non-serious	26	28	Unrelated	Related	Related
Rash maculo-papular	1	Non-serious	80	84	Unrelated	Unrelated	Unrelated
Hyperglycemia	2	Non-serious	92	93	Related	Unrelated	Unrelated
Hypokalemia	2	Non-serious	112	120	Unrelated	Unrelated	Unrelated
Vascular device occlusion	2	Non-serious	155	155	Unrelated	NA	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Nausea	1	Non-serious	177	Unresolved	Related	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305629	Patient number	3085
Demographics:	58-year-old American Indian or Alaska Native female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Categories:	Diarrhea SAE, Grade $\geq$ 3 diarrhea		
Event 2 (PT) Category:	Myositis SAE		
Event 3 (PT) Category:	Myocarditis SAE		
Event 4 (PT) Categories:	Pulmonary embolism Death due to adverse event, SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with unspecified histology, poorly differentiated, ER/PR and HER2 negative, metastatic left breast cancer (T3N2M1) on Study Day – 44.

At screening, sites of disease involvement included breast [left breast tumor, CSE (not otherwise specified) nodule left breast], liver (hepatic nodule segment VII), lymph nodes (left lateral axillary adenopathy, left axillary ganglion), mediastinum (subcarinal ganglion) and bone (multiple bone metastasis).

No past cancer treatments were reported.

No medical or surgical history was reported. The patient's concurrent conditions included arthralgia (hip) and hypothyroidism.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included levothyroxine and tramadol.

On Study Day 1, the patient started treatment with loperamide (total daily dose: 4 mg, PO) for diarrhea.

On Study Day 3, the patient experienced Grade 2 diarrhea (non-serious, related to paclitaxel and ipatasertib). She received treatment with loperamide (details in the table below). On Study Day 17, the event of diarrhea was considered resolved.

On Study Day 28, the patient experienced Grade 1 diarrhea (non-serious, unrelated). She received treatment with loperamide (details in the table below). On Study Day 60, the event of diarrhea was considered resolved.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of atezolizumab was administered on Study Day 57, paclitaxel on Study Day 64 and ipatasertib (400 mg) on Study Day 67.

On Study Day 68, the patient experienced Grade 3 diarrhea (liquid stools up to 7 times per day persisting since 3 days) associated with general discomfort, nausea, and oral intolerance. She denied fever or any other additional manifestation. Upon physical examination abdomen was soft, depressible, painless, with increased airborne noise and no peritoneal signs. On Study Day 71, the event of diarrhea became serious, and she was hospitalized. She received treatment with loperamide (details in the table below), ciprofloxacin, dexamethasone and sodium chloride. Laboratory work-up was within normal range and stool cultures were without major findings. On Study Day 74, the event of diarrhea improved to Grade 2. On Study Day 78, the event of diarrhea improved to Grade 1. On Study Day 79, the event of diarrhea was considered resolved and she was discharged from the hospital.

Due to the event of diarrhea, there was no change in study treatment with atezolizumab, however, study treatment with ipatasertib was reduced to 300 mg on Study Day 95 and Cycle 3 Day 15 of paclitaxel was not administered. The next dose was given on Study Day 95.

The Investigator considered diarrhea, to be related to ipatasertib and paclitaxel and atezolizumab.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	1	Ongoing
Diarrhea	2	PO	71	77

Event 2: Myositis
Event 3: Myocarditis
Event 4: Pulmonary embolism (Pulmonar thromboembolia)

Prior to the events of myositis, myocarditis and pulmonary embolism, the most recent dose of atezolizumab and paclitaxel administered on Study Day 154 and paclitaxel (300 mg) on Study Day 157.

On Study Day 158, the patient experienced fatigue, chest pain and difficulty in walking. Her vitals showed heart rate 39 beats/min. She was diagnosed with serious Grade 3 myositis. On Study Day 159, the patient laboratory work-up showed lactate dehydrogenase 1163, total creatine phosphokinase 226, creatine phosphokinase-MB 370, glutamic-oxaloacetic transaminase 66, gamma-glutamyl transpeptidase 54 (units and normal ranges not reported), and troponin was negative. An ECG showed sinus rhythm, negative T waves in V1 to V4, II III segment, arteriovenous (AV) fistula with an axis minus 70 degrees, and QTc interval of 0.445. In addition, left anterior fascicular block and a diffuse repolarization disorder to d/c myocardial ischemia. An echocardiography showed conserved systolic function. She was diagnosed with life threatening serious Grade 4 myocarditis. She received treatment with morphine and dexamethasone. The patient had persistent symptoms of muscle weakness with greater intensity in the legs. On Study Day 162, the symptoms of dyspnea and chest pain worsened. She also experienced orthopnea, thoracic pain and a stiff chest. She was noted with heart rate of 39 beats/min. Laboratory work-up showed: glutamic-oxaloacetic transaminase: 83, gamma-glutamyl transpeptidase: 63, lactate dehydrogenase: 1284, total creatine phosphokinase: 220, Creatine phosphokinase-MB: 455 and D-dimer was 6.7 mg/L (normal range not reported). On the same day (Study Day 162), she was hospitalized and TEM thoracic ART angio tomography showed no evidence of pulmonary thromboembolism. Relevant vitals throughout the events were not reported. She received treatment with paracetamol, ceftriaxone, dexamethasone, enoxaparin, omeprazole, enoxaparin and oxygen. COVID test was negative on Study Day 162 and Study Day 163. On Study Day 163, the patient died suddenly with chest pain and respiratory failure and pulmonary embolism was concluded as the cause of death (initial intensity was Grade 4). An autopsy was not performed. The events of myositis and myocarditis remained unresolved at the time of patient's death.

Due to the events of myositis and myocarditis, study treatment with atezolizumab and paclitaxel was interrupted on Study Day 154 and ipatasertib was interrupted on Study Day 157 and was never resumed later (see below).

Due to the event of pulmonary embolism, study treatment with atezolizumab, ipatasertib and paclitaxel was permanently discontinued with last dose of atezolizumab, and paclitaxel administered on Study Day 154 and ipatasertib on Study Day 157.

The Investigator considered myositis, myocarditis and pulmonary embolism, to be unrelated to ipatasertib and paclitaxel and related to atezolizumab and other unspecified cause.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Arthralgia	3	Non-serious	2	6	Unrelated	Related	Unrelated
Decreased appetite	2	Non-serious	3	16	Related	Related	Unrelated
Alanine aminotransferase increased	2	Non-serious	7	14	Unrelated	Unrelated	Unrelated
Aspartate aminotransferase increased	1	Non-serious	7	139	Unrelated	Unrelated	Unrelated
Alanine aminotransferase increased	1	Non-serious	14	56	Unrelated	Unrelated	Unrelated
Vomiting	1	Non-serious	18	19	Unrelated	Unrelated	Unrelated
Alopecia	2	Non-serious	29	Unresolved	Unrelated	Related	Unrelated
Vomiting	1	Non-serious	35	42	Related	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	36	Unresolved	Unrelated	Unrelated	Unrelated
Anemia	2	Non-serious	56	70	Unrelated	Related	Unrelated
Alanine aminotransferase increased	2	Non-serious	63	70	Unrelated	Unrelated	Unrelated
Vomiting	1	Non-serious	66	68	Unrelated	Unrelated	Unrelated
Alanine aminotransferase increased	1	Non-serious	92	Unresolved	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	103	133	Unrelated	Unrelated	Unrelated
Blood cholesterol increased	1	Non-serious	152	Unresolved	Related	Unrelated	Unrelated
Hypothyroidism	2	Non-serious	159	Unresolved	Unrelated	Unrelated	Related

Study Number/CRTN:	CO40016/305629	Patient number	3090
Demographics:	54-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Categories:	Suspected COVID-19 Death due to AE, SAE, AE leading to study treatment discontinuation, COVID-19 SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR negative and HER2 negative left breast cancer (T4bN2M1) on Study Day − 40.

At screening, sites of disease involvement included liver (hepatic nodule segment IV and VII), tumor left breast, lymph node (retropectoral ganglion conglomerate and left axillary adenopathy).

No past cancer treatments are reported.

No medical/surgical history was reported. No concurrent conditions were reported.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, atezolizumab and paclitaxel.

No concomitant medications ongoing at Study Day 1 was reported.

Event: Suspected COVID-19 (suspected covid-19 infection)

Prior to the event of suspected COVID-19, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 106 and ipatasertib (400 mg) on Study Day 111.

On Study Day 112, the patient experienced fever (body temperature not reported), pharyngeal pain, nasal congestion, and pharyngeal pain and received symptomatic treatment at home. From Study Day 113 to Study Day 115, her fever continued along with worsening of her general discomfort. On Study Day 116, the patient experienced dyspnea and lung X-ray revealed multifocal pneumonia and suspected severe COVID-19. Subsequently, she was hospitalized. Upon admission, her oxygen saturation was 91% which raised to 95% on binasal cannula. On an unspecified day, oxygen saturation decreased to 92% and then to 91% and she was put on

oxygen support with reservoir mask at 10 L per minute. It was reported that patient might got exposed while being mobilized in taxi for treatment cycle or got infected from her brother. She received treatment with ceftriaxone, hydroxychloroquine, azithromycin, enoxaparin, and paracetamol. On the following day (Study Day 117), a chest tomography revealed poorly defined patched spotlights, peripherally distributed, lustered glass in apical segments of upper and more diffused lobes in middle right lobe, upper and lower left lingula segment and in bilateral basal posterior segment associated with bindings in lower left lingula segment and in bilateral basal posterior segment. A laboratory work-up showed glucose 112 mg/dL, urea 22 mg/dL, creatinine 0.45 mg/dL, WBC count 10100 mil/mm^3, neutrophils 79%, lymphocytes 13%, monocytes 5%, eosinophils 1% and 2% bastons, platelet count 386,000 mil/mm^3, AST 38 U/L, ALT 19 U/L, DHL 703 U/L, protein C-reactive (PCR) 18.6 mg/dL, prothrombin time 13.1 and INR 1.19. Despite of treatment administration, on Study Day 120, her oxygen saturation was decreased to 87% showed progressive deterioration and due to collapse of health system mechanical ventilation was not provided. She also received treatment with hyoscine, dimenhydrinate and fentanyl. On Study Day 121, blood samples showed CPK-MB 29 U/L, creatinine 0.31 mg/dL, glucose 45 mg/dL, DHL 800 U/L, ALP 143 U/L, potassium 2.87 mmol/L, sodium 144 mmol/L, ALT 21 U/L, AST 16 U/L, troponin T < 0.003, urea 23 mg/dL, WBC count 12800×10^3/L, neutrophils 73%, lymphocytes 21%, monocytes 4%, prothrombin time 12.6, INR 1.14, PTT 40, PCR 27.5 mg/dL and fibrinogen 767. On Study Day 124, the patient died due to COVID-19 and progressive deterioration. An autopsy was not performed.

Relevant vitals reported in the table below:

Study Day	**Body temperature** (°C)	**Blood pressure** (mmHg)	**Respiratory rate** (breaths per minute)	**Pulse rate** (beats per minute)
-6	37	118/82	16	72
106	36	120/70	20	74
106	36.6	120/60	20	86
106	36.4	110/70	20	91

Relevant laboratory work-up reported in the table below:

Study Day	**WBC count** (normal range: 4.5-11 $\times 10^3/\mu L$)	**Absolute neutrophil count** (normal range: 1.8-8.2 $\times 10^3/\mu L$)	**Absolute lymphocyte count** (normal range: 1-4.8 $\times 10^3/\mu L$)
-2	11.33	7.02	3.34
91	7.54	4.82	1.97
98	5.77	3.22	2.15
105	4.47	2.34	1.78

Due to this event, study treatment with atezolizumab, paclitaxel and ipatasertib was permanently discontinued with the last dose given on Study Day 106 and Study Day 111 respectively.

The investigator considered suspected COVID-19 to be unrelated to atezolizumab, paclitaxel and ipatasertib and related to other causes.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Hyperglycemia	1	Non-serious	2	Unresolved	Related	Unrelated	Unrelated
Vomiting	1	Non-serious	2	2	Unrelated	Related	Unrelated
Hyperglycemia	2	Non-serious	2	2	Related	Unrelated	Unrelated
Diarrhea	2	Non-serious	3	10	Related	Unrelated	Unrelated
Diarrhea	2	Non-serious	11	17	Related	Unrelated	Unrelated
Alopecia	1	Non-serious	24	Unresolved	Unrelated	Related	Unrelated
Upper respiratory tract infection	2	Non-serious	41	49	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	57	77	Related	Unrelated	Unrelated
Nausea	1	Non-serious	57	77	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	80	97	Related	Unrelated	Unrelated
Nausea	1	Non-serious	92	105	Related	Unrelated	Unrelated

1.2 NARRATIVES FOR PATIENTS WHO DIED DUE TO DISEASE PROGRESSION

Study Number/CRTN:	CO40016/304634	Patient number	3026
Demographics:	50-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Category:	Death due to disease progression		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER/PR negative and HER2 negative left breast cancer (T2N0M0) (histopathology unknown), approximately 2 years and 7 months prior to study entry.

The patient was diagnosed with metastatic disease on Study Day − 50 with ER /PR status unknown and HER2 receptor not assessed in metastatic tissue. At screening, sites of disease involvement included midline (pleura behind the sternum and soft tissue sternum), liver (bilateral segment IVB, V and VI), bone (midline sacrum with a soft tissue tumor), chest (midline nodular infiltrate at the sternum), pleura (nodular infiltrates merging with lymph nodes), liquid pleural cavity, bilateral liver, whole bone, and chest (midline nodular infiltrate).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	Approximately 2 years and 6 months prior to study entry	Approximately 2 years and 4 months prior to study entry
Cancer therapy	Neoadjuvant	Paclitaxel (12 cycles)	Approximately 2 years and 3 months prior to study entry	Approximately 2 years prior to study entry
Surgery	Curative	Left radical mastectomy	Approximately 1 years 11 months prior to study entry	–
Radiotherapy	Metastatic	Sternum (dose:20 cGy; 5 fractions)	−23	−19

No medical/surgical history was reported. The patient′s concurrent conditions included lower back pain, chest pain and hypertension.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included bisoprolol, telmisartan and zoledronic acid.

On Study Day 297, study treatment was permanently discontinued due to symptomatic deterioration (neurologic symptoms, weakness, bone, joints pain and dizziness) with the last dose of atezolizumab given on Study Day 282, paclitaxel on Study Day 289 and ipatasertib on Study Day 290. The patient entered into long-term follow-up.

On Study Day 318, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipataseritib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	5	6	Related	Unrelated	Unrelated
Diarrhea	2	Non-serious	10	11	Related	Unrelated	Unrelated
Diarrhea	2	Non-serious	14	16	Related	Unrelated	Unrelated
Diarrhea	2	Non-serious	18	18	Related	Unrelated	Unrelated
Diarrhea	2	Non-serious	20	23	Related	Unrelated	Unrelated
Rash	2	Non-serious	25	29	No	Related	Unrelated
Diarrhea	2	Non-serious	30	35	Related	Unrelated	Unrelated
Alopecia	2	Non-serious	37	Unresolved	Not Applicable	Unrelated	Related
Diarrhea	2	Non-serious	38	42	Related	Unrelated	Unrelated
Anemia	1	Non-serious	43	120	Not Applicable	Unrelated	Related
Diarrhea	1	Non-serious	44	56	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	76	78	Related	Unrelated	Unrelated
Neutropenia	2	Non-serious	113	120	Unrelated	Unrelated	Related
Anemia	1	Non-serious	157	Unresolved	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	157	184	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	198	205	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	212	233	Unrelated	Unrelated	Related
Blood triglycerides increased	1	Non-serious	254	Unresolved	Unrelated	Related	Unrelated

Study Number/CRTN:	CO40016/304792	Patient number	3048
Demographics:	52-year-old female (Unknown race)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Category:	Rash SAE		
Additional category:	Death due to disease progression		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated-Grade 2, ER/PR negative and HER2 negative left breast cancer (T4N2M1), on Study Day − 56.

At screening, sites of disease involvement included left breast (superior lateral), right axillary lymph node, left side of chest (subcutaneous region on the left lateral face of the chest-abdomen transition-hypochondrium region) and anterior wall of the upper third of the left hemithorax, involving the left subclavian artery, right axillary and inter and retro pectoral lymph node enlargement, as well as prominent prepericardial lymph nodes, bilateral skin nodular formations representing secondary lesions spread throughout the subcutaneous trunk region and liver (nodular lesion in the liver-kidney space).

No past cancer treatments are reported.

No medical/surgical history was reported. The patient′s concurrent conditions included hypertension, thrombosis, pain in extremity (upper left limb) and edema peripheral (upper left limb).

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included hydrochlorothiazide, metamizole, codeine/paracetamol and nifedipine.

Event: Rash

Prior to the event of rash, the most recent dose of atezolizumab was administered on Study Day 1, paclitaxel Study Day 22 and ipatasertib (400 mg) on Study Day 28.

On Study Day 29, at 12:20 hours, Cycle 2 of the atezolizumab infusion started. No pre-medications were reported. Towards the end of atezolizumab infusion, she experienced systemic infusion reaction due to medically significant Grade 2 rash associated with itching and plaques all over body. At 12:58 hours infusion with atezolizumab was completed. She received treatment with diphenhydramine and dexamethasone. Later, on the same day (Study Day 29), the event of rash was considered resolved.

Due to this event, there was no change in the study treatment with ipatasertib and paclitaxel; however, Cycle 2 Day 15 of atezolizumab was delayed and given on Study Day 43.

The Investigator considered rash to be unrelated to paclitaxel and ipatasertib and related to atezolizumab.

On Study Day 106, a radiographic response assessment showed disease progression with new pleural effusion to the left.

On Study Day 113, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and atezolizumab given on Study Day 99 and ipatasertib on Study Day 105. The patient entered into the long-term follow-up.

On Study Day 127, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Infected neoplasm	1	Non-serious	4	15	Unrelated	Unrelated	Unrelated
Blood alkaline phosphatase increased	1	Non-serious	14	63	Unrelated	Unrelated	Related
Anemia	2	Non-serious	21	Unresolved	Unrelated	Unrelated	Related
Hyperglycemia	1	Non-serious	28	63	Related	Unrelated	Unrelated
Weight decreased	1	Non-serious	36	57	Unrelated	Unrelated	Unrelated
Diarrhea	2	Non-serious	43	50	Related	Unrelated	Related

Alopecia	1	Non-serious	57	Unresolved	Unrelated	Unrelated	Related
Hyperglycemia	1	Non-serious	70	85	Related	Unrelated	Unrelated
Blood alkaline phosphatase increased	1	Non-serious	85	Unresolved	Unrelated	Unrelated	Related

Study Number/CRTN:	CO40016/319619	Patient number	3062
Demographics:	52-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Blood glucose increased Grade ≥ 3 hyperglycemia		
Event 2 (PT) Category:	Diabetes mellitus Grade ≥ 3 hyperglycemia		
Additional category:	Death due to disease progression		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated ER/PR negative and HER2 negative right breast cancer (T2NXM1) on Study Day − 86.

On Study Day −41, the patient was diagnosed with metastatic disease with ER/PR negative and HER 2 negative in metastatic tissue. At screening sites of disease involvement included bilateral liver (segment VI and segment IV B), right breast (upper inner quadrant), right lung (segment VIII).

No past cancer treatments are reported.

The patient′s medical history included left ovarian cyst. No surgical history was reported. Concurrent conditions included hypertension, obesity, abdominal pain upper, and hyperglycemia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medication ongoing at Study Day 1 included amlodipine/indapamide/perindopril, timonacic.

Event 1: Blood glucose increased (Elevated level of glucose)
Event 2: Diabetes mellitus

Prior to the events of blood glucose increased and diabetes mellitus, the most recent dose of atezolizumab was administered on Study Day 170, paclitaxel on Study Day 180 and ipatasertib (200 mg) on Study Day 186.

On Study Day 187, the patient presented to the hospital due to severe weakness. A laboratory work-up showed glucose 14.93 mmol/L (normal range: 3.9-5.5 mmol/L). The patient was diagnosed with non-serious Grade 3 blood glucose increased and non-serious Grade 3 diabetes mellitus.

On the same day (Study Day 187), an overall response assessment showed disease progression with new lesions in liver (increased metastasis).

It was reported that diabetes was related to unspecified steroid therapy. The patient received insulin therapy. The events of blood glucose increased, and diabetes mellitus were considered resolving at the time of patient's death (see narrative below).

Relevant laboratory work-up:

Study Day	**Glucose** Normal range: 3.9-5.5 mmol/L	**HbA1c** Normal range: 0-53 mmol/mol
Screening	5.84	43
187	14.93	–
190	17.27	55

There was no change in the study treatment due to the event of diabetes mellitus.

Due to the event of blood glucose increased, there was no change in the study treatment with atezolizumab and paclitaxel. However, study treatment with ipatasertib interrupted after Study Day 186 and later permanently discontinued due to disease progression (see narrative below).

The Investigator considered blood glucose increased and diabetes mellitus to be unrelated to paclitaxel, atezolizumab and ipatasertib and related to disease under study and concomitant medication (unspecified steroid therapy).

On Study Day 190, study treatment was permanently discontinued due to disease progression with the last dose of atezolizumab administered on Study Day 170, paclitaxel on Study Day 180 and ipatasertib on Study Day 186. The patient then entered the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Cisplatin (single cycle)	190	190

On Study Day 211, the patient died due to disease progression. It was unknown whether an autopsy was or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Mucosal inflammation	1	Non-serious	7	29	Unrelated	Unrelated	Unrelated
Dyspnea	1	Non-serious	8	8	Unrelated	Unrelated	Unrelated
Flushing	1	Non-serious	8	8	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	9	11	Related	Unrelated	Unrelated
Vomiting	1	Non-serious	11	11	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	17	17	Related	Unrelated	Unrelated
Nausea	2	Non-serious	19	Resolving	Unrelated	Unrelated	Unrelated
Headache	1	Non-serious	26	86	Unrelated	Unrelated	Unrelated
Eye irritation	1	Non-serious	26	86	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	33	37	Related	Unrelated	Unrelated
Vomiting	1	Non-serious	48	48	Unrelated	Unrelated	Unrelated
Fecal volume increased	1	Non-serious	75	91	Related	Unrelated	Unrelated
Polyneuropathy	2	Non-serious	86	Resolving	Unrelated	Unrelated	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Diarrhea	1	Non-serious	94	98	Related	Unrelated	Unrelated
Diarrhea	2	Non-serious	100	115	Related	Unrelated	Unrelated
Incorrect dose administered	–	Non-serious	114	124	Unrelated	Unrelated	–
Diarrhea	1	Non-serious	122	135	Related	Unrelated	Unrelated
Incorrect dose administered	–	Non-serious	125	127	Unrelated	Unrelated	Unrelated
Product dose omission issue	–	Non-serious	133	134	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	136	137	Related	Unrelated	Unrelated
Hypokalemia	1	Non-serious	142	180	Unrelated	Unrelated	Unrelated
Diarrhea	2	Non-serious	148	160	Related	Unrelated	Unrelated
Hand dermatitis	2	Non-serious	156	Resolving	Unrelated	Unrelated	Unrelated
Asthenia	3	Non-serious	170	Resolving	Unrelated	Unrelated	Unrelated
Hypoalbuminemia	1	Non-serious	170	Resolving	Unrelated	Unrelated	Unrelated
Joint swelling	1	Non-serious	172	Resolving	Unrelated	Unrelated	Unrelated
Fecal volume increased	1	Non-serious	178	185	Related	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304332	Patient number	3093
Demographics:	54-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle) + Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Category:	Death due to disease progression		

The patient was randomized on Study Day – 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR negative and HER2 negative, right breast cancer (T4N1M0), approximately 3 years prior to study entry.

On Study Day – 418, the patient was diagnosed with metastatic disease (ER/PR status was unknown and HER2 status not assessed in metastatic tissue). At screening, sites of disease involvement included left breast, bilateral lungs, peritoneum, bilateral ascites, and bone (TH4, TH11, sacral, bilateral iliac).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Cyclophosphamide and doxorubicin (6 cycles each)	Approximately 2 years and 11 months prior to the study entry	– 982
Surgery	Curative	Right breast radical mastectomy	– 959	–
Radiotherapy	Adjuvant	Scar after right breast mastectomy (dose: 46 cGy); iliac bone (dose: 30 cGy); axillary lymph node (dose: 40 cGy); and sub upper clavicular and right parasternal lymph node (dose: 36 cGy)	– 938	– 905

The patient′s medical history included syncope and hypothyroidism. No other surgical history was reported. Concurrent conditions included pain in extremity, goiter, chronic sinusitis, inguinal hernia, hepatic cyst, and renal cyst.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medication ongoing at Study Day 1 included tramadol.

On Study Day 59, a radiographic response assessment showed disease progression with new lesions in right pleural cavity (pleural effusion).

On Study Day 64, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel, atezolizumab and ipatasertib given on Study Day 43 and Study Day 57 and Study Day 63, respectively. The patient entered into long-term follow-up.

On Study Day 84, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Dyspnea	1	Non-serious	9	19	Related	Related	Unrelated
Neutropenia	2	Non-serious	15	22	Unrelated	Related	Unrelated
Sinus tachycardia	1	Non-serious	16	Unresolved	Unrelated	Unrelated	Unrelated
Anemia	2	Non-serious	22	Unresolved	Unrelated	Related	Unrelated

1.3 NARRATIVES FOR PATIENTS WHO EXPERIENCED SERIOUS ADVERSE EVENT

Study Number/CRTN:	CO40016/319067	Patient number	3001
Demographics:	55-year-old female (race unknown)		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Categories:	Dystonia SAE, AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Mixed connective tissue disease AE leading to study treatment discontinuation		

Event 3 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea
Event 4 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea
Event 5 (PT) Category:	Skin infection SAE
Event 6 (PT) Category:	Vomiting SAE
Event 7 (PT) Categories:	Alanine aminotransferase increased SAE, Grade ≥ 3 hepatotoxicity
Event 8 (PT) Categories:	Aspartate aminotransferase increased SAE, Grade ≥ 3 hepatotoxicity

The patient was randomized on Study Day − 1.

The patient was diagnosed with ductal, poorly differentiated ER/PR negative, and HER2 negative right breast cancer (T3N1cMX) approximately 2 years and 9 months prior to study entry.

On Study Day −33, the patient was diagnosed with advanced unresectable disease with ER/PR negative and HER 2 negative. At screening, sites of disease involvement included lymph nodes (bilateral axillary) and right breast.

No past cancer treatment was reported.

No medical/surgical history was reported. The patient′s concurrent conditions included hypertension, anxiety, breast pain, and blood lactate dehydrogenase increased.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	1	Ongoing

Concomitant medications ongoing at Study Day 1 included famotidine, bisoprolol/hydrochlorothiazide, lorazepam, and tramadol.

Event 1: Dystonia
Event 2: Mixed connective tissue disease

Prior to the event of dystonia, the most recent dose of atezolizumab was administered on Study Day 29, paclitaxel on Study Day 36, and ipatasertib (400 mg) was administered on Study Day 34.

On Study Day 37, the patient experienced Grade 3 dystonia (initial intensity Grade 2, symptoms not reported). On Study Day 42, she was hospitalized. A CT scan and MRI of brain were normal. Hematology and chemistry work-up was within normal range. The cerebrospinal fluid analysis was normal. She received treatment with prednisone. On Study Day 45, the event of dystonia was considered resolved and she was discharged from the hospital.

Prior to the event of mixed connective tissue disease, the most recent dose of atezolizumab was administered on Study Day 29, paclitaxel on Study Day 50, and ipatasertib (400 mg) was administered on Study Day 41.

On Study Day 51, a laboratory work-up showed rheumatoid factor $<$ 10 IU/mL and C-reactive protein 45.2 (units and normal range not reported). The patient was diagnosed with non-serious Grade 2 mixed connective tissue disease. She received treatment with hydroxychloroquine, prednisone, and azathioprine. The event of mixed connective tissue disease remained unresolved at the time of patient's death (see narrative below).

Due to the event of mixed connective tissue disease, there was no change in the study treatment with ipatasertib and paclitaxel.

Due to the event of dystonia, Cycle 2 Day 15 of paclitaxel was delayed and was administered on Study Day 50 and treatment with ipatasertib was interrupted on Study Day 42 and the next was dose given on Study Day 59.

Due to the events of dystonia and mixed connective tissue disease study treatment with atezolizumab was permanently discontinued with the last dose given on Study Day 29.

The Investigator considered dystonia and mixed connective tissue disease to be unrelated to ipatasertib and paclitaxel and related to atezolizumab and other cause (unspecified).

On Study Day 69, the patient experienced Grade 2 diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide.

Event 3: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel and ipatasertib (400 mg) was administered on Study Day 71.

On Study Day 72, the ongoing event of diarrhea worsened to non-serious Grade 3 (more than 7 episodes). Treatment with loperamide was maintained and she also received diphenoxylate/atropine without any improvement; thus, dose of loperamide was increased (details not reported) and on Study Day 73, the event of diarrhea was considered resolved.

Due to the event of diarrhea, there was no change in the study treatment with paclitaxel; however, ipatasertib was interrupted on Study Day 72 and the next dose was given on Study Day 74 at a reduced dose of 300 mg from 400 mg.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel and atezolizumab.

Event 4: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel was administered on Study Day 71 and ipatasertib (300 mg) was administered on Study Day 76.

On Study Day 77, the patient experienced non-serious Grade 3 diarrhea. Treatment with loperamide was maintained. On Study Day 80, the event of diarrhea improved to Grade 1. She further received treatment with cholestyramine. On Study Day 154, the event of diarrhea was considered resolved.

Due to the event of diarrhea, Cycle 4 Day 1 of paclitaxel was delayed and treatment with ipatasertib was interrupted on Study Day 80. The next dose of paclitaxel and ipatasertib (at a reduced dose of 200 mg from 300 mg) was given on Study Day 85.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel and atezolizumab.

The patient received on-study anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Radiotherapy (left breast; 3600 cGy, 12 fractions)	107	123

Event 5: Skin infection
Event 6: Vomiting

Prior to the events of skin infection and vomiting, the most recent dose of paclitaxel and ipatasertib was administered (200 mg) was administered on Study Day 99.

On Study Day 123, the patient was noted with wound on the right breast and new discharge areas. She was diagnosed with Grade 2 skin infection. Treatment vancomycin and cefepime was started. On Study Day 124, she experienced Grade 3 vomiting and Grade 2 abdominal pain (non-serious, unrelated). On Study Day 126, the vomiting became uncontrollable associated

with nausea and ongoing abdominal pain. Subsequently, she was hospitalized. Upon admission, her vitals showed body temperature 98.4°F, pulse 99 bpm, blood pressure 107/69 mmHg, respiratory rate 17 breaths/min, and peripheral capillary oxygen saturation 97%. A chest X-ray showed no radiographic evidence of acute cardiopulmonary disease. A CT scan of abdomen and pelvis showed no acute inflammatory or obstructive abnormality. Later, on the same day (Study Day 126), the event of skin infection was considered worsened to Grade 3. She was also diagnosed with cellulitis. She received treatment with ondansetron, and promethazine. On Study Day 127, the event of vomiting was considered resolved. On Study Day 135, she was discharged from the hospital on doxycycline. On Study Day 149, the event of skin infection was considered resolved. On Study Day 154, the event of abdominal pain was considered resolved.

There was no change in the study treatment due to the events of skin infection and vomiting.

The Investigator considered skin infection to be unrelated to ipatasertib, paclitaxel and atezolizumab and related to disease under study and radiotherapy.

The Investigator considered vomiting to be unrelated to ipatasertib, paclitaxel and atezolizumab and related to radiotherapy and other cause (unspecified).

Event 5: Alanine aminotransferase increased (Elevated ALT)
Event 6: Aspartate aminotransferase increased (Elevated AST)

Prior to the events of alanine aminotransferase increased and aspartate aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 197 and ipatasertib (200 mg) was administered on Study Day 202.

On Study Day 203, a laboratory work-up showed AST 252 U/L (normal range: 0-40 U/L), ALT 220 U/L (normal range: 0-23 U/L), ALP 232 U/L (normal range: 39-117 U/L), and bilirubin 0.3 mg/L (normal range: 0-1.2 mg/dL). The patient was diagnosed with Grade 3 alanine aminotransferase increased and Grade 3 aspartate aminotransferase increased. On Study Day 211, she was hospitalized due to elevated liver enzymes associated with epigastric pain radiating to the back, vomiting and decreased appetite. Treatment with proton pump inhibitor was started, however without response. Ultrasound showed hepatic steatosis but normal common bile duct. It was reported that the elevated liver enzyme was due to azathioprine (given for mixed connective tissue disease from Study Day 187 to Study Day 211) and was thus permanently discontinued. On Study Day 213, the event of ALT increased improved to Grade 2 which further improved to Grade 1 on Study Day 217. On Study Day 219, she was discharged from the hospital. On Study Day 218, the event of alanine aminotransferase increased, and aspartate aminotransferase increased were considered resolved.

Relevant laboratory work-up:

Study Day	**AST** Normal range: 0-40 U/L	**ALT** Normal range: 0-32 U/L	**Total bilirubin** Normal range: 0-1.2 mg/dL	**ALP** Normal range: 39-117 U/L
Screening	40	40	0.2	133
203	252	220	0.3	232
210	371	266	0.2	300
218	20[a]	59[b]	0.6[c]	161[d]

[a]normal range: 0-37 U/L, [b]normal range: 0-65 U/L, [c]normal range: 0.2-1.3 mg/dL, [d]normal range: 39-136 U/L

Due to the events of alanine aminotransferase increased, and aspartate aminotransferase increased Cycle 8 Day 15 was not administered, and the next dose was given on Study Day 225. Treatment with ipatasertib was interrupted after Study Day 210 and the next dose was given on Study Day 232.

The Investigator considered alanine aminotransferase increased, and aspartate aminotransferase increased to be unrelated to ipatasertib, paclitaxel and atezolizumab and related to concomitant medication (azathioprine; given of mixed connective tissue disease).

On Study Day 224, an overall response assessment showed disease progression with new lesions in liver.

On Study Day 241, study treatment with paclitaxel and ipatasertib was permanently discontinued due to disease progression with the last dose of paclitaxel and ipatasertib was administered on Study Day 239. The patient then entered the long-term follow-up.

The patient received on-study anti-cancer therapy as listed in table below:

Treatments	**Start Day**	**Stop Day**
Olaparib	253	378

On Study Day 511, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Constipation	1	Non-serious	7	15	Related	Unrelated	Unrelated
Herpes zoster	1	Non-serious	7	28	Unrelated	Unrelated	Unrelated
Urinary incontinence	2	Non-serious	7	35	Unrelated	Unrelated	Unrelated
Facial pain	1	Non-serious	9	59	Unrelated	Unrelated	Unrelated
Dyspepsia	2	Non-serious	9	113	Unrelated	Unrelated	Unrelated
Headache	1	Non-serious	14	59	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	16	32	Related	Related	Related
Periorbital oedema	2	Non-serious	21	Unresolved	Unrelated	Unrelated	Unrelated
Arthralgia	1	Non-serious	28	59	Related	Related	Related
Peripheral sensory neuropathy	1	Non-serious	35	Unresolved	Unrelated	Unrelated	Unrelated
Mastitis	1	Non-serious	35	154	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	36	59	Related	Related	Related
Urinary tract infection	2	Non-serious	38	45	Unrelated	Unrelated	Unrelated
Mastitis	2	Non-serious	59	73	Unrelated	Unrelated	Not applicable
Rash pustular	2	Non-serious	81	90	Unrelated	Unrelated	Not applicable

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipataseritib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Edema peripheral	1	Non-serious	113	Unresolved	Unrelated	Unrelated	Not Applicable
Hypothyroidism	2	Non-serious	168	Unresolved	Related	Unrelated	Not Applicable
Urinary tract infection	2	Non-serious	211	225	Unrelated	Unrelated	Unrelated
Headache	1	Non-serious	219	Unresolved	Unrelated	Unrelated	Unrelated
Dystonia	1	Non-serious	224	Unresolved	Not Applicable	Not Applicable	Not Applicable

Study Number/CRTN:	CO40016/305639	Patient number	3002
Demographics:	43-year-old Black or African American female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Vomiting SAE		
Event 2 (PT) Category:	Diarrhea SAE		
Event 3 (PT) Category:	Pyrexia SAE		
Event 4 (PT) Category:	Pneumonia SAE		
Event 5 (PT) Category:	Flushing AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR negative and HER2 negative right breast cancer (T2N0M0) approximately 3 years prior to study entry followed by right lumpectomy performed approximately 2 years and 11 months prior to study entry.

The patient was diagnosed with metastatic disease on Study Day −14 with ER /PR negative and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included lymph node (bilateral supraclavicular, left anterior posterior window, bilateral mediastinal and retroperitoneal), right left lower pleural cavity, liver segment 7 and pancreatic tail lesion, right chest pleural metastasis and hepatic liver metastasis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Doxorubicin and cyclophosphamide	Approximately 2 years and 10 months prior to study entry	Approximately 2 years and 9 months prior to study entry
Cancer therapy	Adjuvant	Paclitaxel	Approximately 2 years and 9 months prior to study entry	Approximately 2 years and 7 months prior to study entry
Radiotherapy	Adjuvant	Right breast (dose: 2937 cGy; 11 fractions)	Approximately 2 years and 7 months prior to study entry	Approximately 2 years and 6 months prior to study entry

The patient′s medical history included pleural effusion. Surgical history included female sterilization and ligament operation (right ACL). Concurrent conditions included nausea, back pain, dyspnea, anxiety, seasonal allergy, flank pain, non-cardiac chest pain, decreased appetite and fatigue.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included prochlorperazine, ondansetron and oxycodone/paracetamol.

On Study Day 9, the patient experienced Grade 1 vomiting (non-serious, related to ipatasertib). No treatment was reported for vomiting. Later, on the same day, the event of vomiting was considered resolved.

Event 1: Vomiting

Event 2: Diarrhea

Event 3: Pyrexia (Fever)

Event 4: Pneumonia (Lung infection)

Prior to the events of vomiting, diarrhea, pyrexia and pneumonia, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 1, and ipatasertib (400 mg) on Study Day 11.

On Study Day 11, the patient started paclitaxel infusion at 12:14 hours, during infusion, the patient experienced Grade 3 dyspnea (non-serious, related to paclitaxel; oxygen saturation 81%), Grade 3 anxiety (initial intensity Grade 2; non-serious, unrelated), Grade 1 vomiting, and Grade 1 diarrhea. Subsequently, she was hospitalized. She received treatment with loperamide (details reported in table below) for diarrhea. Later, the infusion of paclitaxel was stopped at 12:20 hours. The patient had history of pleural effusion and she underwent right thoracentesis and 1700 mL of fluid was removed. She received treatment with diphenhydramine, famotidine, methylprednisolone, salbutamol, and prednisone for dyspnea and was kept on oxygen therapy with 4 L oxygen with oxygen saturation 88-89%. Her symptoms resolved 10 minutes post treatment. On Study Day 11, the events of vomiting and diarrhea were considered resolved.

Prior to the events of pyrexia and pneumonia, the most recent dose of atezolizumab was administered on Study Day 1, paclitaxel and ipatasertib (400 mg) on Study Day 11.

On Study Day 13, her vitals showed body temperature 39°C with tachycardia (heart rate not reported) and hypotension (blood pressure not reported). A laboratory work-up showed WBC count 6.4 $\times 10^3/\mu L$ (normal range: 4.2-10.2 $\times 10^3/\mu L$). A chest X-ray revealed worsening in diffused right lung infiltrate with persisting moderate right effusion. The patient was diagnosed with Grade 2 pyrexia and Grade 3 pneumonia, leading to prolonged hospitalization. On Study Day 15, a pleural catheter was placed for the drainage of pleural fluid with leads to improvement in dyspnea. At 15:23 hours, a laboratory work-up showed troponin level 0.203 (normal range: 0-0.45; units not reported), and at 21:40 hours, 0.160 (normal range: 0-0.45). A blood culture was negative. She received treatment with vancomycin and cefepime for pyrexia and pneumonia. On Study Day 18, the events of pyrexia and pneumonia were considered resolved and she was discharged from the hospital. On Study Day 21, the event of anxiety was considered resolved. On Study Day 32, the event of dyspnea was considered resolved

Loperamide details:

Indication	Loperamide daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	8	PO	1	2
Diarrhea	2	PO	7	10
Diarrhea	4	PO	11	11

Relevant laboratory values listed in the table below:

Study Day	**WBC count** (normal range: 4.6-10.2 $\times$ $10^3/\mu L$)	**Absolute neutrophil count** (normal range: 2-6.9 $\times$ $10^3/\mu L$)	**Absolute lymphocyte count** (normal range: 0.6-3.7 $\times$ $10^3/\mu L$)	**Body temperature** (°C)
– 4	4.6	3	1.1	35.9
11	5.6	4.1	0.8	36.7
21	7.6	4.4	1.9	—

Due to the events of vomiting and diarrhea, there was no change in study treatment with ipatasertib and atezolizumab; however, Cycle 1 Day 8 of paclitaxel was delayed, and the next dose given on Study Day 11.

Due to the events of pyrexia and pneumonia, there was no change in study treatment with atezolizumab; however, Cycle 1 Day 15 of paclitaxel was delayed and study treatment with ipatasertib was interrupted on Study Day 12. The next dose was given on Study Day 21.

The Investigator considered vomiting to be related to ipatasertib and paclitaxel and unrelated to atezolizumab.

The Investigator considered diarrhea to be related to paclitaxel and unrelated to ipatasertib and atezolizumab.

The Investigator considered pyrexia and pneumonia to be unrelated to atezolizumab, ipatasertib and paclitaxel and related to other causes (unspecified).

Event 5: Flushing

Prior to the event of flushing, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 21 and ipatasertib (400 mg) on Study Day 22.

On Study Day 32, at 15:43 hours, the patient started treatment with paclitaxel infusion. The infusion was started slow and within 22 minutes, the patient experienced Grade 3 dyspnea (non-serious, related to paclitaxel; oxygen saturation 91% on room air) and Grade 2 face flushing. The paclitaxel infusion was stopped at 16:06 hours. She received 2 L oxygen therapy and treatment with diphenhydramine, methylprednisolone and sodium chloride for flushing and dyspnea. Post treatment, her vitals improved, and oxygen saturation was 97%. On Study Day 32, the event of flushing was considered resolved.

Due to this event, there was no change in study treatment with ipatasertib and atezolizumab; however, paclitaxel was permanently discontinued with the last dose given on Study Day 32.

The Investigator considered flushing, to be unrelated to atezolizumab and ipatasertib and related to paclitaxel and other causes (unspecified).

On Study Day 39, a radiographic response assessment showed disease progression

On Study Day 44, study treatment with atezolizumab and ipatasertib was permanently discontinued due to disease progression with the last dose of atezolizumab given on Study Day 32 and ipatasertib on Study Day 38. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Sacituzumab (6 cycles), eribulin (2 cycles), docetaxel (4 cycles), bevacizumab (4 cycles), gemcitabine (6 cycles), carboplatin (6 cycles), letrozole and abemaciclib	45	172

On Study Day 535, the patient died due to disease progression. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Atezolizumab)	Causality (Ipatasertib)	Causality (Paclitaxel)
Retching	1	Non-serious	1	1	Unrelated	Unrelated	Unrelated
Pleural effusion	2	Non-serious	19	Unresolved	Unrelated	Unrelated	Unrelated
Chills	2	Non-serious	21	21	Unrelated	Unrelated	Unrelated
Nausea	1	Non-serious	21	21	Unrelated	Unrelated	Unrelated
Fatigue	1	Non-serious	23	Unresolved	Unrelated	Related	Related
Diarrhea	1	Non-serious	23	Unresolved	Unrelated	Related	Related

Study Number/CRTN:	CO40016/318263	Patient number	3004
Demographics:	63-year-old Asian female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		

Cohort:	Cohort C
Event 1 (PT) Category:	Hyperglycemia Grade ≥ 3 hyperglycemia
Event 2 (PT) Category:	Lymphoedema SAE
Event 3 (PT) Category:	Urinary tract infection SAE
Event 4 (PT) Category:	Febrile neutropenia SAE
Event 5 (PT) Categories:	Pneumonitis SAE, Grade ≥ 2 pneumonitis

The patient was randomized on Study Day 1.

The patient was diagnosed with ductal, poorly differentiated, ER/PR negative and HER2 negative metastatic right breast cancer (T2N3M1) on Study Day −35.

At screening sites of disease involvement included right breast, right cervical neck, lymph node (right supraclavicular and right axillary and right cervical), right bone scapula and right supraclavicular lymph node.

No past cancer treatments are reported.

The patient′s medical history included tumor pain. Surgical history included left shoulder operation. Concurrent conditions included diabetes mellitus and hypertension.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included linagliptin/metformin, irbesartan, simvastatin, glimepiride, and amlodipine.

Event 1: Hyperglycemia

Prior to the event of hyperglycemia, the most recent dose of atezolizumab was administered on Study Day 29, paclitaxel on Study Day 36 and ipatasertib (400 mg) on Study Day 42.

On Study Day 43, a laboratory work-up showed glucose 337 mg/dL and the patient was diagnosed with non-serious Grade 3 hyperglycemia. No treatment was reported for this event. On Study Day 49, the event of hyperglycemia was considered resolved.

Relevant laboratory values listed in the table below:

Study Day	**Glucose** (normal range: 70-100 mg/dL)
– 2	115
43	337
49	113

Due to the event of hyperglycemia, there was no change in the study treatment with paclitaxel. However, study treatment with atezolizumab wasinterrupted on Study Day 30 and next dose given on Study Day 56 and ipatasertib was interrupted on Study Day 43 and next dose was given on Study Day 50 at a reduced dose of 300 mg from 400 mg.

The Investigator considered hyperglycemia to be related to atezolizumab and ipatasertib and unrelated to paclitaxel.

Event 2: Lymphedema

Prior to the event of lymphedema, the most recent dose of atezolizumab was administered on Study Day 29, ipatasertib (400 mg) on Study Day 42. and paclitaxel on Study Day 43.

On Study Day 49, the patient presented due to edema in right arm after waking up. An angio CT-scan showed normal venous system but diffused upper extremity swelling. The patient was diagnosed with Grade 1 lymphedema in right arm, leading to hospitalization. The event occurred due to no position change during sleeping. She received treatment with ketorolac, *Vitis vinifera* seed and aceclofenac. On Study Day 51, the event of lymphedema was considered resolved and she was discharged from the hospital.

There was no change in the study treatment due to the event of lymphedema.

The Investigator considered lymphedema to be unrelated to ipatasertib, paclitaxel and atezolizumab and related to other causes (no position change during sleeping).

Event 3: Urinary tract infection

Event 4: Febrile neutropenia

Event 5: Pneumonia

Prior to the events of urinary tract infection, febrile neutropenia and pneumonia, the most recent dose of atezolizumab was administered on Study Day 56, paclitaxel on Study Day 70 and ipatasertib (400 mg) on Study Day 73.

On Study Day 74, the patient′s experienced fever (body temperature was 38.4°C). A laboratory work-up showed WBC count 0.66 × $10^3/\mu L$ (normal range: 4-10 × $10^3/\mu L$), absolute neutrophil count 48% (normal range: 40-75%), absolute lymphocyte count 43.9% (normal range: 20-50%), and C-reactive protein 29.76 (normal range: 0-0.50 mg/dL). She was diagnosed with Grade 3 urinary tract infection (urinalysis not reported) and Grade 4 febrile neutropenia, leading to hospitalization. She received treatment with ciprofloxacin, cefepime, filgrastim and propacetamol. On Study Day 77, a CT-scan showed Grade 2 pneumonitis in both lungs. She received treatment with methylprednisolone, sulfamethoxazole/trimethoprim, codeine, levofloxacin and meropenem for pneumonitis. On Study Day 106, the events of urinary tract infection, pneumonitis and febrile neutropenia were considered resolved and she was discharged from the hospital.

Relevant laboratory values listed in the table below:

Study Day	**WBC count** (normal range: 4-10 × $10^3\mu L$)	**Neutrophils** (normal range: 40-75%)	**Lymphocytes** (normal range: 20-50%)	**Body temperature** (°C)
− 2	6.52	59.4	31.1	36.7
74	0.66	48	43.9	38.4
75	0.35	37.1	52.1	—
76	0.60	35	56.1	—
78	2.68	64.7	28.3	—
106	6.09	78.8	15.8	—

Due to the events of febrile neutropenia, urinary tract infection and pneumonitis, study treatment with atezolizumab was interrupted on Study Day 56, paclitaxel on Study Day 70 and ipatasertib on Study Day 73 and was later never resumed as per physician′s decision (see narrative below).

The Investigator considered febrile neutropenia and urinary tract infection to be unrelated to ipatasertib, atezolizumab and related to paclitaxel.

The Investigator considered pneumonitis to be and unrelated to ipatasertib, atezolizumab and related to atezolizumab and concurrent illness.

On Study Day 134, study treatment was permanently discontinued as per physician′s decision (the patient did not decide to discontinue the study treatment because of any one adverse event, but because of the judgement that the administration of the drug would jeopardize her in

the overall state of the subject) with the last dose atezolizumab administered on Study Day 58, paclitaxel on Study Day 70 and ipatasertib on Study Day 73. The patient then entered the long-term follow-up.

On Study Day 151, an overall response assessment showed disease progression.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Doxorubicin and cyclophosphamide	152	Ongoing

On Study Day 421, the patient was lost to follow-up.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	6	73	Related	Unrelated	Unrelated
Nausea	1	Non-serious	6	Unresolved	Unrelated	Unrelated	Related
Mucosal inflammation	1	Non-serious	15	22	Unrelated	Unrelated	Related
Neuropathy peripheral	1	Non-serious	36	Resolving	Unrelated	Unrelated	Related
Weight decreased	2	Non-serious	36	Resolving	Unrelated	Unrelated	Unrelated
Anemia	2	Non-serious	50	64	Unrelated	Unrelated	Related
Hyperglycemia	2	Non-serious	70	74	Related	Related	Unrelated
Anemia	3	Non-serious	74	75	Unrelated	Unrelated	Related
Nausea	1	Non-serious	76	80	Unrelated	Unrelated	Related
Platelet count decreased	3	Non-serious	78	83	Unrelated	Unrelated	Related

Study Number/CRTN:	CO40016/318264	Patient number	3007
Demographics:	63-year-old Asian female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Category:	Cholecystitis SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER negative, PR positive, HER 2 negative, locally recurrent left breast cancer (T2NXMX) on Study Day -662.

On Study Day −64, the patient was diagnosed with metastatic disease with ER/PR negative, and HER2 negative in metastatic tissue. At screening sites of disease involvement included left lower lobe of lung and bilateral multiple lung metastasis.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Doxorubicin and cyclophosphamide	-648	-585
Cancer therapy	Neoadjuvant	Paclitaxel	-564	-501
Surgery	Curative	Left breast lumpectomy	-462	NA
Radiotherapy	Adjuvant	Left breast (50 cGy, 19 fractions)	-69	-41

No medical or surgical history was reported. No concurrent condition was reported.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab. The same day, she also started loperamide prophylactically (total daily dose: 4 mg) for diarrhea.

Concomitant medication ongoing at Study Day 1 included aceclofenac.

Event: Cholecystitis

Prior to the event of cholecystitis, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 101 and ipatasertib (300 mg) on Study Day 104.

On Study Day 105, the patient experienced Grade 1 pyrexia (body temperature not reported; non-serious, unrelated). On the same day (Study Day 105), a laboratory work-up showed CRP 5.93 (units and normal range not reported). A blood culture revealed *Citrobacter freundii.* She received treatment with paracetamol and ciprofloxacin for the event of fever. On Study Day 107, the event of pyrexia was considered resolved. On the same day (Study Day 107), an abdomen and pelvic CT scan revealed Grade 1 (initial intensity) cholecystitis. There was no evidence of abdominal metastasis. On Study Day 112, her CRP was 1.32. On Study Day 127, the patient was hospitalized. On Study Day 128, a laparoscopic cholecystectomy was performed. Later, on the same day (Study Day 128), she experienced Grade 1 procedural pain (non-serious, unrelated). She received treatment with cefixime and cefazolin. On Study Day 129, the most extreme Grade for cholecystitis was assessed as Grade 3. Later the same day (Study Day 129), her CRP was 1.03, the event of cholecystitis was considered resolved and she was discharged from the hospital. On Study Day 139, the event of procedural pain was considered resolved.

Due to the event of cholecystitis, study treatment with ipatasertib, paclitaxel and atezolizumab was interrupted. The next dose of ipatasertib and paclitaxel was administered on Study Day 147, and atezolizumab on Study Day 154.

The Investigator considered cholecystitis, to be unrelated to ipatasertib, paclitaxel and atezolizumab and related to other causes (unspecified).

On Study Day 283, radiographic response assessment showed disease progression. On the same day (Study Day 283), study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and atezolizumab administered on Study Day 270 and ipatasertib administered on Study Day 275. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine	283	343
Cisplatin and gemcitabine	343	406
Resection of metastatic site in left lung	476	NA
Gemcitabine and carboplatin	497	Ongoing

On Study Day 865, the long-term follow-up was completed by study team.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Myalgia	1	Non-serious	8	45	Unrelated	Related	Unrelated
Neutropenia	3	Non-serious	15	31	Unrelated	Related	Unrelated
Rash	1	Non-serious	16	22	Related	Unrelated	Unrelated
Diarrhea	2	Non-serious	17	207	Related	Unrelated	Unrelated
Decreased appetite	1	Non-serious	69	Unresolved	Unrelated	Unrelated	Unrelated
Oedema peripheral	1	Non-serious	86	93	Unrelated	Related	Unrelated
Neuropathy peripheral	2	Non-serious	86	Unresolved	Unrelated	Related	Unrelated
Cystitis	1	Non-serious	161	166	Unrelated	Unrelated	Unrelated
Cough	1	Non-serious	179	181	Unrelated	Unrelated	Unrelated
Dermatitis acneiform	1	Non-serious	209	229	Unrelated	Unrelated	Unrelated
Neuropathy peripheral	2	Non-serious	213	Unresolved	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	267	275	Related	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305145	Patient number	3008
Demographics:	46-year-old Black or African American female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		

Event 1 (PT) Category:	Pneumonitis Grade $\geq$ 2 pneumonitis
Event 2 (PT) Category:	Musculoskeletal chest pain SAE
Event 3 (PT) Category:	Cholecystitis SAE

The patient was randomized on Study Day -1.

The patient was diagnosed with ductal, moderately differentiated (Grade 2), ER/PR and HER 2 negative, metastatic right breast cancer (T4N3M1) on Study Day -103.

At screening, sites of disease involvement included breast (right breast mass), lymph node (right axillary, right lower paratracheal and multiple lymphadenopathy), liver (liver metastasis 1 right lobe segment 8, liver metastasis 2 right lobe segment 5/6 and multiple liver metastasis) and lung (malignant right pleural thickening and right lymphangitis carcinomatosis right lung).

No past cancer treatments were reported.

The patient′s medical history included aspiration pleural cavity and pulmonary embolism. Surgical history included caesarean section. Concurrent conditions included intracranial aneurysm, depression, epilepsy, and gastroesophageal reflux disease.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included omeprazole, tramadol, and morphine sulfate.

Event 1: Pneumonitis

Prior to the event of pneumonitis, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 43 and ipatasertib (400 mg) on Study Day 49.

On Study Day 62, the patient was diagnosed with non-serious Grade 2 pneumonitis (symptoms and diagnostic details not reported). No treatment was administered for the event of pneumonitis. The event of pneumonitis remained unresolved at the time of patient's death (see narrative below).

Due to the event of pneumonitis, there was no change in study treatment with paclitaxel, however, study treatment with ipatasertib and atezolizumab was interrupted and ipatasertib was

resumed at a reduced dose of 300 mg from 400 mg on Study Day 64, and atezolizumab was resumed on Study Day 85.

The Investigator considered pneumonitis, to be unrelated to paclitaxel and related to ipatasertib and atezolizumab.

Event 2: Musculoskeletal chest pain (Chest wall pain)

Prior to the event of musculoskeletal chest pain, the most recent dose of atezolizumab was administered on Study Day 43, paclitaxel on Study Day 64 and ipatasertib (300 mg) on Study Day 66.

On Study Day 67, the patient experienced serious Grade 3 musculoskeletal chest pain associated with breathlessness; however, denied fever. Subsequently, she was hospitalized. The blood tests results were unremarkable and did not suggest any infection. On Study Day 68, CT pulmonary angiogram excluded pulmonary embolus but showed worsening areas of consolidation in the lung and possible lytic lesions in sternum which were not there in the baseline scan. Treatment with tramadol and morphine sulfate was maintained for pain relief and she further received treatment with enoxaparin; following which her condition improved and she was feeling better. On Study Day 69, the event of musculoskeletal chest pain was considered resolved and she was discharged from the hospital.

There was no change in study treatment due to the event of musculoskeletal chest pain.

The Investigator considered musculoskeletal chest pain, to be unrelated to paclitaxel, ipatasertib and atezolizumab and related to disease under study.

On Study Day 104, radiographic response assessment showed disease with new lesions in bone (bilateral small volume bony deposits).

On Study Day 111, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and atezolizumab administered on Study Day 99 and ipatasertib administered on Study Day 105. The patient entered into the long-term follow-up.

Event 3: Cholecystitis

Prior to the event of cholecystitis, study treatment with paclitaxel, atezolizumab and ipatasertib was already discontinued.

On Study Day 116, the patient was feeling unwell, experienced overall weakness with right sided abdominal pain, constipation, and Grade 2 vomiting (non-serious, related to paclitaxel). Blood culture was performed (details not reported). She was suspected with cholecystitis. On Study Day 118, she was hospitalized. Vitals showed body temperature 37.7°C, heart rate 100 beats/min, respiration rate 20 breaths/min and oxygen saturation 99% on room air. She received treatment with dexamethasone, ondansetron, cyclizine, piperacillin/tazobactam,

docusate, hyoscine, oxycodone, and metoclopramide. On Study Day 119, the event of vomiting was considered resolved. On Study Day 120, an ultrasound showed multiple gallstones with normal kidneys, pancreas, and spleen. Thus, the diagnosis of Grade 3 cholecystitis was confirmed. The event of cholecystitis remained unresolved at the time of patient's death.

The Investigator considered cholecystitis, to be unrelated to paclitaxel, ipatasertib and atezolizumab and related to disease under study.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Gemcitabine and carboplatin	120	148
Epirubicin	169	169

On Study Day 207, the patient died due to disease progression. It was unknown whether an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious / Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**	**Causality (Atezolizumab)**
Dizziness	1	Non-serious	1	Unresolved	Related	Unrelated	Unrelated
Nausea	2	Non-serious	1	30	Related	Unrelated	Unrelated
Hypoacusis	1	Non-serious	9	13	Unrelated	Unrelated	Unrelated
Constipation	1	Non-serious	11	13	Unrelated	Unrelated	Unrelated
Pyrexia	1	Non-serious	15	19	Unrelated	Unrelated	Unrelated
Fatigue	1	Non-serious	15	Unresolved	Unrelated	Related	Unrelated
Dry mouth	1	Non-serious	15	Unresolved	Unrelated	Unrelated	Unrelated
Diarrhea	2	Non-serious	16	18	Related	Unrelated	Unrelated
Pruritus	1	Non-serious	17	28	Related	Unrelated	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Diarrhea	1	Non-serious	18	27	Related	Unrelated	Unrelated
Nausea	1	Non-serious	23	24	Unrelated	Related	Unrelated
Proctalgia	1	Non-serious	25	Unresolved	Unrelated	Unrelated	Unrelated
Constipation	2	Non-serious	28	Unresolved	Unrelated	Unrelated	Unrelated
Nausea	1	Non-serious	39	Unresolved	Unrelated	Related	Related
Vomiting	1	Non-serious	39	47	Unrelated	Related	Related
Fatigue	2	Non-serious	39	Unresolved	Related	Related	Related
Lethargy	2	Non-serious	39	Unresolved	Related	Related	Related
Dizziness	2	Non-serious	48	62	Related	Unrelated	Unrelated
Visual impairment	2	Non-serious	48	62	Related	Unrelated	Unrelated
Vomiting	2	Non-serious	48	62	Related	Unrelated	Unrelated
Pruritus	1	Non-serious	60	Unresolved	Unrelated	Unrelated	Unrelated
Vascular access site pain	2	Non-serious	73	Unresolved	Unrelated	Unrelated	Unrelated
Back pain	2	Non-serious	73	Unresolved	Unrelated	Unrelated	Unrelated
Oral candidiasis	1	Non-serious	76	83	Unrelated	Unrelated	Unrelated
Onychalgia	1	Non-serious	83	Unresolved	Unrelated	Related	Unrelated
Rash	2	Non-serious	111	Unknown	Related	Unrelated	Related

Study Number/CRTN:	CO40016/305639	Patient number	3009
Demographics:	60-year-old Black or African American female		

Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)
Cohort:	Cohort C
Event 1 (PT) Category:	Urinary tract infection SAE
Event 2 (PT) Category:	Dehydration SAE

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, ER negative, PR positive and HER 2 negative, right breast cancer (T4N2M0, histological grade unknown) on Study Day -822.

On Study Day −29, the patient was diagnosed with metastatic disease with ER/PR and HER 2 negative in metastatic tissue. At screening sites of disease involvement included breast (chest wall nodule).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Doxorubicin and cyclophosphamide	-783	-743
Cancer therapy	Neoadjuvant	Docetaxel	-776	-652
Surgery	Curative	Left breast radical mastectomy	-597	NA
Radiotherapy	Neoadjuvant / adjuvant	Lymph node (supraclavicular), left breast and bone (left mid chest wall) (dose: 5000 cGy, 25 fractions)	-514	-479
Radiotherapy	Adjuvant	Bone (left chest wall boost) (dose: 1000 cGy, 5 fractions)	-481	-472
Radiotherapy	Adjuvant	Bone (left chest wall boost) (dose: 1000 cGy, 5 fractions)	-478	-472

The patient′s medical history included diverticulum. Surgical history included bilateral knee arthroplasty. Concurrent conditions included type 2 diabetes mellitus, hyperlipidemia, hypertension, osteoarthritis, peripheral motor neuropathy, lymphoedema (left arm and hand), pruritus (other, left chest wall itch), musculoskeletal chest pain (left chest wall pain) and cardiomegaly.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included furosemide, amlodipine, losartan, atorvastatin, carvedilol, hydrocodone bitartrate/paracetamol, sitagliptin phosphate, gabapentin, hydroxyzine, and potassium chloride.

On Study Day 28, the patient experienced Grade 2 dehydration (non-serious, unrelated). The patient received treatment with sodium chloride.

Event 1: Urinary tract infection
Event 2: Dehydration

Prior to the events of urinary tract infection and dehydration, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 42 and ipatasertib (300 mg) on Study Day 48.

On Study Day 49, the patient experienced Grade 2 abdominal pain (non-serious, related to ipatasertib), intractable Grade 2 nausea (non-serious. related to ipatasertib and paclitaxel) and vomiting attributed to chemotherapy with body temperature 36.7°C. A urinalysis showed 1+ bacteria, white blood cells 174 (normal range: 0-6, units not reported) and leukocyte esterase in large amount. The patient was diagnosed with serious Grade 3 urinary tract infection and Grade 3 worsening of dehydration, leading to hospitalization (for observation). On the same day (Study Day 49), she was also noted with acute kidney injury with creatinine:1.5 mg/dL (normal range: 0.52-1.21 mg/dL) and blood urea nitrogen: 25 mg/dL (normal range: 7-18 mg/dL). It was reported that acute kidney injury was attributed to dehydration which was considered due to nausea, vomiting, and poor oral intake. Relevant laboratory work-up throughout the events was not reported. She received treatment with ceftriaxone sodium, ondansetron, calcium chloride/potassium chloride/sodium lactate and sodium chloride; following which her diet was progressed from clear liquid to soft, which she was able to tolerate. On Study Day 52, her creatinine was 1.3 mg/dL and blood urea nitrogen 16 mg/dL. On the same day (Study Day 52), the event of abdominal pain was considered resolved. On Study Day 53, the event of nausea improved to Grade 1. On the same day (Study Day 53), the event of urinary tract infection and serious Grade 3 event of dehydration were considered resolved and she was discharged from the hospital. The event of nausea and non-serious Grade 2 event of dehydration remained unresolved at the time of patient′s death (see below).

Due to the events of urinary tract infection and dehydration (serious), study treatment with paclitaxel, ipatasertib and atezolizumab was interrupted and was the next dose was administered on Study Day 70.

The Investigator considered urinary tract infection and dehydration (serious), to be related to paclitaxel, ipatasertib and atezolizumab.

On Study Day 91, radiographic response assessment showed disease progression and the study treatment was permanently discontinued with the last dose of paclitaxel and atezolizumab administered on Study Day 85 and ipatasertib administered on Study Day 90. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Gemcitabine and carboplatin	93	190
Capecitabine	198	504
Sacituzumab govitecan	525	525

On Study Day 550, the patient died due to failed to thrive. Underlying cancer was not considered as contribution factor. It was unknown whether an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious / Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**	**Causality (Atezolizumab)**
Nausea	1	Non-serious	5	18	Related	Related	Unrelated
Vomiting	1	Non-serious	13	13	Related	Related	Unrelated
Nausea	2	Non-serious	19	42	Related	Unrelated	Unrelated
Decreased appetite	1	Non-serious	19	Resolving	Related	Unrelated	Unrelated
Fatigue	1	Non-serious	19	42	Related	Related	Unrelated
Depression	1	Non-serious	19	42	Unrelated	Unrelated	Unrelated
Anxiety	1	Non-serious	19	42	Unrelated	Unrelated	Unrelated
Nausea	1	Non-serious	43	48	Related	Related	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Dysgeusia	1	Non-serious	45	Unresolved	Unrelated	Related	Unrelated
Headache	1	Non-serious	54	63	Unrelated	Unrelated	Unrelated
Dizziness	1	Non-serious	54	Unresolved	Unrelated	Unrelated	Unrelated
Dyspnea	2	Non-serious	54	57	Unrelated	Unrelated	Unrelated
Gastroesophageal reflux disease	1	Non-serious	59	Unresolved	Unrelated	Related	Unrelated
Pruritus	2	Non-serious	72	Unresolved	Unrelated	Unrelated	Unrelated
Musculoskeletal chest pain	2	Non-serious	81	Unresolved	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304448	Patient number	3012
Demographics:	58-year-old Asian female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Rash maculo-papular Grade ≥ 3 rash		
Event 2 (PT) Category:	Hyperglycemia (First episode) Grade ≥ 3 hyperglycemia		
Event 3 (PT) Category:	Hyperglycemia (Second episode) Grade ≥ 3 hyperglycemia		
Event 4 (PT) Categories:	Hyperglycemia (Third episode) AE leading to study treatment discontinuation, Grade ≥ 3 hyperglycemia		
Event 5 (PT) Categories:	Diabetic ketoacidosis		

	SAE, AE leading to study treatment discontinuation, Grade ≥ 3 hyperglycemia
Event 6 (PT) Category:	Hyperglycemia (Fourth episode) Grade ≥ 3 hyperglycemia
Event 7 (PT) Categories:	Hyperglycemia (Fifth episode) AE leading to study treatment discontinuation, Grade ≥ 3 hyperglycemia

The patient was randomized on Study Day − 2.

The patient was initially diagnosed with ductal, poorly differentiated, ER positive, PR negative and HER2 negative, left breast cancer (T2N1miMX) on Study Day −771 following left breast biopsy on the same day.

On Study Day −738, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative in metastatic tissue, following left sentinel node biopsy on the same day. On Study Day −38, the patient was diagnosed with locally recurrent disease. At screening sites of disease involvement included lymph nodes (left internal mammary lymph node, right level 1 right axillary lymph node, peritracheal node and right level 2 right axillary node).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Simple mastectomy of left breast and other surgery of left lymph node	-738	NA
Cancer therapy	Adjuvant	Anastrozole	-695	-35

The patient's medical history included neutrophil toxic granulation present. No surgical history was reported. Concurrent conditions included asthma, rhinitis allergic, dermatitis atopic, hyperlipidemia, osteoarthritis (bilateral knees), osteopenia, glucose tolerance impaired, urticaria, dyshidrotic eczema, hyperglycemia, lymphocyte count decreased, and monocyte count decreased.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included montelukast sodium, azelastine hydrochloride, salbutamol sulfate, fluticasone propionate/salmeterol xinafoate, olopatadine

hydrochloride, tiotropium bromide, beclomethasone dipropionate, cetirizine hydrochloride, calcium carbonate/cholecalciferol, fish oil and dexamethasone and loperamide.

Event 1: Rash maculo-papular

Prior to the event of rash maculo-papular, the most recent dose of paclitaxel was administered on Study Day 8, atezolizumab and ipatasertib (400 mg) on Study Day 15.

On Study Day 16, within 24 hours of end of atezolizumab infusion, the patient experienced non-serious Grade 2 (initial intensity) rash maculo-papular on chest which was considered as systemic infusion reaction. On Study Day 17, the rash spread to legs, arms, back and then on all over the body and was considered worsened to Grade 3. She received treatment with dexamethasone, prednisone, and hydroxyzine for the event of rash maculo-papular. On Study Day 20, the rash was only present on arms and the event improved Grade 2. On Study Day 22, the event of rash maculo-papular further improved to Grade 1. She further received treatment with triamcinolone. On Study Day 34, the event of rash maculo-papular was considered resolved.

Due to the event of rash maculo-papular, there was no change in study treatment with paclitaxel, however, study treatment with atezolizumab was interrupted on Study Day 29 and was resumed on Study Day 99, ipatasertib was interrupted on Study Day 32 and was resumed on Study Day 33.

The Investigator considered rash maculo-papular, to be related to ipatasertib and atezolizumab, and unrelated to paclitaxel.

Event 2: Hyperglycemia (First episode)

Prior to the event of hyperglycemia (first episode), the most recent dose of paclitaxel and atezolizumab was administered on Study Day 29, ipatasertib (400 mg) on Study Day 33.

On Study Day 34, a laboratory work-up showed fasting glucose: 319 mg/dL (normal range: 60-159 mg/dL), leading to diagnosis of non-serious Grade 3 hyperglycemia (first episode). Relevant laboratory work-up is reported in the table below. She received treatment with metformin, isophane insulin, insulin glargine and insulin lispro (details in the table below). On Study Day 41, the event of hyperglycemia improved to Grade 2.

Due to the event of hyperglycemia, study treatment with atezolizumab was interrupted on Study Day 29 and was resumed on Study Day 99, ipatasertib was reduced to 300 mg on Study Day 43, and paclitaxel was interrupted after Study Day 57 and was resumed on Study Day 78.

The Investigator considered hyperglycemia (first episode), to be unrelated to paclitaxel and related to ipatasertib, atezolizumab and other cause (unspecified).

Event 3: Hyperglycemia (Second episode)

Prior to the event of hyperglycemia (second episode), the most recent dose of atezolizumab was administered on Study Day 29, ipatasertib (400 mg) on Study Day 33 and paclitaxel on Study Day 36.

On Study Day 42, a laboratory work-up showed glucose: 196 mg/dL (normal range: 60-159 mg/dL) and potassium: 3.3 mEq/L (normal range: 3.5-5.3 mEq/L), leading to diagnosis of non-serious Grade 2 (initial intensity) hyperglycemia (second episode) and Grade 1 hypokalemia (non-serious, related to ipatasertib and atezolizumab). Relevant laboratory work-up is reported in the table below. Treatment with metformin, isophane insulin, insulin glargine and insulin lispro was maintained. On Study Day 55, the event of hyperglycemia (second episode) worsened to Grade 3. On Study Day 56, the event of hypokalemia was considered resolved.

There was no change in study treatment due to the event of hyperglycemia (second episode).

The Investigator considered hyperglycemia (second episode), to be unrelated to paclitaxel and related to ipatasertib and atezolizumab.

Event 4: Hyperglycemia (Third episode)
Event 5: Diabetic ketoacidosis
Event 6: Hyperglycemia (Fourth episode)
Event 7: Hyperglycemia (Fifth episode)

Prior to the event of hyperglycemia (third episode), the most recent dose of atezolizumab was administered on Study Day 29, paclitaxel on Study Day 43 and ipatasertib (300 mg) on Study Day 48.

On Study Day 56, in the afternoon, the patient′s laboratory work-up showed fasting glucose 347 mg/dL (normal range: 60-159 mg/dL) and HbA1c: 10.2 % (normal range: 4.6-6 %), leading to diagnosis of non-serious Grade 3 hyperglycemia (third episode) and Grade 1 glycosylated hemoglobin increased (non-serious, unrelated). Relevant laboratory work-up is reported in the table below. She received treatment with isophane insulin. On Study Day 57, the patient experienced Grade 2 vomiting (non-serious, related to paclitaxel and atezolizumab). No treatment was administered for the event of vomiting.

Prior to the events of diabetic ketoacidosis and hyperglycemia (fourth episode), the most recent dose of atezolizumab was administered on Study Day 29, ipatasertib (300 mg) on Study Day 48 and paclitaxel on Study Day 57.

On Study Day 58, a laboratory work-up showed blood glucose 730 mg/dL (normal range not reported), sodium 132 mEq/L (normal range: 133-145 mEq/L), potassium 3.7 mEq/L (normal range: 3.5-5.3 mEq/L), phosphorus 1.1 mg/dL (normal range: 2.7-4.5 mg/dL), magnesium

0.7 mg/dL (normal range: 1.7-2.3 mg/dL), creatinine: 0.23 μmol/L (normal range: 53-106 μmol/L). Arterial blood gas analysis showed pH 7.13. The patient was diagnosed with serious Grade 4 diabetic ketoacidosis along with Grade 3 dehydration (non-serious, related to paclitaxel), Grade 1 acute kidney injury (non-serious, unrelated), Grade 1 hyperkalemia, Grade 3 hypophosphatemia, Grade 3 hypomagnesemia (all non-serious, related to ipatasertib and atezolizumab), Grade 1 white blood cell count increased (non-serious, related to ipatasertib and paclitaxel, WBC count not reported), Grade 1 immature granulocyte count increased (non-serious, related to ipatasertib and paclitaxel, immature granulocyte count not reported). Subsequently, she was hospitalized (in ICU). Relevant laboratory work-up is reported in the table below. She received treatment with magnesium sulfate, calcium chloride/potassium chloride/sodium lactate, potassium chloride and glucose. On the same day (Study Day 58), the events of hypomagnesemia and hyperkalemia were considered resolved; however, she was noted with Grade 1 hypokalemia (non-serious, related to ipatasertib and atezolizumab). On Study Day 59, the events of vomiting, acute kidney injury, white blood cell count increased and immature granulocyte count increased were considered resolved. On Study Day 60, the event of dehydration was considered resolved. On Study Day 61, the events of diabetic ketoacidosis and hypokalemia were considered resolved and she was discharged from the hospital. On Study Day 63, the event of hypophosphatemia was considered resolved. On Study Day 69, the event of hyperglycemia (third episode) improved to Grade 2.

On Study Day 70, ongoing event of hyperglycemia (glucose 220 mg/dL) was reported as non-serious Grade 2 event. Relevant laboratory work-up is reported in the table below. Treatment with metformin, isophane insulin, insulin glargine and insulin lispro was maintained On an unspecified day, the event of hyperglycemia (fourth episode) worsened to Grade 3. On Study Day 76, the event of hyperglycemia (fourth episode) improved to Grade 1 and later was considered resolved on the same day (Study Day 76).

Prior to the event of hyperglycemia (fifth episode), the most recent dose of atezolizumab was administered on Study Day 29, ipatasertib (300 mg) on Study Day 48 and paclitaxel on Study Day 78.

On Study Day 84, the patient experienced blurred vision and neuropathy but without worsening. A laboratory work-up showed glucose 266 mg/dL (normal range: 60-159 mg/dL), leading to diagnosis of non-serious Grade 3 hyperglycemia (fifth episode). Relevant laboratory work-up is reported in the table below. On Study Day 85, she was also noted with Grade 2 type 1 diabetes mellitus (non-serious, related to ipatasertib and atezolizumab, laboratory work-up was not reported for this day). She received treatment with metformin, isophane insulin, insulin glargine and insulin lispro (details in the table below). On Study Day 91, the event of hyperglycemia (fifth episode) was considered resolved. The event of type 1 diabetes mellitus remained unresolved at the time of patient's death (see below).

The event of glycosylated hemoglobin increased remained unresolved at the time of patient's death (see narrative below).

Due to the event of hyperglycemia (third episode) and diabetic ketoacidosis paclitaxel was interrupted after Study Day 57 and was resumed on Study Day 78.

Due to event of hyperglycemia (fourth and fifth episode), there was no change in study treatment with paclitaxel.

Due to these events, treatment with atezolizumab was interrupted after Study Day 29 and was resumed on Study Day 99 and paclitaxel was interrupted after Study Day 57 and was resumed on Study Day 78.

Due to the events of hyperglycemia (third and fifth episode) and diabetic ketoacidosis, study treatment with ipatasertib was permanently discontinued with last dose administered on Study Day 48.

The Investigator considered hyperglycemia (third episode) and diabetic ketoacidosis, to be unrelated to paclitaxel and related to ipatasertib and atezolizumab.

The Investigator considered hyperglycemia (fourth episode), to be unrelated to paclitaxel and related to ipatasertib, atezolizumab and other cause (unspecified).

The Investigator considered hyperglycemia (fifth episode), to be unrelated to paclitaxel, ipatasertib and related to atezolizumab.

Relevant laboratory work-up:

Study Day	**Glucose** Normal range: 60-159 mg/dL	**HbA1c** Normal range: 4.6-6%
Screening (– 13)	96	6.0
1	160	—
7	116	—
14	124	—
22	152	—
28	159	—
34	319	—
35	295	—
42	196	—
56	347	10.2
57	340	
58	127	—
58	75	—
	730*	—
61	174	—

Study Day	Glucose Normal range: 60-159 mg/dL	HbA1c Normal range: 4.6-6%
63	273*	—
70	220	—
77	159	—
84	266	—
91	100	—
98	122	—
105	132	—
139	172	—
140	256	7.7

*normal range not reported

Hyperglycemia treatment details:

Treatment	Indication	Dose (Units: mg)	Route	Frequency	Start day	Stop day
Metformin	Hyperglycemia	500	PO	QD	35	44
Isophane insulin	Hyperglycemia	100*	SC	PRN	37	61
Metformin	Hyperglycemia	1500	PO	QD	44	Ongoing
Isophane insulin	Hyperglycemia	13*	SC	BID	61	Ongoing
Insulin glargine	Hyperglycemia	—	SC	PRN	69	Ongoing
Insulin lispro	Hyperglycemia	—	SC	PRN	69	Ongoing

*Units: U

On Study Day 107, radiographic response assessment showed disease progression.

On Study Day 113, study treatment was permanently discontinued due to disease progression with the last dose of atezolizumab and paclitaxel administered on Study Day 99 and Study Day 106, respectively. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day

Atezolizumab and paclitaxel	113	225
Capecitabine	247	341
Pegylated liposomal doxorubicin	366	394
Sacituzumab govitecan hziy	429	590
Eribulin	604	611
Doxorubicin and cyclophosphamide	625	646
Carboplatin and gemcitabine	667	737

On Study Day 780, the patient died due to disease progression. It was unknown whether an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious / Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**	**Causality (Atezolizumab)**
Fatigue	2	Non-serious	2	56	Related	Related	Related
Diarrhea	1	Non-serious	5	7	Related	Related	Related
Nausea	1	Non-serious	6	12	Related	Related	Related
Blood lactate dehydrogenase increased	1	Non-serious	7	7	Unrelated	Unrelated	Unrelated
Anti-islet cell antibody positive	1	Non-serious	7	Unresolved	Unrelated	Unrelated	Unrelated
Anti-islet cell antibody positive	1	Non-serious	7	Unresolved	Unrelated	Unrelated	Unrelated
Anti-gad antibody positive	1	Non-serious	7	Unresolved	Unrelated	Unrelated	Unrelated
Eosinophil percentage increased	1	Non-serious	7	21	Unrelated	Unrelated	Unrelated
Basophil percentage increased	1	Non-serious	7	7	Unrelated	Unrelated	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Arthralgia	1	Non-serious	9	22	Unrelated	Related	Related
Abdominal discomfort	1	Non-serious	10	28	Related	Related	Related
Chills	1	Non-serious	13	14	Unrelated	Related	Unrelated
Alanine aminotransferase increased	1	Non-serious	14	34	Related	Related	Related
White blood cell count decreased	2	Non-serious	14	21	Related	Related	Unrelated
Neutrophil count decreased	2	Non-serious	14	21	Related	Related	Unrelated
Metamyelocyte percentage increased	1	Non-serious	21	22	Unrelated	Unrelated	Unrelated
Immature granulocyte percentage increased	1	Non-serious	22	28	Unrelated	Unrelated	Unrelated
Diarrhea	2	Non-serious	24	63	Related	Related	Related
Peripheral sensory neuropathy	1	Non-serious	25	Unresolved	Unrelated	Related	Unrelated
Monocyte percentage decreased	1	Non-serious	28	35	Unrelated	Unrelated	Unrelated
Basophil percentage increased	1	Non-serious	28	35	Unrelated	Unrelated	Unrelated
Nausea	1	Non-serious	30	Unresolved	Unrelated	Related	Related
Vision blurred	1	Non-serious	33	Unresolved	Unrelated	Unrelated	Related
Muscle spasms	1	Non-serious	33	36	Unrelated	Unrelated	Unrelated
Hyponatremia	1	Non-serious	34	35	Unrelated	Unrelated	Related
Hypomagnesaemia	1	Non-serious	42	56	Related	Unrelated	Related

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
White blood cell count decreased	1	Non-serious	42	56	Related	Related	Related
Lymphocyte count decreased	1	Non-serious	42	56	Related	Related	Unrelated
Alopecia	2	Non-serious	43	Unresolved	Unrelated	Related	Unrelated
Hyponatremia	1	Non-serious	56	Unresolved	Unrelated	Unrelated	Related
Carbon dioxide decreased	1	Non-serious	56	Unresolved	Unrelated	Unrelated	Unrelated
Blood cholesterol increased	1	Non-serious	56	Unresolved	Unrelated	Unrelated	Unrelated
Low density lipoprotein increased	1	Non-serious	56	Unresolved	Unrelated	Unrelated	Unrelated
Embolism	1	Non-serious	58	Unresolved	Unrelated	Unrelated	Unrelated
Prothrombin time prolonged	1	Non-serious	58	Unresolved	Unrelated	Unrelated	Unrelated
Hyperkalemia	1	Non-serious	58	58	Related	Unrelated	Related
Blood chloride decreased	1	Non-serious	58	58	Related	Unrelated	Related
Red blood cell count decreased	1	Non-serious	59	63	Related	Related	Unrelated
Anemia	2	Non-serious	59	66	Related	Related	Unrelated
Hematocrit decreased	1	Non-serious	59	66	Related	Related	Unrelated
Platelet count decreased	1	Non-serious	59	63	Related	Related	Unrelated
Lymphocyte count decreased	2	Non-serious	59	70	Related	Related	Unrelated
Alanine aminotransferase increased	1	Non-serious	63	70	Related	Unrelated	Related
Aspartate aminotransferase increased	1	Non-serious	63	66	Related	Related	Related

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Hypoalbuminemia	1	Non-serious	63	70	Related	Related	Related
Immature granulocyte count increased	1	Non-serious	63	70	Related	Related	Unrelated
Hyponatremia	1	Non-serious	66	77	Unrelated	Unrelated	Related
Blood chloride decreased	1	Non-serious	66	Unresolved	Related	Unrelated	Related
Red blood cell count decreased	1	Non-serious	66	70	Related	Related	Unrelated
Carbon dioxide decreased	1	Non-serious	70	77	Unrelated	Unrelated	Unrelated
Eosinophil percentage increased	1	Non-serious	77	98	Related	Related	Unrelated
Basophil percentage increased	1	Non-serious	77	91	Related	Related	Unrelated
Hypothyroidism	2	Non-serious	84	Unresolved	Unrelated	Unrelated	Related
Alanine aminotransferase increased	1	Non-serious	84	91	Related	Related	Related
Aspartate aminotransferase increased	1	Non-serious	84	91	Related	Related	Related
Monocyte percentage decreased	1	Non-serious	84	91	Related	Related	Unrelated
Hyponatremia	1	Non-serious	91	140	Unrelated	Unrelated	Related
Weight increased	1	Non-serious	98	Unresolved	Unrelated	Unrelated	Unrelated
Basophil percentage increased	1	Non-serious	98	Unresolved	Related	Related	Unrelated
Monocyte percentage decreased	1	Non-serious	98	139	Related	Related	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Lymphocyte count decreased	1	Non-serious	105	139	Related	Related	Unrelated

Study Number/CRTN:	CO40016/305639	Patient number	3016
Demographics:	62-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Peripheral motor neuropathy AE leading to study treatment discontinuation		
Event 3 (PT) Category:	Fatigue AE leading to study treatment discontinuation		
Event 4 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 5 (PT) Categories:	Cardiac arrest Deaths due to adverse event, SAE		

A narrative for this patient is available in Section 1.1 Narratives for patients who died due to an adverse event(s).

Study Number/CRTN:	CO40016/306603	Patient number	3024
Demographics:	49-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Gastroenteritis norovirus SAE		
Event 2 (PT) Category:	Aspartate aminotransferase increased Grade ≥3 hepatotoxicity		
Event 3 (PT) Category:	Diarrhea Grade ≥3 diarrhea		
Event 4 (PT) Category:	Pyrexia SAE		
Event 5 (PT) Category:	Hypertransaminasaemia SAE		
Event 6 (PT) Category:	Fatigue SAE		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR negative and HER2 negative left breast cancer (T2N1M0) approximately 1 years and 9 months prior to study entry.

The patient was diagnosed with metastatic disease on Study Day − 36 with ER /PR negative and HER2 negative disease in metastatic tissue following left bed mastectomy. At screening, sites of disease involvement included lymph node (subcarinal) and left chest wall, left pleural effusion, anterior chest wall soft tissue thickening and bone (left 3rd costochondral junction and left frontal).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	Approximately 1 years 9 months prior to study entry	Approximately 1 years 7 months prior to study entry
Cancer therapy	Neoadjuvant	Carboplatin and paclitaxel (6 cycles each)	Approximately 1 years 6 months prior to study entry	Approximately 1 years 6 months prior to study entry
Surgery	Curative	Left simple mastectomy	Approximately 1 years 5 months prior to study entry	—
Radiotherapy	Adjuvant	Left chest wall (dose: 5000 cGy; 25 fractions)	Approximately 1 years 3 months prior to study entry	Approximately 1 years 2 months prior to study entry
Cancer therapy	Adjuvant	Capecitabine (2 cycles)	Approximately 1 years 2 months prior to study entry	Approximately 1 years 1 months prior to study entry

The patient′s medical history included hypotension, cardiac murmur, endometriosis, and hypothyroidism. No surgical history was reported. Concurrent conditions included depression, post-traumatic stress disorder, hot flush, neuropathy peripheral, fatigue, chest pain, back pain, Ehlers Danlos syndrome, psychogenic seizure, presyncope, dehydration, anxiety, autonomic nervous system imbalance, progesterone decreased, attention deficit hyperactivity disorder, cognitive disorder and myoclonic dystonia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included cholecalciferol, methylphenidate, clonidine, quetiapine, bupropion, paracetamol, ibuprofen, gabapentin, and hydrocodone/paracetamol.

On Study Day 2, the patient experienced Grade 1 gastroesophageal reflux disease (event occurred within 24 hours after end of atezolizumab infusion) (non-serious, related). She received treatment with calcium carbonate, lansoprazole, rabeprazole and pantoprazole for gastroesophageal reflux disease. The event remained unresolved at the time of patient′s death (see narrative below).

Due to the event of Grade 1 neuropathy peripheral (non-serious, related), study treatment with paclitaxel was reduced from 80 mg/m^2 to 65 mg/m^2 on Study Day 85.

Event 1: Gastroenteritis norovirus (Norovirus gastroenteritis)

Event 2: Aspartate aminotransferase increased (Elevated AST)

Prior to the events of gastroenteritis norovirus and aspartate aminotransferase increased, the most recent dose of atezolizumab was administered on Study Day 141, paclitaxel on Study Day 148 and ipatasertib (400 mg) on Study Day 148.

On Study Day 146, the patient experienced Grade 2 diarrhea (non-serious, related). She received treatment with loperamide for diarrhea. On the following day (Study Day 147), the event of diarrhea was considered resolved.

On Study Day 149, the patient presented to the hospital with symptoms of nausea, vomiting, non-stop diarrhea (5 times) and Grade 1 pyrexia (body temperature: 101.4°F; non-serious, unrelated). A blood and urine cultures were without any growth. A stool pathogen panel was positive for norovirus, and she was diagnosed with Grade 3 gastroenteritis norovirus. Later, on the same day (Study Day 149), a laboratory work-up showed AST 466 U/L (normal range: 15-37 U/L) and she was diagnosed with non-serious Grade 3 aspartate aminotransferase increased and Grade 2 alanine aminotransferase increased (ALT not reported for this day; non-serious, unrelated). She received treatment with sodium chloride, cefepime and metronidazole for pyrexia. On the following day (Study Day 150), the patient was hospitalized. As per physician, the symptoms occurred due to event of gastroenteritis norovirus. She further received treatment with rabeprazole, sodium chloride, magnesium sulfate and pantoprazole. On Study Day 151, the events of gastroenteritis norovirus and pyrexia were considered resolved. On the following day (Study Day 152), the patient was discharged from the hospital. On Study Day 159, the events of aspartate aminotransferase increased, and alanine aminotransferase increased were considered resolved.

Grade changes for elevated AST are reported in the table below:

Event	Study Day	Grade change
Elevated AST	151	1
Elevated AST	152	2
Elevated AST	155	1

Relevant laboratory values listed in the table below:

Study Day	**WBC count** (normal range: 4.8-10.8 $\times$ $10^3/\mu L$)	**Absolute neutrophil count** (normal range: 1.5-6.5 $\times$ $10^3/\mu L$)	**Absolute lymphocyte count** (normal range: 1.2-3.4 $\times$ $10^3/\mu L$)
– 3	5.1	—	—
141	3.9	2.2	1.1
148	3.7	2.3	1.1

Relevant laboratory values listed in the table below:

Study Day	**AST** (normal range: 15-37 U/L)	**ALT** (normal range: 14-59 U/L)	**ALP** (normal range: 50-136 U/L)	**Total bilirubin** (normal range: 0.2-1 mg/dL)
-3	34	46	138	0.2
148	12	21	99	0.2
155	60	111	110	0.2

Due to the event of gastroenteritis norovirus, there was no change in study treatment with paclitaxel and atezolizumab; however, study treatment with ipatasertib was interrupted on Study Day 150 and next dose given on Study Day 153.

There was no change in the study treatment due to the event of aspartate aminotransferase increased.

The Investigator considered events of gastroenteritis norovirus and aspartate aminotransferase increased to be unrelated to paclitaxel, ipatasertib and atezolizumab and related to concurrent illness (unspecified).

Event 3: Diarrhea

Prior to the event of diarrhea, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 168, and ipatasertib (400 mg) on Study Day 171.

On Study Day 172, the patient experienced non-serious Grade 3 diarrhea (12 episodes). A stool sample for *Clostridium*. difficile, *Salmonella,* shigella, Shiga, *E*. coli, and Campylobacter was negative. She received treatment with loperamide. On the following day (Study Day 173), the event of diarrhea was considered resolved.

Loperamide details:

Indication	Loperamide daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	1	3
Diarrhea	2	PO	4	4
Diarrhea	4	PO	5	6
Diarrhea	4	PO	16	16
Diarrhea	4	PO	18	18
Diarrhea	2	PO	19	24
Diarrhea	4	PO	25	26
Diarrhea	2	PO	27	27
Diarrhea	2	PO	30	33
Diarrhea	2	PO	36	43
Diarrhea	8	PO	44	44
Diarrhea	2	PO	48	55
Diarrhea	2	PO	57	57
Diarrhea	2	PO	63	63
Diarrhea	2	PO	67	74
Diarrhea	6	PO	75	75
Diarrhea	2	PO	76	76
Diarrhea	6	PO	90	90
Diarrhea	2	PO	92	92
Diarrhea	6	PO	95	95
Diarrhea	2	PO	96	96
Diarrhea	6	PO	101	101
Diarrhea	2	PO	102	102
Diarrhea	4	PO	103	103
Diarrhea	2	PO	104	104
Diarrhea	4	PO	107	107
Diarrhea	6	PO	108	108
Diarrhea	4	PO	114	114
Diarrhea	4	PO	119	119
Diarrhea	2	PO	129	129
Diarrhea	2	PO	135	135
Diarrhea	2	PO	146	146
Diarrhea	8	PO	149	149

Indication	Loperamide daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	157	158
Diarrhea	8	PO	172	172
Diarrhea	4	PO	189	189

Due to the event of diarrhea, there was no change in study treatment with paclitaxel and atezolizumab; however, study treatment with ipatasertib was interrupted on Study Day 172 and further resumed at a reduced dose of 300 mg from 400 mg on Study Day 174.

The Investigator considered diarrhea to be related to paclitaxel, ipatasertib and atezolizumab.

On Study Day 210, the patient complaints of cough and shortness of breath. A chest X-ray revealed left pleural effusion and she received treatment with amoxicillin/clavulanic acid.

Event 4: Pyrexia (fever)

Event 5: Hypertransaminasaemia (transaminitis)

Prior to the events of pyrexia and hypertransaminasaemia, the most recent dose of ipatasertib (300 mg) was administered on Study Day 188, atezolizumab and paclitaxel on Study Day 210.

On Study Day 214, the patient completed her left sided thoracentesis is morning. Later, on the same day, the patient presented to the emergency department due to Grade 2 pyrexia (initial intensity Grade 1; body temperature 101.1°F). She received treatment with azithromycin for pyrexia.

On Study Day 216, at 11:55 hours, a laboratory work-up showed AST 110 U/L (normal range: 15-37 U/L). Later, at 22:21 hours, her AST worsened to 505 U/L (normal range: 15-37 U/L) and she was diagnosed with Grade 1 hypertransaminasaemia. Subsequently, she was hospitalized. During the hospitalization, she complaints of labored breathing and vitals showed body temperature 103.3°F. A COVID-19 test was not performed. A chest X-ray revealed left lower lobe opacification and effusion. The pleural fluid analysis was consistent with malignant effusion. She received treatment with paracetamol, piperacillin/tazobactam, lidocaine, and methylprednisolone. On Study Day 218, the event of pyrexia was considered resolved. On Study Day 220, the event of hypertransaminasaemia worsened to Grade 3. On Study Day 223, the patient was discharged from the hospital with prednisone for hypertransaminasaemia. On Study Day 225, the event of hypertransaminasaemia was considered resolved.

Relevant laboratory values listed in the table below:

Study Day	**AST** (normal range: 15-37 U/L)	**ALT** (normal range: 14-59 U/L)	**ALP** (normal range: 50-136 U/L)	**Total bilirubin** (normal range: 0.2-1 mg/dL)
−3	34	46	138	0.2
210	19	23	103	0.3
216	110 505	—	—	—
217	640	571*	—	—
218	148	391*	—	—
220	11	158*	—	—
221	—	110*	—	—

*normal range: 13-56 U/L

Due to the events of pyrexia and hypertransaminasaemia, study treatment with ipatasertib was interrupted after Study Day 188, paclitaxel and atezolizumab was interrupted on Study Day 210 and never resumed due to disease progression (see narrative below).

The Investigator considered pyrexia to be unrelated to paclitaxel, ipatasertib and atezolizumab and related to disease under study.

The Investigator considered hypertransaminasaemia to be related to atezolizumab and unrelated to paclitaxel and ipatasertib.

On Study Day 224, a radiographic response assessment showed disease progression with new lesions in left lung (pleura).

Event 6: Fatigue

Prior to the event of fatigue, the most recent dose of ipatasertib (300 mg) was administered on Study Day 188, atezolizumab and paclitaxel on Study Day 210.

On Study Day 228, the patient presented to the emergency department with Grade 3 fatigue and weakness. On the following day (Study Day 229), the patient was hospitalized and to rule out sepsis. A chest CT-angiogram revealed consolidation in left lower lobe and chest X-ray

showed slight interval decrease in size of left pleural effusion. A laboratory work-up showed no abnormality. No treatment was reported for this event. On Study Day 230, the event of fatigue was considered resolved and she was discharged from the hospital.

Action taken with the study treatment was reported as not applicable.

The Investigator considered fatigue to be unrelated to atezolizumab, paclitaxel and ipatasertib and related to disease under study.

On Study Day 242, study treatment was permanently discontinued due to disease progression with the last dose of ipatasertib given on Study Day 188, atezolizumab and paclitaxel given on Study Day 210. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Ladiratuzumab (2 cycles)	243	278

On Study Day 435, the patient died due to disease progression. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Nausea	1	Non-serious	1	29	Related	Related	Related
Cough	1	Non-serious	1	50	Unrelated	Unrelated	Unrelated
Dry mouth	1	Non-serious	1	Unresolved	Related	Related	Related
Oropharyngeal pain	1	Non-serious	2	15	Unrelated	Unrelated	Unrelated
Hyperhidrosis	1	Non-serious	2	110	Unrelated	Unrelated	Unrelated
Aspartate aminotransferase increased	2	Non-serious	7	15	Related	Related	Related
Alanine aminotransferase increased	1	Non-serious	7	15	Related	Related	Related
Blood lactate dehydrogenase increased	1	Non-serious	7	15	Related	Related	Related

Balance disorder	1	Non-serious	8	Unresolved	Related	Related	Related
Rash	1	Non-serious	19	120	Related	Related	Related
Vomiting	2	Non-serious	21	22	Related	Related	Related
Neutropenia	2	Non-serious	29	36	Related	Related	Related
Diarrhea	2	Non-serious	39	45	Related	Related	Related
Constipation	1	Non-serious	45	48	Unrelated	Unrelated	Unrelated
Anemia	1	Non-serious	50	110	Related	Related	Related
Muscle spasms	1	Non-serious	52	Unresolved	Related	Related	Related
Fatigue	2	Non-serious	58	Unresolved	Related	Related	Related
Epistaxis	1	Non-serious	67	91	Related	Related	Related
Diarrhea	1	Non-serious	75	76	Related	Related	Related
Diarrhea	2	Non-serious	90	97	Related	Related	Related
Nail bed tenderness	1	Non-serious	91	141	Related	Related	Related
Cognitive disorder	2	Non-serious	97	99	Related	Related	Related
Vomiting	1	Non-serious	97	98	Related	Unrelated	Unrelated
Oropharyngeal pain	1	Non-serious	98	102	Unrelated	Unrelated	Unrelated
Headache	1	Non-serious	98	100	Unrelated	Unrelated	Unrelated
Urinary tract infection	2	Non-serious	98	105	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	101	109	Related	Related	Related
Hypercalcemia	1	Non-serious	105	110	Related	Related	Related
Nausea	1	Non-serious	110	111	Related	Related	Related
Diarrhea	1	Non-serious	114	115	Related	Related	Related
Diarrhea	1	Non-serious	119	120	Related	Related	Related
Tinnitus	1	Non-serious	124	Unresolved	Related	Related	Related
Eyelid function disorder	1	Non-serious	124	Unresolved	Related	Related	Related
Hypoacusis	1	Non-serious	124	Unresolved	Related	Related	Related

Diarrhea	1	Non-serious	129	130	Related	Related	Related
Diarrhea	1	Non-serious	135	137	Related	Related	Related
Anemia	2	Non-serious	144	152	Unrelated	Unrelated	Unrelated
Mucosal inflammation	1	Non-serious	151	157	Related	Related	Related
Headache	1	Non-serious	151	152	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	157	159	Related	Related	Related
Seasonal allergy	1	Non-serious	166	Unresolved	Unrelated	Unrelated	Unrelated
Breath odor	1	Non-serious	183	Unresolved	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	189	190	Related	Related	Related
Productive cough	1	Non-serious	200	214	Unrelated	Unrelated	Unrelated
Diarrhea	2	Non-serious	213	215	Related	Related	Related
Diarrhea	2	Non-serious	217	218	Related	Related	Related
Cough	1	Non-serious	219	221	Unrelated	Unrelated	Unrelated
Wheezing	2	Non-serious	236	242	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304331	Patient number	3029
Demographics:	63-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Category:	Tumor necrosis SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR negative and HER2 negative advanced unresectable right breast cancer (T4N1M0) on Study Day – 49, followed by right breast biopsy performed on the same day.

At screening, sites of disease involvement included right breast, right axillary lymph node A, B and C.

No past cancer treatments are reported.

The patient′s medical history included appendicitis. Surgical history included appendicectomy and blood transfusion. Concurrent conditions included chronic tonsillitis, essential hypertension, hypertensive heart disease, cardiac failure, pancreatitis chronic, hemangioma of liver, liver disorder, pyelonephritis chronic, fibrocystic breast disease, diabetes mellitus, left ventricular hypertrophy, adrenal adenoma, cholecystitis chronic, ovarian cyst, uterine leiomyoma, spinal disorder, and aortic arteriosclerosis.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included hydrochlorothiazide/ramipril, trimetazidine and metformin.

Event: Tumor necrosis

Prior to the event of tumor necrosis, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 157 and ipatasertib (400 mg) on Study Day 163.

On Study Day 169, the patient′s weekly breast ultrasound scan showed growth formation which was heterogenic in structure with cyst formation. She was diagnosed with Grade 1 tumor necrosis. On Study Day 224, during a scheduled visit for biopsy procedure, a physical examination revealed hyperemic skin thinning of right breast; thus, the patient had high risk of right breast external opening formation. Subsequently, the event of tumor necrosis was assessed to have worsened to Grade 3, leading to hospitalization for surgery. On Study Day 227, a right sided mastectomy with lymph nodes dissection was performed and on Study Day 235themicroscopic study showed breast tissue with 9 cm defined formation, 300 mL reddish fluid emitting at resection and grey-yellow tissues on left side due to a lot of hemorrhages. It also revealed breast tissue with defined infiltrating Grade 3 ductal carcinoma, and therapeutical path morphosis I-II with negative tumor edge. It was reported that six lymph nodes were dissected and showed chronic lymphadenitis (KI-83%). The patient required daily dressings and observation; thus, her hospitalization was prolonged to abide all sanitary hygienic products (dressing) taking into consideration to complete the resection. On Study Day 249, the event of tumor necrosis was considered resolved and she was discharged from the hospital.

Due to this event, study treatment with atezolizumab, paclitaxel and ipatasertib was interrupted and never resumed (see narrative below).

The Investigator considered tumor necrosis to be related atezolizumab, paclitaxel, ipatasertib and disease under study.

Study treatment was permanently discontinued as during the surgery for tumor necrosis, all target lesions were resected, hence patient would no longer participate in the study. The last dose of paclitaxel and atezolizumab was given on Study Day 211 and ipatasertib on Study Day 217. The patient then entered the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Radiotherapy to the post-operative scar area	277	277

On Study Day 811, the patient was discontinued from the study as study was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Alopecia	2	Non-serious	21	Unresolved	Related	Unrelated	Related
Diarrhea	1	Non-serious	31	31	Related	Unrelated	Unrelated
Nausea	2	Non-serious	33	46	Related	Unrelated	Related
Diarrhea	1	Non-serious	45	50	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	59	62	Related	Unrelated	Unrelated
Intestinal mucosal atrophy	1	Non-serious	64	Unresolved	Related	Unrelated	Unrelated
Gastrointestinal disorder	1	Non-serious	64	Unresolved	Unrelated	Unrelated	Unrelated
Hyperbilirubinemia	1	Non-serious	71	85	Related	Related	Related
Respiratory disorder	2	Non-serious	79	82	Unrelated	Unrelated	Unrelated
Weight decreased	1	Non-serious	197	Unresolved	Unrelated	Unrelated	Related

Study Number/CRTN:	CO40016/318721	Patient number	3030
Demographics:	71-year-old female (Race unknown)		

Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)
Cohort:	Cohort C
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea
Event 2 (PT) Categories:	Autoimmune hepatitis SAE, AE leading to Study treatment discontinuation

The patient was randomized on Study Day − 6.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER2 negative, right breast cancer (T2N1M1) on Study Day − 57.

On Study Day − 36, ER/PR and HER2 negative disease was diagnosed in metastatic tissue. At screening sites of disease involvement included right lung (prevertebral right basal and nodule under pleural apical right), right breast (supero-external paramedian) and right lymph nodes (axillary and mediastinal lymph nodes).

No past cancer treatments were reported.

No medical or surgical history was reported. Concurrent conditions included osteoarthritis, back pain, dust allergy and seasonal allergy.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

No concomitant medication ongoing at Study Day 1 was reported.

On Study Day 2, the patient received loperamide prophylactically (total daily dose: 2 mg, PO) for diarrhea.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 7.

On Study Day 8, the patient experienced non-serious Grade 1 (initial intensity) diarrhea without general health disorder. No diagnostic test was performed. Unspecified rehydration was given and she received treatment with diosmectite and loperamide. Grade changes and loperamide

treatment details for the event of diarrhea are reported in the table below. On Study Day 149, the event of diarrhea was considered resolved.

Grade changes for diarrhea:

Study Day	Grade changes for diarrhea
15	2
43	1
46	2
47	3
50	1
57	3
64	1

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	2	2
Diarrhea	2	PO	9	12
Diarrhea	2	PO	14	14
Diarrhea	4	PO	15	16
Diarrhea	4	PO	18	18
Diarrhea	4	PO	20	20
Diarrhea	4	PO	31	31
Diarrhea	4	PO	37	37
Diarrhea	4	PO	40	40
Diarrhea	6	PO	43	43
Diarrhea	8	PO	44	44
Diarrhea	4	PO	45	45
Diarrhea	12	PO	46	46
Diarrhea	10	PO	47	49
Diarrhea	8	PO	50	50
Diarrhea	10	PO	51	52
Diarrhea	6	PO	53	53
Diarrhea	4	PO	58	60
Diarrhea	4	PO	62	63
Diarrhea	4	PO	68	68
Diarrhea	8	PO	69	70

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	74	74
Diarrhea	8	PO	75	75
Diarrhea	4	PO	77	77
Diarrhea	4	PO	86	86
Diarrhea	4	PO	93	93
Diarrhea	4	PO	96	96
Diarrhea	4	PO	98	98
Diarrhea	4	PO	100	100
Diarrhea	4	PO	102	102
Diarrhea	4	PO	104	105
Diarrhea	4	PO	114	114
Diarrhea	4	PO	121	121
Diarrhea	4	PO	124	124
Diarrhea	4	PO	126	126
Diarrhea	4	PO	129	130
Diarrhea	8	PO	131	131
Diarrhea	4	PO	132	134
Diarrhea	8	PO	135	135
Diarrhea	4	PO	136	136
Diarrhea	4	PO	157	160
Diarrhea	4	PO	201	206
Diarrhea	4	PO	211	211

There was no change in study treatment due to the event of diarrhea.

The Investigator considered diarrhea, to be related to ipatasertib, paclitaxel and atezolizumab.

Event 2: Autoimmune hepatitis

Prior to the event of autoimmune hepatitis, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 156 and ipatasertib (400 mg) on Study Day 159.

On Study Day 160, the patient experienced abdominal pain. A CT scan showed hypotonia of bile ducts, evoking angiocholitis. She was diagnosed with bile duct infection along with hepatic cytolysis, anicteric cholestasis, inflammatory syndrome and serious Grade 3 autoimmune hepatitis (laboratory work-up was not reported for this day). Subsequently, she was hospitalized and received treatment with ceftriaxone, metronidazole, prednisone, tramadol, corticosteroid (unspecified) and prednisolone metasulfobenzoate sodium. The inflammatory syndrome

reduced well with disappearance of the hyperleukocytosis. Relevant laboratory work-up is reported in the table below. On an unspecified day, CRP reduced to 24.4 mg/L (normal range not reported). Abdominal pain also decreased; however, she had tenderness in the right hypochondrium. On Study Day 166, she experienced a resurgence of fever (body temperature not reported) with the appearance of a biological inflammatory syndrome without any infectious syndrome. On Study Day 168, her laboratory work-up showed albumin: 29 g/L (normal range not reported). It was reported that cytolysis and cholestasis persisted and increased. On Study Day 170, a cholangio MRI was performed (details not reported). On Study Day 172, she was discharged from the hospital. On Study Day 357, the event of autoimmune hepatitis was considered resolved.

Due to the event of autoimmune hepatitis, study treatment with ipatasertib, paclitaxel and atezolizumab was permanently discontinued with last dose of atezolizumab administered on Study Day 156, paclitaxel on Study Day 219 and ipatasertib on Study Day 235. The patient entered into the long-term follow-up.

The Investigator considered autoimmune hepatitis, to be unrelated to ipatasertib, paclitaxel and related to atezolizumab.

Relevant laboratory work-up:

Study Day	**AST** Normal range 13-40 U/L	**ALT** Normal range 7-40 U/L	**Total bilirubin** Normal range: 0-21 μmol/L	**ALP** Normal range: 45-149 U/L	**GGT** (units and normal range not reported)	**CRP** (normal value: $<$5 mg/L)
Screening	14	10	9	176	—	—
163	55*	52*	3@	350%	—	—
165	109*	77*	—	407%	343	24.3
168	257*	127*	—	552%	554	133
175	109#	151#	8.6$	1163^	—	—
178	53#	101#	8.6$	829^	—	—
182	28#	45#	10.3$	568^	—	—
189	24#	22#	8.6$	373^	—	—
196	26#	23#	8.6$	253^	—	—

Study Day	AST Normal range 13-40 U/L	ALT Normal range 7-40 U/L	Total bilirubin Normal range: 0-21 μmol/L	ALP Normal range: 45-149 U/L	GGT (units and normal range not reported)	CRP (normal value: < 5 mg/L)
203	26[#]	25[#]	10.3[$]	209[^]	—	—
217	38[#]	26[#]	3.4[$]	206[^]	—	—
224	85[#]	54[#]	5.1[$]	276[^]	—	—
224	85[#]	54[#]	5.1[$]	276[^]	—	—
226	85[+]	54[+]	—	276[+]	248	—
231	251[#]	241[#]	5.1[$]	400[^]	—	—
232	251[#]	241[#]	5.1[$]	400[^]	—	—
239	516[#]	904[#]	6.8[$]	457[^]	720	—
247	270[#]	614[#]	8.6[$]	476[^]	—	—

[*]Normal range: 10-35 U/L, [#]normal range: 0-35 U/L, [@]normal range: 0-17 μmol/L, [$]normal range: 2-21 μmol/L, [%]normal range: 35-105 U/L, [^]normal range: 30-120 U/L, units: UI/L; [+]normal range not reported

On Study Day 423, a radiographic response assessment showed disease progression with new lesions in right side of brain (single cortical right parieto-temporo-occipital location measuring 24 × 13 mm with peripheral edema).

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Radiotherapy to brain (stereotaxic) (dose: 33 cGy and 3 fractions)	457	462
Capecitabine	504	510
Pegylated liposomal doxorubicin hydrochloride	721	Ongoing

On Study Day 892, the patient was discontinued from the study as per Sponsor's and physician's decision.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Arthralgia	1	Non-serious	8	36	Unrelated	Unrelated	Unrelated
Asthenia	2	Non-serious	8	Resolving	Related	Related	Related
Arthralgia	2	Non-serious	8	36	Unrelated	Unrelated	Unrelated
Nausea	1	Non-serious	15	Resolving	Unrelated	Related	Unrelated
Rhinitis	1	Non-serious	29	36	NA	Unrelated	Unrelated
Erythema	2	Non-serious	29	36	Related	Unrelated	Related
Anemia	1	Non-serious	43	149	Unrelated	Unrelated	Unrelated
Nasopharyngitis	1	Non-serious	81	92	NA	Unrelated	Unrelated
Tooth infection	2	Non-serious	98	118	Unrelated	Unrelated	Unrelated
Dry eye	2	Non-serious	127	142	Unrelated	Unrelated	Unrelated
Chest pain	1	Non-serious	149	191	NA	Unrelated	Unrelated
Hypertension	2	Non-serious	150	Resolving	Unrelated	Unrelated	Unrelated
Paresthesia	1	Non-serious	153	156	Related	Related	Unrelated
Anxiety	2	Non-serious	156	Resolving	Unrelated	Unrelated	Unrelated
Paresthesia	1	Non-serious	205	Resolving	Unrelated	Related	Unrelated
Muscle spasms	1	Non-serious	226	Resolving	Unrelated	Unrelated	Unrelated
Hypothyroidism	1	Non-serious	231	Unresolved	Unrelated	Unrelated	Unrelated
Hot flush	1	Non-serious	233	247	Unrelated	Unrelated	NA
Balance disorder	2	Non-serious	247	308	Unrelated	Unrelated	Unrelated
Amnesia	1	Non-serious	247	Resolving	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304785	Patient number	3035
Demographics:	36-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Category:	Urinary tract infection SAE		

The patient was randomized on Study Day – 3.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR negative and HER2 negative left breast cancer (T2N0M0) approximately 2 years and 3 months prior to study entry.

The patient was diagnosed with metastatic disease on Study Day – 41 with ER /PR and HER2 disease not reported in the metastatic tissue. At screening, sites of disease involvement included lymph node (midline subcarinal lymph node enlargement).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	Approximately 2 years and 2 months prior to study entry	Approximately 2 years prior to study entry
Cancer therapy	Neoadjuvant	Paclitaxel (dose: 4 cycles)	Approximately 1 years and 11 months prior to study entry	Approximately 1 years and 9 months prior to study entry
Surgery	Curative	Left radical mastectomy	Approximately 1 years and 7 months prior to study entry	–
Radiotherapy	Adjuvant	Left breast (dose:5000 cGy)	Approximately 1 years and 3 months prior to study entry	Approximately 1 years and 2 months prior to study entry

No medical/surgical history was reported. The patient′s concurrent conditions included calculus urinary, factor V Leiden mutation and blood lactate dehydrogenase increased.

At screening, the patient′s ECOG Performance Status was 1.

At screening, urinalysis showed:

Study Day	**Urine pH** (normal range: 5-6; units not reported)	**Urine specific gravity** (normal range: 1.015-1.025; units not reported)	**Urine glucose**	**Urine protein**
− 24	6	1.020	0 (Absent)	+ 1 (Trace)

On Study Day 1, the patient received her first study treatment with ipatasertib, atezolizumab and paclitaxel.

No concomitant medications ongoing at Study Day 1 was reported.

Event: Urinary tract infection

Prior to the event of urinary tract infection, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 2.

On Study Day 3, the patient experienced fever (body temperature not reported for this day) and dysuria. A laboratory work-up showed leukocytes 16.100/mm^3, bands 161/mm^3 and neutrophils 13.556/mm^3. Urinalysis showed leukocytes 40 cells per microscopic field, RBC count 20 cells per microscopic field, hemoglobin (2 ±) and negative nitrite was reported. The patient was diagnosed with Grade 3 urinary tract infection, leading to hospitalization. The double J stent was removed. She received treatment with cefuroxime, ketoprofen and levofloxacin for urinary tract infection. On Study Day 5, the patient was discharged from the hospital. On Study Day 6, the event of urinary tract infection was improved to Grade 2. On Study Day 14, the event of urinary tract infection was considered resolved.

Relevant laboratory values listed in the table below:

Study Day	**WBC count** (normal range: 3600-11000/μL)	**Absolute neutrophil count** (normal range: 1500-7900/μL)	**Absolute lymphocyte count** (normal range: 1000-5500/μL)
− 24	9870	5073	3612
− 4	9220	5698	2701
8	9310	5437	2951
15	7960	4394	2850

There was no change in the study treatment due to the event of urinary tract infection.

The Investigator considered urinary tract infection to be unrelated to atezolizumab, paclitaxel and ipatasertib and related to other causes (unspecified).

On Study Day 138, a radiographic response assessment showed disease progression with new lesion in pancreas (expansive hypodense lesion in the topography of the pancreatic head), lymph node (left peripancreatic lymph node enlargement), brain (bilateral left and right cerebellar hemisphere), lymph node (left axillary lymph node enlargement and left cervical level and right mediastinal lymph node enlargement) and study treatment was permanently discontinued with the last dose of ipatasertib given on Study Day 113, atezolizumab and paclitaxel on Study Day 127 respectively. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Carboplatin and gemcitabine (single cycle each)	143	143

On Study Day 192, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Decreased appetite	1	Non-serious	3	30	Related	Related	Related
Nausea	1	Non-serious	3	30	Unrelated	Unrelated	Related
Cough	1	Non-serious	14	Resolving	Unrelated	Related	Related
Fungal skin infection	2	Non-serious	25	37	Unrelated	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	36	Resolving	Unrelated	Unrelated	Related
Headache	2	Non-serious	38	38	Unrelated	Unrelated	Related
Alopecia	2	Non-serious	44	Resolving	Unrelated	Unrelated	Related
Vaginal discharge	1	Non-serious	44	67	Unrelated	Unrelated	Unrelated
Hyperphosphatemia	1	Non-serious	57	70	Unrelated	Unrelated	Unrelated
Paronychia	1	Non-serious	75	Resolving	Unrelated	Unrelated	Related
Hypothyroidism	1	Non-serious	75	Resolving	Unrelated	Related	Unrelated

Mucosal inflammation	2	Non-serious	89	95	Unrelated	Unrelated	Related
Abdominal pain upper	1	Non-serious	115	Resolving	Unrelated	Unrelated	Unrelated
Headache	1	Non-serious	120	Resolving	Unrelated	Unrelated	Unrelated
Aspartate aminotransferase increased	2	Non-serious	127	Resolving	Related	Related	Related
Alanine aminotransferase increased	2	Non-serious	127	Resolving	Related	Related	Related
Lipase increased	4	Non-serious	130	Resolving	Related	Related	Unrelated
Contusion	1	Non-serious	143	168	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/318813	Patient number	3046
Demographics:	49-year-old American Indian or Alaska Native female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Category:	Tumor fistulisation SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with unspecified, poorly differentiated ER/PR and HER 2 negative, right breast cancer (T4bN1M1) on Study Day -81.

At screening sites of disease involvement included lung (left major pulmonary nodule and bilateral pulmonary nodules), breast (right) and lymph node (right axillary).

No past cancer treatments were reported.

No medical or surgical history was reported. No concurrent condition was reported.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

No concomitant medication ongoing at Study Day 1 was reported.

Event: Tumor fistulisation (Left breast tumor fistulization)

Prior to the event of tumor fistulisation, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 43 and ipatasertib (400 mg) on Study Day 49.

On Study Day 54, the patient was noted with left breast tumor necrosis with fistulization towards the skin of the breast associated with the persistent drainage. She was diagnosed with Grade 1 (initial intensity) tumor fistulisation. No diagnostic test was performed. She received treatment with diclofenac. On an unspecified day, the event worsened to Grade 3. On Study Day 102, she was hospitalized. On the same day (Study Day 102), on-study palliative 'other' surgery of right breast was performed. On Study Day 104, the event of tumor fistulisation was considered resolved and she was discharged from the hospital.

There was no change in study treatment due to the event of tumor fistulisation.

The Investigator considered tumor fistulisation, to be unrelated to ipatasertib, paclitaxel and atezolizumab and related to other cause (unspecified).

On Study Day 221, radiographic response assessment showed disease progression with new lesions in right lung (upper right lobe and right medial basal segment).

On Study Day 246, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and atezolizumab administered on Study Day 212 and ipatasertib administered on Study Day 218. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine	290	321
Radiotherapy to brain (holocraneal) (dose: 3000 cGy and 10 fractions)	352	352
Carboplatin	387	387

On Study Day 394, the patient died due to COVID-19 infection. Underlying cancer was considered as contribution factor. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Diarrhea	1	Non-serious	1	20	Related	Unrelated	Unrelated
Accidental overdose	1	Non-serious	22	22	Related	Unrelated	Unrelated
Nasopharyngitis	1	Non-serious	54	57	Unrelated	Unrelated	Unrelated
Dermatitis contact	1	Non-serious	71	81	Unrelated	Unrelated	Unrelated
Neuropathy peripheral	3	Non-serious	85	Unresolved	Unrelated	Related	Unrelated
Hypothyroidism	1	Non-serious	85	120	Unrelated	Unrelated	Related
Diarrhea	2	Non-serious	87	89	Related	Unrelated	Unrelated
Diarrhea	2	Non-serious	94	101	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	114	121	Related	Unrelated	Unrelated
Mucosal inflammation	1	Non-serious	120	127	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/318144	Patient number	3047
Demographics:	83-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Categories:	Diarrhea SAE, Grade $\geq$ 3 diarrhea		
Event 2 (PT) Category:	Gamma-glutamyl transferase increased Grade $\geq$ 3 hepatotoxicity		

Event 3 (PT) Category:	Nausea SAE
Event 4 (PT) Categories:	Pneumonitis SAE, AE leading to study treatment discontinuation, Grade ≥ 2 pneumonitis

The patient was randomized on Study Day 1.

The patient was diagnosed with ductal, moderately differentiated, ER/PR and HER2 negative, metastatic left breast cancer (T3N1M1) on Study Day − 61.

At screening sites of disease involvement included mediastinum (left anterior mediastinum), lymph node (right supraclavicular, left axillary, midline mediastinal), lungs (right lobe of left lung, upper left lobe), liver (midline segment IVB, midline adjacent) and bone (sternum and bilateral costal bow).

No past cancer treatments were reported.

The patient′s medical history included neck pain, nausea, left breast pain and blood creatinine increased. No surgical history was reported. Concurrent conditions included hypertension, dyslipidemia, blood urea increased, and blood lactate dehydrogenase increased.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included acetylsalicylic acid/aluminum glycinate/magnesium carbonate, atenolol, chlortalidone, simvastatin, tramadol and metamizole sodium.

The patient received loperamide prophylactically (total daily dose: 4 mg, PO) for diarrhea from Study Day 1 to Study Day 7.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of atezolizumab was administered on Study Day 1, paclitaxel on Study Day 8 and ipatasertib (400 mg) on Study Day 9.

On Study Day 10, the patient experienced Grade 2 (initial intensity) intermittent diarrhea with low food intake. She received treatment with loperamide (details in the table below). It was reported that she experienced 6 episodes of diarrhea in a day without improvement despite the treatment. On Study Day 12, she experienced fever (body temperature 38°C). On the same day (Study Day 12), the event of diarrhea worsened to Grade 3 and she was hospitalized. A

laboratory work-up showed absolute neutrophil count: 1554 /μL (normal range: 1700-8000 /μL) and WBC count: 2230 /μL (normal range: 3500-10500 /μL); thus, febrile neutropenia was ruled out. She also received hydration therapy and further treatment with ciprofloxacin, butylscopolamine, dimenhydrinate, ondansetron and ranitidine. Later, her fever resolved. On Study Day 14, the event of diarrhea was considered resolved. On Study Day 15, she was discharged from the hospital.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	1	7
Diarrhea	2	PO	8	8
Diarrhea	16	PO	9	9
Diarrhea	22	PO	10	10
Diarrhea	24	PO	11	11
Diarrhea	20	PO	12	12
Diarrhea	2	PO	16	16
Diarrhea	2	PO	21	21
Diarrhea	4	PO	22	23
Diarrhea	6	PO	24	24
Diarrhea	8	PO	25	26
Diarrhea	22	PO	27	28
Diarrhea	6	PO	30	30
Diarrhea	12	PO	31	31
Diarrhea	18	PO	32	32
Diarrhea	12	PO	33	34
Diarrhea	14	PO	35	35
Diarrhea	18	PO	36	36
Diarrhea	10	PO	37	37
Diarrhea	18	PO	38	39
Diarrhea	12	PO	40	40
Diarrhea	18	PO	41	42
Diarrhea	16	PO	43	43
Diarrhea	18	PO	44	48
Diarrhea	2	PO	51	53

Due to the event of diarrhea, Cycle 1 Day 15 of atezolizumab and paclitaxel was delayed, ipatasertib was interrupted on Study Day 11. The next dose was given on Study Day 22.

The Investigator considered diarrhea, to be related to ipatasertib, and unrelated to paclitaxel and atezolizumab.

Event 2: Gamma-glutamyltransferase increased (Gamma GT increase)

Prior to the event of gamma-glutamyltransferase increased, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 22 and ipatasertib (300 mg) on Study Day 28.

On Study Day 29, the patient was noted with non-serious Grade 1 (initial intensity) gamma-glutamyltransferase increased. GGT value was not reported throughout the event.

On Study Day 31, the patient experienced Grade 1 diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide (details in the table above).

On Study Day 36, the patient was noted with Grade 2 lymphopenia (non-serious, related to ipatasertib). On Study Day 40, the event of lymphopenia worsened to Grade 3. No treatment was administered for the event of lymphopenia.

On Study Day 43, the event of gamma-glutamyltransferase increased worsened to Grade 3. No treatment was administered for the event of gamma-glutamyltransferase increased. The event of gamma-glutamyltransferase increased remained unresolved at the time of patient's death (see narrative below).

There was no change in study treatment due to the event of gamma-glutamyltransferase increased.

The Investigator considered gamma-glutamyltransferase increased, to be related to ipatasertib and unrelated to paclitaxel and atezolizumab.

Relevant laboratory work-up:

Study Day	**AST** Normal range 8-32 U/L	**ALT** Normal range 4-33 U/L	**Total bilirubin** Normal range: 0-1.2 mg/dL	**ALP** Normal range: 35-105 U/L
Screening (1)	45	17	0.38	113
8	29	14	0.55	89
12	22	13	—	—
22	26	17	0.48	94

Study Day	AST Normal range 8-32 U/L	ALT Normal range 4-33 U/L	Total bilirubin Normal range: 0-1.2 mg/dL	ALP Normal range: 35-105 U/L
29	23	16	0.65	83
36	22	15	0.67	121
43	31	20	0.47	241
53	48	31	0.72	—
56	—	—	0.70	—
57	45	40	0.55	114
58	—	—	0.68	—
59	29	25	0.58	89
62	35	31	0.36	96
64	37	39	0.35	—
102	37	41	0.60	131

Event 3: Nausea
Event 4: Pneumonitis

Prior to the event of nausea, the most recent dose of paclitaxel, atezolizumab and ipatasertib (200 mg) was administered on Study Day 43.

On Study Day 44, the patient experienced Grade 1 (initial intensity) nausea. On Study Day 45, the event of nausea worsened to Grade 2. On Study Day 49, the event of nausea worsened to Grade 3 along with low ingestion of food, and she was hospitalized. Physical examination revealed good general condition (flushed, hydrated, afebrile, and eupneic). She was well-informed to time and space oriented. Her ECOG score of 2. An echocardiography showed segmental contractility and preserved dimensions. She was on intermittent tachypnea venturi mask and received treatment with ondansetron, metamizole sodium, dexamethasone, ranitidine, vitamin B complex, dimenhydrinate/fructose/glucose/pyridoxine hydrochloride, bromopride, magnesium sulfate, potassium chloride and potassium phosphate dibasic/potassium phosphate monobasic for the event of nausea, following which her diet improved.

Prior to the event of pneumonitis, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 43 and ipatasertib (200 mg) on Study Day 49.

On Study Day 51, the event of nausea improved to Grade 2, however, she experienced Grade 3 asthenia (related). On the same day (Study Day 51), the patient's hospitalization was prolonged. She received treatment with normal saline; however due to venous hydration, she was congested and treatment with furosemide was started. On Study Day 53, she experienced dyspnea. In the afternoon, dyspnea worsened. She was moved to ICU and venturi mask was replaced with nasal catheter. A Chest X-ray and blood cultures were performed (details not reported). On Study Day 56, a chest CT showed several diffuse changes confirming pneumonitis (initial Grade 2 on study day 51 and most extreme Grade 3 on study day 53). She was continued under non-invasive oxygen ventilation. She further received treatment with methylprednisolone, piperacillin sodium/tazobactam sodium, fenoterol, ipratropium, hydrocortisone, infliximab, prednisone, sulfamethoxazole, trimethoprim, amiodarone and diltiazem. On Study Day 71, the events of nausea and pneumonitis were considered resolved and she was discharged from the hospital with naso-enteral tube for diet and medication.

Relevant laboratory work-up:

Study Day	**WBC count** Normal range: 3500-10500/μL	**Neutrophil count** Normal range: 1700-8000/μL	**Lymphocyte count** Normal range: 900-2900/μL
Screening (1)	7470	5326	1389
52	10710	8140	1414
53	10310	8867	866
53	8620	7499	336
54	7790	6333	834
55	9670	7446	1460
56	12280	10561	1044
57	11730	9912	962
58	12530	11290	702
59	11500	10131	736
60	20020	16356	1582
61	19240	15815	1635
62	20670	16722	1860
64	23310	21911	932
67	14230	11925	1395
69	15380	12150	1707

Due to the event of nausea, study treatment with was interrupted and due to the event of pneumonitis, study treatment with ipatasertib, paclitaxel and atezolizumab was permanently discontinued with last dose of paclitaxel and atezolizumab administered on Study Day 43 and ipatasertib on Study Day 49. The patient entered into long-term follow-up.

The Investigator considered nausea, to be related to ipatasertib, paclitaxel and atezolizumab.

The Investigator considered pneumonitis, to be unrelated to ipatasertib and paclitaxel and related to atezolizumab.

On Study Day 119, the patient was hospitalized due to Grade 3 emphysematous cystitis (serious, causality reported as NA, probably related previous hospitalization). A laboratory work-up showed leukocytes 9740 and creatinine 0.55 (units and normal ranges not reported). She received treatment with ceftriaxone, diltiazem, ranitidine, prednisone, mirtazapine, metoclopramide, butyl scopolamine, metamizole sodium, sodium picosulfate, codeine, morphine, amikacin, piperacillin/tazobactam and naloxone. On Study Day 123, a chest X-ray results were worsened compared to previous exam (done on Study Day 56) and she was diagnosed with Grade 2 (initial intensity) pneumonia (serious; causality reported as NA). On the same day (Study Day 123), laboratory work-up showed leukocytes 10220. On Study Day 125, leukocytes were 6730.

On Study Day 127, the patient died due to breast cancer and the event of pneumonia. An autopsy was not performed. The events of lymphopenia, diarrhea and emphysematous cystitis remained unresolved at the time of patient's death.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Vomiting	1	Non-serious	4	6	Related	Unrelated	Unrelated
Hyponatremia	2	Non-serious	12	14	Unrelated	Unrelated	Unrelated
Lymphopenia	3	Non-serious	12	22	Related	Related	Unrelated
Anemia	2	Non-serious	12	52	Unrelated	Related	Unrelated
Insomnia	1	Non-serious	19	28	Unrelated	Unrelated	Unrelated
Hyperglycemia	2	Non-serious	22	102	Related	Unrelated	Unrelated
Hypoalbuminemia	1	Non-serious	22	29	Related	Unrelated	Unrelated
Hypokalemia	1	Non-serious	22	36	Related	Unrelated	Unrelated
Blood lactate dehydrogenase increased	1	Non-serious	22	102	Unrelated	Unrelated	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Nausea	1	Non-serious	26	29	Related	Related	Unrelated
Vomiting	1	Non-serious	27	29	Related	Related	Unrelated
Diarrhea	2	Non-serious	27	31	Related	Related	Unrelated
Hyponatremia	1	Non-serious	29	56	Related	Unrelated	Unrelated
Blood alkaline phosphatase increased	1	Non-serious	36	Unresolved	Related	Related	Related
Alkalosis	1	Non-serious	36	Unresolved	Related	Related	Related
Lymphopenia	2	Non-serious	36	39	Related	Unrelated	Unrelated
Aspartate aminotransferase increased	1	Non-serious	40	43	Related	Related	Related
Neutropenia	1	Non-serious	40	43	Unrelated	Related	Unrelated
Hypertension	2	Non-serious	40	40	NA	NA	NA
Tachycardia	1	Non-serious	40	40	Unrelated	Unrelated	Unrelated
Hypokalemia	1	Non-serious	43	55	Related	Unrelated	Unrelated
Headache	1	Non-serious	67	67	NA	NA	NA

Study Number/CRTN:	CO40016/304792	Patient number	3048
Demographics:	52-year-old female (Unknown race)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Category:	Rash SAE		
Additional category:	Death due to disease progression		

A narrative for this patient is available in Section 1.2 Narratives for patients who died due to disease progression.

Study Number/CRTN:	CO40016/304664	Patient number	3051
Demographics:	63-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Categories:	Diarrhea SAE, Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Febrile neutropenia SAE		
Event 3 (PT) Category:	Fatigue SAE		
Event 4 (PT) Category:	Dehydration SAE		
Event 5 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER2 negative, left breast cancer (T1N1M0) approximately 3 years and 6 months prior to study entry.

On Study Day -368, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative in metastatic tissue. At screening, sites of disease involvement included lung (right basal, right medial apex, right pleural effusion, right hilar node and right mediastinal) and brain (left frontal lobe).

Past cancer treatments are listed in the table below:

Type of treatment	**Therapy Setting/Intent**	**Treatments details**	**Start Day**	**Stop Day**
Surgery	Curative	Axillary Dissection of left breast	Approximately 3 years and 6 months prior to study entry	NA

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Doxorubicin, cyclophosphamide, and paclitaxel	Approximately 3 years and 5 months prior to study entry	Approximately 2 years and 11 months prior to study entry
Radiotherapy	Adjuvant	Breast (Left breast; dose: 50 cGy and 25 fractions) (Supraclavicular; dose: 48 cGy and 25 fractions)	Approximately 2 years and 10 months prior to study entry	Approximately 2 years and 9 months prior to study entry
Radiotherapy	Metastatic	Lung (Right upper pulmonary lobe; dose: 48 cGy and 4 fractions)	-322	-313

No medical history was reported. The patient′s surgical history included hip arthroplasty and laparoscopy. Concurrent conditions included depression, hypercholesterolemia, osteoarthritis, endometriosis, hypertension, anxiety, and fatigue.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included atorvastatin, paracetamol, hydralazine, metoprolol, diazepam, ibuprofen, mirtazapine, and escitalopram.

The patient received loperamide prophylactically (total daily dose: 4 mg, PO) for diarrhea on Study Day 2.

Event 1: Diarrhea
Event 2: Febrile neutropenia

Prior to the events of diarrhea and febrile neutropenia, the most recent dose of atezolizumab was administered on Study Day 1, paclitaxel on Study Day 8 and ipatasertib (400 mg) on Study Day 12.

On Study Day 13, the patient experienced Grade 3 diarrhea and was hospitalized for investigations and hydration. Up on examination she was noted with fever (temperature 38.1°C) and laboratory work-up showed neutrophil count 0.84×10^9/L (normal range: 1.8-7.7 $\times 10^9$/L). The patient was diagnosed with Grade 3 febrile neutropenia. Relevant laboratory work-up and vitals are reported in the table below. Stool and blood cultures were negative. She received treatment with codeine, potassium and magnesium for the event of diarrhea, ondansetron for nausea and piperacillin/tazobactam for febrile neutropenia. Later, her fever subsided, with no

source found. On Study Day 15, the event of febrile neutropenia was considered resolved. On Study Day 18, the event of diarrhea was considered resolved and she was discharged from the hospital.

Relevant laboratory work-up:

Study Day	**WBC count** Normal range: 4-11 $\times$ 10^9/L	**Neutrophil count** Normal range: 1.8-7.7 $\times$ 10^9/L	**Lymphocyte count** Normal range: 1-4 $\times$ 10^9/L	**Body temperature** °C
Screening	7.1	4.97	0.96	36.3
13	1.9	0.84	0.73	38.1
15	4.7	2.66	1.03	—

Due to the event of diarrhea, Cycle 1 Day 15 of paclitaxel and atezolizumab was not administered and the next dose was given on Study Day 30 (Cycle 2 Day 1). Treatment with ipatasertib was interrupted on Study Day 14 and was resumed on Study Day 29.

Due to the event of febrile neutropenia, there was no change in study treatment with paclitaxel, however, study treatment with ipatasertib was reduced to 300 mg on Study Day 29 and Cycle 1 Day 15 of atezolizumab was not administered and the next dose was given on Study Day 30.

The Investigator considered diarrhea, to be related to ipatasertib and atezolizumab, and unrelated to paclitaxel.

The Investigator considered febrile neutropenia, to be related to ipatasertib and paclitaxel, and unrelated to atezolizumab.

Event 3: Fatigue (Worsening fatigue)
Event 4: Dehydration

Prior to the events of fatigue and dehydration, the most recent dose of atezolizumab was administered on Study Day 1, paclitaxel on Study Day 8 and ipatasertib (400 mg) on Study Day 13.

On Study Day 28, the patient experienced Grade 2 fatigue associated with Grade 2 dehydration, leading to hospitalization. Laboratory work-up was not clinically significant. No treatment was administered for the event of fatigue, and she received treatment with sodium chloride for dehydration. On Study Day 30, her laboratory work-up showed sodium: 141 mmol/L (normal range 135-145 mmol/L), potassium: 4.2 mmol/L (normal range: 3.5-5.2 mmol/L). On the same day (Study Day 30), the event of fatigue improved to Grade 1 and event of dehydration was considered resolved and she was discharged from the hospital. The event of fatigue remained unresolved at the time of patient’s death (see narrative below).

Due to the events of fatigue and dehydration, Cycle 2 Day 1 of paclitaxel and atezolizumab was delayed and the next dose was given on Study Day 30. Treatment with ipatasertib was interrupted on Study Day 30 and was resumed on Study Day 31.

The Investigator considered fatigue and dehydration, to be related to ipatasertib, paclitaxel and atezolizumab.

Event 5: Diarrhea (second episode)

Prior to the event of diarrhea, the most recent dose of atezolizumab was administered on Study Day 30, paclitaxel on Study Day 36 and ipatasertib (300 mg) on Study Day 41.

On Study Day 42, the patient experienced non-serious Grade 3 diarrhea. Unspecified treatment was administered for the event of diarrhea. On Study Day 43, the event of diarrhea was considered resolved.

Due to the event of diarrhea, there was no change in study treatment with atezolizumab, however, study treatment with ipatasertib was interrupted on Study Day 43 and was resumed on Study Day 57 and paclitaxel was reduced to 65 mg/m^2 from 80 mg/m^2 on Study Day 57.

The Investigator considered diarrhea, to be related to ipatasertib and paclitaxel and unrelated to atezolizumab.

Loperamide treatment details:

Indication	**Total daily dose** (Units: mg)	**Route**	**Start day**	**Stop day**
Diarrhea	4	PO	2	2
Diarrhea	4	PO	3	6
Diarrhea	12	PO	7	8
Diarrhea	16	PO	9	12
Diarrhea	8	PO	31	36
Diarrhea	4	PO	38	39
Diarrhea	4	PO	58	59
Diarrhea	4	PO	67	70
Diarrhea	4	PO	73	73
Diarrhea	10	PO	75	75
Diarrhea	6	PO	76	77
Diarrhea	4	PO	86	90
Diarrhea	6	PO	91	91
Diarrhea	4	PO	93	95
Diarrhea	8	PO	96	96

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	97	100
Diarrhea	2	PO	103	105
Diarrhea	4	PO	114	117
Diarrhea	8	PO	118	118

On Study Day 114, a radiographic response assessment showed disease progression with new lesions in brain (right frontal lobe).

On Study Day 148, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and atezolizumab administered on Study Day 113 and ipatasertib on Study Day 118. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Radiotherapy to brain (bilatetal frontal and occipital lobes, left temporal lobe,) (dose: 120 cGy and 1 fraction)	142	142
Radiotherapy to brain (hippocampal sparing) (dose: 30 cGy and 10 fractions)	224	235
Vinorelbine	379	386
Carboplatin and Gemcitabine	414	Ongoing

On Study Day 543, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Hemorrhoids	1	Non-serious	21	Resolving	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	44	71	Related	Unrelated	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Mucosal inflammation	1	Non-serious	94	113	Unrelated	Related	Unrelated
Rash maculo-papular	1	Non-serious	114	148	Related	Related	Unrelated

Study Number/CRTN:	CO40016/304331	Patient number	3054
Demographics:	59-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Category:	Tumor necrosis SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with “other” moderately differentiated, ER/PR and HER2 negative, locally advanced unresectable left breast cancer (T4N1M0) on Study Day − 90 following left breast biopsy on the same day.

At screening sites of disease involvement included breast (formation in left breast, lesion in left breast upper outer quadrant and lesion in left breast lower outer quadrant), soft tissue (skin fold) and lymph nodes (axillary lymph node left side A and axillary lymph node left side B).

No past cancer treatments were reported.

The patient’s medical history included Grade 1 cervical polyp. Surgical history included polypectomy. Concurrent conditions included Grade 1 pericarditis, Grade 1 hepatic cyst, Grade 1 renal cyst, Grade 1 uterine leiomyoma, Grade 1 spinal meningeal cyst, Grade 1 goiter, Grade 1 autonomic nervous system imbalance, Grade 1 metabolic cardiomyopathy and fibroma of head soft tissue.

At screening, the patient’s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included quercetin, metoprolol and temgicoluril.

Event: Tumor necrosis

Prior to the event of tumor necrosis, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 212 and ipatasertib (400 mg) on Study Day 217.

On Study Day 224, the patient was diagnosed with Grade 2 (initial intensity) tumor necrosis (symptoms and diagnostic details not reported for this day). No treatment was administered for the event.

On Study Day 279, a CT scan showed stable response but she experienced worsening of pain syndrome in left breast which was radiating to left axillary area and had bursting sensation and itching. On Study Day 292, a physical examination showed deformed left breast with 7 cm conglomeration observed in lower quadrant, 1 cm ulceration in lower edge which was nodular non-uniform, tightly merged to front chest wall, with sero-hemorrhagic discharge. On the same day (Study Day 292), the event of tumor necrosis became serious, and she was hospitalized.

On Study Day 295, palliative mastectomy with thoracic muscles of left breast and palliative left lymph node resection were performed. On Study Day 303, a macroscopic observation showed $6 \times 4 \times 7$ cm formation in breast tissue. A microscopic examination showed defined infiltrating in-breast tissue carcinoma and Grade 2 therapeutical pathomorphosis. Tumor edge was negative. It was reported that 12 lymph nodes were dissected, all lymph nodes were negative. On Study Day 307, immune-histochemistry revealed ER/PR negative and KI 35%. The patient required daily dressings and observation; thus, hospitalization was prolonged to abide all sanitary and hygienic procedure (dressings) in consideration of the complete resection. On Study Day 314, the event of tumor necrosis was considered resolved and she was discharged from the hospital.

Due to the event of tumor necrosis, study treatment with atezolizumab and paclitaxel was interrupted on Study Day 268 and ipatasertib was interrupted on Study Day 254 and was later never resumed (see narrative below).

The Investigator considered tumor necrosis, to be related to ipatasertib, paclitaxel and atezolizumab.

On Study Day 314, study treatment was permanently discontinued due to other reason (all target lesions were resected during the surgery thus the patient no longer participant in the study) with last dose of paclitaxel and atezolizumab administered on Study Day 268 and ipatasertib on Study Day 254. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Radiotherapy to left cervical supraclavicular, axillary, parasternal lymph nodes and front chest wall left side (dose: 5000 cGy, fractions not reported)	351	393

On Study Day 753, the patient was discontinued from the study as study was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Epistaxis	1	Non-serious	15	15	Unrelated	Related	Unrelated
Alopecia	2	Non-serious	20	523	Unrelated	Related	Unrelated
Alanine aminotransferase increased	1	Non-serious	29	36	Related	Related	Related
Neutropenia	1	Non-serious	113	120	Unrelated	Related	Unrelated
Leukopenia	1	Non-serious	113	120	Unrelated	Related	Unrelated
Hyperkalemia	2	Non-serious	120	127	Related	Related	Unrelated
Leukopenia	1	Non-serious	155	198	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	182	187	Related	Unrelated	Unrelated
Hyperbilirubinemia	1	Non-serious	203	212	Related	Related	Related
Diarrhea	2	Non-serious	209	212	Unrelated	Unrelated	Unrelated
Neutropenia	1	Non-serious	212	230	Unrelated	Related	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipataseritib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Leukopenia	1	Non-serious	212	230	Unrelated	Related	Unrelated
Diarrhea	2	Non-serious	218	218	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	246	250	Related	Unrelated	Unrelated
Nail dystrophy	2	Non-serious	257	Unresolved	Unrelated	Related	Unrelated
Leukopenia	1	Non-serious	259	268	Unrelated	Related	Unrelated

Study Number/CRTN:	CO40016/304784	Patient number	3055
Demographics:	45-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Category:	Pleural effusion SAE		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with unspecified, well differentiate, ER/PR and HER2 negative, left breast cancer (T4bN0M0) approximately 5 years prior to study entry.

On Study Day -37, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative in metastatic tissue. At screening sites of disease involvement included pleura (other right lower lobe pleura nodule), lung (nodule in apical region in the right lobe lung and nodule in the anterior region in the right lobe lung and bilateral sparse nodules in the lungs), liver (hepatic nodule in the right lobe vii region, hepatic nodule in the right lobe vii/vi region and sparse nodules in the liver parenchyma), bone (osteolytic lesion on right costal arch), kidney (lump on the anterior aspect of the left kidney), lymph nodes (right thoracic region, gastro-hepatic and right renal) and right pleural effusion.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Doxorubicin and cyclophosphamide	Approximately 5 years prior to study entry	Approximately 5 years prior to study entry
Surgery	Curative	Simple mastectomy of left breast	Approximately 4 years and 10 months prior to study entry	NA
Cancer therapy	Adjuvant	Doxorubicin, cyclophosphamide, and paclitaxel	Approximately 4 years and 9 months prior to study entry	Approximately 4 years and 6 months prior to study entry
Radiotherapy	Adjuvant	Breast (left breast and left supraclavicular fossa; dose: 5040 cGy and 28 fractions)	Approximately 4 years and 4 months prior to study entry	Approximately 4 years and 2 months prior to study entry

The patient′s medical history included aspartate aminotransferase increased and alanine aminotransferase increased. No surgical history was reported. No concurrent condition was reported.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

No concomitant medication ongoing at Study Day 1 was reported.

Event: Pleural effusion (Worsening of pleural effusion)

Prior to the event of pleural effusion, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 15 and ipatasertib (400 mg) on Study Day 21.

On Study Day 23, the patient experienced Grade 1 intermittent and non-productive cough (non-serious, unrelated). Upon auscultation vesicular murmur were decreased. A chest X-ray showed Grade 1 (initial intensity) right pleural effusion (worsening of non-target lesion). No treatment was administered for the event. On Study Day 29, the event of pleural effusion worsened to Grade 3 and she was hospitalized. On Study Day 30, a thoracentesis was performed with drainage of 2 liters of serous fluid. On Study Day 33, pleurodesis was performed. On Study Day 36, the chest drain removed. On the same day (Study Day 36), the event of pleural effusion was considered resolved and she was discharged from the hospital.

There was no change in study treatment due to the event of pleural effusion.

The Investigator considered pleural effusion, to be unrelated to ipatasertib, paclitaxel and atezolizumab, and related to disease under study.

On Study Day 57, a radiographic response assessment showed disease progression with new lesions in lymph node (right retropectoral lymph nodes), lung (compressive atelectasis of part of the right lower lobe) and right adrenal gland (nodular thickening).

On Study Day 64, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and atezolizumab administered on Study Day 57 and ipatasertib on Study Day 64. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Gemcitabine	98	158
Capecitabine and zoledronic acid monohydrate	189	Ongoing

On Study Day 446, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious / Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**	**Causality (Atezolizumab)**
Diarrhea	2	Non-serious	4	23	Related	Related	Unrelated
Nausea	1	Non-serious	4	30	Related	Related	Unrelated
Vomiting	1	Non-serious	4	4	Related	Related	Unrelated
Pain	1	Non-serious	6	Resolving	Unrelated	Related	Unrelated
Dermatitis allergic	1	Non-serious	14	17	Unrelated	Related	Unrelated
Anemia	1	Non-serious	15	Resolving	Unrelated	Related	Unrelated
Stomatitis	2	Non-serious	19	47	Unrelated	Related	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Chest pain	1	Non-serious	24	24	Unrelated	Unrelated	Unrelated
Alanine aminotransferase increased	1	Non-serious	29	57	Unrelated	Related	Unrelated
Chest pain	2	Non-serious	30	30	Unrelated	Unrelated	Unrelated
Headache	1	Non-serious	30	30	Unrelated	Unrelated	Unrelated
Alopecia	1	Non-serious	30	Unresolved	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	32	41	Related	Related	Unrelated
Chest pain	2	Non-serious	32	36	Unrelated	Unrelated	Unrelated
Hypoalbuminemia	2	Non-serious	36	43	Unrelated	Unrelated	Unrelated
Blood alkaline phosphatase increased	1	Non-serious	36	57	Unrelated	Related	Unrelated
Nausea	1	Non-serious	36	Resolving	Unrelated	Unrelated	Unrelated
Diarrhea	2	Non-serious	42	42	Related	Related	Unrelated
Diarrhea	2	Non-serious	43	57	Related	Related	Unrelated
Diarrhea	1	Non-serious	58	66	Related	Related	Unrelated

Study Number/CRTN:	CO40016/305113	Patient number	3060
Demographics:	44-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Influenza SAE		
Event 2 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		

The patient was randomized on Study Day – 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR negative and HER2 negative left breast cancer (T2N3M0), approximately 2 years prior to study entry.

The patient was diagnosed with metastatic disease on an unknown date with ER /PR and HER2 negative in metastatic tissue. At screening, sites of disease involvement included left breast (axilla lesion).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Docetaxel, fluorouracil, epirubicin and cyclophosphamide (unknown dose)	Approximately 1 years and 10 months prior to study entry	Approximately 1 years and 4 months prior to study entry
Surgery	Curative	Left lymph node (axillary dissection)	Approximately 1 years 5 months prior to study entry	–
Radiotherapy	Adjuvant	Left breast and supraclavicular fossa (unknown dose)	Approximately 1 years and 4 months prior to study entry	Approximately 1 years and 4 months prior to study entry

No medical/surgical history was reported. The patient′s concurrent conditions included pain in extremity (left arm).

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included calcium carbonate, paracetamol, and ibuprofen.

Event: Influenza

Prior to the event of influenza, the most recent dose of atezolizumab was administered on Study Day 55, paclitaxel on Study Day 62 and ipatasertib (400 mg) on Study Day 65.

On Study Day 66, the patient presented to the department with flue and high body temperature of 39°C. A blood test was performed, and results showed no neutropenia. She was diagnosed with Grade 2 influenza, leading to hospitalization. She received treatment with oseltamivir for influenza. On the following day (Study Day 67), the patient was discharged from the hospital. On Study Day 92, the event of influenza was considered resolved.

Relevant laboratory values listed in the table below:

Study Day	**WBC count** (normal range: 4-10 $\times$ 10^9/L)	**Absolute neutrophil count** (normal range: 2-7 $\times$ 10^9/L)	**Absolute lymphocyte count** (normal range: 1-3 $\times$ 10^9/L)	**Body temperature** (°C)
– 14	9.6	7.3	1.52	36.8
62	5.1	3.23	1.4	36.7
92	7.7	4.96	1.9	37

Due to this event, Cycle 3 Day 8 of paclitaxel was delayed and was given on Study Day 62, Cycle 3 Day 15 of atezolizumab was not administered. Treatment with ipatasertib was interrupted on Study Day 66. The next dose of atezolizumab and ipatasertib was given on Study Day 85.

The Investigator considered influenza to be unrelated to atezolizumab, paclitaxel and ipatasertib and related to other causes (unspecified).

Event 2: Diarrhea

Prior to the event of diarrhea, the most recent dose of atezolizumab was administered on Study Day 393, paclitaxel on Study Day 400, and ipatasertib (400 mg) on Study Day 404.

On Study Day 405, the patient experienced non-serious Grade 3 diarrhea. It was reported that she was going hourly but then received treatment with loperamide which settled her diarrhea. On Study Day 407, the event of diarrhea improved to Grade 1 and remained unresolved at the time of study discontiunation.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	1	Ongoing
Diarrhea	2	PO	405	407

There was no change in the study treatment due to the event of diarrhea.

The Investigator considered diarrhea to be related to atezolizumab and paclitaxel and unrelated to ipatasertib.

On Study Day 673, a radiographic response assessment showed disease progression with new lesion in left breast (pec major).

On Study Day 722, study treatment was permanently discontinued due to disease progression with the last dose of atezolizumab given on Study Day 708, paclitaxel on Study Day 715 and ipatasertib on Study Day 721. The patient entered into the long-term follow-up.

On Study Day 750, the patient was discontinued from the study as study was terminated as per physician decision (LTFU terminated by the Sponsor).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	1	100	Related	Unrelated	Unrelated
Nausea	1	Non-serious	8	322	Related	Related	Unrelated
Fatigue	1	Non-serious	8	281	Related	Unrelated	Related
Abdominal pain	1	Non-serious	8	8	Related	Unrelated	Related
Epistaxis	1	Non-serious	8	8	Related	Unrelated	Related
Arthralgia	1	Non-serious	96	98	Unrelated	Unrelated	Unrelated
Back pain	1	Non-serious	108	Unresolved	Not Applicable	Unrelated	Unrelated
Mucosal inflammation	1	Non-serious	124	Unresolved	Related	Related	Unrelated
Hot flush	1	Non-serious	168	Unresolved	Unrelated	Unrelated	Unrelated
Headache	1	Non-serious	209	210	Unrelated	Unrelated	Unrelated

Dyspepsia	1	Non-serious	228	597	Unrelated	Unrelated	Unrelated
Gastroesophageal reflux disease	1	Non-serious	236	Unresolved	Unrelated	Unrelated	Related
Gingivitis	1	Non-serious	242	Unresolved	Related	Unrelated	Related
Fatigue	2	Non-serious	272	275	Unrelated	Unrelated	Unrelated
Dyspnea	1	Non-serious	281	Unresolved	Unrelated	Unrelated	Unrelated
Anxiety	1	Non-serious	281	297	Unrelated	Unrelated	Unrelated
Nail ridging	1	Non-serious	336	Unresolved	Unrelated	Unrelated	Related
Fatigue	1	Non-serious	406	475	Related	Unrelated	Related
Herpes zoster	1	Non-serious	417	424	Unrelated	Unrelated	Unrelated
Fatigue	3	Non-serious	476	491	Unrelated	Related	Unrelated
Epistaxis	1	Non-serious	557	644	Unrelated	Unrelated	Related
Fatigue	1	Non-serious	568	588	Related	Unrelated	Related
Fatigue	3	Non-serious	589	602	Unrelated	Unrelated	Related
Dyspnea	1	Non-serious	637	Unresolved	Unrelated	Unrelated	Related
Vision blurred	1	Non-serious	649	Unresolved	Related	Unrelated	Unrelated

Study Number/CRTN:	CO40016/318721	Patient number	3067
Demographics:	58-year-old female (Unknown race)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle)+Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Rash pruritic Grade ≥ 3 rash		
Event 2 (PT) Category:	General physical health deterioration SAE		
Event 3 (PT) Categories:	Covid-19 SAE, COVID-19 SAE		

The patient was randomized on Study Day − 11.

The patient was initially diagnosed with other histology, poorly differentiated, ER/PR negative and HER2 negative left breast cancer (T4N3M0), on Study Day − 57.

The patient was diagnosed with metastatic disease on an unknown day with ER /PR negative and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included formation in left breast (underlying mass with cutaneous infiltrate, and multiple retro-pectoral and supraclavicular axillary adenomegalies).

No past cancer treatments were reported.

The patient′s medical history included post procedural inflammation. No surgical history was reported. Concurrent conditions included drug hypersensitivity (penicillin), hypercholesterolemia, hypertension, deafness, hypothyroidism, and skin cancer (left breast).

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included levothyroxine, pristinamycin, ibuprofen, bisoprolol/hydrochlorothiazide, and spironolactone.

Event 1: Rash pruritic (skin rash all over the body, itchy)

Prior to the event of rash pruritic, the most recent dose of atezolizumab was administered on Study Day 1, paclitaxel on Study Day 7 and ipatasertib (400 mg) on Study Day 12.

On Study Day 13, she developed Grade 3 itchy rash pruritic all over body covering 80% of the body surface. It was reported that her tolerance to treatment was poor thus skin rash was considered related to hives and study treatment administration. Her body temperature was 39.1°C. She received treatment with desloratadine and corticosteroid (unspecified). Re-assessment was performed post 48 hours of treatment and advised to increase the treatment dose from 1 mg/kg to 2 mg/kg. On Study Day 43, the event of rash pruritic was considered resolved.

Due to the event of rash pruritic, Cycle 1 Day 15 of atezolizumab and paclitaxel was not administered, and the next dose was given on Study Day 36. Study treatment with ipatasertib was interrupted on Study Day 14 and the next dose was given on Study Day 38.

The Investigator considered rash pruritic to be unrelated to paclitaxel and related to atezolizumab and ipatasertib.

On Study Day 70, the patient was noted with Grade 3 anemia (initial intensity Grade 2; non-serious, unrelated). On Study Day 105, she was noted with Grade 3 hypokalemia (non-serious, unrelated) (potassium level not reported for this day). On the following day (Study Day 106), she was diagnosed with Grade 2 acute kidney injury (non-serious, unrelated; lab work-up not reported for this day). On Study Day 127, the event of acute kidney injury was considered resolved.

Event 2: General physical health deterioration (deterioration in general condition)

Prior to the event of general physical health deterioration, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 131 and ipatasertib (400 mg) on Study Day 98.

On Study Day 144, the patient was noted with Grade 3 general physical health deterioration associated with nausea, asthenia, hypotension without tachycardia, fever (vitals not reported) and mottling with no desaturation, oozing left breast, permeation nodules on left breast level associated with purulent and foul-smelling discharge, sacrum pressure ulcers, and bilateral lower limb edema. Laboratory work-up showed hypokalemia (potassium level not reported for this day), hyponatremia, acute renal failure, and inflammatory syndrome (lab work-up not reported). Subsequently, she was hospitalized. She received right heel dressings for pressure sores and oozing left breast and treatment with potassium chloride, glucose/potassium chloride/sodium chloride (to repair breast dressing which was very smelly and oozing), levothyroxine, paracetamol, and morphine. The pressure ulcer in sacrum and right heel was treated with biatain, 1 L bionolyte 5% per 24 hours. She further received treatment with tinzaparin. On Study Day 146, a laboratory work-up showed serum creatinine of 115 μmol/L (normal range not reported) and stable C-reactive protein: 80 (units and normal range not reported). She received continued hydration with 2 g of potassium in 1 L of bionylte, treatment with magnesium chloride, fentanyl, ketamine, metoclopramide, and midazolam administered over 15 minutes. An improvement was noted in phlebitis pain and in lower limb edema. On Study Day 153, her vitals improved with no fever and nausea. She then received treatment with glucose 1-phosphate disodium. During hospitalization, the patient complained of mild pain without dyspnea. Upon examination, she was oriented (GCS: 15), non-confused with no sensory motor deficit, no meningeal and cerebellar syndrome. The examination showed two ulcerative necrotic lesions covered with hyperalgic fibrin on skin with one extension of the nipple of about 12 cm in diameter and 5 cm deep and other 10 cm in diameter in axillary extension connected to the subcutaneous fistula and 2nd orifice more internal less than 2 cm in diameter. It was reported that, pain on visual analogue scale was 2/10 outside treatment and 8/10 while dressing the left breast wound. She further received treatment with oxycodone (20 mg continuous dose everyday) along with 10 mg bolus with a refractory period of 1 hour and increased dosing to 30 mg maximum per day. On an unspecified day, the event of general physical health deterioration improved. On Study Day 151, the event of hypokalemia was considered resolved. The event of general physical health deterioration was considered resolving at the time of patient's death (see narrative below).

Due to the event of general physical health deterioration, Cycle 6 Day 1 of atezolizumab and paclitaxel was delayed, and the next dose was given on Study Day 152 and treatment with ipatasertib was interrupted on Study Day 98 and later never resumed due to due non-compliance to study drug.

The Investigator considered general physical health deterioration to be unrelated to ipatasertib, paclitaxel and atezolizumab and related to disease under study.

Treatment with ipatasertib was permanently discontinued due to non-compliance to study drug with the last dose given on Study Day 98.

Event 3: COVID-19 (COVID 19 infection)

Prior to the event of COVID-19, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 152.

On Study Day 154, during the ongoing hospitalization, her vitals showed blood pressure 140/80 mmHg, heart rate 100 bpm and oxygen saturation of 95% ambient air. She had no fever. A PCR test was performed, and the patient was diagnosed with Grade 3 moderate but typical COVID-19 with frosted glass opacities (without crazy paving crosslinks) and appearance of subpleural topography especially in the basal segment of upper right lobe and in the middle lobe with no condensations on radiography examination. She received treatment with ceftriaxone, macrogol and oxycodone. On Study Day 173, a follow-up chest CT-scan showed a clear improvement in the ground glass areas and the disappearance of bilateral pleural effusion thus, the event of COVID-19 was considered resolved. On the following day (Study Day 174), she was discharged from the hospital. On Study Day 179, the test for COVID-19 was reported negative.

Vitals reported in the table below:

Study Day	Body temperature (°C)	Pulse rate (beats per minute)	Respiratory rate (breaths per minute)	Blood pressure
− 23	37.9	62	16	134/77
152 (14:00 hours)	37.5	80	16	120/75
152 (18:15 hours)	37.7	87	16	138/91
152(19:50 h ours)	37.7	92	16	137/92

Relevant laboratory work-up reported in the table below:

Study Day	**WBC count** (normal range: 3.8-11 $\times$ 10^9/L)	**Absolute neutrophil count** (normal range: 1500-7500/μL)	**Absolute lymphocyte count** (normal range: 1000-4800/μL)
-6	7200*	5285	958**
152	3.16	2594	259
165	2.21	1019	356
167	4.73	3027	544

*normal range: 4000-11000/μL, **normal range: 1500-7500/μL

Due to the event of COVID-19, Cycle 7 Day 1 of paclitaxel and atezolizumab was delayed on Study Day 152 and next dose was given on Study Day 180.

The Investigator considered COVID-19 to be unrelated to ipatasertib, paclitaxel and atezolizumab and related to disease under study.

On Study Day 183, an overall response assessment showed disease progression.

On Study Day 195, the study treatment was permanently discontinued due to disease progression with the last dose of atezolizumab given on Study Day 180 and paclitaxel on the Study Day 195. The patient then entered the long-term follow-up phase.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	**Start Day**	**Stop Day**
Paclitaxel (3 cycles)	209	222

On Study Day 304, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Back pain	2	Non-serious	7	Unresolved	Unrelated	Unrelated	Unrelated
Diarrhea	2	Non-serious	11	120	Related	Related	Related
Decreased appetite	3	Non-serious	15	Unresolved	Unrelated	Unrelated	Unrelated
Mucosal inflammation	1	Non-serious	15	36	Unrelated	Related	Unrelated
Influenza	2	Non-serious	18	35	Unrelated	Unrelated	Unrelated
Vomiting	1	Non-serious	36	64	Unrelated	Related	Related
Nausea	2	Non-serious	43	200	Related	Related	Unrelated
Asthenia	1	Non-serious	43	304	Related	Related	Related
Phlebitis	3	Non-serious	70	209	Unrelated	Unrelated	Unrelated
Dizziness	1	Non-serious	108	108	Unrelated	Unrelated	Unrelated
Fall	1	Non-serious	108	108	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304787	Patient number	3077
Demographics:	64-year-old Black or African American female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Categories:	Large intestine perforation SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER2 negative, locally advanced unresectable right breast cancer (T3N2M0) on Study Day −63.

At screening sites of disease involvement included breast (upper lateral quadrant and left skin thickening) and lymph nodes (left axillary).

No past cancer treatments were reported.

No medical or surgical history was reported. No concurrent condition was reported.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medication ongoing at Study Day 1 included morphine.

Event: Large intestine perforation (Perforation in the sigmoid)

Prior to the event of large intestine perforation, the most recent dose of atezolizumab, paclitaxel and ipatasertib (400 mg) was administered on Study Day 31.

On Study Day 35, the patient experienced Grade 2 abdominal pain. Symptomatic treatment was administered with metamizole, tramadol, ranitidine, bromopride and ondansetron. On Study Day 39, abdomen CT scan revealed pneumoperitoneum and urgent surgery was recommended. On Study Day 40, the patient was stable and had improvement in abdominal pain. She was admitted to the hospital and underwent abdominal rectosigmoidectomy and terminal colostomy without complication. She received treatment with cefazolin and metronidazole. An anatomopathological examination concluded Grade 3 large intestine perforation and transmural inflammatory process. She further received treatment with ciprofloxacin. On Study Day 45, she was discharged from the hospital in a stable condition. On Study Day 49, she was stable without complications. On Study Day 59, she was well and without complications and her routine laboratory work-up showed not clinically significant changes. On the same day (Study Day 59), the event of large intestine perforation was considered resolved.

Due to the event of large intestine perforation, study treatment with ipatasertib, paclitaxel and atezolizumab was permanently discontinued with last dose of atezolizumab, paclitaxel and ipatasertib administered on Study Day 31. The patient entered into long-term follow-up.

The Investigator considered large intestine perforation, to be related to ipatasertib and atezolizumab and unrelated to paclitaxel.

On Study Day 133, a radiographic response assessment showed disease progression with new lesions in lymph nodes (upper mediastinum).

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Paclitaxel, cisplatin and gemcitabine	95	350
'Other' palliative surgery of left breast	226	NA
Cisplatin and gemcitabine	257	Ongoing

On Study Day 606, the patient died due to 'other' cause (companion was unable to inform). It was unknown if underlying cancer was a contribution factor or not. An autopsy was not performed.

Other AE experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Pruritus	1	Non-serious	13	13	Related	Related	Related

Study Number/CRTN:	CO40016/304891	Patient number	3080
Demographics:	49-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Categories:	Pneumonia SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was diagnosed with ductal, poorly differentiated, ER/PR and HER2 negative, metastatic right breast cancer (T4N2M1) on Study Day − 58.

At screening, sites of disease involvement included lymph nodes (right axillary node, bilateral mediastinal node, and bilateral nodal metastases), lung (left lower pulmonary lobe, right upper pulmonary lobe and multiple bilateral) and breast (right).

Past cancer treatment is listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Metastatic	Right breast (dose: 2000 cGy, 5 fractions)	-31	-27

No medical or surgical history was reported. No concurrent condition was reported.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medication ongoing at Study Day 1 included loperamide.

Event: Pneumonia

Prior to the event of pneumonia, the most recent dose of atezolizumab was administered on Study Day 1, paclitaxel on Study Day 8 and ipatasertib (400 mg) on Study Day 11.

On Study Day 12, the patient was hospitalized due to Grade 2 pneumonia (presenting signs, symptoms and confirmatory assessment details not reported). A chest X-ray was normal. Relevant laboratory work-up is reported in the table below. She received treatment with meropenem and acyclovir. On Study Day 15, a chest X-ray was performed (results not reported). On Study Day 16, CT head showed no brain metastasis. On Study Day 23, MRI head showed no evidence of meningoencephalitis. On Study Day 26, a chest X-ray showed suspicion for infection. On Study Day 34, she was discharged from the hospital. On Study Day 35, the patient was noted with breathlessness and dehydration and was re-hospitalized. On the same day (Study Day 35), a chest X-ray showed persisting infiltration throughout both lungs. She received further treatment with flucloxacillin, gentamicin, piperacillin sodium/tazobactam sodium, sodium chloride, folic acid, omeprazole, amoxicillin, ciprofloxacin, ibuprofen, codeine phosphate, morphine sulfate and prednisolone. On Study Day 36, a chest X-ray and CT chest abdomen and pelvis showed pneumonitis and disease progression in breast and lungs (non-target lesions). On Study Day 37, unspecified laboratory work-up was performed (results not reported). On Study Day 44, the event of pneumonia was considered resolved and she was discharged from the hospital.

Due to the event of pneumonia, there was no change in study treatment with ipatasertib, however, study treatment with atezolizumab and paclitaxel was permanently discontinued with last dose administered on Study Day 1 and Study Day 8, respectively.

The Investigator considered pneumonia, to be unrelated to ipatasertib, paclitaxel, and atezolizumab and related to disease under study and concurrent illness (unspecified).

Relevant laboratory work-up:

Study Day	**WBC count** Normal range: 4-10 $\times$ 10^9/L	**Neutrophils** Normal range: 2-7 $\times$ 10^9/L	**Lymphocytes** Normal range: 1.1-5 $\times$ 10^9/L
Screening (−7)	8.2	5.4	1.9
12	8	6.5	1
35	7.3	5.2	1.3
37	9.2	6.1	1.6

On Study Day 35, study treatment with ipatasertib was permanently discontinued as per physician's decision (because patient's health deteriorated, and subsequent CT scans showed progression) with the last dose of ipatasertib administered on Study Day 14. The patient entered into the long term follow up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	**Start Day**	**Stop Day**
Carboplatin	44	84

On Study Day 147, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious / Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**	**Causality (Atezolizumab)**
Constipation	1	Non-serious	3	4	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	5	6	Related	Related	Unrelated
Fatigue	2	Non-serious	5	Unresolved	Related	Related	Unrelated
Flushing	1	Non-serious	8	8	Unrelated	Related	Unrelated

Study Number/CRTN:	CO40016/304680	Patient number	3081
Demographics:	65-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Blood alkaline phosphatase increased Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Categories:	Immune-mediated lung disease SAE, Grade ≥ 2 pneumonitis		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR negative and HER2 negative right breast cancer (T2N3M0) approximately 3 years and 4 months prior to study entry.

On Study Day – 77, the patient was diagnosed with metastatic disease with ER/PR unknown and HER2 receptor not assessed in metastatic tissue. At screening, sites of disease involvement included midline mediastinum, liver (segment II, IVA and IVB), lymph node midline and right lung (segment 9 and 10) and left pleural fluid.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	Approximately 3 years and 2 months prior to study entry	Approximately 3 years prior to study entry
Cancer therapy	Adjuvant	Paclitaxel (12 cycles)	Approximately 2 years and 11 months prior to study entry	Approximately 2 years and 8 months prior to study entry
Radiotherapy	Adjuvant	Axillary cervical supraclavicular nodes (dose: 5000 cGy)	Approximately 2 years and 7 months prior to study entry	Approximately 2 years and 5 months prior to study entry
Surgery	Curative	Right breast	–160	–
Surgery	Curative	Right breast	–117	–

No medical/surgical history was reported. The patient′s concurrent conditions included hypertension and cancer pain.

At screening, the patient's ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included candesartan, hydrochlorothiazide, bisoprolol and paracetamol.

Event 1: Blood alkaline phosphatase increased (alkaline phosphatase level increase)

Prior to the event of blood alkaline phosphatase increased, the most recent dose of atezolizumab was given on Study Day 1, paclitaxel on Study Day 9, and ipatasertib (400 mg) on Study Day 19.

On Study Day 20, a laboratory work-up showed ALP 437 U/L (normal range: 38-126 U/L), ALT 79 U/L (normal range: 0-34 U/L), AST 80 U/L (normal range: 14-36 U/L) and total bilirubin 0.72 mg/dL (normal range: 0.2-1.3 mg/dL). The patient was diagnosed with non-serious Grade 2 blood alkaline phosphatase increased. No treatment was reported for this event. On Study Day 43, the patient was noted with Grade 2 aspartate aminotransferase increased (non-serious, unrelated; AST 172 U/L normal range: 14-36 U/L). On Study Day 65, the event of blood alkaline phosphatase increased worsened to Grade 3. On Study Day 93, the event of blood alkaline phosphatase increased was considered resolved. The event of aspartate aminotransferase increased was resolving at the time of patient's death (see narrative below).

Relevant laboratory values listed in the table below:

Study Day	**AST** (normal range: 14-36 U/L)	**ALT** (normal range: 0-34 U/L)	**ALP** (normal range: 38-126 U/L)	**Total bilirubin** (normal range: 0.2-1.3 mg/dL)
-13	69	39	112	0.87
20	80	79	437	0.72
30	46	33	177	0.75
37	38	26	141	0.61
43	172	116	457	0.66
58	50	47	204	0.72
64	114	61	948	0.82

72	50	38	291	0.82
79	51	31	166	0.5
93	40	22	121	0.66
100	54	29	137	0.56
107	56	32	158	0.56

There was no change in the study treatment with ipatasertib and paclitaxel due to the event of blood alkaline phosphatase increased; however, study treatment with atezolizumab was interrupted on Study Day 2 and the next dose was given on Study Day 30.

The Investigator considered blood alkaline phosphatase increased to be unrelated to ipatasertib and paclitaxel and related to atezolizumab and disease under study.

Event 2: Immune-mediated lung disease (Suspicion of immune-mediated pneumonitis)

Prior to the event of immune-mediated lung disease, the most recent dose of atezolizumab and paclitaxel was given on Study Day 43, and ipatasertib (400 mg) on Study Day 50.

On Study Day 55, a CT-scan was performed, and the patient was suspected with interstitial pneumonia. She had no symptoms of infection including fever, cough, and increased WBC count. On Study Day 58, an X-ray was performed, and diagnosis of Grade 2 immune-mediated lung disease was made, leading to hospitalization. She received treatment with clarithromycin and paracetamol for immune-mediated lung disease. On Study Day 65, the event of immune-mediated lung disease was considered resolved and she was discharged from the hospital.

Relevant laboratory values listed in the table below:

Study Day	**WBC count** (normal range: 4-10 $\times$ $10^3/\mu L$)	**Absolute neutrophil count** (normal range: 1.8-7.7 $\times$ $10^3/\mu L$)	**Absolute lymphocyte count** (normal range: 1.1-6.5 $\times$ $10^3/\mu L$)
-1	9.11	7.04	1.03
58	16.46	13.32	1.96
64	6.74	3.68	2.02

Due to this event, Cycle 3 Day 1 of atezolizumab and paclitaxel was delayed and treatment with ipatasertib was interrupted on Study Day 50. The next dose was given on Study Day 65.

The Investigator considered immune-mediated lung disease to be unrelated to ipatasertib and paclitaxel and related to atezolizumab.

On Study Day 106, an overall response assessment showed disease progression.

On Study Day 107, the patient was discontinued from the study treatment due to disease progression with the last dose of atezolizumab given on Study Day 93, paclitaxel on Study Day 100 and ipatasertib on Study Day 106. The patient then entered the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine	119	Ongoing

On Study Day 257, the patient died due to disease progression (as per public records). No information regarding autopsy was reported.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Blood glucose increased	1	Non-serious	9	20	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	41	42	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	52	65	Related	Unrelated	Related
Anemia	2	Non-serious	58	Resolving	Unrelated	Related	Unrelated
Blood alkaline phosphatase increased	1	Non-serious	100	Resolving	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305629	Patient number	3085
Demographics:	58-year-old American Indian or Alaska Native female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		

Event 1 (PT) Categories:	Diarrhea SAE, Grade ≥ 3 diarrhea
Event 2 (PT) Category:	Myositis SAEs
Event 3 (PT) Category:	Myocarditis SAEs
Event 4 (PT) Categories:	Pulmonary embolism Death due to adverse events, SAE, AE leading to Study treatment discontinuation

A narrative for this patient is available in Section 1.1 Narratives for patients who died due to an adverse event(s).

Study Number/CRTN:	CO40016/305145	Patient number	3086
Demographics:	66-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Gastroenteritis SAE		
Event 2 (PT) Category:	Pyrexia SAE		
Event 3 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		
Event 4 (PT) Category:	Neuropathy peripheral (Grade 1) AE leading to study treatment discontinuation		
Event 5 (PT) Category:	Acute kidney injury SAE		

The patient was randomized on Study Day – 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER2 negative, right breast cancer (T2N1M1) on Study Day – 49.

On Study Day − 36, ER and HER2 negative, PR status was unknown disease was diagnosed in metastatic tissue. At screening sites of disease involvement included breast (right breast mass), lymph node (right axillary lymph node, right small axillary sub pectoral lymphadenopathy and right small volume right axillary lymph node) and bone (bilateral diffuse bone metastasis).

No past cancer treatment was reported.

The patient′s medical history included menopause. Surgical history included cholecystectomy. Concurrent conditions included diverticulum, hypothyroidism, hypertension, migraine, and arthralgia.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included candesartan, levothyroxine, amitriptyline, and paracetamol.

Event 1: Gastroenteritis (Infective gastereneritus)
Event 2: Pyrexia

Prior to the events of gastroenteritis and pyrexia, the most recent dose of atezolizumab was administered on Study Day 1, paclitaxel was administered on Study Day 8 and ipatasertib (400 mg) was administered on Study Day 13.

On Study Day 5, the patient experienced intermittent Grade 2 (initial intensity Grade 1) diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide for the event of diarrhea. On Study Day 7, she experienced Grade 1 dyspepsia (non-serious, related to ipatasertib and paclitaxel). She received treatment with omeprazole for the event of dyspepsia. On Study Day 13, she had bowel movement after every 30 minutes of food intake, approximately 8 to 10 times in a day.

On Study Day 14, the patient presented with increased bowel frequency since 3 days, vague cramping in central abdomen, Grade 1 nausea (non-serious, related). She was noted with Grade 2 pyrexia (body temperature: 38.4°C) and diagnosed with Grade 3 gastroenteritis, leading to hospitalization. Her blood pressure was 120/80 mmHg. A laboratory work-up showed: neutrophils 2.0 $\times 10^9$/L (normal range: 1.7-6.2 $\times 10^9$/L), glomerular filtration rate: 86, creatinine: 65 μmol/L (normal range: 50-98 μmol/L), sodium 134 mmol/L (normal range: 133-146 mmol/L), potassium 4.1 mmol/L (normal range: 3.5-5.3 mmol/L) and magnesium 0.68 mmol/L (normal range: 0.7-1 mmol/L). She did not have any other local infection symptoms. She received treatment with piperacillin sodium/tazobactam sodium, enoxaparin, cetirizine, cyclizine and ondansetron. She was still experiencing bowels movements 4 to 5 times a day, although no blood or mucous was present. She also felt lightheaded and dizzy and had reduced oral intake

due to diarrhea. Later, her vitals showed body temperature 37.5°C, blood pressure 115/65 mmHg, heart rate 78 beats/min, respiratory rate 18 breaths/min and oxygen saturation 95 %. Blood culture was negative for methicillin-resistant *Staphylococcus aureus*; *Clostridium difficile* glutamate dehydrogenase test was negative. Feces cultures was negative for *Salmonella*; *Shigella*, *Esherichia coli,* and *Campylobacter*. Later, on the same day (Study Day 14), the event of pyrexia resolved. Her symptoms improved over the next 2 days and on Study Day 16, the event of gastroenteritis was considered resolved. On Study Day 18, she was discharged from the hospital. On Study Day 76, the event of dyspepsia was considered resolved. On Study Day 77, the event of nausea was considered resolved. The event of diarrhea was intermitted but remained unresolved at the time of study discontinuation (see below).

Due to the event of gastroenteritis and pyrexia, Cycle 1 Day 15 of paclitaxel and atezolizumab was not administered. Study treatment with ipatasertib was interrupted after Study Day 13. The next dose of study treatment with paclitaxel, atezolizumab and ipatasertib (at a reduced dose of 300 mg) was given on Study Day 29.

The Investigator considered gastroenteritis, to be related to ipatasertib and unrelated to paclitaxel (causality with atezolizumab was not reported).

The Investigator considered pyrexia, to be related to paclitaxel and unrelated to ipatasertib and atezolizumab.

Relevant vital signs:

Study Day	**Body temperature** °C
Screening (−7)	36.6
14	38.2
	38.4
	37.5

The patient experienced three non-serious events of neuropathy peripheral from Study Day 175 to Study Day 230 (details in the AE table below) and received treatment with pyridoxine form Study Day 176 to Study Day 196 for neuropathy peripheral.

Event 3: Neuropathy peripheral (Peripheral neuropathy)
Event 4: Neuropathy peripheral (Peripheral neuropathy; Grade 1)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 225 and paclitaxel (200 mg) on Study Day 230.

On Study Day 231, the pre-existing event of non-serious neuropathy peripheral worsened to Grade 3. No treatment was administered for the event of neuropathy peripheral Prior to the

event of neuropathy peripheral (Grade 1), the most recent dose of paclitaxel was administered on Study Day 225, atezolizumab on Study Day 239 and paclitaxel (200 mg) on Study Day 244.

. On Study Day 252, the event of non-serious neuropathy peripheral improved to Grade 1, but remained unresolved at the time of study discontinuation.

Due to both the events of neuropathy peripheral, there was no change in study treatment with ipatasertib and atezolizumab, however, study treatment with paclitaxel was permanently discontinued with last dose administered on Study Day 225.

The Investigator considered neuropathy peripheral (Grade 3), to be unrelated to ipatasertib and atezolizumab and related to paclitaxel and procedure (unspecified).

The Investigator considered neuropathy peripheral (Grade 1), to be unrelated to ipatasertib and atezolizumab and related to paclitaxel.

Event 5: Acute kidney injury

Prior to the event of acute kidney injury, the most recent dose of atezolizumab was administered on Study Day 267 and ipatasertib (200 mg) on Study Day 272.

On Study Day 280, a laboratory work-up showed creatinine 197 μmol/L (normal range: 50-98 μmol/L) and urea 7.9 mmol/L (normal range: 2.5-7.8 mmol/L), leading to diagnosis of serious Grade 2 (initial intensity) acute kidney injury. Later, on the same day (Study Day 280), the event of acute kidney injury worsened to Grade 3. On Study Day 281, she was hospitalized. She received treatment with unspecified IV fluids and prednisolone; following which the event of acute kidney injury improved to Grade 2. Later, on the same day (Study Day 281), she was discharged from the hospital. On Study Day 288, the event of acute kidney injury was considered resolved.

Due to the event of acute kidney injury, study treatment with ipatasertib was interrupted on Study Day 273, Cycle 11 Day 1 of atezolizumab was not administered. The next dose was given on Study Day 309.

The Investigator considered acute kidney injury, to be unrelated to ipatasertib and paclitaxel and related to atezolizumab.

Relevant laboratory work-up:

Study Day	Creatinine Normal range : 50-98 μmol/L	Urea Normal range : 2.5-7.8 mmol/L
Screening	57	2.8
280	197	7.9
	195	7.7
281	205	8.4
283	145	9.4
283	145	9.4
288	93	6.6

On Study Day 758, the study treatment and study was permanently discontinued due to other reason (the patient entered to post trial assessment program) with last dose of atezolizumab administered on Study Day 744 and ipatasertib on Study Day 750.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Dyspepsia	1	Non-serious	4	5	Unrelated	Related	Unrelated
Rash	1	Non-serious	16	35	NA	Unrelated	Unrelated
Lethargy	1	Non-serious	35	252	Unrelated	Related	Unrelated
Nausea	1	Non-serious	93	Unresolved	Related	Unrelated	Unrelated
Vulvovaginal discomfort	1	Non-serious	163	177	NA	Unrelated	Unrelated
Urge incontinence	1	Non-serious	170	170	Unrelated	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	175	195	Unrelated	Related	Unrelated
Neuropathy peripheral	2	Non-serious	196	223	Unrelated	Related	Unrelated
Depressed mood	1	Non-serious	199	204	Unrelated	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	224	230	Unrelated	Related	Unrelated
Blood thyroid stimulating hormone increased	1	Non-serious	262	283	Unrelated	Unrelated	Related
Thirst	1	Non-serious	273	282	Unrelated	Related	Related

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Migraine	1	Non-serious	322	418	Unrelated	Unrelated	Unrelated
Acute kidney injury	2	Non-serious	350	357	Unrelated	NA	Related
Pain in extremity	1	Non-serious	373	679	Unrelated	Unrelated	Unrelated
Vulvovaginal discomfort	2	Non-serious	382	429	Unrelated	NA	Unrelated
Fatigue	1	Non-serious	413	702	Unrelated	NA	Unrelated
Dry skin	1	Non-serious	429	Unresolved	Unrelated	Unrelated	Unrelated
Arthralgia	1	Non-serious	432	Unresolved	Related	Unrelated	Related
Arthralgia	1	Non-serious	432	532	Unrelated	Unrelated	Unrelated
Rash	1	Non-serious	442	491	Unrelated	NA	Unrelated
Vulvovaginal pruritus	1	Non-serious	444	Unresolved	Unrelated	NA	Unrelated
Bone pain	1	Non-serious	637	Unresolved	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305629	Patient number	3090
Demographics:	54-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Categories:	Suspected COVID-19 Death due to adverse event, SAE, AE leading to study treatment discontinuation, COVID-19 SAE		

A narrative for this patient is available in Section 1.1 Narratives for patients who died due to an adverse event(s).

Study Number/CRTN:	CO40016/304792	Patient number	3091
Demographics:	51-year-old Black or African American female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Categories:	Rash SAE, Grade ≥ 3 rash		
Event 2 (PT) Categories:	Hypersensitivity SAE, AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR negative and HER2 negative left breast cancer (T3N1M1) on Study Day − 79.

The patient was diagnosed with metastatic disease on Study Day − 77 with ER/PR negative and HER2 negative disease. At screening, sites of disease involvement included left breast (laterals and inferior quadrants) and lymph node (left axillary and inter pectoral and retro pectoral) and left lung (pleural effusion).

No past cancer treatments are reported.

No medical/surgical history was reported. The patient′s concurrent conditions included hypertension and headache.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, atezolizumab and paclitaxel.

Concomitant medication ongoing at Study Day 1 included losartan.

Event 1: Rash

Prior to the event of rash, the most recent dose of atezolizumab was administered on Study Day 1, paclitaxel on Study Day 8 and ipatasertib (400 mg) on Study Day 13.

On Study Day 14, the patient presented to the emergency room with Grade 2 rash all over body and face associated with itching and high fever (body temperature not reported). She also complaints about lesions inside the mouth making her difficult to eat. She received treatment

with metamizole. Her laboratory work-up was unaltered. Urine and blood test were reported negative. On Study Day 17, the event of rash worsened to Grade 3, leading to hospitalization. She then received treatment with hydroxyzine and prednisone. On Study Day 20, the event of rash was considered resolved and she was discharged from the hospital.

Due to the event of rash, Cycle 1 Day 15 of atezolizumab and paclitaxel was not administered, treatment with ipatasertib was interrupted on Study Day 15. The next dose of study treatment was given on Study Day 29.

The Investigator considered rash to be related to ipatasertib and atezolizumab and unrelated to paclitaxel.

Event 2: Hypersensitivity (allergic reaction)

Prior to the event of hypersensitivity, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 99 and ipatasertib (400 mg) on Study Day 101.

On Study Day 104, the patient presented to the emergency room with rash (erythema plus sensibility increase) all over the body and face associated with edema and high fever (body temperature not reported). Her laboratory work-up was unaltered. Urine and blood test were reported negative. The patient was diagnosed with Grade 3 hypersensitivity, leading to hospitalization (initial intensity Grade 2). She received treatment with prednisone, promethazine and metamizole for hypersensitivity. On Study Day 108, the event of hypersensitivity was considered resolved and she was discharged from the hospital.

Due to the event of hypersensitivity, study treatment with atezolizumab, paclitaxel and ipatasertib was permanently discontinued with the last dose of atezolizumab and paclitaxel was given on Study Day 99 and ipatasertib on Study Day 104. The patient entered into the long-term follow-up.

The Investigator considered hypersensitivity, to be related to atezolizumab and unrelated to ipatasertib and paclitaxel.

On Study Day 167, a radiographic response assessment showed disease progression.

On Study Day 701, the patient was discontinued from the study as study was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Alopecia	1	Non-serious	20	Unresolved	Unrelated	Related	Unrelated
Anemia	2	Non-serious	21	190	Unrelated	Related	Unrelated
Alanine aminotransferase increased	1	Non-serious	28	43	Related	Related	Related
Non-cardiac chest pain	2	Non-serious	36	36	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	39	47	Related	Related	Unrelated
Hypertension	3	Non-serious	92	92	Unrelated	Unrelated	Unrelated
Asthenia	1	Non-serious	92	Unresolved	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	96	103	Related	Related	Unrelated
Arthralgia	2	Non-serious	102	157	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304878	Patient number	3102
Demographics:	67-year-old Asian female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Category:	Pyrexia SAE		

The patient was randomized on Study Day − 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR negative and HER2 negative right breast cancer (T4N3cM1), on Study Day − 65, prior to study entry.

At screening, sites of disease involvement included lymph node (right medial and lateral axilla, right infraclavicular and right supraclavicular), right breast and right overlying breast.

No past cancer treatments are reported.

The patient′s medical history included pulmonary tuberculosis and thyroid mass. No surgical history was reported. Concurrent conditions included right breast pain, lymph node pain and osteopenia.

At screening, the patient′s ECOG Performance Status was 0.

Relevant laboratory work-up reported in the table below:

Study Day	**WBC count** (normal range: 4-10 × 10^3/μL)	**Neutrophils** (normal range:50-75%)	**Lymphocytes** (normal range: 20-44%)	**Body temperature** (°C)
-13	6.1	55.3	37.2	36.7

On Study Day 1, the patient received her first study treatment with ipatasertib paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included paracetamol/tramadol, fexofenadine and levocetirizine.

Event: Pyrexia (fever)

Prior to the event of pyrexia, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 9.

On Study Day 10, the patient experienced Grade 1 pyrexia (body temperature around 37°C) along with Grade 1 asthenia (non-serious, related), Grade 1 decreased appetite and Grade 1 dizziness (both non-serious, unrelated). She received treatment with ketorolac, ciprofloxacin, and paracetamol. On the following day (Study Day 11), the patient experienced Grade 1 skin rash (non-serious related to ipatasertib and atezolizumab) and received treatment with chlorphenamine. On Study Day 13, the event of pyrexia worsened to Grade 2 (body temperature 39.3°C), leading to hospitalization. A laboratory work-up showed WBC count 2, hemoglobin 11.6, platelet count 230, absolute neutrophil count 1190 (units and normal range not reported for all). Test for influenza A and B was negative. A chest X-ray did not show any active lung lesion. A test for COVID-19 was negative. She further received treatment with piperacillin/tazobactam, paracetamol and ketorolac. On Study Day 14, the event of dizziness was considered resolved. On Study Day 15, the event of pyrexia was considered resolved. On Study Day 16, the event of decreased appetite was considered resolved. On Study Day 21, the event of rash was considered resolved. On Study Day 22, the patient was discharged from the hospital. The event of asthenia remained unresolved at the time of patient′s death (see narrative below).

Due to this event, Cycle 1 Day 8 of paclitaxel was not administered, and Cycle 1 Day 15 was delayed and was administered on Study Day 22. Cycle 1 Day 15 of atezolizumab was not administered and the next dose was administered on Study Day 30. Study treatment with

ipatasertib was interrupted on Study Day 11 and the next dose was given on Study Day 22 (400 mg).

The Investigator considered pyrexia to be unrelated to ipatasertib and paclitaxel and related to atezolizumab.

On Study Day 162, an overall response assessment showed disease progression.

On Study Day 170, study treatment was permanently discontinued due to disease progression with the last dose of atezolizumab given on Study Day 128, paclitaxel on Study Day 156 and ipatasertib on Study Day 162. The patient then entered the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	**Start Day**	**Stop Day**
Doxorubicin and cyclophosphamide (6 cycles each)	170	275
Eribulin (single cycle)	350	358

On Study Day 378, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious / non-serious**	**Onset Day**	**Resolution Day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**	**Causality (Atezolizumab)**
Alopecia	2	Non-serious	22	Unresolved	Unrelated	Related	Unrelated
Urticaria	1	Non-serious	22	22	Unrelated	Related	Unrelated
Productive cough	1	Non-serious	35	51	Related	Related	Related
Peripheral sensory neuropathy	2	Non-serious	38	Unresolved	Unrelated	Related	Unrelated
Pneumonitis	1	Non-serious	55	107	Related	Unrelated	Related
Myalgia	1	Non-serious	62	63	Unrelated	Related	Unrelated
Lymphedema	1	Non-serious	74	Unresolved	Unrelated	Related	Unrelated
Myalgia	1	Non-serious	76	97	Unrelated	Related	Unrelated

Hyperthyroidism	1	Non-serious	86	170	Unrelated	Unrelated	Related
Axillary pain	1	Non-serious	166	Unresolved	Unrelated	Unrelated	Unrelated

1.4 NARRATIVES FOR PATIENTS WHO DISCONTINUED STUDY TREATMENT DUE TO AN ADVERSE EVENT

Study Number/CRTN:	CO40016/319067	Patient number	3001
Demographics:	55-year-old female (race unknown)		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Categories:	Dystonia SAE, AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Mixed connective tissue disease AE leading to study treatment discontinuation		
Event 3 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 4 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 5 (PT) Category:	Skin infection SAE		
Event 6 (PT) Category:	Vomiting SAE		
Event 7 (PT) Categories:	Alanine aminotransferase increased SAE, Grade ≥ 3 hepatotoxicity		
Event 8 (PT) Categories:	Aspartate aminotransferase increased SAE, Grade ≥ 3 hepatotoxicity		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/305639	Patient number	3002
Demographics:	43-year-old Black or African American female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Vomiting SAE		
Event 2 (PT) Category:	Diarrhea SAE		
Event 3 (PT) Category:	Pyrexia SAE		
Event 4 (PT) Category:	Pneumonia SAE		
Event 5 (PT) Category:	Flushing AE leading to study treatment discontinuation		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304448	Patient number	3012
Demographics:	58-year-old Asian female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Rash maculo-papular Grade ≥ 3 rash		
Event 2 (PT) Category:	Hyperglycemia (First episode) Grade ≥ 3 hyperglycemia		
Event 3 (PT) Category:	Hyperglycemia (Second episode) Grade ≥ 3 hyperglycemia		

Event 4 (PT) Categories:	Hyperglycemia (Third episode) AE leading to study treatment discontinuation, Grade ≥ 3 hyperglycemia
Event 5 (PT) Categories:	Diabetic ketoacidosis SAE, AE leading to study treatment discontinuation, Grade ≥ 3 hyperglycemia
Event 6 (PT) Category:	Hyperglycemia (Fourth episode) Grade ≥ 3 hyperglycemia
Event 7 (PT) Categories:	Hyperglycemia (Fifth episode) AE leading to study treatment discontinuation, Grade ≥ 3 hyperglycemia

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304880	Patient number	3014
Demographics:	65-year-old Asian female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Hyperglycemia Grade ≥ 3 hyperglycemia		
Event 3 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		

The patient was randomized on Study Day 1.

The patient was diagnosed with lobular, ER/PR and HER2 negative, metastatic right breast cancer (T2N1M1, histological grade unknown) on Study Day -42.

At screening, sites of disease involvement included right breast, lymph node (metastatic lymph nodes in the left paraaortic space and hepatoduodenal ligament) and bone (multiple bone metastasis).

No past cancer treatments were reported.

No medical or surgical history was reported. The patient′s concurrent conditions included Grade 1 hypertension, Grade 1 hyperlipidemia, Grade 1 breast pain, Grade 1 myoclonus, Grade 1 right facial paralysis, intracranial aneurysm, and type 2 diabetes mellitus.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included fimasartan potassium trihydrate, rosuvastatin, rebamipide, codeine phosphate/ibuprofen/paracetamol, oxycodone, loperamide and levocetirizine.

Event 1: Peripheral sensory neuropathy

Prior to the event of peripheral sensory neuropathy, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 57 and ipatasertib (400 mg) on Study Day 63.

On Study Day 64, the patient experienced non-serious Grade 1 (initial intensity) peripheral sensory neuropathy (signs and symptoms not reported). She received treatment with pregabalin and duloxetine for the event of peripheral sensory neuropathy. On Study Day 288, the event of peripheral sensory neuropathy worsened to Grade 3. On Study Day 393, the event of peripheral sensory neuropathy improved to Grade 2. The event of peripheral sensory neuropathy remained unresolved at the time of patient′s death (see below).

Due to the event of peripheral sensory neuropathy, there was no change in study treatment with ipatasertib and atezolizumab, however, study treatment with paclitaxel was permanently discontinued with last dose administered on Study Day 281.

The Investigator considered peripheral sensory neuropathy, to be related to ipatasertib and unrelated to paclitaxel and atezolizumab.

Event 2: Hyperglycemia

Prior to the event of hyperglycemia, the most recent dose of atezolizumab was administered on Study Day 253, paclitaxel on Study Day 260, and ipatasertib (200 mg) on Study Day 265.

On Study Day 266, the patient’s laboratory work-up showed blood glucose: 336 mg/dL (normal range: 70-110 mg/dL). She was diagnosed with non-serious Grade 3 hyperglycemia. No treatment was administered for the event. On Study Day 274, the event of hyperglycemia was considered resolved.

Due to the event of hyperglycemia, study treatment with atezolizumab, paclitaxel and ipatasertib was interrupted. The next dose of paclitaxel was administered on Study Day 274, atezolizumab and ipatasertib on Study Day 281.

The Investigator considered hyperglycemia, to be related to ipatasertib and unrelated to paclitaxel and atezolizumab.

Relevant laboratory work-up:

Study Day	**Glucose** Normal range: 70-110 mg/dL	**HbA1c** Normal range: 4-6%
Screening	120	7.4
266	336	—
274	100	—

Event 3: Aspartate aminotransferase increased

Prior to the event of aspartate aminotransferase increased, the most recent dose of atezolizumab and ipatasertib (200 mg) on Study Day 533.

On Study Day 533, the patient's laboratory work-up showed: AST 66 U/L (normal range: 13-34 U/L). On Study Day 534, she was diagnosed with non-serious Grade 1 (initial intensity) aspartate aminotransferase increased. No treatment was administered for the event. On Study Day 617, the event of aspartate aminotransferase increased worsened to Grade 3.

On the same day (Study Day 617), radiographic response assessment showed disease progression with new lesions in right lung (small lobulated nodule in right lower lobe).

On Study Day 619, the event of aspartate aminotransferase increased improved to Grade 2.

There was no change in study treatment due to the event of aspartate aminotransferase increased.

On Study Day 624, study treatment was permanently discontinued due to disease progression with the last dose of atezolizumab administered on Study Day 603 and ipatasertib administered on Study Day 609. The patient entered into the long-term follow-up.

On Study Day 729, the event of aspartate aminotransferase increased was considered resolved.

The Investigator considered aspartate aminotransferase increased, to be unrelated to ipatasertib, paclitaxel and atezolizumab and related to disease under study.

Relevant laboratory work-up:

Study Day	AST Normal range: 13-34 U/L	ALT Normal range: 5-46 U/L	Total bilirubin Normal range: 0.4-1.5 mg/dL	ALP Normal range: 50-155 U/L
Screening (– 6)	23	8	0.3	196
533	66	26	0.5	208
547	39	7	0.3	163
561	70	10	0.5	226
575	40	6	0.4	257
589	51	7	0.5	288
603	73	12	0.6	233
617	271	30	0.9	293
	214	—	—	—
619	135	—	—	—
624	149	24	0.7	261

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine	624	Ongoing

On Study Day 801, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Pyrexia	1	Non-serious	6	6	Unrelated	Related	Unrelated
Nausea	1	Non-serious	6	365	Unrelated	Related	Unrelated
Dyspepsia	1	Non-serious	6	365	Unrelated	Related	Unrelated
Pyrexia	1	Non-serious	14	14	Unrelated	Related	Unrelated
Stomatitis	1	Non-serious	15	106	Unrelated	Related	Unrelated
Alopecia	1	Non-serious	15	534	Unrelated	Related	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Diarrhea	2	Non-serious	15	477	Related	Unrelated	Unrelated
Rash	1	Non-serious	27	477	Related	Unrelated	Unrelated
Cough	1	Non-serious	27	36	Unrelated	Unrelated	Unrelated
Skin exfoliation	1	Non-serious	36	106	Unrelated	Related	Unrelated
Decreased appetite	1	Non-serious	43	Unresolved	Unrelated	Related	Unrelated
Anemia	2	Non-serious	57	Unresolved	Unrelated	Related	Unrelated
Neutrophil count decreased	4	Non-serious	84	90	Unrelated	Related	Unrelated
Weight decreased	1	Non-serious	113	Unresolved	Unrelated	Related	Unrelated
Edema	1	Non-serious	127	477	Unrelated	Related	Unrelated
Hyperglycemia	2	Non-serious	183	204	Related	Unrelated	Unrelated
Alanine aminotransferase increased	1	Non-serious	204	211	Unrelated	Unrelated	Unrelated
Aspartate aminotransferase increased	1	Non-serious	204	211	Unrelated	Unrelated	Unrelated
Fatigue	1	Non-serious	232	Unresolved	Unrelated	Related	Unrelated
Neutrophil count decreased	3	Non-serious	266	274	Unrelated	Related	Unrelated
Alanine aminotransferase increased	1	Non-serious	309	323	Unrelated	Unrelated	Unrelated
Aspartate aminotransferase increased	1	Non-serious	309	323	Unrelated	Unrelated	Unrelated
Dental caries	1	Non-serious	379	Unresolved	Unrelated	Unrelated	Unrelated
Cough	1	Non-serious	407	434	Unrelated	Unrelated	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Pyrexia	1	Non-serious	419	434	Related	Unrelated	Related
Arthralgia	1	Non-serious	449	561	Unrelated	Unrelated	Unrelated
Rhinitis allergic	1	Non-serious	477	491	Unrelated	Unrelated	Unrelated
Pyrexia	1	Non-serious	549	554	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	566	619	Related	Unrelated	Related

Study Number/CRTN:	CO40016/305639	Patient number	3016
Demographics:	62-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Peripheral motor neuropathy AE leading to study treatment discontinuation		
Event 3 (PT) Category:	Fatigue AE leading to study treatment discontinuation		
Event 4 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 5 (PT) Categories:	Cardiac arrest Death due to adverse event, SAE		

A narrative for this patient is available in Section 1.1 Narratives for patients who died due to an adverse event(s).

Study Number/CRTN:	CO40016/306603	Patient number	3020

Demographics:	46-year-old White female
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)
Cohort:	Cohort C
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation

The patient was randomized on Study Day – 2.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER 2 negative, right breast cancer (T2N1M0) approximately 3 years and 6 months prior to study entry.

On Study Day – 57, the patient was diagnosed with metastatic disease with ER/PR and HER 2 negative in metastatic tissues. At screening sites of disease involvement included lymph node (right axillary, retro pectoral nodes and mediastinal nodes) and bone (right sclerotic lesion right femur and right intertrochanteric right femur).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Doxorubicin and cyclophosphamide	Approximately 3 years and 5 months prior to study entry	Approximately 3 years and 3 months prior to study entry
Cancer therapy	Neoadjuvant	Leuprorelin acetate	Approximately 3 years and 5 months prior to study entry	Approximately 3 years and 1 month prior to study entry
Cancer therapy	Neoadjuvant	Paclitaxel	Approximately 3 years and 3 months prior to study entry	Approximately 3 years and 1 month prior to study entry
Surgery	Curative	Simple mastectomy of right breast	Approximately 3 years prior to study entry	NA
Radiotherapy	Adjuvant	Right breast (chest wall) (dose: 5000 cGy and 25 fraction)	Approximately 3 years prior to study entry	Approximately 2 years and 11 months prior to study entry

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Capecitabine	Approximately 2 years and 11 months prior to study entry	-861

No medical or surgical history was reported. The patient′s concurrent conditions included gastroesophageal reflux disease, seasonal allergy, hiatus hernia, vitamin D deficiency, anxiety, hepatic steatosis, pulmonary mass, insomnia and lichen striatus.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included cholecalciferol, loperamide and lidocaine/prilocaine.

Event: Neuropathy peripheral (Peripheral neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of atezolizumab was administered on Study Day 57, paclitaxel on Study Day 64 and ipatasertib (400 mg) on Study Day 70.

On Study Day 71, the patient experienced non-serious Grade 1 (initial intensity) neuropathy peripheral (signs and symptoms not reported). No treatment was administered for the event. On Study Day 148, the event of neuropathy peripheral worsened to Grade 2. On Study Day 176, the event of neuropathy peripheral improved to Grade 1. On Study Day 225, the event of neuropathy peripheral again worsened to Grade 2. The event of neuropathy peripheral remained unresolved at the time of study discontinuation.

Due to the event of neuropathy peripheral, there was no change in study treatment with ipatasertib and atezolizumab, however, study treatment with paclitaxel was permanently discontinued with last dose administered on Study Day 210.

The Investigator considered neuropathy peripheral, to be related to paclitaxel and unrelated to ipatasertib and atezolizumab.

On Study Day 277, radiographic response assessment showed disease progression with new lesions in right axillary lymph node (equivocal).

On Study Day 440, a repeat radiographic response assessment showed disease progression with new lesions lymph node (aortopulmonary window node and mesenteric nodes) and bone (left femoral diaphysis).

On Study Day 461, study treatment was permanently discontinued due to disease progression with the last dose of ipatasertib administered on Study Day 413 and atezolizumab on Study Day 433. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Sacituzumab govitecan	475	733
Bevacizumab and capecitabine	774	Ongoing

On Study Day 908, the patient was discontinued from the study as study was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Nausea	1	Non-serious	1	1	Related	Unrelated	Unrelated
Dizziness	1	Non-serious	1	1	Related	Unrelated	Unrelated
Nausea	1	Non-serious	1	1	Related	Unrelated	Unrelated
Fatigue	1	Non-serious	3	141	Unrelated	Related	Unrelated
Constipation	1	Non-serious	3	19	Unrelated	Unrelated	Unrelated
Rhinorrhea	1	Non-serious	3	29	Unrelated	Related	Unrelated
Paresthesia	1	Non-serious	3	85	Unrelated	Unrelated	Unrelated
Dental discomfort	1	Non-serious	3	112	Related	Unrelated	Related
Headache	1	Non-serious	6	6	Unrelated	Unrelated	Unrelated
Gastroesophageal reflux disease	1	Non-serious	13	Unresolved	Related	Related	Related

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Dry mouth	1	Non-serious	13	118	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	18	19	Unrelated	Unrelated	Unrelated
Nausea	1	Non-serious	19	19	Unrelated	Unrelated	Unrelated
Vomiting	1	Non-serious	19	19	Unrelated	Unrelated	Unrelated
Rash maculo-papular	1	Non-serious	19	85	Unrelated	Unrelated	Related
Dizziness	1	Non-serious	19	19	Unrelated	Unrelated	Unrelated
Insomnia	1	Non-serious	21	Unresolved	Related	Related	Related
Neutropenia	2	Non-serious	29	36	Related	Related	Related
Diarrhea	1	Non-serious	36	36	Unrelated	Unrelated	Unrelated
Wound	2	Non-serious	39	Unresolved	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	44	64	Related	Related	Related
Neutropenia	2	Non-serious	49	57	Related	Related	Related
Abdominal distension	1	Non-serious	50	71	Unrelated	Unrelated	Unrelated
Anemia	1	Non-serious	57	141	Unrelated	Related	Unrelated
Constipation	1	Non-serious	65	118	Unrelated	Unrelated	Unrelated
Dry eye	1	Non-serious	67	112	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	72	118	Related	Related	Related
Pain	1	Non-serious	105	154	Unrelated	Unrelated	Unrelated
Postoperative wound infection	2	Non-serious	117	176	Unrelated	Unrelated	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Pruritus	1	Non-serious	121	141	Unrelated	Unrelated	Unrelated
Lymphadenopathy	1	Non-serious	131	160	Related	Related	Related
Hypersomnia	1	Non-serious	152	168	Related	Related	Related
Pruritus	1	Non-serious	154	213	Unrelated	Unrelated	Unrelated
Fatigue	1	Non-serious	176	274	Related	Related	Related
Paresthesia	1	Non-serious	177	366	Unrelated	Unrelated	Unrelated
Lymphoedema	1	Non-serious	177	Unresolved	Unrelated	Unrelated	Unrelated
Oedema	1	Non-serious	212	494	Unrelated	Related	Unrelated
Dysphagia	2	Non-serious	244	274	Unrelated	Unrelated	Unrelated
Bone pain	1	Non-serious	260	494	Unrelated	Unrelated	Unrelated
Abdominal distension	1	Non-serious	274	366	Unrelated	Unrelated	Unrelated
Constipation	1	Non-serious	274	Unresolved	Unrelated	Unrelated	Unrelated
Urinary tract infection	2	Non-serious	294	301	Unrelated	Unrelated	Related
Abdominal pain	1	Non-serious	294	366	Unrelated	Unrelated	Unrelated
Back pain	1	Non-serious	294	366	Unrelated	Unrelated	Unrelated
Hypoesthesia	1	Non-serious	336	366	Unrelated	Unrelated	Unrelated
Wound infection	2	Non-serious	377	384	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304332	Patient number	3022
Demographics:	57-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Rash papular Grade ≥ 3 rash		
Event 2 (PT) Category:	Autoimmune hepatitis AE leading to study treatment discontinuation		
Event 3 (PT) Category:	Aspartate aminotransferase increased AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated, ER/PR negative and HER2 negative right breast cancer (T4N1M1) on Study Day − 29.

At screening, sites of disease involvement included right breast and right lung (segment 6), right side of chest, right axillary lymph node, bilateral lung, bone (right IV, V ribs) and bone Th1.

No past cancer treatments are reported.

No medical/surgical history was reported. The patient′s concurrent condition included renal cyst.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 was reported.

Event 1: Rash papular (Papular rash on body)

Prior to the event of rash papular, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 15 and ipatasertib (400 mg) on Study Day 21.

On Study Day 22, the patient experienced non-serious Grade 3 rash papular all over the body except head. She received treatment with loratadine and prednisolone for rash papular. On Study Day 33 the event of rash was considered resolved.

There was no change in the study treatment due to the event of rash papular.

The Investigator considered rash papular to be related to atezolizumab and unrelated to paclitaxel and ipatasertib.

Event 2: Autoimmune hepatitis

Prior to the event of autoimmune hepatitis, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 197 and ipatasertib (400 mg) on Study Day 203.

On Study Day 204, a laboratory work-up showed ALP 142.1 U/L (normal range: 42-98 U/L), ALT 182 U/L (normal range: 4-36 U/L) and AST 177 U/L (normal range: 8-33 U/L) and the patient was diagnosed with non-serious Grade 3 autoimmune hepatitis. On the following day (Study Day 205), a PCR test for synevo-hepatitis C virus and hepatitis B virus was negative. She received treatment with phospholipids, *Cynara cardunculus* extract, arginine/betaine/betaine hydrochloride and prednisolone. On Study Day 215, the event of autoimmune hepatitis was considered resolved.

Due to the event of autoimmune hepatitis, study treatment with paclitaxel was delayed and the next dose was administered on Study Day 253 (Cycle 10 Day 1), atezolizumab and ipatasertib was permanently discontinued with the last dose administered on Study Day 197 and Study Day 203, respectively.

The Investigator considered autoimmune hepatitis to be unrelated to paclitaxel and ipatasertib and related to atezolizumab.

Event 3: Aspartate aminotransferase increased (Increasing of AST)

Prior to the event of aspartate aminotransferase increased, the most recent dose of paclitaxel was administered on Study Day 295.

On Study Day 279, a laboratory work-up showed ALT 92 U/L (normal range: 4-36 U/L) and the patient was diagnosed with Grade 1 alanine aminotransferase increased (non-serious, related to paclitaxel).

On Study Day 307, a laboratory work-up showed AST 102 U/L (normal range: 8-33 U/L) and the patient was diagnosed with non-serious Grade 2 aspartate aminotransferase increased. She received treatment with phospholipids. On Study Day 288, the event of alanine aminotransferase increased was considered resolved. The event of aspartate aminotransferase increased remained unresolved at the time of patient's death (see narrative below).

Relevant laboratory values listed in the table below:

Study Day	**AST** (normal range: 8-33 U/L)	**ALT** (normal range: 4-36 U/L)	**ALP** (normal range: 42-98 U/L)	**Bilirubin** (normal range: 4.27-20.52 μmol/L)
-2	42	11	81.2	12
204	177	182	142.1	12.8
208	153	167	132.9	11.3
211	69	144	126.3	13.6
215	25	55	90.5	14.9
223	28	26	77.7	15
229	32	24	78	10.8
237	40	27	86	10.5
244	26	35	75.6	11
251	85	75	96.8	12.2
260	64	73	100	13
267	21	60	129.2	12.4
279	68	92	127.5	13.1
286	37	47	119.5	12.9
295	71	53	104	10.6
307	102	90	115	11.4
316	110	89	115	11.6
323	100	92	115	11.6
335	105	43	120.1	10.8

Due to the event of aspartate aminotransferase increased, study treatment with paclitaxel was permanently discontinued with the last dose administered on Study Day 295. The patient entered into the long-term follow-up.

The Investigator considered aspartate aminotransferase increased to be related to paclitaxel and unrelated to ipatasertib.

On Study Day 391, a radiographic response assessment showed disease progression with new lesions in right bone (ilium) and mediastinum lymph node.

On Study Day 648, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Diarrhea	1	Non-serious	1	1	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	4	8	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	11	21	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	29	49	Related	Unrelated	Unrelated
Alopecia	2	Non-serious	32	142	Unrelated	Unrelated	Related
Rash papular	1	Non-serious	46	54	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	57	64	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	67	77	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	87	88	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	92	94	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	96	105	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	116	133	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	178	189	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	198	203	Related	Unrelated	Unrelated
Weight decreased	1	Non-serious	229	Unresolved	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/318721	Patient number	3030
Demographics:	71-year-old female (Race unknown)		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Categories:	Autoimmune hepatitis SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304784	Patient number	3044
Demographics:	44-year-old female (Unknown race)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Category:	Diarrhea AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with not otherwise specified, poorly differentiated ER/PR negative and HER2 negative right breast cancer (T2N0M1) approximately 2 years and 4 months prior to study entry.

On Study Day – 54, the patient was diagnosed with ER/PR negative and HER2 negative in metastatic tissue. At screening, sites of disease involvement included lung (pulmonary nodule of the anterior segment of the left upper lobe and bilateral other pulmonary nodules).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right mastectomy	Approximately 2 years 2 months prior to study entry	NA
Cancer therapy	Adjuvant	Doxorubicin, cyclophosphamide, and docetaxel (4 cycles each)	Approximately 2 years prior to study entry	Approximately 1 years 7 months prior to study entry

No medical/surgical history was reported. No concurrent conditions were reported.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 was reported.

The patient was discontinued from the study treatment with paclitaxel as per physician′s decision with the last dose of paclitaxel given on Study Day 759.

Prior to the event of diarrhea, the patient was noted with multiple events of diarrhea (please refer to table below for details). She received treatment with loperamide.

Event	Most extreme grade	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Diarrhea	2	843	843	Related	Unrelated	Unrelated
Diarrhea	2	847	847	Related	Unrelated	NA
Diarrhea	2	853	853	Related	Unrelated	NA
Diarrhea	2	881	881	Related	Unrelated	Unrelated
Diarrhea	1	883	883	Related	Unrelated	Unrelated

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of atezolizumab was given on Study Day 906 and ipatasertib (400 mg) on Study Day 909.

On Study Day 910, the patient experienced non-serious Grade 1 diarrhea. She received treatment with loperamide for diarrhea. Later, on the same day, the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	1	2
Diarrhea	2	PO	3	6
Diarrhea	2	PO	7	10
Diarrhea	4	PO	11	22
Diarrhea	2	PO	38	38
Diarrhea	2	PO	42	42
Diarrhea	2	PO	46	46
Diarrhea	2	PO	49	49
Diarrhea	2	PO	60	60
Diarrhea	2	PO	63	63
Diarrhea	2	PO	66	66
Diarrhea	2	PO	70	70
Diarrhea	2	PO	74	74
Diarrhea	2	PO	101	102
Diarrhea	4	PO	103	103
Diarrhea	2	PO	104	106
Diarrhea	2	PO	119	119
Diarrhea	2	PO	125	125
Diarrhea	4	PO	128	129
Diarrhea	2	PO	132	132
Diarrhea	2	PO	147	147
Diarrhea	2	PO	151	151
Diarrhea	4	PO	152	152
Diarrhea	2	PO	154	154
Diarrhea	2	PO	156	156
Diarrhea	4	PO	182	182
Diarrhea	2	PO	198	199
Diarrhea	2	PO	207	207
Diarrhea	2	PO	215	215
Diarrhea	2	PO	257	257
Diarrhea	2	PO	260	260
Diarrhea	4	PO	355	355
Diarrhea	4	PO	370	370

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	371	371
Diarrhea	2	PO	383	383
Diarrhea	2	PO	392	392
Diarrhea	2	PO	399	399
Diarrhea	2	PO	415	415
Diarrhea	4	PO	425	425
Diarrhea	2	PO	451	451
Diarrhea	2	PO	455	456
Diarrhea	2	PO	478	478
Diarrhea	2	PO	482	482
Diarrhea	2	PO	504	505
Diarrhea	2	PO	532	532
Diarrhea	2	PO	539	539
Diarrhea	2	PO	567	567
Diarrhea	2	PO	594	594
Diarrhea	2	PO	597	628
Diarrhea	2	PO	609	609
Diarrhea	2	PO	644	644
Diarrhea	2	PO	650	650
Diarrhea	2	PO	672	672
Diarrhea	2	PO	700	700
Diarrhea	2	PO	707	707
Diarrhea	2	PO	721	721
Diarrhea	2	PO	726	726
Diarrhea	2	PO	735	735
Diarrhea	2	PO	736	736
Diarrhea	2	PO	753	753
Diarrhea	2	PO	843	843
Diarrhea	2	PO	847	847
Diarrhea	2	PO	853	853
Diarrhea	2	PO	881	881
Diarrhea	2	PO	883	883
Diarrhea	2	PO	910	910

Due to the event od diarrhea and as per physician′s decision (patient to enter roll over study), study treatment with atezolizumab was permanently discontinued with the last dose administered on Study Day 906.

On Study Day 913, the patient was discontinued from the study treatment with ipatasertib as per physician′s decision (patient to enter roll over study) with the last dose of ipatasertib given on Study Day 912.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel and atezolizumab.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Asthenia	1	Non-serious	3	30	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	7	49	Related	Unrelated	Related
Back pain	1	Non-serious	17	31	Unrelated	Unrelated	Related
Alopecia	2	Non-serious	29	823	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	35	42	Unrelated	Unrelated	Related
Pain in extremity	1	Non-serious	40	45	Unrelated	Unrelated	Unrelated
Neutropenia	2	Non-serious	49	56	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	58	74	Related	No	Related
Upper respiratory tract infection	2	Non-serious	77	83	Unrelated	Unrelated	Unrelated
Leukopenia	1	Non-serious	101	106	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	101	113	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	101	106	Related	Unrelated	Related

Vulvovaginal dryness	1	Non-serious	114	Unresolved	Unrelated	Unrelated	Related
Irritability	1	Non-serious	114	295	Unrelated	Unrelated	Related
Memory impairment	1	Non-serious	114	Unresolved	Unrelated	Unrelated	Related
Asthenia	1	Non-serious	114	185	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	119	119	Related	Unrelated	Related
Neutropenia	2	Non-serious	120	141	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	126	126	Related	Unrelated	Related
Diarrhea	1	Non-serious	128	129	Related	Unrelated	Related
Diarrhea	1	Non-serious	132	132	Related	Unrelated	Related
Hypercholesterolemia	1	Non-serious	141	Unresolved	Related	Unrelated	Unrelated
Hypertriglyceridemia	2	Non-serious	141	322	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	147	147	Related	Unrelated	Related
Neutropenia	1	Non-serious	148	158	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	151	156	Related	Unrelated	Related
Hyperglycemia	1	Non-serious	168	176	Related	Unrelated	Unrelated
Leukopenia	1	Non-serious	176	183	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	176	219	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	182	182	Related	Unrelated	Related
Leukopenia	2	Non-serious	190	219	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	198	199	Related	Unrelated	Related
Pain	1	Non-serious	214	218	NA	Yes	Related
Diarrhea	1	Non-serious	215	215	Yes	Yes	Related
Blood alkaline phosphatase increased	1	Non-serious	219	239	NA	Unrelated	Related

High density lipoprotein increased	1	Non-serious	219	239	NA	Unrelated	Related
Covid-19	2	Non-serious	224	233	NA	Unrelated	Unrelated
Neutropenia	2	Non-serious	239	246	NA	Unrelated	Related
Diarrhea	1	Non-serious	257	257	Related	Unrelated	Related
Flatulence	1	Non-serious	259	268	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	260	260	Related	Unrelated	Related
Leukopenia	1	Non-serious	273	659	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	273	659	Unrelated	Unrelated	Related
Leukopenia	1	Non-serious	301	308	Related	Related	Related
Neutropenia	1	Non-serious	301	308	Related	Related	Related
High density lipoprotein increased	1	Non-serious	308	322	Unrelated	Unrelated	Unrelated
Leukopenia	1	Non-serious	322	337	Related	Related	Related
Neutropenia	2	Non-serious	322	337	Related	Related	Related
Back pain	1	Non-serious	353	Unresolved	Unrelated	Unrelated	Unrelated
Leukopenia	2	Non-serious	357	365	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	357	365	Unrelated	Unrelated	Related
Onychomadesis	2	Non-serious	373	409	Unrelated	Unrelated	Related
Nail infection	2	Non-serious	373	384	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	383	383	Related	Unrelated	Related
Leukopenia	1	Non-serious	386	407	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	386	407	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	392	392	Related	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	394	Unresolved	Unrelated	Unrelated	Related

Diarrhea	1	Non-serious	399	399	Related	Unrelated	Unrelated
Hypertriglyceridemia	1	Non-serious	407	911	Unrelated	Unrelated	Unrelated
Leukopenia	2	Non-serious	413	420	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	413	420	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	415	415	Related	Unrelated	Unrelated
Nail infection	2	Non-serious	416	424	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	425	425	Related	Unrelated	Unrelated
Hyponatremia	1	Non-serious	434	441	Unrelated	No	Unrelated
Leukopenia	1	Non-serious	441	448	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	441	448	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	451	451	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	455	456	Related	Unrelated	Unrelated
Neutropenia	2	Non-serious	469	505	Unrelated	Unrelated	Related
Leukopenia	1	Non-serious	476	505	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	478	478	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	482	482	Related	Unrelated	No
Diarrhea	1	Non-serious	505	505	Unrelated	Unrelated	Related
Leukopenia	1	Non-serious	526	533	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	526	533	Unrelated	Unrelated	Related
Hyperglycemia	1	Non-serious	526	533	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	532	532	Related	Unrelated	Related
Blood lactate dehydrogenase increased	1	Non-serious	533	547	Related	Related	Related
Diarrhea	2	Non-serious	539	539	Related	Unrelated	Related
Skin hyperpigmentation	1	Non-serious	542	554	Unrelated	Unrelated	Unrelated
Leukopenia	1	Non-serious	554	575	Unrelated	Unrelated	Related

Neutropenia	1	Non-serious	554	561	Unrelated	Unrelated	Related
Hyperglycemia	1	Non-serious	554	589	Related	Unrelated	Unrelated
Dermatitis allergic	2	Non-serious	574	Unresolved	Related	Related	Unrelated
Hot flush	2	Non-serious	586	Unresolved	Unrelated	Unrelated	Related
Leukopenia	1	Non-serious	591	604	Related	Related	Related
Neutropenia	1	Non-serious	591	604	Related	Related	Related
Diarrhea	1	Non-serious	594	594	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	597	597	Related	Unrelated	Related
Hyperglycemia	1	Non-serious	604	610	Related	Unrelated	Unrelated
Leukopenia	1	Non-serious	610	659	Related	Related	Related
Neutropenia	2	Non-serious	610	631	Related	Related	Related
Blood lactate dehydrogenase increased	1	Non-serious	610	617	Related	Related	Related
Neutropenia	2	Non-serious	638	659	Related	Related	Related
Diarrhea	1	Non-serious	644	644	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	650	650	Related	Unrelated	Unrelated
Weight increased	1	Non-serious	661	Unresolved	Unrelated	Unrelated	Unrelated
Neutropenia	2	Non-serious	666	673	Related	Related	Related
Leukopenia	2	Non-serious	666	673	Unrelated	Unrelated	Related
Diarrhea	2	Non-serious	672	672	Related	Unrelated	Unrelated
Blood lactate dehydrogenase increased	1	Non-serious	673	701	Unrelated	Unrelated	Unrelated
Anemia	1	Non-serious	687	694	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	700	700	Related	Unrelated	Unrelated
Leukopenia	1	Non-serious	701	716	Unrelated	Unrelated	Related
Neutropenia	1	Non-serious	701	716	Unrelated	Unrelated	Related
Diarrhea	1	Non-serious	707	707	Related	Unrelated	Unrelated

Blood lactate dehydrogenase increased	1	Non-serious	716	722	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	721	721	Related	Related	Related
Leukopenia	1	Non-serious	722	743	Related	Related	Related
Neutropenia	2	Non-serious	722	729	Related	Related	Related
Diarrhea	1	Non-serious	726	726	Related	Related	Related
Diarrhea	1	Non-serious	735	735	Related	Related	Related
Diarrhea	1	Non-serious	736	736	Related	Related	Related
Diarrhea	1	Non-serious	753	753	Related	Unrelated	Unrelated
Leukopenia	1	Non-serious	757	805	Unrelated	Unrelated	Unrelated
Neutropenia	2	Non-serious	757	777	Unrelated	Unrelated	Unrelated
Neutropenia	1	Non-serious	791	805	Related	Related	NA
Leukopenia	1	Non-serious	820	833	Related	Related	Unrelated
Neutropenia	1	Non-serious	820	833	Related	Related	Unrelated
Leukopenia	1	Non-serious	848	861	Related	Related	Unrelated
Neutropenia	2	Non-serious	848	861	Related	Related	NA
Leukopenia	1	Non-serious	883	Unresolved	Related	Related	Unrelated
Neutropenia	1	Non-serious	903	Unresolved	Unrelated	Related	NA

Study Number/CRTN:	CO40016/318144	Patient number	3047
Demographics:	83-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Categories:	Diarrhea SAE, Grade ≥ 3 diarrhea		
Event 2 (PT)	Gamma-glutamyl transferase increased		

Category:	Grade ≥ 3 hepatotoxicity
Event 3 (PT) Category:	Nausea SAE
Event 4 (PT) Categories:	Pneumonitis SAE, AE leading to study treatment discontinuation, Grade ≥ 2 pneumonitis

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/319083	Patient number	3057
Demographics:	50-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Category:	Neutrophil count decreased AE leading to study treatment discontinuation		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER2 negative, left breast cancer (T1cN0M0) approximately 7 years and 4 months following left lymph node biopsy.

On Study Day −35, the patient was diagnosed with locally recurrent advanced unresectable, metastatic disease with ER/PR and HER2 negative in metastatic tissues. At screening sites of disease involvement included chest (left wall mass and left additional thoracic adenopathy), and lymph nodes (lateral retro pectoral node and left axillary).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Left breast lumpectomy	Approximately 7 years prior to study entry	NA
Cancer therapy	Adjuvant	Docetaxel and cyclophosphamide	Approximately 7 years prior to study entry	Approximately 7 years prior to study entry
Radiotherapy	Adjuvant	Breast (left breast; total dose: 6080 cGy, 26 fractions) (lumpectomy bed; 1600 cGy, 16 fractions)	Approximately 7 years prior to study entry	Approximately 7 years prior to study entry

The patient's medical history included tobacco use. No surgical history was reported. Concurrent conditions included fatigue and arthralgia (left shoulder radiating down arm).

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

No concomitant medication ongoing at Study Day 1 was reported.

The patient was noted with multiple episodes of neutrophil count decreased (details in the AE table below) from Study Day 64 to Study Day 497. The patient received treatment with filgrastim for neutrophil count decreased.

Event: Neutrophil count decreased

Prior to the event of neutrophil count decreased, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 505 and ipatasertib (200 mg) on Study Day 511.

On Study Day 512, the patient′s laboratory work-up showed neutrophil count 1000 cells/μL (normal range: 1800-8000 cells/μL). She was diagnosed with non-serious Grade 3 neutrophil count decreased. Relevant laboratory work-up is reported in the table below. Unspecified treatment was administered for the event. On Study Day 519, the event of neutrophil count decreased was considered resolved.

Due to the event of neutrophil count decreased, there was no change in study treatment with atezolizumab, however, study treatment with ipatasertib was interrupted on Study Day 512 and the next dose was given Study Day 519. Treatment with paclitaxel was permanently discontinued with last dose administered on Study Day 505.

The Investigator considered neutrophil count decreased, to be related to paclitaxel and unrelated to ipatasertib and atezolizumab.

Relevant laboratory work-up:

Study Day	**WBC count** Normal range: 4.5-13 $\times$ $10^3/\mu L$	**Neutrophil count** Normal range: 1800-8000 cells/μL	**Lymphocyte count** Normal range: 1200-5200 cells/μL
Screening	4.2	2400	1200
512	2.5	1000	1000
519	4.0	1600	1100

On Study Day 841, the patient discontinued the study as she entered post trial access program and last dose of ipatasertib was administered on Study Day 805, and atezolizumab on Study Day 827.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious / Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality (Ipatasertib)**	**Causality (Paclitaxel)**	**Causality (Atezolizumab)**
Nausea	1	Non-serious	2	197	Unrelated	Related	Unrelated
Paresthesia	1	Non-serious	7	15	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	8	477	Unrelated	Related	Unrelated
Nasal congestion	1	Non-serious	13	29	Unrelated	Unrelated	Unrelated
Stomatitis	1	Non-serious	15	29	Unrelated	Related	Related
Dysgeusia	1	Non-serious	15	197	Unrelated	Related	Unrelated
Cognitive disorder	1	Non-serious	37	Unresolved	Unrelated	Related	Unrelated
Neuropathy peripheral	1	Non-serious	41	197	Unrelated	Related	Related
Headache	1	Non-serious	42	197	Unrelated	Unrelated	Unrelated
Neutrophil count decreased	2	Non-serious	64	70	Related	Related	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Fatigue	1	Non-serious	70	169	Related	Related	Unrelated
Myalgia	1	Non-serious	70	197	Unrelated	Related	Unrelated
Neutrophil count decreased	2	Non-serious	85	92	Unrelated	Related	Unrelated
Neutrophil count decreased	2	Non-serious	99	113	Unrelated	Related	Unrelated
Insomnia	1	Non-serious	113	Unresolved	Unrelated	Unrelated	Unrelated
Neutrophil count decreased	2	Non-serious	120	127	Unrelated	Related	Unrelated
Neutrophil count decreased	3	Non-serious	141	148	Unrelated	Related	Unrelated
Onycholysis	1	Non-serious	155	163	Unrelated	Related	Unrelated
Neutrophil count decreased	2	Non-serious	155	183	Unrelated	Related	Unrelated
Fatigue	2	Non-serious	169	197	Unrelated	Related	Unrelated
Neutrophil count decreased	2	Non-serious	183	197	Unrelated	Related	Unrelated
Arthralgia	1	Non-serious	194	281	Unrelated	Related	Related
Fatigue	1	Non-serious	197	Unresolved	Unrelated	Related	Unrelated
Neutrophil count decreased	3	Non-serious	204	211	Related	Related	Unrelated
Neutrophil count decreased	1	Non-serious	211	232	Related	Related	Unrelated
Blood cholesterol increased	1	Non-serious	225	Unresolved	Related	Unrelated	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Neutrophil count decreased	2	Non-serious	232	239	Related	Related	Unrelated
Neutrophil count decreased	2	Non-serious	260	281	Unrelated	Related	Unrelated
Anxiety	2	Non-serious	275	Unresolved	Unrelated	Unrelated	Unrelated
Arthralgia	2	Non-serious	281	309	Unrelated	Unrelated	Unrelated
Neutrophil count decreased	2	Non-serious	288	302	Unrelated	Related	Unrelated
Vulvovaginal dryness	2	Non-serious	308	Unresolved	Unrelated	Related	Unrelated
Neutrophil count decreased	2	Non-serious	337	365	Related	Related	Unrelated
Neutrophil count decreased	2	Non-serious	372	379	Related	Related	Unrelated
Arthralgia	1	Non-serious	379	Unresolved	Unrelated	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	414	610	Unrelated	Related	Related
Neutrophil count decreased	2	Non-serious	456	463	Related	Related	Unrelated
Neutrophil count decreased	2	Non-serious	477	484	Unrelated	Related	Unrelated
Hypomagnesaemia	1	Non-serious	484	505	Unrelated	Unrelated	Unrelated
Neutrophil count decreased	3	Non-serious	491	497	Unrelated	Related	Unrelated
Hypomagnesaemia	1	Non-serious	512	519	Unrelated	Unrelated	Unrelated
Procedural pain	1	Non-serious	575	701	Unrelated	NA	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Rhinitis allergic	2	Non-serious	631	813	Unrelated	Unrelated	Unrelated
Influenza like illness	1	Non-serious	719	721	Unrelated	NA	Unrelated
Tooth abscess	3	Non-serious	738	771	Unrelated	NA	Unrelated
Pruritus	1	Non-serious	792	Unresolved	Unrelated	NA	Unrelated
Pruritus	1	Non-serious	792	Unresolved	Unrelated	NA	Unrelated
Hypomagnesaemia	1	Non-serious	799	813	Unrelated	NA	Unrelated
Urinary tract infection	2	Non-serious	825	841	Unrelated	NA	Unrelated
Procedural pain	2	Non-serious	836	839	Unrelated	NA	Unrelated

Study Number/CRTN:	CO40016/304787	Patient number	3061
Demographics:	75-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Category:	Hyperbilirubinemia Grade ≥ 3 hepatotoxicity		
Event 4 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 5 (PT) Categories:	Alanine aminotransferase increased AE leading to study treatment discontinuation, Grade ≥ 3 hepatotoxicity		
Event 6 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 7 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 8 (PT) Categories:	Aspartate aminotransferase increased AE leading to study treatment discontinuation, Grade ≥ 3 hepatotoxicity		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR negative and HER2 negative advanced unresectable right breast cancer (T4bN1M0), on Study Day −76.

The patient was diagnosed with metastatic disease on an unspecified day with ER /PR negative and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included right breast (side and lateral lower quadrant) and axillary right lymph node.

No past cancer treatments are reported.

No medical/surgical history was reported. The patient′s concurrent conditions included hypertension.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included hydrochlorothiazide and losartan.

Event 1: Aspartate aminotransferase increased (AST increase)

Event 2: Alanine aminotransferase increased (ALT increase)

Event 3: Hyperbilirubinemia

Prior to the events of aspartate aminotransferase increased, alanine aminotransferase increased and hyperbilirubinemia the most recent dose of atezolizumab was administered on Study Day 29, paclitaxel on Study Day 36 and ipatasertib (400 mg) on Study Day 49.

On Study Day 56, the Cycle 3 Day 1 laboratory work-up showed AST 328 U/L (normal range: 5-34 U/L), ALT 329 U/L (normal range: 8-42 U/L), total bilirubin 4.17 mg/dL (normal range: 0-1 mg/dL) and lipase 217 U/L (normal range: 3-60 U/L). The patient was diagnosed with non-serious Grade 3 aspartate aminotransferase increased, Grade 3 alanine aminotransferase increased, Grade 3 hyperbilirubinemia and Grade 3 lipase increased (non-serious, related). She received treatment with prednisone. Post re-evaluation, she was asymptomatic with no clinical complaints. On Study Day 59, the event of AST increased improved to Grade 2 which further improved to Grade 1 on Study Day 64. On Study Day 71, the events of aspartate aminotransferase increased, alanine aminotransferase increased, and hyperbilirubinemia were considered resolved. The event of lipase increased was considered resolving at the time of study discontinuation.

Due to the event of aspartate aminotransferase increased, Cycle 2 Day 15 of paclitaxel and atezolizumab was not administered, and Cycle 3 Day 1 was delayed and given on Study Day 73; however, study treatment with ipatasertib was interrupted on Study Day 50 and the next dose was given on Study Day 73 at a reduced dose of 300 mg.

Due to the events of alanine aminotransferase increased, and hyperbilirubinemia, there was no change in the study treatment with atezolizumab; however, Cycle 2 Day 15 of paclitaxel was not administered, and Cycle 3 Day 1 was delayed and given on Study Day 73. Study treatment with ipatasertib was interrupted on Study Day 50 and the next dose was given on Study Day 73 at a reduced dose of 300 mg.

The Investigator considered aspartate aminotransferase increased, alanine aminotransferase increased, and hyperbilirubinemia to be related atezolizumab, paclitaxel and ipatasertib.

Event 4: Aspartate aminotransferase increased (AST increase)

Event 5: Alanine aminotransferase increased (Increase ALT)

Prior to the events of aspartate aminotransferase increased and alanine aminotransferase increased, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 73 and ipatasertib (300 mg) on Study Day 78.

On Study Day 79, Cycle 4 Day 8 laboratory work-up showed AST 203 U/L (normal range: 5-34 U/L) and ALT 306 U/L (normal range: 8-42 U/L). The patient was diagnosed with non-serious Grade 3 aspartate aminotransferase increased and Grade 3 alanine aminotransferase increased. MRI abdomen was normal. She received treatment with prednisone. On Study Day 93, the event of ALT increased improved to Grade 1 and the event of aspartate aminotransferase increased was considered resolved. On Study Day 107, the event of alanine aminotransferase increased was considered resolved.

Due to the event of aspartate aminotransferase increased and alanine aminotransferase increased, Cycle 3 Day 15 of paclitaxel was not administered, and Cycle 4 Day 1 was delayed and given on study treatment Study Day 94. Treatment with ipatasertib was interrupted on Study Day 80 and next dose was given on Study Day 101 (300 mg).

Due to the event of aspartate aminotransferase increased, study treatment with atezolizumab was interrupted after Cycle 3 and due to the event of alanine aminotransferase increased, atezolizumab was permanently discontinued with the last dose given on Study Day 73 (Cycle 3 Day 1).

The Investigator considered aspartate aminotransferase increased, alanine aminotransferase increased to be related atezolizumab, paclitaxel and ipatasertib.

Event 6: Aspartate aminotransferase increased (AST increase)

Event 7: Alanine aminotransferase increased (ALT increase)

Prior to the events of aspartate aminotransferase increased and alanine aminotransferase increased, the most recent dose of paclitaxel was administered and on Study Day 101 and ipatasertib (300 mg) on Study Day 120.

On Study Day 121, Cycle 5 Day 1 laboratory work-up showed AST 363 U/L (normal range: 5-34 U/L) and ALT 290 U/L (normal range: 8-42 U/L), total bilirubin 2.15 mg/dL (normal range: 0-1 mg/dL) and ALP 714 U/L (normal range: 30-105 U/L). The patient was diagnosed with non-serious Grade 3 aspartate aminotransferase increased, non-serious Grade 3 alanine aminotransferase increased, Grade 1 blood alkaline phosphatase increased and Grade 1 hyperbilirubinemia (both non-serious; related to ipatasertib). She received treatment with prednisone. On Study Day 128, the event of AST increased improved to Grade 1. Later the same day (Study Day 128), the events of aspartate aminotransferase, alanine aminotransferase

increased, blood alkaline phosphatase increased, and hyperbilirubinemia were considered resolved.

There was no change in the study treatment with paclitaxel due to the events of aspartate aminotransferase increased and alanine aminotransferase increased; however, study treatment with ipatasertib was interrupted on Study Day 122 and the next dose was given on Study Day 129.

The Investigator considered aspartate aminotransferase increased and alanine aminotransferase increased to be related to ipatasertib and unrelated to paclitaxel and atezolizumab.

Event 8: Aspartate aminotransferase increased (AST increased)

Prior to the event of aspartate aminotransferase increased, the most recent dose of paclitaxel was administered and on Study Day 129 and ipatasertib (300 mg) on Study Day 134.

On Study Day 135, a laboratory work-up showed AST 98 U/L (normal range: 5-34 U/L), ALT 157 U/L (normal range: 8-42 U/L), total bilirubin 1.67 mg/dL (normal range: 0-1 mg/dL) and alkaline phosphatase 302 U/L (normal range: 30-105 U/L). The patient was diagnosed with non-serious Grade 1 aspartate aminotransferase increased, Grade 2 alanine aminotransferase increased, Grade 2 hyperbilirubinemia and Grade 2 blood alkaline phosphatase increased (all non-serious, related). Her treatment with prednisone was maintained. On Study Day 170, the event of blood alkaline phosphatase increased was considered resolved. On Study Day 191, the event of aspartate aminotransferase increased was considered resolved. On Study Day 205, the event of hyperbilirubinemia was considered resolved. On Study Day 212, the event of alanine aminotransferase increased was considered resolved.

Relevant laboratory values listed in the table below:

Study Day	**AST** (normal range: 5-34 U/L)	**ALT** (normal range: 8-42 U/L)	**ALP** (normal range: 30-105 U/L)	**Total bilirubin** (normal range: 0-1 mg/dL)
-8	29	17	69	0.9
56	328	329	298	4.17
59	133	219	278	2.03
64	70	145	228	1.77
71	41	67	144	1.71

79	203	306	189	1.42
86	91	234	1698	1.33
93	30	79	139	1.74
100	36	68	84	1.14
107	33	20	112	0.97
121	363	290	714	2.15
126	166	217	398	1.59
128	92	178	252	1.26
135	98	157	302	1.67
149	63	79	298	1.42
156	74	87	199	1.23
163	39	45	129	1.4
170	46	40	85	1.17
177	61	43	70	1.4
184	48	66	68	1.45
191	28	37	55	1.02
205	33	39	64	0.8
212	39	32	59	1.11
219	39	26	53	1
238	59	66	236	0.66

There was no change in the study treatment with paclitaxel due to the event of aspartate aminotransferase increased; however, study treatment with ipatasertib was permanently discontinued with the last dose given on Study Day 156.

The Investigator considered aspartate aminotransferase increased to be related to ipatasertib and paclitaxel.

On Study Day 239, study treatment with paclitaxel was permanently discontinued due to other reason (the patient chose to discontinue due to recurrent adverse event related to chemotherapy) with the last dose of paclitaxel given on Study Day 213. The patient then entered the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Surgery of right breast	254	–
Radiotherapy to right breast (dose: 5005 cGy; 29 fractions)	337	365

On Study Day 742, the patient was discontinued from the study as study was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Diarrhea	1	Non-serious	6	23	Related	Related	Related
Diarrhea	2	Non-serious	38	50	Related	Related	Related
Neutropenia	2	Non-serious	42	56	Related	Related	Related
Asthenia	2	Non-serious	102	125	Related	Related	Unrelated
Leukopenia	2	Non-serious	107	121	Related	Related	Unrelated
Blood alkaline phosphatase increased	1	Non-serious	121	128	Related	Unrelated	Unrelated
Hyperbilirubinemia	1	Non-serious	121	128	Related	Unrelated	Unrelated
Hyperglycemia	1	Non-serious	121	128	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	132	134	Related	Related	NA
Diarrhea	1	Non-serious	139	140	Related	Related	Unrelated
Hyperglycemia	1	Non-serious	149	Resolving	Related	Related	Unrelated

Asthenia	2	Non-serious	150	396	Related	Related	Unrelated
Neuropathy peripheral	1	Non-serious	154	Resolving	Related	Related	Related
Pruritus	1	Non-serious	158	171	Related	Related	Unrelated
Neutropenia	1	Non-serious	163	170	Related	Related	Unrelated
Rash	2	Non-serious	178	184	Related	Related	Unrelated
Neutropenia	2	Non-serious	184	191	Unrelated	Related	Unrelated
Neutropenia	3	Non-serious	219	238	NA	Related	NA

Study Number/CRTN:	CO40016/304203	Patient number	3063
Demographics:	55-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day − 1.

The patient was initially diagnosed with ductal, poorly differentiated ER/PR negative and HER2 negative left breast cancer (T1N0M0) on Study Day − 919.

On Study Day −43, the patient was diagnosed with metastatic disease with ER/PR negative and HER 2 negative in metastatic tissue. At screening sites of disease involvement included lymph nodes (left mediastinal, neck, axillary, and internal mammary).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Docetaxel and cyclophosphamide (4 cycles each)	− 873	− 810
Surgery	Curative	Left sentinel lymph node biopsy	− 765	NA
Surgery	Curative	Left simple mastectomy	− 35	NA

The patient's medical history included intraductal proliferative breast lesion. No surgical history was reported. Concurrent conditions included tinnitus, hypertension, post menopause, fatigue,

anxiety, dermatitis contact, activated partial thromboplastin time prolonged, blood cholesterol increased, and insomnia.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included lisinopril and loratadine.

Event: Neuropathy peripheral (Neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of atezolizumab, paclitaxel, and ipatasertib (400 mg) was administered on Study Day 29.

On Study Day 29, the patient was diagnosed with non-serious Grade 1 neuropathy peripheral (presenting signs and symptoms not reported). She received treatment with gabapentin. On Study Day 204, the event of neuropathy peripheral worsened to Grade 2. The event of neuropathy peripheral remained unresolved at the time of patient′s death (see narrative below).

Due to this event, there was no change in the study treatment with atezolizumab and ipatasertib; however treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 323.

The Investigator considered neuropathy peripheral to be unrelated to atezolizumab and ipatasertib and related to paclitaxel, and other cause (unspecified).

On Study Day 446, an overall response assessment showed disease progression.

On Study Day 449, study treatment with atezolizumab and ipatasertib was permanently discontinued due to disease progression with the last dose of atezolizumab administered on Study Day 435, and ipatasertib on Study Day 441. The patient then entered the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine	449	531
Methotrexate	548	Ongoing

On Study Day 608, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipataseritib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Hyperglycemia	1	Non-serious	1	8	Unrelated	Unrelated	Unrelated
Constipation	1	Non-serious	4	36	Unrelated	Related	Unrelated
Dysgeusia	2	Non-serious	5	176	Unrelated	Related	Unrelated
Diarrhea	2	Non-serious	11	435	Related	Related	Unrelated
Abdominal pain	1	Non-serious	12	43	Related	Related	Unrelated
Back pain	1	Non-serious	12	43	Related	Related	Unrelated
White blood cell count decreased	1	Non-serious	15	29	Unrelated	Related	Unrelated
Herpes zoster	2	Non-serious	20	36	Unrelated	Unrelated	Unrelated
Cough	1	Non-serious	29	73	Unrelated	Unrelated	Unrelated
Alopecia	2	Non-serious	29	Unresolved	Unrelated	Related	Unrelated
Conjunctivitis	2	Non-serious	32	43	Unrelated	Unrelated	Unrelated
Anemia	1	Non-serious	36	Unresolved	Related	Related	Unrelated
Fatigue	2	Non-serious	36	Unresolved	Related	Related	Unrelated
Alanine aminotransferase increased	1	Non-serious	36	66	Related	Related	Unrelated
Upper respiratory tract infection	2	Non-serious	38	50	Unrelated	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipataseritib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Rash	1	Non-serious	38	58	Unrelated	Unrelated	Unrelated
Nausea	1	Non-serious	41	Unresolved	Related	Related	Unrelated
Jugular vein thrombosis	2	Non-serious	50	Unresolved	Unrelated	Related	Unrelated
Dyspnea	1	Non-serious	113	225	Unrelated	Related	Unrelated
Vomiting	1	Non-serious	117	117	Unrelated	Unrelated	Unrelated
Weight decreased	2	Non-serious	120	Unresolved	Related	Related	Related
Skin hyperpigmentation	1	Non-serious	134	386	Unrelated	Related	Unrelated
Hypokalemia	1	Non-serious	141	148	Unrelated	Unrelated	Related
Pruritus	1	Non-serious	169	176	Unrelated	Related	Unrelated
Hypertriglyceridemia	1	Non-serious	225	309	Related	Unrelated	Related
Rash	1	Non-serious	251	267	Unrelated	Unrelated	Unrelated
Musculoskeletal chest pain	1	Non-serious	251	288	Unrelated	Unrelated	Unrelated
Headache	1	Non-serious	255	258	Unrelated	Unrelated	Unrelated
Upper respiratory tract infection	2	Non-serious	272	295	Unrelated	Unrelated	Unrelated
Abdominal pain	1	Non-serious	321	337	Related	Related	Unrelated
Edema peripheral	1	Non-serious	323	365	Unrelated	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Headache	2	Non-serious	330	Unresolved	Unrelated	Unrelated	Unrelated
Rash	2	Non-serious	358	393	Related	Unrelated	Related
Fall	1	Non-serious	383	Unresolved	Unrelated	Not Applicable	Unrelated
Depression	1	Non-serious	386	Unresolved	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305247	Patient number	3066
Demographics:	69-year-old female (race unknown)		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day − 4.

The patient was diagnosed with ductal, moderately differentiated ER negative, PR positive and HER2 negative metastatic left breast cancer (TXNXM1) on Study Day − 55.

At screening sites of disease involvement included lung (bilateral, right lower and inferior lobe) and bone.

No past cancer treatment was reported.

The patient′s medical history included fibroadenoma of breast, uterine leiomyoma, and carpal tunnel syndrome. Surgical history included skin cyst excision, hysterectomy, thyroidectomy, breast tumor excision, and fracture treatment (malleolus fracture). Concurrent conditions included glaucoma, back pain, constipation, dry skin, edema peripheral, hemorrhoids, and hypothyroidism.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included levothyroxine, Chondrus cripus/lidocaine/titanium, and latanoprost.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel, atezolizumab was administered on Study Day 29, and ipatasertib (400 mg) was administered on Study Day 34.

On Study Day 35, the patient experienced non-serious Grade 1 diarrhea. On Study Day 40, the event of diarrhea worsened to Grade 3. She received treatment with loperamide (details in the table below). On Study Day 44, the event of diarrhea improved to Grade 2. On Study Day 46, the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	5	5
Diarrhea	6	PO	6	7
Diarrhea	4	PO	18	19
Diarrhea	6	PO	20	20
Diarrhea	4	PO	45	45
Diarrhea	2	PO	59	59
Diarrhea	4	PO	77	78
Diarrhea	2	PO	171	171
Diarrhea	4	PO	172	172
Diarrhea	2	PO	173	174
Diarrhea	2	PO	176	177
Diarrhea	6	PO	178	178
Diarrhea	4	PO	179	181
Diarrhea	6	PO	182	184
Diarrhea	4	PO	185	186
Diarrhea	2	PO	187	191
Diarrhea	4	PO	200	200
Diarrhea	2	PO	206	210
Diarrhea	2	PO	213	213

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	217	218
Diarrhea	2	PO	234	234
Diarrhea	2	PO	239	240
Diarrhea	2	PO	243	243
Diarrhea	2	PO	245	245
Diarrhea	2	PO	258	258
Diarrhea	2	PO	267	267
Diarrhea	2	PO	368	368

Due to this event, there was no change in the study treatment with atezolizumab; however, Cycle 2 Day 15 of paclitaxel was delayed and treatment with ipatasertib was interrupted on Study Day 45. The next dose of paclitaxel and ipatasertib (at a reduced dose of 300 mg from 400 mg) was administered on Study Day 50.

The Investigator considered diarrhea to be related to atezolizumab, ipatasertib and paclitaxel.

On Study Day 110, the patient was diagnosed with Grade 1 neuropathy peripheral on finger and toes (non-serious, related to paclitaxel). No treatment was given for the event.

Event 2: Neuropathy peripheral (Neuropathy; hands and feet)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel, atezolizumab was administered on Study Day 227, and ipatasertib (300 mg) was administered on Study Day 230.

On Study Day 231, the ongoing event of neuropathy peripheral worsened and spread to hands and feet and was considered Grade 2 (presenting signs and symptoms not reported). No treatment was given for the event. On Study Day 355, the event of neuropathy peripheral of hands resolved and neuropathy peripheral of feet improved the patient Grade 1. The event of neuropathy peripheral (feet) remained unresolved at the time of study discontinuation.

Due to this event, there was no change in the study treatment with atezolizumab and ipatasertib; however treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 269.

The Investigator considered neuropathy peripheral to be unrelated to atezolizumab and ipatasertib and related to paclitaxel.

On Study Day 386, an overall response assessment showed disease progression with new lesions in liver (segment VI) and study treatment with atezolizumab and ipatasertib was

permanently discontinued with the last dose of atezolizumab administered on Study Day 381, and ipatasertib on Study Day 385. The patient then entered the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine	409	576
Pegylated liposomal doxorubicin	583	Ongoing

On Study Day 723, the patient was discontinued from the study as long term follow-up was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Diarrhea	1	Non-serious	5	6	Related	Related	Related
Flatulence	2	Non-serious	17	46	Related	Related	Related
Alopecia	2	Non-serious	23	325	Unrelated	Related	Unrelated
Epistaxis	1	Non-serious	40	75	Related	Related	Related
Insomnia	2	Non-serious	46	75	Unrelated	Unrelated	Unrelated
Weight increased	2	Non-serious	50	Unresolved	Related	Unrelated	Unrelated
Respiratory tract infection viral	1	Non-serious	65	71	Unrelated	Unrelated	Unrelated
Hypercalcemia	1	Non-serious	71	73	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	109	131	Related	Related	Related
Constipation	1	Non-serious	109	131	Related	Related	Related

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Dry eye	1	Non-serious	135	145	Related	Related	Related
Paronychia	2	Non-serious	152	206	Related	Unrelated	Unrelated
Nail disorder	2	Non-serious	164	349	Related	Related	Related
Nail disorder	2	Non-serious	164	356	Related	Related	Related
Asthenia	2	Non-serious	172	349	Related	Related	Related
Rash	1	Non-serious	172	263	Related	Related	Related
Diarrhea	2	Non-serious	172	193	Not Applicable	Related	Related
Abdominal pain	1	Non-serious	175	193	Related	Related	Related
Hypercalcemia	1	Non-serious	198	241	Unrelated	Unrelated	Unrelated
Hypertension	1	Non-serious	199	230	Related	Related	Related
Diarrhea	1	Non-serious	207	242	Related	Unrelated	Unrelated
Eczema	1	Non-serious	245	259	Related	Related	Related
Diarrhea	1	Non-serious	245	262	Related	Unrelated	Unrelated
Hypertension	1	Non-serious	269	Unresolved	Related	Unrelated	Unrelated
Hand dermatitis	1	Non-serious	290	368	Unrelated	Unrelated	Related
Spinal pain	1	Non-serious	349	Unresolved	Unrelated	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Cough	1	Non-serious	358	373	Unrelated	Not Applicable	Unrelated
Fatigue	1	Non-serious	387	622	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/319619	Patient number	3068
Demographics:	58-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Category:	Polyneuropathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, moderately differentiated ER/PR negative and HER2 negative right breast cancer (T1N1M0) approximately 3 years and 5 months prior to study entry.

On Study Day – 49, the patient was diagnosed with metastatic disease with ER/PR negative and HER2 negative in metastatic tissue. At screening, sites of disease involvement included right lymph node (upper part of pulmonary hilus) and right lung (V segment and IX segment) and bone (vertebra L1 and Th12).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right simple mastectomy	Approximately 3 years and 1 month prior to study entry	NA
Cancer therapy	Adjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	Approximately 3 years and 1 month prior to study entry	Approximately 2 years and 11 months prior to study entry
Cancer therapy	Adjuvant	Docetaxel (4 cycles)	Approximately 2 years and 9 months prior to study entry	Approximately 2 years and 7 months prior to study entry
Radiotherapy	Adjuvant	Right chest wall, supraclavicular, axillary (dose: 5000 cGy; 25 fractions)	Approximately 2 years and 7 months prior to study entry	Approximately 2 years and 6 months prior to study entry

No medical/surgical history was reported. The patient′s concurrent conditions included hypertension, aortic aneurysm, spinal osteoarthritis, and hemorrhoids.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included metoprolol and zofenopril.

Event: Polyneuropathy

Prior to the event of polyneuropathy, the most recent dose of atezolizumab and paclitaxel was given on Study Day 157 and ipatasertib (400 mg) on Study Day 162.

On Study Day 171, the patient was noted with non-serious Grade 1 polyneuropathy (diagnostic details not reported). On Study Day 214, the event worsened to Grade 2. She received treatment with *Borago officinalis* seed oil/nicotinic acid/pantothenic acid/pyridoxine/riboflavin/selenium/thioctic acid/vitamin B1 (unspecified)/vitamin E (unspecified). The event of polyneuropathy was resolving at the time of patient′s death (see narrative below).

There was no change in the study treatment with ipatasertib and atezolizumab; however, study treatment with paclitaxel was reduced from 80 mg/m^2 to 65 mg/m^2 on Study Day 199 and then paclitaxel was permanently discontinued with the last dose given on Study Day 213.

The Investigator considered polyneuropathy to be related to paclitaxel and unrelated to ipatasertib and atezolizumab.

On Study Day 372, an overall response assessment showed disease progression with new lesions in brain (left frontal lobe, corpus callosum, thalamus and left cerebellum) and neck (spinal cord at C3/C4).

On Study Day 373, the patient was discontinued from the study treatment due to disease progression with the last dose of atezolizumab given on Study Day 339 and ipatasertib on Study Day 359. The patient then entered the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Radiotherapy to brain (dose: 4000 cGy; 5 fractions)	375	379
Radiotherapy to spinal cord in area of Th12	386	390

On Study Day 465, the patient died due to disease progression. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Blood pressure increased	2	Non-serious	1	1	Unrelated	Unrelated	Unrelated
Constipation	1	Non-serious	5	6	Unrelated	Unrelated	Unrelated
Rash papular	1	Non-serious	8	36	Related	Unrelated	Unrelated
Blood pressure increased	1	Non-serious	8	8	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	10	11	Related	Unrelated	Unrelated
Neutropenia	2	Non-serious	15	51	Unrelated	Unrelated	Related
Chest discomfort	3	Non-serious	22	22	Unrelated	Unrelated	Related

Flushing	3	Non-serious	22	22	Unrelated	Unrelated	Related
Anemia	2	Non-serious	29	135	Related	Related	Related
Headache	1	Non-serious	31	31	Unrelated	Unrelated	Unrelated
Headache	1	Non-serious	33	33	Unrelated	Unrelated	Unrelated
Rash	2	Non-serious	40	44	Related	Related	Related
Tumor inflammation	1	Non-serious	46	47	Related	Related	Related
Rash	1	Non-serious	79	81	Related	Unrelated	Related
Stomatitis	1	Non-serious	88	Resolving	Related	Unrelated	Unrelated
Eye disorder	2	Non-serious	94	97	Unrelated	Unrelated	Related
Rash	1	Non-serious	108	109	Related	Unrelated	Unrelated
Bronchitis	2	Non-serious	113	124	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	135	142	Unrelated	Unrelated	Related
Anemia	1	Non-serious	142	241	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	149	157	Unrelated	Unrelated	Related
Hyperbilirubinemia	1	Non-serious	227	269	Related	Unrelated	Unrelated
Headache	2	Non-serious	283	283	Unrelated	Unrelated	Unrelated
Pruritus	2	Non-serious	315	321	Unrelated	Related	Unrelated
Autoimmune hypothyroidism	1	Non-serious	339	Resolving	Unrelated	Related	Unrelated
Pneumonitis	1	Non-serious	353	361	Unrelated	Related	Unrelated
Peripheral motor neuropathy	3	Non-serious	361	Resolving	Unrelated	Unrelated	Unrelated
Hypercholesterolemia	1	Non-serious	373	Resolving	Unrelated	Unrelated	Unrelated
Hyperbilirubinemia	1	Non-serious	373	Resolving	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/306603	Patient number	3072
Demographics:	78-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Category:	Dyspnea AE leading to study treatment discontinuation		

The patient was randomized on Study Day – 1.

The patient was initially diagnosed with comedo-ductal, poorly differentiated, ER/PR negative and HER2 positive right breast cancer (T1cN0MX) approximately 2 years and 7 months prior to study entry.

On Study Day – 71, the patient was diagnosed with metastatic disease with ER/PR negative and HER2 negative in metastatic disease. At screening, sites of disease involvement included lung (left lower lobe, right lower lobe nodules and bilateral pulmonary nodules) and left pelvis bone.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right partial mastectomy and right sentinel lymph node	Approximately 2 years and 5 months prior to study entry	=
Cancer therapy	Adjuvant	Paclitaxel and trastuzumab	Approximately 2 years and 5 months prior to study entry	Approximately 2 years and 2 months prior to study entry
Cancer therapy	Adjuvant	Trastuzumab	Approximately 2 years and 2 months prior to study entry	Approximately 1 year and 6 months prior to study entry
Radiotherapy	Adjuvant	Right breast (dose: 4256 cGy; 16 fractions)	Approximately 2 years prior to study entry	Approximately 2 years prior to study entry
Radiotherapy	Adjuvant	Right breast boost (dose: 1000 cGy; 4 fractions)	Approximately 2 years prior to study entry	Approximately 1 year 11 months prior to study entry

No medical history was reported. The patient′s surgical history included left knee arthroplasty, appendicectomy, bilateral cataract operation and cholecystectomy. Concurrent conditions included hypertension, hyperlipidemia, irritable bowel syndrome, arthritis, deafness, sinus tachycardia, intraocular pressure increased, insomnia and urinary tract infection.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included calcium carbonate, lisinopril, melatonin, metoprolol, ezetimibe, fish oil, *Prunus cerasus* and travoprost.

Event: Dyspnea (Intermittent shortness of breath)

Prior to the event of dyspnea, the most recent dose of atezolizumab and paclitaxel was given on Study Day 524 and ipatasertib (300 mg) on Study Day 527.

On Study Day 466, the patient experienced Grade 1 dyspnea exertional (non-serious, unrelated). On Study Day 482, she experienced Grade 1 chest pain (non-serious, unrelated). No treatment was given for these events. On Study Day 497, the event of chest pain was considered resolved.

On Study Day 528, dyspnea exertional resolved; however the patient experienced non-serious Grade 2 dyspnea. she received unspecified treatment for this event. The event of dyspnea remained unresolved at the time of study discontinuation.

Due to this event, there was no change in the study treatment with ipatasertib and atezolizumab; however, study treatment with paclitaxel was reduced from 80 mg/m^2 to 65 mg/m^2 on Study Day 692 and then paclitaxel was permanently discontinued with the last dose given on Study Day 706.

The Investigator considered dyspnea to be unrelated to ipatasertib and atezolizumab related to paclitaxel and other causes (unspecified).

On Study Day 846, the patient was discontinued from the study treatment and study due to transitioned to PTAP with the last dose of atezolizumab and ipatasertib given on the same day (Study Day 846).

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Constipation	1	Non-serious	2	11	Unrelated	Unrelated	Unrelated
Dizziness	1	Non-serious	2	14	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	11	23	Related	Related	Related
Onycholysis	1	Non-serious	15	Unresolved	Unrelated	Unrelated	Related
Cough	1	Non-serious	21	37	Unrelated	Unrelated	Unrelated
Rhinorrhea	1	Non-serious	21	Unresolved	Unrelated	Unrelated	Unrelated
Epistaxis	1	Non-serious	21	23	Unrelated	Unrelated	Unrelated
Oropharyngeal pain	1	Non-serious	21	23	Unrelated	Unrelated	Unrelated
Alopecia	2	Non-serious	26	Unresolved	Related	Related	Related
Rash	1	Non-serious	27	30	Related	Related	Related
Constipation	1	Non-serious	30	31	Unrelated	Unrelated	Unrelated
Nausea	1	Non-serious	37	86	Related	Related	Related
Diarrhea	1	Non-serious	45	57	Related	Related	Related
Arthralgia	1	Non-serious	51	Unresolved	Unrelated	Unrelated	Unrelated
Muscle spasms	1	Non-serious	65	170	Related	Related	Related
Diarrhea	1	Non-serious	65	73	Related	Related	Related
Diarrhea	2	Non-serious	74	77	Related	Related	Related
Constipation	1	Non-serious	81	84	Unrelated	Unrelated	Unrelated
Oropharyngeal pain	1	Non-serious	91	114	Unrelated	Unrelated	Unrelated
Nasopharyngitis	1	Non-serious	100	114	Unrelated	Unrelated	Unrelated
Flatulence	1	Non-serious	100	742	Related	Related	Related
Flushing	1	Non-serious	101	Unresolved	Related	Related	Related

Nausea	1	Non-serious	102	258	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	102	356	Related	Unrelated	Unrelated
Seasonal allergy	1	Non-serious	114	Unresolved	Unrelated	Unrelated	Unrelated
Gastroesophageal reflux disease	1	Non-serious	213	328	Unrelated	Related	Unrelated
Constipation	1	Non-serious	213	Unresolved	Unrelated	Related	Unrelated
Rash	1	Non-serious	219	231	Unrelated	Unrelated	Unrelated
Edema peripheral	1	Non-serious	243	Unresolved	Unrelated	Unrelated	Unrelated
Hemorrhoids	1	Non-serious	348	Unresolved	Unrelated	Unrelated	Unrelated
Neuropathy peripheral	1	Non-serious	412	Unresolved	Unrelated	Unrelated	Related
COVID-19	1	Non-serious	458	467	Unrelated	Unrelated	Unrelated
Chest pain	1	Non-serious	473	476	Unrelated	Unrelated	Unrelated
Anemia	1	Non-serious	524	761	Unrelated	Unrelated	Related
Arthralgia	1	Non-serious	582	Unresolved	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	595	595	Related	Unrelated	Unrelated
Dizziness	1	Non-serious	601	601	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	623	Unresolved	Related	Unrelated	Unrelated
Arthralgia	1	Non-serious	623	Unresolved	Unrelated	Unrelated	Unrelated
Abdominal discomfort	1	Non-serious	681	Unresolved	Unrelated	Unrelated	Unrelated
Pulmonary embolism	1	Non-serious	695	Unresolved	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304331	Patient number	3074
Demographics:	68-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Category:	Encephalopathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day − 1.

The patient was diagnosed with poorly differentiated not otherwise specified ER/PR negative and HER2 negative metastatic right breast cancer (T4N2M1) on Study Day − 58, following right breast biopsy on the same day.

At screening sites of disease involvement included lymph nodes (sub-aortal and right axillary), and right breast.

No past cancer treatment was reported.

No medical/surgical history was reported. The patient′s concurrent conditions included varicose vein (lower extremities; Grade 2), peripheral venous disease (Grade 2), ovarian cyst (left; Grade 1), myocardial ischemia, arteriosclerosis coronary artery (Grade 1), spinal pain (Grade1), pulmonary fibrosis (Grade 1), and degenerative bone disease (Grade 1).

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included trimetazidine, acetylsalicylic acid/magnesium hydroxide, rosuvastatin, diosmin/hesperidin, and heparin.

Event: Encephalopathy

Prior to the event of encephalopathy, the most recent dose of paclitaxel was administered on Study Day 337, atezolizumab, and ipatasertib (400 mg) on Study Day 372.

On Study Day 373, laboratory work-up showed D-dimer 663 ng/mL, albumin 40 g/L (normal range not reported) and normal procalcitonin. The patient was diagnosed with non-serious Grade 2 encephalopathy (symptoms and further assessments not reported). She received treatment with prochlorperazine, lactose/peptone, thioctic acid, ipidacrine, and thiotriazoline. The event of encephalopathy remained unresolved at the time of study discontinuation.

Due to this event, there was no change in the study treatment with atezolizumab and ipatasertib; however, treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 337.

The Investigator considered encephalopathy to be unrelated to atezolizumab and ipatasertib and related to paclitaxel.

On Study Day 1135, study treatment with atezolizumab and ipatasertib and study was permanently discontinued as patient stared PTA program with the last dose of atezolizumab administered on Study Day 1114, and ipatasertib on Study Day 1121.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Neutropenia	2	Non-serious	8	57	Unrelated	Related	Unrelated
Alopecia	2	Non-serious	25	Unresolved	Unrelated	Related	Unrelated
Diarrhea	2	Non-serious	37	42	Related	No	Unrelated
Anemia	1	Non-serious	71	246	Unrelated	Related	Unrelated
Nail discoloration	1	Non-serious	81	Unresolved	Unrelated	Related	Unrelated
Polyneuropathy	2	Non-serious	92	Unresolved	Unrelated	Related	Unrelated
Neutropenia	3	Non-serious	134	156	Related	Related	Unrelated
Neutropenia	2	Non-serious	162	190	Unrelated	Related	Unrelated
Leukopenia	1	Non-serious	162	190	Unrelated	Related	Unrelated
Alanine aminotransferase increased	1	Non-serious	183	211	Unrelated	Not Applicable	Unrelated
Neutropenia	1	Non-serious	225	274	Related	Related	Unrelated
Leukopenia	1	Non-serious	225	267	Related	Related	Unrelated
Anemia	1	Non-serious	253	442	Unrelated	Related	Unrelated
Neutropenia	1	Non-serious	295	302	Unrelated	Related	Unrelated
Rash maculo-papular	1	Non-serious	307	311	Related	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Neutropenia	1	Non-serious	309	322	Unrelated	Related	Unrelated
Leukopenia	1	Non-serious	309	322	Unrelated	Related	Unrelated
Pulmonary embolism	2	Non-serious	319	489	Unrelated	Unrelated	Unrelated
Neutropenia	1	Non-serious	337	351	Unrelated	Related	Unrelated
Hypercholesterolemia	1	Non-serious	512	Unresolved	Unrelated	Unrelated	Unrelated
Glomerular filtration rate decreased	2	Non-serious	638	Unresolved	Unrelated	Not Applicable	Unrelated

Study Number/CRTN:	CO40016/319619	Patient number	3076
Demographics:	65-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Category:	Polyneuropathy AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with mucinous moderately differentiated ER/PR negative and HER2 negative left breast cancer (T2N0M0) on Study Day − 924.

On Study Day −172, the patient was diagnosed with metastatic disease with ER/PR negative and HER 2 negative in metastatic tissue. At screening sites of disease involvement included lung (left IV and X segment and right side).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	– 778	– 715
Cancer therapy	Adjuvant	Paclitaxel (12 cycles)	– 694	– 617
Radiotherapy	Adjuvant	Left breast area (5250 cGy and 21 fractions)	– 595	– 565

No medical/surgical history was reported. Concurrent conditions included anal fistula, dyslipidemia, depression, hypothyroidism, and glaucoma.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included sertraline, trazodone, levothyroxine, and dorzolamide.

Event: Polyneuropathy

Prior to the event of polyneuropathy, the most recent dose of atezolizumab was administered on Study Day 198, paclitaxel, and ipatasertib (300 mg) on Study Day 205.

On Study Day 205, the patient was diagnosed with non-serious Grade 1 polyneuropathy (presenting signs and symptoms not reported). No treatment was given for the event. The event of polyneuropathy remained resolving at the time of patient's death (see narrative below).

Due to this event, there was no change in the study treatment with atezolizumab and ipatasertib; however, treatment with paclitaxel was permanently discontinued with the last dose given on Study Day 212.

The Investigator considered polyneuropathy to be unrelated to atezolizumab and ipatasertib and related to paclitaxel.

On Study Day 269, an overall response assessment showed disease progression with new lesions in liver (segment IV and VI).

On Study Day 282, study treatment with atezolizumab and ipatasertib was permanently discontinued due to disease progression with the last dose of atezolizumab administered on Study Day 268, and ipatasertib on Study Day 273. The patient then entered the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Carboplatin (10 cycles)	289	352
Capecitabine	381	Ongoing

On Study Day 507, the patient died due to disease progression. It was unknown if an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipataseritib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Anemia	2	Non-serious	8	240	Unrelated	Related	Unrelated
Diarrhea	2	Non-serious	10	21	Related	Unrelated	Unrelated
Leukopenia	1	Non-serious	15	36	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	35	35	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	39	41	Related	Unrelated	Unrelated
Alopecia	1	Non-serious	43	Resolving	Unrelated	Related	Related
Myalgia	1	Non-serious	63	63	Unrelated	Related	Unrelated
Myalgia	1	Non-serious	65	65	Unrelated	Related	Unrelated
Myalgia	1	Non-serious	69	69	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	69	70	Related	Unrelated	Unrelated

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Myalgia	1	Non-serious	93	94	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	101	114	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	125	127	Related	Unrelated	Unrelated
Abnormal sensation in eye	2	Non-serious	130	Resolving	Unrelated	Related	Unrelated
Diarrhea	2	Non-serious	158	163	Related	Unrelated	Unrelated
Skin lesion	1	Non-serious	182	198	Unrelated	Unrelated	Related
Overdose	–	Non-serious	191	191	Unrelated	Unrelated	Unrelated
Conjunctivitis	2	Non-serious	200	211	Unrelated	Unrelated	Unrelated
Anemia	1	Non-serious	254	282	Unrelated	Unrelated	Unrelated
Product dose omission in error	–	Non-serious	274	274	Unrelated	Unrelated	Not reported

Study Number/CRTN:	CO40016/304787	Patient number	3077
Demographics:	64-year-old Black or African American female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Categories:	Large intestine perforation SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/312641	Patient number	3078
Demographics:	55-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER2 negative, left breast cancer (T1cN2aMX) on Study Day − 645.

On Study Day − 76, the patient was diagnosed with metastatic disease with ER/PR and HER2 receptor negative in metastatic tissue. At screening, sites of disease involvement included lymph nodes (right hilar) and bone (spine).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Epirubicin, cyclophosphamide and docetaxel	-630	-508
Surgery	Curative	'Other' surgery of left breast	-475	NA
Radiotherapy	Adjuvant	Left breast and internal mammary chain and level II - IV axillary lymph nodes (dose unknown, 15 fractions)	-421	-401
Radiotherapy	Adjuvant	Breast boost (dose unknown, 5 fractions)	-400	-394

The patient's medical history included pneumonia. No surgical history was reported. No concurrent condition was reported.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

No concomitant medication ongoing at Study Day 1 was reported.

Event: Neuropathy peripheral (Peripheral neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of atezolizumab was administered on Study Day 1, paclitaxel on Study Day 8 and ipatasertib (400 mg) on Study Day 13.

On Study Day 14, the patient was noted with non-serious Grade 1 (initial intensity) neuropathy peripheral. No treatment was administered for the event. On Study Day 58, the event of neuropathy peripheral worsened to Grade 2. On Study Day 79, the event of neuropathy peripheral worsened to Grade 3. On Study Day 114, the event of neuropathy peripheral improved to Grade 1. The event of neuropathy peripheral remained unresolved at the time of patient′s death (see narrative below).

Due to the event of neuropathy peripheral, there was no change in study treatment with ipatasertib and atezolizumab, however, study treatment with paclitaxel was permanently discontinued with last dose administered on Study Day 65.

The Investigator considered neuropathy peripheral, to be related to paclitaxel, and unrelated to ipatasertib and atezolizumab.

On Study Day 110, a radiographic response assessment showed disease progression with new lesions in lymph nodes (right-sided retrocrural nodes and left renal artery lymph node) and soft tissue (gastro hepatic space soft tissue).

On Study Day 135, study treatment with ipatasertib and atezolizumab was permanently discontinued due to disease progression with the last dose of atezolizumab and ipatasertib administered on Study Day 100 and Study Day 106, respectively. The patient entered into the long term follow up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine	114	170
Carboplatin	202	362
Radiotherapy to brain (dose: 2100 cGy, 1 fraction)	226	226

On Study Day 455, the patient died due to disease progression. It was unknown whether an autopsy was performed or not.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Fatigue	1	Non-serious	4	Unresolved	Related	Related	Unrelated
Nausea	1	Non-serious	4	30	Related	Related	Unrelated
Thirst	1	Non-serious	4	37	Related	Related	Unrelated
Vision blurred	1	Non-serious	4	37	Related	Unrelated	Unrelated
Neutropenia	2	Non-serious	7	14	Related	Related	Unrelated
White blood cell count decreased	2	Non-serious	7	14	Related	Related	Unrelated
Musculoskeletal pain	2	Non-serious	7	30	Unrelated	Unrelated	Unrelated
Nasal crusting	1	Non-serious	10	14	Unrelated	Related	Unrelated
Epistaxis	1	Non-serious	10	14	Unrelated	Related	Unrelated
Epistaxis	1	Non-serious	23	27	Unrelated	Related	Unrelated
Rash	1	Non-serious	23	31	Related	Related	Unrelated
Hordeolum	1	Non-serious	23	31	Unrelated	Unrelated	Unrelated
Nasopharyngitis	1	Non-serious	23	32	Unrelated	Unrelated	Unrelated
Cough	1	Non-serious	30	86	Unrelated	Unrelated	Unrelated
Oropharyngeal pain	1	Non-serious	42	86	Unrelated	Unrelated	Unrelated
Dyspnea	1	Non-serious	42	102	Unrelated	Unrelated	Unrelated
Oral candidiasis	1	Non-serious	42	65	Unrelated	Related	Unrelated
Abdominal pain	2	Non-serious	43	43	Unrelated	Unrelated	Unrelated
Neutropenia	2	Non-serious	71	77	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	73	Unresolved	Related	Related	Unrelated
Posterior reversible encephalopathy syndrome	3	Serious	177	199	Related	Unrelated	Related

Study Number/CRTN:	CO40016/304891	Patient number	3080
Demographics:	49-year-old White female		

Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)
Cohort:	Cohort C
Event (PT) Categories:	Pneumonia SAE, AE leading to study treatment discontinuation

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304332	Patient number	3082
Demographics:	68-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR negative (HER2 receptor not assessed) right breast cancer (T2N1M0) approximately 4 years and 1 month prior to study entry.

The patient was diagnosed with metastatic disease on Study Day – 93 with ER /PR negative and HER2 negative disease. At screening, sites of disease involvement included lymph node (right lung, segment 3, right conglomerate of left nodes upper clavicular, greater pectoral muscle small pectoral muscle, right neck, right basal and broncho pulmonal) and bilateral lung.

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Right radical mastectomy	Approximately 4 years prior to study entry	–
Cancer therapy	Adjuvant	Cyclophosphamide, doxorubicin, and fluorouracil (4 cycles each)	Approximately 3 years and 11 months prior to study entry	Approximately 3 years and 9 months prior to study entry

The patient′s medical history included cholelithiasis. Surgical history included cholecystectomy and appendicectomy. Concurrent conditions included arthralgia (right shoulder) and splenic granuloma.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, atezolizumab and paclitaxel.

No concomitant medications ongoing at Study Day 1 was reported.

Event: Neuropathy peripheral (Peripheral neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of atezolizumab was administered on Study Day 113, paclitaxel and ipatasertib (200 mg) on Study Day 120.

On Study Day 121, the patient was diagnosed with non-serious Grade 1 neuropathy peripheral (assessment details not reported). She received treatment with cyanocobalamin/cytidine/disodium uridine/folic acid, ipidacrine, pentoxifylline, choline alfoscerate, cytidine, thioctic acid and pregabalin for neuropathy peripheral. The event of neuropathy peripheral remained unresolved at the time of study discontinuation.

Relevant grade changes reported in the table below:

Event	Study Day	Grade change
Peripheral neuropathy	150	3
Peripheral neuropathy	175	2
Peripheral neuropathy	887	3

Due to the event of neuropathy peripheral, there was no change in the study treatment with ipatasertib and atezolizumab; however, study treatment with paclitaxel was initially reduced from 80 mg/m^2 to 65 mg/m^2 on Study Day 176 and later permanently discontinued with the last dose given on Study Day 883.

The Investigator considered neuropathy peripheral to be related to paclitaxel and unrelated to atezolizumab and ipatasertib.

On Study Day 966, study treatment was permanently discontinued as per physician′s decision (for safety and patient interest) with the last dose of ipatasertib given on Study Day 693 and atezolizumab on Study Day 883. The patient entered into the long-term follow-up.

On Study Day 986, the patient was discontinued from the study as long term follow up was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Diarrhea	1	Non-serious	5	5	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	7	21	Related	Unrelated	Unrelated
Alopecia	1	Non-serious	17	561	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	30	49	Related	Unrelated	Unrelated
Accidental overdose	1	Non-serious	65	65	Unrelated	Unrelated	Unrelated
Accidental overdose	1	Non-serious	80	81	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	85	86	Related	Unrelated	Unrelated
Rib fracture	1	Non-serious	167	223	Unrelated	Unrelated	Unrelated
Cerebrovascular insufficiency	3	Non-serious	887	Unresolved	Unrelated	Related	Unrelated

Study Number/CRTN:	CO40016/305629	Patient number	3085
Demographics:	58-year-old American Indian or Alaska Native female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Categories:	Diarrhea SAE, Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Myositis SAE		
Event 3 (PT) Category:	Myocarditis SAE		
Event 4 (PT) Categories:	Pulmonary embolism Death due to adverse event, SAE, AE leading to Study treatment discontinuation		

A narrative for this patient is available in Section 1.1 Narratives for patients who died due to an adverse event(s).

Study Number/CRTN:	CO40016/305145	Patient number	3086
Demographics:	66-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Gastroenteritis SAE		
Event 2 (PT) Category:	Pyrexia SAE		
Event 3 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		
Event 4 (PT) Category:	Neuropathy peripheral (Grade 1) AE leading to study treatment discontinuation		
Event 5 (PT) Category:	Acute kidney injury SAE		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304785	Patient number	3088
Demographics:	51-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity		

Event 3 (PT) Categories:	Aspartate aminotransferase increased AE leading to study treatment discontinuation, Grade ≥ 3 hepatotoxicity
Event 4 (PT) Categories:	Alanine aminotransferase increased (Second episode) AE leading to study treatment discontinuation, Grade ≥ 3 hepatotoxicity

The patient was randomized on Study Day 1.

The patient was initially diagnosed with unspecified histology, moderately differentiated, ER/PR and HER2 negative, right breast cancer (TXN1M1) approximately 2 years and 9 months prior to study entry.

On Study Day – 91, the patient was diagnosed with metastatic disease with ER/PR and HER2 negative in metastatic tissue. At screening sites of disease involvement included lymph node (right axillary lymph node in superficial chain, right cervical VI lymph node and midline infiltrated at the cervical level V).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Surgery	Curative	Radical mastectomy of right breast and right sentinel lymph node iopsy	-783	NA
Cancer therapy	Adjuvant	Tamoxifen	-728	-90
Radiotherapy	Adjuvant	Right breast (dose: 5000 cGy, 25 fractions)	-726	-721

No medical or surgical history was reported. The patient′s concurrent condition included pain in the right upper limb.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included codeine phosphate/paracetamol and amitriptyline.

The patient received treatment with loperamide (total daily dose: 4 mg, PO) for diarrhea from Study Day 1 to Study Day 15.

On Study Day 16, the patient experienced Grade 1 diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide (details in the table below). On Study Day 52, the event of diarrhea was considered resolved.

On Study Day 65, the patient experienced another episode of Grade 1 diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide (details in the table below). On Study Day 89, the event of diarrhea was considered resolved.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of atezolizumab, paclitaxel and ipatasertib (400 mg) was administered on Study Day 101.

On Study Day 102, the patient experienced non-serious Grade 3 diarrhea. No diagnostic test was performed. She received treatment with loperamide (details in the table below). On Study Day 108, the event of diarrhea was considered resolved.

Due to the event of diarrhea, there was no change in study treatment with paclitaxel and atezolizumab, however, study treatment with ipatasertib was reduced to 300 mg on Study Day 115.

The Investigator considered diarrhea, to be related to ipatasertib and unrelated to paclitaxel and atezolizumab.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	1	15
Diarrhea	2	PO	18	52
Diarrhea	2	PO	76	89
Diarrhea	12	PO	102	108

Event 2: Alanine aminotransferase increased (ALT elevation)

Prior to the event of alanine aminotransferase increased, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 129 and ipatasertib (300 mg) on Study Day 135.

On Study Day 142, a laboratory work-up showed ALT 178 U/L (normal range: 0-35 U/L) and AST 123 U/L (normal range: 14-36 U/L), leading to diagnosis of non-serious Grade **3** alanine aminotransferase increased and Grade 2 aspartate aminotransferase increased (non-serious, related to atezolizumab). Relevant laboratory work-up is reported in the table below. She received treatment with prednisone. On Study Day 147, the events of alanine aminotransferase increased and aspartate aminotransferase increased were considered resolved.

Due to the event of alanine aminotransferase increased, there was no change in study treatment with ipatasertib and paclitaxel, however, study treatment with atezolizumab was interrupted on Study Day 129 and was resumed on Study Day 170.

The Investigator considered alanine aminotransferase increased, to be unrelated to ipatasertib and paclitaxel and related to atezolizumab.

Relevant laboratory work-up:

Study Day	**AST** Normal range: 14-36 U/L	**ALT** Normal range: 0-35 U/L	**Bilirubin** Normal range: 0-1.3 mg/dL	**ALP** Normal range: 38-126 U/L
Screening (1)	31	24	0.3	106
142	123	178	0.5	137
148	46	58	0.4	99
156	21	24	0.3	87
170	46	62	0.3	84
177	37	41	0.4	77
184	72	87	0.4	95
198	207	340	0.3	138
200	100	248	—	—
204	67	141	0.4	118
207	39	85	—	—
213	67	120	0.4	96
218	41	84	0.3	94
226	47	58	0.3	77
233	210	262	0.4	95
235	272	377	—	—
240	109	288	—	—
243	67	204	—	—
249	35	78	0.4	94
256	37	57	0.3	93
263	69	87	0.3	72
277	131	245	0.3	81
281	68	168	0.3	80
283	44	106	—	—
288	35	60	0.6	71
297	25	27	0.4	61

Event 3: Aspartate aminotransferase increased (AST elevation)
Event 4: Alanine aminotransferase increased (ALT elevation; second episode)

Prior to the events of aspartate aminotransferase increased and alanine aminotransferase increased (second episode), the most recent dose of paclitaxel and atezolizumab was administered on Study Day 184 and ipatasertib (300 mg) on Study Day 190.

On Study Day 198, a laboratory work-up showed ALT 340 U/L (normal range: 0-35 U/L) and AST 207 U/L (normal range: 14-36 U/L), leading to diagnosis of asymptomatic non-serious Grade 3 aspartate aminotransferase increased and non-serious Grade 3 alanine aminotransferase increased (second episode). Grade changes for the events of aspartate aminotransferase increased and alanine aminotransferase increased (second episode) were reported in the table below. Relevant laboratory work-up is reported in the table above. She received treatment with prednisone. On Study Day 296, the events of aspartate aminotransferase increased and alanine aminotransferase increased (second episode) were considered resolved.

Due to the events of aspartate aminotransferase increased and alanine aminotransferase increased (second episode), study treatment with paclitaxel was first interrupted on Study Day 233, resumed on Study Day 249, and then later dose was reduced to 65 mg/m^2 on Study Day 288. Treatment with atezolizumab was first interrupted on Study Day 184 and was later permanently discontinued with last dose administered on Study Day 184. Study treatment with ipatasertib was first interrupted on Study Day 204, resumed on Study Day 218, again interrupted on Study Day 232, again resumed on Study Day 249 and later was permanently discontinued with last dose administered on Study Day 269.

The Investigator considered aspartate aminotransferase increased, to be unrelated to ipatasertib and paclitaxel and related to atezolizumab.

The Investigator considered alanine aminotransferase increased (second episode), to be related to ipatasertib, paclitaxel and atezolizumab.

Grade changes for aspartate aminotransferase increased:

Study Day	Grade changes for aspartate aminotransferase increased
200	1
233	3
240	2
263	1
277	2
281	1

Grade changes for alanine aminotransferase increased (second episode):

Study Day	Grade changes for alanine aminotransferase increased (second episode)
204	2
207	1
213	2
218	1
233	3
246	2
249	1
277	3
281	2
288	1

On Study Day 782, the study was permanently discontinued due to other reason (the patient moved to post trial assessment) with last dose of paclitaxel administered on Study Day 753.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Decreased appetite	2	Non-serious	31	68	Related	Related	Unrelated
Insomnia	2	Non-serious	33	445	Unrelated	Unrelated	Unrelated
Weight decreased	1	Non-serious	36	44	Unrelated	Unrelated	Unrelated
Pruritus	1	Non-serious	51	76	Related	Unrelated	Unrelated
Upper respiratory tract infection	2	Non-serious	80	90	Unrelated	Unrelated	Unrelated
Decreased appetite	2	Non-serious	102	108	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	127	178	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	189	192	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	260	267	Related	Unrelated	Unrelated
Pruritus	2	Non-serious	308	319	Unrelated	Unrelated	Unrelated
Pruritus	1	Non-serious	375	382	Unrelated	Unrelated	Unrelated
Headache	1	Non-serious	418	433	NA	Unrelated	NA
Vitreous detachment	1	Non-serious	418	Unresolved	NA	Unrelated	NA

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Pruritus	1	Non-serious	418	515	NA	Related	NA
Depression	1	Non-serious	418	464	NA	Unrelated	Unrelated
Hypertriglyceridemia	2	Non-serious	486	569	NA	Unrelated	NA
Pruritus	1	Non-serious	535	627	Unrelated	Related	Unrelated
Contrast media reaction	1	Non-serious	614	614	NA	Unrelated	NA
Dysphonia	1	Non-serious	617	630	NA	Unrelated	NA
Dermatitis acneiform	1	Non-serious	637	647	NA	Unrelated	NA
Dyslipidemia	2	Non-serious	654	Unresolved	NA	Unrelated	NA
Cellulitis	2	Non-serious	723	731	NA	Unrelated	NA

Study Number/CRTN:	CO40016/304929	Patient number	3089
Demographics:	51-year-old Asian female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle) + Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR negative and HER2 negative, left breast cancer (T3N1MX), approximately 4 years and 10 months prior to study entry following left simple mastectomy.

The patient was diagnosed with locally recurrent disease approximately 3 years 4 months prior to the study entry, and on Study Day – 73 the patient was diagnosed with locally advanced unresectable disease with ER/PR negative and HER2 negative in recurrent/metastatic tissue. At screening, sites of disease involvement included lymph nodes (left supraclavicular and right upper jugular), lung (right lower lobe) and soft tissue (left scalene muscle)

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Adjuvant	Epirubicin and cyclophosphamide (4 cycles each)	Approximately 4 years and 8 months prior to the study entry	Approximately 4 years and 6 months prior to the study entry
Cancer therapy	Adjuvant	Paclitaxel (Cycle: unknown)	Approximately 4 years and 6 months prior to the study entry	Approximately 4 years and 3 months prior to the study entry
Cancer therapy	Adjuvant	Docetaxel (4 cycles)	Approximately 3 years and 7 months prior to the study entry	Approximately 3 years prior to the study entry
Radiotherapy	Adjuvant	Left supraclavicular fossa and level III of the axilla (dose: unknown)	Approximately 2 years and 11 months prior to the study entry	Approximately 2 years and 10 months prior to the study entry
Cancer therapy	Adjuvant	Paclitaxel nanoparticle albumin-bound and carboplatin (6 cycles each)	−784	−630

No medical or surgical history and concurrent conditions were reported.

At screening, the patient's ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medication ongoing at Study Day 1 included vitamin D (unspecified).

On Study Day 134, the patient developed Grade 1 neuropathy peripheral (non-serious, related to paclitaxel; symptoms not reported). No treatment was administered for this event.

Event: Neuropathy peripheral (Peripheral neuropathy)

Prior to the event of neuropathy peripheral, the most recent dose of paclitaxel, ipatasertib (400 mg) and atezolizumab was administered on Study Day 176

On Study Day 177, the ongoing event of neuropathy peripheral worsened to Grade 2 (signs and symptoms not reported). No treatment was reported for the event. The event of neuropathy peripheral remained unresolved at the time of study discontinuation.

Due to the event of neuropathy peripheral, there was no change in study treatment with ipatasertib and atezolizumab; however, paclitaxel was permanently discontinued with the last dose administered on Study Day 190.

The Investigator considered neuropathy peripheral to be related to paclitaxel and unrelated to ipatasertib and atezolizumab.

On Study Day 475, a radiographic response assessment showed disease progression with new lesions in bone (intrathecal metastases in lumbar spine).

On the same day (Study Day 475), study treatment with atezolizumab and ipatasertib was permanently discontinued due to disease progression with the last dose of atezolizumab administered on Study Day 442 and ipatasertib on Study Day 448. The patient entered into long-term follow-up.

On Study Day 728, the patient was permanently discontinued from the study as LTFU was terminated by Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Constipation	1	Non-serious	3	Unresolved	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	4	Unresolved	Related	Unrelated	Unrelated
Toothache	1	Non-serious	10	Unresolved	Unrelated	Unrelated	Unrelated
Rash erythematous	2	Non-serious	13	20	Related	Unrelated	Unrelated
Periorbital edema	1	Non-serious	16	Unresolved	Related	Unrelated	Unrelated
Pruritis	1	Non-serious	22	300	Related	Unrelated	Unrelated
Rash erythematous	1	Non-serious	22	29	Related	Unrelated	Unrelated
Mouth ulceration	1	Non-serious	24	36	Unrelated	Related	Unrelated

Event	Most extreme grade	Serious/Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Insomnia	1	Non-serious	33	Unresolved	Unrelated	Unrelated	Unrelated
Rash	1	Non-serious	37	39	Related	Unrelated	Unrelated
Mouth ulceration	1	Non-serious	73	99	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	78	112	Unrelated	Related	Unrelated
Dry eye	1	Non-serious	107	134	Unrelated	Related	Unrelated
Rash	1	Non-serious	134	Unresolved	Related	Unrelated	Unrelated
Decreased appetite	1	Non-serious	148	169	Unrelated	Related	Unrelated
Fatigue	1	Non-serious	148	Unresolved	Unrelated	Related	Unrelated
Nail disorder	1	Non-serious	176	Unresolved	Unrelated	Related	Unrelated
Tooth infection	2	Non-serious	191	199	Unrelated	NA	Unrelated
Oropharyngeal pain	2	Non-serious	193	196	Unrelated	Unrelated	NA
Retinal tear	1	Non-serious	208	Unresolved	Unrelated	NA	Unrelated
Intentional product misuse	NA	Non-serious	253	253	NA	NA	NA
Abdominal pain upper	1	Non-serious	420	Unresolved	Unrelated	NA	NA
Vomiting	1	Non-serious	420	428	Unrelated	NA	Unrelated
Diarrhea	1	Non-serious	420	Resolving	Unrelated	NA	Unrelated

Study Number/CRTN:	CO40016/305629	Patient number	3090
Demographics:	54-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Categories:	Suspected COVID-19 Death due to AE, SAE, AE leading to study treatment discontinuation, COVID-19 SAE		

A narrative for this patient is available in Section 1.1 Narratives for patients who died due to an adverse event(s).

Study Number/CRTN:	CO40016/304792	Patient number	3091
Demographics:	51-year-old Black or African American female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Categories:	Rash SAE, Grade $\geq$ 3 rash		
Event 2 (PT) Categories:	Hypersensitivity SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304332	Patient number	3094
Demographics:	63-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle) + Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Category:	Autoimmune hepatitis AE leading to study treatment discontinuation		

The patient was randomized on Study Day 1.

The patient was diagnosed with ductal, moderately differentiated, ER/PR negative and HER2 negative, metastatic left breast cancer (T3N2M1), on Study Day − 51.

At screening, sites of disease involvement included left breast, right lung S3, lymph nodes (left axillary and interpectoral and right conglomerate of lymph nodes in right lung radix)

No past cancer treatments were reported.

The patient′s medical history included hepatitis B and pneumonia. No surgical history was reported. Concurrent conditions included renal cyst and inguinal hernia.

At screening, the patient′s ECOG Performance Status was 1. At screening, hepatitis B surface antigen, anti-hepatitis B core antibody, and anti-hepatitis C antibody were negative.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

No concomitant medications ongoing on Study Day 1 were reported.

Event: Autoimmune hepatitis

Prior to the event of autoimmune hepatitis, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 348 and ipatasertib (300 mg) on Study Day 356.

On Study Day 362, the patient was noted with Grade 2 alanine aminotransferase increased (non-serious, related) and Grade 1 aspartate aminotransferase increased (non-serious, related to ipatasertib and paclitaxel). On Study Day 365, the event of aspartate aminotransferase

increased was considered resolved. On Study Day 368, the event of alanine aminotransferase increased.

Later, on the same day (Study Day 368), a laboratory work-up showed ALT 267 U/L (normal range: 4-36 U/L), AST 189 U/L (normal range: 8-33 U/L), ALP 399.1 U/L (normal range: 53-141 U/L) and bilirubin 12.6 μmol/L (normal range: 4.27-20.52 μmol/L). The patient was diagnosed with non-serious Grade 3 autoimmune hepatitis. Treatment for the event included methylprednisolone. On Study Day 378, the event of autoimmune hepatitis was considered resolved.

Relevant laboratory work-up:

Study Day	**AST** Normal range : 8-33 U/L	**ALT** Normal range : 4-36 U/L	**Bilirubin** Normal range: 4.27-20.52 μmol/L	**ALP** Normal range: 53-141 U/L	**LDH** Normal range: 225-450 U/L
Screening	16	16	13.4	85.3	484
362	92	97	13	295	482
368	189	267	12.6	399.1	524
371	36	102	11.8	267	358
378	20	39	11	169	390

Due to the event of autoimmune hepatitis, the study treatment with paclitaxel and ipatasertib was interrupted after Study Day 348 and Study Day 356 respectively. The next dose of paclitaxel was given on Study Day 413 and ipatasertib on Study Day 420. Treatment with atezolizumab was permanently discontinued with the last dose administered on Study Day 348.

The Investigator considered autoimmune hepatitis to be unrelated to paclitaxel and ipatasertib and related to atezolizumab and concurrent illness.

On Study Day 441, a radiographic response assessment showed disease progression with new lesions in liver (segment 6).

On Study Day 454, study treatment with ipatasertib and paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel administered on Study Day 434 and ipatasertib on Study Day 440. The patient entered into long-term follow-up.

On Study Day 950, the patient was permanently discontinued from the study as LTFU was terminated by Sponsor.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious/Non-serious**	**Onset day**	**Resolution day / Outcome**	**Causality** (Ipatasertib)	**Causality** (Paclitaxel)	**Causality** (Atezolizumab)
Diarrhea	1	Non-serious	5	5	Unrelated	Unrelated	Unrelated
Hyperthermia	1	Non-serious	7	7	Related	Unrelated	Unrelated
Hyperthermia	1	Non-serious	13	14	Unrelated	Unrelated	Unrelated
Hypertension	2	Non-serious	14	14	Unrelated	Unrelated	Unrelated
Neutropenia	2	Non-serious	15	22	Unrelated	Related	Unrelated
Tonsillitis	2	Non-serious	16	20	Unrelated	Unrelated	Unrelated
Rash erythematous	1	Non-serious	16	18	Unrelated	Unrelated	Related
Alopecia	2	Non-serious	22	Unresolved	Unrelated	Related	Unrelated
Diarrhea	2	Non-serious	30	30	Related	Unrelated	Unrelated
Neutropenia	2	Non-serious	36	43	Unrelated	Related	Unrelated
Diarrhea	2	Non-serious	37	39	Related	Unrelated	Unrelated
Accidental overdose	1	Non-serious	50	56	Unrelated	Unrelated	Unrelated
Neutropenia	2	Non-serious	71	83	Unrelated	Related	Unrelated
Neutropenia	2	Non-serious	98	111	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	120	121	Related	Unrelated	Unrelated
Neutropenia	2	Non-serious	126	138	Unrelated	Related	Unrelated
Neutropenia	2	Non-serious	154	166	Unrelated	Related	Unrelated
Neutropenia	2	Non-serious	238	250	Unrelated	Related	Unrelated

Event	Most extreme grade	Serious/Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Dysphonia	2	Non-serious	263	275	Unrelated	Unrelated	Unrelated
Neuropathy peripheral	2	Non-serious	295	332	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	349	353	Related	Related	Unrelated
Alanine aminotransferase increased	2	Non-serious	362	368	Related	Related	Related
Aspartate aminotransferase increased	1	Non-serious	362	365	Related	Related	Unrelated
Rash	1	Non-serious	381	390	Unrelated	Unrelated	Related
Neutropenia	2	Non-serious	427	434	Unrelated	Related	Unrelated

Study Number/CRTN:	CO40016/318813	Patient number	3101
Demographics:	38-year-old American Indian or Alaska Native female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle) + Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Categories:	Alanine aminotransferase increased AE leading to study treatment discontinuation, AESI: Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Categories:	Aspartate aminotransferase increased AE leading to study treatment discontinuation, AESI: Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Categories:	Blood alkaline phosphatase increased AE leading to study treatment discontinuation, AESI: Grade ≥ 3 hepatotoxicity		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ″other″ moderately differentiated, ER/PR negative and HER2 negative right breast cancer (T3N1M0), approximately 3 years prior to study entry.

On Study Day −49, the patient was diagnosed with metastatic disease with ER/PR status unknown and HER2 status not assessed in metastatic tissue. At screening, sites of disease involvement included lymph nodes (midline retroperitoneum, midline upper pretracheal and left cervical IV), lung (left upper lobe), bilateral ovarian tumor and pelvis (left acetabulum).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Carboplatin and docetaxel (6 cycles each)	Approximately 2 years and 11 months prior to the study entry	−921
Surgery	Curative	Right breast modified radical mastectomy and right lymph node axillary dissection	−874	NA
Radiotherapy	Adjuvant	Right breast (dose: unknown, 25 fractions)	−826	−794

No medical or surgical history and concurrent condition was reported.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

No concomitant medications ongoing on Study Day 1 were reported.

Event 1: Alanine aminotransferase increased
Event 2: Aspartate aminotransferase increased
Event 3: Blood alkaline phosphatase increased (alkaline phosphatase increased)

Prior to the events of alanine aminotransferase increased, aspartate aminotransferase increased, and blood alkaline phosphatase increased, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 29 and ipatasertib (400 mg) on Study Day 35.

On Study Day 36, the patient was noted with non-serious Grade 3 events of alanine aminotransferase increased, aspartate aminotransferase increased, and blood alkaline phosphatase increased with ALT 340 U/L, AST 192 U/L and ALP 701 U/L. On Study Day 39, the event of aspartate aminotransferase increased improved to Grade 2. On Study Day 43, the event of blood alkaline phosphatase increased improved to Grade 2 and alanine aminotransferase increased improved to Grade 1. No treatment was given for these events. On Study Day 43, the event of aspartate aminotransferase increased was considered resolved. On

Study Day 50, alanine aminotransferase increased was considered resolved. On Study Day 150, blood alkaline phosphatase increased was considered resolved.

Relevant chemistry work-up:

Study Day	**AST** Normal range: 0-32 U/L	**ALT** Normal range: 0-33 U/L	**ALP** Normal range: 35-104 U/L	**Bilirubin** Normal range: 0.1-1 mg/dL
Screening	16	11	102	0.28
36	192	340	701	0.45
43	27	70	421	0.28
45	24	46	371	0.33
50	20	27	253	0.48
57	18	19	177	0.23
64	20	19	140	0.26
71	19	16	119	0.22
85	21	16	132	0.25
92	16	12	118	0.3
99	15	11	109	0.29
113	22	16	152	0.29
120	14	10	113	0.16
127	14	11	107	0.13
141	23	12	109	0.27
150	22	12	98	0.24

There was no change in the study treatment with paclitaxel due to the event of blood alkaline phosphatase increased; however, due to the events of alanine aminotransferase increased, aspartate aminotransferase increased, Cycle 2 Day of paclitaxel was not administered and the next dose was given on Study Day 51.

Due to the events of alanine aminotransferase increased, aspartate aminotransferase increased, and blood alkaline phosphatase increased, study treatment with atezolizumab and ipatasertib was permanently discontinued with the last dose administered on Study Day 29 and Study Day 35 respectively.

The Investigator considered alanine aminotransferase increased and aspartate aminotransferase increased, to be related to ipatasertib and atezolizumab and unrelated to paclitaxel.

The Investigator considered blood alkaline phosphatase increased, to be related to ipatasertib and unrelated to paclitaxel and atezolizumab.

On Study Day 145, a radiographic response assessment showed disease progression with new lesions in lymph node (midline para-aortic).

On Study Day 150, study treatment with paclitaxel was permanently discontinued due to disease progression with the last dose of paclitaxel given on Study Day 142. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Cisplatin and gemcitabine (3 cycles each)	151	219
Radiotherapy to left acetabulum bone (dose: 7000 cGy, 7 fractions)	166	172
Capecitabine (2 cycles)	232	267
Doxorubicin and cyclophosphamide (4 cycles each)	270	334

On Study Day 366, the patient died due to COVID-19 infection. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day/ Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Pain in extremity	1	Non-serious	114	140	Unrelated	Unrelated	Unrelated
Hypercalcemia	2	Non-serious	141	Unresolved	NA	Unrelated	NA

1.5 NARRATIVES FOR PATIENTS WHO BECAME PREGNANT WHILE IN THE STUDY

No patient became pregnant while in the study.

1.6 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥3 HYPERGLYCEMIA

Study Number/CRTN:	CO40016/318263	Patient number	3004
Demographics:	63-year-old Asian female		

Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)
Cohort:	Cohort C
Event 1 (PT) Category:	Hyperglycemia Grade ≥ 3 hyperglycemia
Event 2 (PT) Category:	Lymphoedema SAE
Event 3 (PT) Category:	Urinary tract infection SAE
Event 4 (PT) Category:	Febrile neutropenia SAE
Event 5 (PT) Categories:	Pneumonitis SAE, Grade ≥ 2 pneumonitis

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304448	Patient number	3012
Demographics:	58-year-old Asian female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Rash maculo-papular Grade ≥ 3 rash		
Event 2 (PT) Category:	Hyperglycemia (First episode) Grade ≥ 3 hyperglycemia		
Event 3 (PT) Category:	Hyperglycemia (Second episode) Grade ≥ 3 hyperglycemia		
Event 4 (PT) Categories:	Hyperglycemia (Third episode) AE leading to study treatment discontinuation, Grade ≥ 3 hyperglycemia		
Event 5 (PT)	Diabetic ketoacidosis		

Categories:	SAE, AE leading to study treatment discontinuation, Grade ≥ 3 hyperglycemia
Event 6 (PT) Category:	Hyperglycemia (Fourth episode) Grade ≥ 3 hyperglycemia
Event 7 (PT) Categories:	Hyperglycemia (Fifth episode) AE leading to study treatment discontinuation, Grade ≥ 3 hyperglycemia

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304880	Patient number	3014
Demographics:	65-year-old Asian female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Hyperglycemia Grade ≥ 3 hyperglycemia		
Event 3 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		

A narrative for this patient is available in Section 1.4 Narratives for patients who discontinued study treatment due to an adverse event.

Study Number/CRTN:	CO40016/304787	Patient number	3052
Demographics:	59-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		

Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea
Event 2 (PT) Category:	Diarrhea (second episode) Grade ≥ 3 diarrhea
Event 3 (PT) Category:	Hyperglycemia Grade ≥ 3 hyperglycemia
Event 4 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER2 negative, locally advanced unresectable right breast cancer (T3N1M0) on Study Day − 62.

At screening sites of disease involvement included breast (right lateral upper quadrant and right skin thickening) and lymph nodes (right axillary).

No past cancer treatments were reported.

No medical or surgical history was reported. The patient′s concurrent conditions included constipation, hypertension, glaucoma, rhinitis allergic, intervertebral disc protrusion and epilepsy.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medications ongoing at Study Day 1 included losartan, acetylsalicylic acid, carbamazepine, hydrochlorothiazide, and lamotrigine.

The patient received loperamide prophylactically (total daily dose: 4 mg, PO) for diarrhea from Study Day 1 to Study Day 15.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of atezolizumab was administered on Study Day 1, paclitaxel on Study Day 8 and ipatasertib (400 mg) on Study Day 10.

On Study Day 11, the patient experienced non-serious Grade 3 diarrhea. No diagnostic test was reported. Treatment with loperamide was maintained (details in the table below). On Study Day 12, the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	1	15
Diarrhea	8	PO	16	19
Diarrhea	12	PO	20	20
Diarrhea	4	PO	21	21
Diarrhea	4	PO	29	35
Diarrhea	4	PO	37	38
Diarrhea	2	PO	39	40
Diarrhea	2	PO	42	44
Diarrhea	2	PO	46	47
Diarrhea	2	PO	58	68
Diarrhea	2	PO	70	71
Diarrhea	4	PO	74	74
Diarrhea	2	PO	76	76
Diarrhea	4	PO	93	94
Diarrhea	4	PO	96	100
Diarrhea	4	PO	103	104
Diarrhea	4	PO	115	124
Diarrhea	4	PO	126	126
Diarrhea	4	PO	128	130
Diarrhea	4	PO	143	144
Diarrhea	4	PO	146	146
Diarrhea	4	PO	148	149

There was no change in study treatment due to the event of diarrhea.

The Investigator considered diarrhea, to be related to ipatasertib, and unrelated to paclitaxel and atezolizumab.

On Study Day 13, the patient experienced Grade 2 diarrhea (non-serious, related to ipatasertib). Treatment with loperamide was maintained (details in the table above).

Event 2: Diarrhea (Grade 3; second episode)

Prior to the event of diarrhea (second Grade 3 episode), the most recent dose of atezolizumab was administered on Study Day 1, paclitaxel on Study Day 8 and ipatasertib (400 mg) on Study Day 14.

On Study Day 15, the ongoing event of diarrhea worsened to non-serious Grade 3. No diagnostic test was reported. Treatment with loperamide was maintained (details in the table above). On Study Day 19, the event of Grade 3 diarrhea improved to Grade 2.

There was no change in study treatment due to the event of diarrhea.

The Investigator considered diarrhea, to be related to ipatasertib, and unrelated to paclitaxel and atezolizumab.

On Study Day 44, the Grade 2event of diarrhea was considered resolved.

Event 3: Hyperglycemia

Prior to the event of hyperglycemia, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 114 and ipatasertib (400 mg) on Study Day 119.

On Study Day 120, the patient′s laboratory work-up showed blood glucose: 408 mg/dL (normal range: 70-99 mg/dL) and she was diagnosed with non-serious Grade 2 (initial intensity) hyperglycemia. Hyperglycemia grade changes are reported in the table below. She received treatment with metformin (details in the table below). On Study Day 169, the event of hyperglycemia was considered resolved.

Due to the event of hyperglycemia, there was no change in study treatment with paclitaxel and atezolizumab, however, study treatment ipatasertib dose was reduced to 300 mg on Study Day 142.

The Investigator considered hyperglycemia, to be related to ipatasertib, paclitaxel and atezolizumab.

Hyperglycemia grade changes:

Study Day	Hyperglycemia grade changes
142	1
148	2
155	3
169	1

Hyperglycemia treatment details:

Treatment	Indication	Dose (Units: mg)	Route	Frequency	Start day	Stop day
Metformin	Hyperglycemia	850	PO	BID	121	Ongoing

Relevant laboratory work-up:

Study Day	Glucose Normal range: 70-99 mg/dL)	HbA1c Normal range: 4-5.7%
Screening (−9)	89	5.5
120	408	—
127	327	—
141	153	—
142	—	9.3
148	191	—
155	257	—
169	90	7.6

Event 4: Alanine aminotransferase increased (Increased ALT)

Prior to the event of alanine aminotransferase increased, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 142 and ipatasertib (300 mg) on Study Day 147.

On Study Day 148, the patient′s laboratory work-up showed AST 104 U/L (normal range 5-34 U/L), ALT 247.0 U/L (normal range 8-42 U/L), total bilirubin 1.45 mg/dL (normal range: 0-1 mg/dL) and ALP 186.0 U/L (normal range: 30-105 U/L) leading to diagnosis of non-serious Grade 3 (initial intensity) alanine aminotransferase increased, Grade 1 aspartate aminotransferase increased, Grade 1 blood alkaline phosphatase increased, and Grade 1 blood bilirubin increased (all non-serious, related). Relevant laboratory work-up is reported in the table below. Unspecified treatment was administered for the events of alanine aminotransferase increased and aspartate aminotransferase increased. On Study Day 155, the events of aspartate aminotransferase increased, and blood bilirubin increased were considered resolved. On Study Day 169, the event of blood alkaline phosphatase increased was considered resolved. The event of alanine aminotransferase increased was resolving at the time of study discontinuation.

Alanine aminotransferase increased grade changes:

Study Day	Alanine aminotransferase increased grade changes
155	2
169	1
176	3
183	1
197	2
211	1

Relevant laboratory work-up:

Study Day	**AST** Normal range 5-34 U/L	**ALT** Normal range 8-42 U/L	**Total bilirubin** Normal range: 0-1 mg/dL	**ALP** Normal range: 30-105 U/L
Screening (– 9)	27.0	42.0	0.59	83.0
148	104.0	247.0	1.45	186.0
155	55.0	114.0	0.92	210.0
169	28.0	54.0	1.07	107.0
176	79.0	301.0	1.10	151.0
183	18.0	71	1.07	138.0
197	36.0	126.0	1.14	124.0
211	52.0	55.0	0.81	135.0

Due to the event of alanine aminotransferase increased, there was no change in study treatment with paclitaxel and atezolizumab, however, study treatment with ipatasertib was interrupted on Study Day 149 and was resumed on Study Day 170.

The Investigator considered alanine aminotransferase increased, to be related to ipatasertib, paclitaxel and atezolizumab.

On Study Day 176, the patient was noted with Grade 1 blood alkaline phosphate increased, Grade 1 aspartate aminotransferase increased, and Grade 1 blood bilirubin increased (all non-serious, unrelated; lab work up in the table above). On Study Day 183, the event of aspartate aminotransferase increased was considered resolved. On Study Day 211, the event of blood bilirubin was considered resolved. The event of blood alkaline phosphate increased was resolving at the time of study discontinuation.

On Study Day 188, a radiographic response assessment showed disease progression with new lesions in right breast (right side top square and right side upper square quadrant, injury flow).

On Study Day 213, study treatment was permanently discontinued due to disease progression with last dose of paclitaxel and atezolizumab administered on Study Day 184 and ipatasertib on Study Day 190. The patient entered into long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
'Other' curative surgery of right breast	234	NA
Radiotherapy to breast (right breast and supraclavicular fossa) (dose: 5000 cGy and 200 fractions)	275	324

On Study Day 395, the patient lost to follow-up.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Nausea	1	Non-serious	30	Resolving	Related	Related	Related
Asthenia	1	Non-serious	58	58	Unrelated	Related	Unrelated
Tremor	1	Non-serious	58	58	Unrelated	Related	Unrelated
Hyperhidrosis	1	Non-serious	58	58	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	93	98	Related	Related	Related
Aspartate aminotransferase increased	1	Non-serious	99	113	Related	Related	Related
Alanine aminotransferase increased	2	Non-serious	99	141	Related	Related	Related
Abdominal pain	3	Non-serious	101	110	Related	Related	Related
Myalgia	1	Non-serious	115	136	Related	Related	Related
Neutropenia	2	Non-serious	127	141	Related	Related	Related
Pruritus	1	Non-serious	142	158	Related	Related	Related
Vomiting	2	Non-serious	145	146	Related	Related	Related

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Hyperglycemia	1	Non-serious	176	Resolving	Related	Related	Related

Study Number/CRTN:	CO40016/319619	Patient number	3062
Demographics:	52-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Blood glucose increased Grade ≥ 3 hyperglycemia		
Event 2 (PT) Category:	Diabetes mellitus Grade ≥ 3 hyperglycemia		
Additional category:	Death due to disease progression		

A narrative for this patient is available in Section 1.2 Narratives for patients who died due to disease progression.

1.7 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥3 DIARRHEA

Study Number/CRTN:	CO40016/319067	Patient number	3001
Demographics:	55-year-old female (race unknown)		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Categories:	Dystonia SAE, AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Mixed connective tissue disease AE leading to study treatment discontinuation		
Event 3 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		

Event 4 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea
Event 5 (PT) Category:	Skin infection SAE
Event 6 (PT) Category:	Vomiting SAE
Event 7 (PT) Categories:	Alanine aminotransferase increased SAE, Grade ≥ 3 hepatotoxicity
Event 8 (PT) Categories:	Aspartate aminotransferase increased SAE, Grade ≥ 3 hepatotoxicity

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304784	Patient number	3005
Demographics:	45-year-old White female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, histological grade unknown, ER/PR negative and HER2 negative left breast cancer (TXNXM1) on Study Day − 85.

At screening sites of disease involvement included lymph node (left supraclavicular, left axillary enlargement and right supraclavicular) and left breast quadrants.

No past cancer treatments are reported.

The patient′s medical history included constipation. No surgical history was reported. Concurrent conditions included hypertension, anxiety, abdominal pain upper, hypothyroidism, headache, left breast pain, abdominal pain, hepatomegaly, and hepatic steatosis.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included fluoxetine, levothyroxine, Olmesartan, hydrochlorothiazide, tramadol and metamizole.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 1 and ipatasertib (400 mg) on Study Day 6.

On Study Day 6, the patient experienced first episode of non-serious Grade 1 diarrhea. On the following day (Study Day 7), the event of diarrhea worsened to Grade 3. She received treatment with loperamide (details reported in the table below). On Study Day 9, the event of diarrhea improved to Grade 2. On Study Day 11, diarrhea was improved to Grade 1. On Study Day 12, the first episode of diarrhea was considered resolved.

Due to the event of diarrhea, there was no change in the study treatment with atezolizumab and paclitaxel. However, study treatment with ipatasertib was interrupted on Study Day 8 and the next dose was administered on Study Day 29 at a reduced dose of 300 mg from 400 mg.

The Investigator considered diarrhea to be unrelated to paclitaxel and atezolizumab and related to ipatasertib and other causes (unspecified).

On Study Day 46, the patient experienced Grade 2 diarrhea (non-serious, related to ipatasertib). She received treatment with loperamide. On the following day (Study Day 47), the event of diarrhea was considered resolved.

On Study Day 66, the patient experienced another episode of Grade 2 diarrhea (non-serious, unrelated). She received treatment with loperamide. On Study Day 68, diarrhea was considered resolved.

Event 2: Diarrhea

Prior to the event of diarrhea, the most recent dose of atezolizumab was administered on Study Day 58, paclitaxel on Study Day 65 and ipatasertib (300 mg) on Study Day 71.

On Study Day 70, the patient experienced non-serious Grade 2 diarrhea. On Study Day 71, the event pf diarrhea worsened to Grade 3. She received treatment with loperamide. On Study Day 72, the event of diarrhea improved to Grade 1 and later on the same day (Study Day 72), the event of diarrhea was considered resolved.

Loperamide details:

Indication	Loperamide daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	Loperamide	PO	7	12
Diarrhea	Loperamide	PO	46	47
Diarrhea	Loperamide	PO	66	67
Diarrhea	Loperamide	PO	68	68
Diarrhea	Loperamide	PO	70	70
Diarrhea	Loperamide	PO	71	71
Diarrhea	Loperamide	PO	72	72

Due to the event of diarrhea, study treatment with atezolizumab was interrupted on Study Day 58, paclitaxel on Study Day 65 and ipatasertib on Study Day 71 and later never resumed due to disease progression (see narrative below).

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel and atezolizumab.

On Study Day 115, an overall response assessment showed disease progression with new lesions in bilateral sparse hypo vascular nodules and bone minor oval lesions on lumbar vertebral bodies and right iliac bone.

Study treatment was permanently discontinued due to disease progression with the last dose atezolizumab administered on Study Day 58, paclitaxel on Study Day 65 and ipatasertib on Study Day 71. The patient then entered the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Cyclophosphamide and doxorubicin (6 cycles each)	124	213
Surgery for left breast	324	—
Left plastron breast and left supraclavicular fossa (dose: 30 cGy, 10 fractions)	399	412
Brain (dose: 30 cGy, 10 fractions)	409	412
Gemcitabine and carboplatin (single cycle each)	444	444

On Study Day 455, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Erythema	2	Non-serious	1	1	Unrelated	Unrelated	Related
Oxygen saturation decreased	1	Non-serious	1	1	Unrelated	Unrelated	Related s
Tremor	2	Non-serious	1	1	Unrelated	Unrelated	Unrelated
Vision blurred	2	Non-serious	1	1	Unrelated	Unrelated	Related
Dizziness	2	Non-serious	1	1	Unrelated	Unrelated	Related
Amenorrhea	1	Non-serious	11	Resolving	Unrelated	Unrelated	Related
Pyrexia	1	Non-serious	14	14	Unrelated	Unrelated	Unrelated
Alopecia	1	Non-serious	19	Resolving	Unrelated	Unrelated	Related
Cough	2	Non-serious	59	86	Unrelated	Unrelated	Unrelated
Insomnia	2	Non-serious	25	29	Unrelated	Unrelated	Unrelated
Pneumonia	2	Non-serious	73	83	Unrelated	Unrelated	Unrelated
Dyspnea	2	Non-serious	73	Resolving	Unrelated	Unrelated	Unrelated
Tumor pain	2	Non-serious	82	Resolving	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/305639	Patient number	3016
Demographics:	62-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Peripheral motor neuropathy AE leading to study treatment discontinuation		

Event 3 (PT) Category:	Fatigue AE leading to study treatment discontinuation
Event 4 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity
Event 5 (PT) Categories:	Cardiac arrest Death due to adverse event, SAE

A narrative for this patient is available in Section 1.1 Narratives for patients who died due to an adverse event(s).

Study Number/CRTN:	CO40016/306603	Patient number	3024
Demographics:	49-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Gastroenteritis norovirus SAE		
Event 2 (PT) Category:	Aspartate aminotransferase increased Grade ≥3 hepatotoxicity		
Event 3 (PT) Category:	Diarrhea Grade ≥3 diarrhea		
Event 4 (PT) Category:	Pyrexia SAE		
Event 5 (PT) Category:	Hypertransaminasaemia SAE		
Event 6 (PT) Category:	Fatigue SAE		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/318721	Patient number	3030
Demographics:	71-year-old female (Race unknown)		

Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)
Cohort:	Cohort C
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea
Event 2 (PT) Categories:	Autoimmune hepatitis SAE, AE leading to Study treatment discontinuation

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/318144	Patient number	3032
Demographics:	67-year-old female (Race unknown)		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was diagnosed with tubular, poorly differentiated, ER/PR and HER 2 negative, metastatic, locally advanced unresectable left breast cancer (T4dN3M0) on Study Day -64.

At screening sites of disease involvement included left breast and lymph node (left axillary and left retro pectoral).

Past cancer treatment is listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Radiotherapy	Other	Left breast (20 cGy, 5 fractions)	-30	-14

The patient's medical history included lymphocyte count decreased, amylase increased, Grade 1 hypocalcemia and tumor hemorrhage. No surgical history was reported. Concurrent conditions included hypothyroidism and anemia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab. On the same day (Study Day 1), she started loperamide prophylactically (total daily dose: 4 mg, details in the table below).

No concomitant medication ongoing at Study Day 1 was reported.

The patient experienced multiple non-serious events of diarrhea (details in the AEs table below) from Study Day 6 to Study Day 74 and she received loperamide for these events (details in the AE table below).

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 71 and ipatasertib (400 mg) on Study Day 74.

On Study Day 75, the patient experienced non-serious Grade 3 diarrhea. No laboratory test was performed. She received treatment with loperamide (details in the table below). On the same day (Study Day 75), the event of diarrhea was considered resolved.

Due to the event of diarrhea, there was no change in study treatment with atezolizumab, however, study treatment with ipatasertib was first interrupted from Study Day 75 to Study Day 78, and later was reduced to 300 mg on Study Day 85.

The Investigator considered diarrhea to be related to ipatasertib and atezolizumab and unrelated to paclitaxel.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	1	136

On Study Day 190, study treatment was permanently discontinued as per physician′s decision (the patient responded to the study treatment but after re-evaluation she was eligible for breast surgery) with the last dose of paclitaxel and atezolizumab administered on Study Day 155 and ipatasertib on Study Day 161. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Unspecified curative surgery of right 'other'	196	NA
Capecitabine	266	482
Radiotherapy to right chest (breast) (dose: 180 cGy and 25 fractions)	302	345

On Study Day 828, the patient was discontinued from the study as study was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipataseritib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Anemia	2	Non-serious	1	8	NA	NA	Unrelated
Tri-iodothyronine increased	1	Non-serious	1	57	Unrelated	Unrelated	Unrelated
Hypocalcemia	1	Non-serious	1	29	Unrelated	Unrelated	Unrelated
Myalgia	1	Non-serious	2	5	NA	Related	NA
Nausea	1	Non-serious	5	5	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	6	7	Related	Unrelated	Unrelated
Anemia	1	Non-serious	8	15	NA	NA	Unrelated
Hyperglycemia	1	Non-serious	8	15	Related	Unrelated	Unrelated
Diarrhea	1	Non-serious	10	24	Related	Unrelated	Unrelated
Urinary tract infection	2	Non-serious	10	29	Unrelated	Unrelated	Related
Lymphopenia	3	Non-serious	15	29	Unrelated	Related	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Leukopenia	1	Non-serious	15	29	Related	Related	Related
Hypokalemia	1	Non-serious	15	15	Unrelated	Unrelated	Unrelated
Anemia	2	Non-serious	15	Unresolved	Related	Related	Related
Vomiting	1	Non-serious	29	29	Related	Related	Related
Lymphopenia	2	Non-serious	29	64	NA	NA	Unrelated
Blood lactate dehydrogenase increased	1	Non-serious	36	43	Unrelated	Unrelated	Unrelated
Alopecia	2	Non-serious	37	Resolving	Unrelated	Related	Unrelated
Breast pain	1	Non-serious	40	40	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	41	49	Related	Unrelated	Unrelated
Lipase increased	3	Non-serious	57	85	Related	Related	Related
Blood lactate dehydrogenase decreased	1	Non-serious	57	64	NA	NA	Unrelated
Diarrhea	2	Non-serious	68	74	Related	Unrelated	Unrelated
Hyperglycemia	1	Non-serious	71	85	Related	Unrelated	Unrelated
Eosinophilia	1	Non-serious	71	85	Related	Related	Related
Lymphopenia	2	Non-serious	71	92	Related	Related	Related
Mean cell volume decreased	2	Non-serious	71	92	Unrelated	Unrelated	Unrelated
Hypocalcemia	1	Non-serious	85	92	Unrelated	Unrelated	Unrelated
Eosinophilia	1	Non-serious	92	113	Related	Related	Related

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Lymphopenia	2	Non-serious	92	113	Related	Related	Related
Diarrhea	2	Non-serious	96	97	Unrelated	Unrelated	Unrelated
Pyrexia	1	Non-serious	99	99	Unrelated	Unrelated	Unrelated
Eosinophilia	1	Non-serious	120	141	Related	Related	Related

Study Number/CRTN:	CO40016/304787	Patient number	3034
Demographics:	46-year-old female (Unknown race)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 3 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR negative and HER2 negative left breast cancer (T3N0M0), on Study Day − 204.

The patient was diagnosed with metastatic disease on an unknown day with ER /PR negative and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included left breast (lateral upper quadrant).

No past cancer treatment was reported.

No medical/surgical history was reported. No concurrent conditions were reported.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 was reported.

Event 1: Diarrhea

Prior to the event of diarrhea, the most recent dose of atezolizumab was administered on Study Day 198, paclitaxel on Study Day 205 and ipatasertib (400 mg) on Study Day 207.

On Study Day 208, the patient experienced non-serious Grade 3 diarrhea. She received treatment with loperamide. On Study Day 211, the event of diarrhea was considered resolved.

There was no change in the study treatment due to the event of diarrhea.

The Investigator considered diarrhea to be related to atezolizumab, paclitaxel and ipatasertib.

Event 2: Diarrhea

Prior to the second Grade 3 event of diarrhea, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 212 and ipatasertib (400 mg) on Study Day 213.

On Study Day 214, the patient experienced Grade 3 diarrhea. She experienced approximately 8 episodes of diarrhea and received treatment with loperamide. On Study Day 218, the event of diarrhea was considered resolved.

There was no change in the study treatment with atezolizumab and paclitaxel due to this event; however, study treatment with ipatasertib was reduced from 400 mg to 300 mg on Study Day 226.

The Investigator considered event of diarrhea to be related to atezolizumab, paclitaxel and ipatasertib.

On Study Day 371, the patient experienced Grade 1 diarrhea (non-serious, related). On Study Day 372, the event of diarrhea worsened to Grade 2. She received treatment with loperamide. On Study Day 378, the event of diarrhea was considered resolved.

Event 3: Diarrhea

Prior to the third Grade 3 event of diarrhea, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 422 and ipatasertib (300 mg) on Study Day 424.

On Study Day 425, the patient experienced non-serious Grade 1 diarrhea. On Study Day 433, the event of diarrhea worsened to Grade 3. She was oriented to maintain anti-diarrheal diet,

water intake and received treatment with loperamide. On Study Day 441, the event of diarrhea was considered resolved.

Loperamide details:

Indication	Loperamide daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	2	13
Diarrhea	4	PO	15	27
Diarrhea	4	PO	30	51
Diarrhea	4	PO	71	85
Diarrhea	4	PO	90	106
Diarrhea	4	PO	114	115
Diarrhea	4	PO	119	122
Diarrhea	4	PO	125	126
Diarrhea	4	PO	128	128
Diarrhea	16	PO	208	211
Diarrhea	4	PO	212	212
Diarrhea	4	PO	214	220
Diarrhea	4	PO	371	372
Diarrhea	4	PO	374	378
Diarrhea	8	PO	425	450

Due to the event of diarrhea, Cycle 16 Day 15 and Cycle 17 Day 1 of paclitaxel and atezolizumab was not administered, and study treatment with ipatasertib was interrupted on Study Day 436. The next dose of paclitaxel and ipatasertib was given on Study Day 457 and atezolizumab on Study Day 464.

The Investigator considered event of diarrhea to be related to atezolizumab, paclitaxel and ipatasertib.

On Study Day 611, study treatment was permanently discontinued as per physician′s decision (due to low adherence to the protocol and the patient's desire to interrupt treatment) with the last dose of paclitaxel and atezolizumab given on Study Day 562 and ipatasertib on Study Day 582. The patient entered into the long-term follow-up.

On Study Day 797, the patient was discontinued from the study as study was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Accidental overdose	1	Non-serious	22	22	Related	Unrelated	Unrelated
Diarrhea	2	Non-serious	91	93	Unrelated	Related	Related
Neuropathy peripheral	1	Non-serious	127	146	Related	Related	Related
Oedema peripheral	1	Non-serious	130	147	Related	Related	Related
Headache	1	Non-serious	194	199	Related	Related	Related
Pain in extremity	1	Non-serious	194	461	Related	Related	Related
Dyslipidemia	2	Non-serious	225	Resolving	Unrelated	Unrelated	Unrelated
Headache	2	Non-serious	234	238	Related	Related	Related
Headache	1	Non-serious	243	243	Related	Related	Related
Headache	1	Non-serious	252	253	Related	Related	Related
Pyrexia	1	Non-serious	261	265	Unrelated	Unrelated	Unrelated
Asthenia	2	Non-serious	261	287	Unrelated	Unrelated	Unrelated
Tremor	1	Non-serious	261	261	Unrelated	Unrelated	Unrelated
Pain	1	Non-serious	262	302	Unrelated	Unrelated	Unrelated
Pruritus	1	Non-serious	265	274	Unrelated	Unrelated	Unrelated
Hyperglycemia	1	Non-serious	267	281	Related	Related	Related
Aspartate aminotransferase increased	2	Non-serious	267	282	Related	Related	Related
Alanine aminotransferase increased	1	Non-serious	267	281	Related	Related	Related
Pyrexia	1	Non-serious	298	301	Related	Related	Related
Spinal pain	2	Non-serious	318	461	Unrelated	Unrelated	Unrelated
Pain in extremity	2	Non-serious	318	461	Unrelated	Unrelated	Unrelated

Anemia	1	Non-serious	351	414	Related	Related	Related
Rhinitis	1	Non-serious	400	400	Unrelated	Unrelated	Unrelated
Neuropathy peripheral	2	Non-serious	402	461	Related	Related	Related
Anemia	1	Non-serious	421	428	Related	Related	Related
Blood alkaline phosphatase increased	1	Non-serious	421	428	Related	Related	Related
Blood alkaline phosphatase increased	1	Non-serious	449	456	Related	Related	Related
Blood alkaline phosphatase increased	1	Non-serious	505	Resolving	Related	Related	Related
Arthralgia	2	Non-serious	506	580	Unrelated	Unrelated	Unrelated
Spinal pain	2	Non-serious	506	580	Unrelated	Unrelated	Unrelated
Anemia	1	Non-serious	519	Resolving	Related	Related	Related
Leukopenia	1	Non-serious	519	590	Related	Related	Related
Headache	2	Non-serious	534	566	Unrelated	Unrelated	Unrelated
Asthenia	2	Non-serious	562	Resolving	Related	Related	Related
Nausea	1	Non-serious	562	568	Related	Related	Related
Vomiting	1	Non-serious	567	568	Related	Related	Related
Vertigo	2	Non-serious	577	Resolving	Related	Related	Related

Study Number/CRTN:	CO40016/304787	Patient number	3037
Demographics:	48-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with mucinous, ER/PR negative and HER2 negative left breast cancer (T4bN1M1) on Study Day − 43.

At screening, sites of disease involvement included liver (right lobe liver, segment VII and segment VIII), breast left (peri areolar thickening of the skin), and liver (segment V, transition between segments VII and VIII and segment VI).

No past cancer treatments are reported.

No medical/surgical history was reported. No concurrent conditions were reported.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, atezolizumab and paclitaxel.

Concomitant medications ongoing at Study Day 1 included zolpidem and escitalopram.

Prior to the event of diarrhea, the patient was noted with multiple events of diarrhea (please refer to table below for details). She received treatment with loperamide.

Event	Most extreme grade	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Diarrhea	1	38	41	Related	Related	Related
Diarrhea	2	42	43	Related	Unrelated	Unrelated
Diarrhea	2	50	50	Related	Unrelated	Unrelated
Diarrhea	2	72	72	Related	Unrelated	Unrelated
Diarrhea	2	76	77	Related	Unrelated	Unrelated

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of atezolizumab was administered on Study Day 86, paclitaxel on Study Day 93 and ipatasertib (400 mg) on Study Day 97.

On Study Day 98, the patient experienced non-serious Grade 3 diarrhea. Grade change during the event course is reported in the table below. She received treatment with loperamide. On Study Day 107, the event of diarrhea was considered resolved.

Loperamide details:

Indication	Loperamide daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	Loperamide	PO	2	4
Diarrhea	Loperamide	PO	8	28
Diarrhea	Loperamide	PO	32	44
Diarrhea	Loperamide	PO	46	46
Diarrhea	Loperamide	PO	72	77
Diarrhea	Loperamide	PO	79	79
Diarrhea	Loperamide	PO	87	87
Diarrhea	Loperamide	PO	98	107
Diarrhea	Loperamide	PO	98	98
Diarrhea	Loperamide	PO	101	106
Diarrhea	Loperamide	PO	143	163

Relevant grade changes reported in the table below:

Event	Study Day	Grade change
Diarrhea	99	2
Diarrhea	106	3
Diarrhea	107	2

There was no change in the study treatment due to the event of diarrhea.

The Investigator considered diarrhea to be related to atezolizumab, paclitaxel and ipatasertib.

On Study Day 132, a radiographic response assessment showed disease progression with new lesion in bone (lytic lesion in T4 and T5, L1 and right iliac wing, dorsal 5, 6 E 11 E, and low back 1).

On Study Day 213, study treatment with ipatasertib, atezolizumab, paclitaxel and was permanently discontinued due to disease progression with the last dose of ipatasertib administered on Study Day 171, atezolizumab, and paclitaxel on Study Day 185. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Capecitabine and zoledronic acid	210	Ongoing
Radiotherapy (thoracic and lumbar spine) (dose: 2000 cGy; 5 fractions)	279	287

On Study Day 790, the patient was discontinued from the study as study was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Infusion related reaction	1	Non-serious	1	1	Unrelated	Related	Unrelated
Diarrhea	2	Non-serious	144	145	Related	Related	Related
Diarrhea	2	Non-serious	148	156	Related	Related	Related
Diarrhea	1	Non-serious	180	183	Related	Unrelated	Unrelated

Study Number/CRTN:	CO40016/318144	Patient number	3047
Demographics:	83-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Categories:	Diarrhea SAE, Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Gamma-glutamyl transferase increased Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Category:	Nausea SAE		
Event 4 (PT) Categories:	Pneumonitis SAE, AE leading to study treatment discontinuation, Grade ≥ 2 pneumonitis		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/318146	Patient number	3049
Demographics:	34-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR negative and HER2 negative right breast cancer (T3N0M0), approximately 2 years and 4 months, prior to study entry.

The patient was diagnosed with metastatic disease on Study Day − 58 with ER /PR negative and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included liver (nodule in segment VI and other nodules) and lymph node (enlargement in hepatic hilo).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Doxorubicin and cyclophosphamide (4 cycles each)	Approximately 2 years and 3 months prior to study entry	Approximately 2 years and 1 months prior to study entry
Cancer therapy	Neoadjuvant	Paclitaxel (12 cycles)	Approximately 2 years prior to study entry	Approximately 1 years and 10 months prior to study entry
Surgery	Curative	Right radical mastectomy and right axillary dissection	Approximately 1 years and 8 months prior to study entry	−
Cancer therapy	Adjuvant	Capecitabine (6 cycles)	Approximately 1 years and 7 months prior to study entry	Approximately 1 years and 2 months prior to study entry
Radiotherapy	Adjuvant	Breast and supraclavicular fossa (dose: 50 cGy; 28 fractions)	Approximately 1 years and 6 months prior to study entry	Approximately 1 years and 4 months prior to study entry

The patient′s medical history included appendicitis. No surgical history was reported. Concurrent conditions included depression, abdominal pain upper and insomnia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

Concomitant medications ongoing at Study Day 1 included zolpidem, sertraline, metamizole and gabapentin.

On Study Day 68, the patient was diagnosed with Grade 1 diarrhea (non-serious, related to ipatasertib). No treatment was reported for this event. Later, on the same day, the event of diarrhea was considered resolved.

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 97 and ipatasertib (400 mg) on Study Day 104.

On Study Day 105, the patient was diagnosed with non-serious Grade 3 diarrhea. Unspecified treatment was given for the event. Later, on the same day (Study Day 105), the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	2	5
Diarrhea	4	PO	6	20
Diarrhea	2	PO	27	27
Diarrhea	6	PO	30	30
Diarrhea	4	PO	31	31
Diarrhea	14	PO	32	32
Diarrhea	4	PO	33	35
Diarrhea	4	PO	37	37
Diarrhea	4	PO	39	39
Diarrhea	4	PO	41	41
Diarrhea	4	PO	44	44
Diarrhea	4	PO	46	47

There was no change in the study treatment due to the event of diarrhea.

The Investigator considered diarrhea to be related to ipatasertib and unrelated to paclitaxel and to atezolizumab.

On Study Day 96, a radiographic response assessment showed disease progression with new lesion in bone (T8 vertebrae).

On Study Day 111, study treatment was permanently discontinued due to disease progression with the last dose of paclitaxel and atezolizumab given on Study Day 97 and ipatasertib on Study Day 104. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	Start Day	Stop Day
Gemcitabine and cisplatin	120	Ongoing

On Study Day 480, the patient was lost to follow-up.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Nausea	1	Non-serious	3	13	Related	Related	Related
Diarrhea	2	Non-serious	4	20	Related	Unrelated	Unrelated
Rash	1	Non-serious	8	Resolving	Related	Unrelated	Unrelated
Fatigue	2	Non-serious	28	Resolving	Related	Related	Related
Abdominal pain	1	Non-serious	32	48	Related	Unrelated	Unrelated
Hypercholesterolemia	1	Non-serious	54	110	Related	Unrelated	Unrelated
Low density lipoprotein increased	1	Non-serious	54	Resolving	Related	Unrelated	Unrelated
Nausea	1	Non-serious	64	Resolving	Related	Related	Related
Decreased appetite	1	Non-serious	108	Resolving	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304664	Patient number	3051
Demographics:	63-year-old White female		

Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)
Cohort:	Cohort C
Event 1 (PT) Categories:	Diarrhea SAE, Grade ≥ 3 diarrhea
Event 2 (PT) Category:	Febrile neutropenia SAE
Event 3 (PT) Category:	Fatigue SAE
Event 4 (PT) Category:	Dehydration SAE
Event 5 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304787	Patient number	3052
Demographics:	59-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Diarrhea (second episode) Grade ≥ 3 diarrhea		
Event 3 (PT) Category:	Hyperglycemia Grade ≥ 3 hyperglycemia		
Event 4 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity		

A narrative for this patient is available in Section 1.6 narratives for patients who experienced Grade ≥ 3 hyperglycemia.

Study Number/CRTN:	CO40016/305113	Patient number	3060
Demographics:	44-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Influenza SAE		
Event 2 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/305247	Patient number	3066
Demographics:	69-year-old female (race unknown)		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Neuropathy peripheral AE leading to study treatment discontinuation		

A narrative for this patient is available in Section 1.4 Narratives for patients who discontinued study treatment due to an adverse event.

Study Number/CRTN:	CO40016/305629	Patient number	3085
Demographics:	58-year-old American Indian or Alaska Native female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		

Cohort:	Cohort C
Event 1 (PT) Categories:	Diarrhea SAE, Grade ≥ 3 diarrhea
Event 2 (PT) Category:	Myositis SAEs
Event 3 (PT) Category:	Myocarditis SAE
Event 4 (PT) Categories:	Pulmonary embolism Death due to adverse event, SAE, AE leading to Study treatment discontinuation

A narrative for this patient is available in Section 1.1 Narratives for patients who died due to an adverse event(s).

Study Number/CRTN:	CO40016/304785	Patient number	3088
Demographics:	51-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Categories:	Aspartate aminotransferase increased AE leading to study treatment discontinuation, Grade ≥ 3 hepatotoxicity		
Event 4 (PT) Categories:	Alanine aminotransferase increased (Second episode) AE leading to study treatment discontinuation, Grade ≥ 3 hepatotoxicity		

A narrative for this patient is available in Section 1.4 Narratives for patients who discontinued study treatment due to an adverse event.

Study Number/CRTN:	CO40016/304787	Patient number	3096

Demographics:	53-year-old White female
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)
Cohort:	Cohort C
Event (PT) Category:	Diarrhea Grade ≥ 3 diarrhea

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated ER/PR negative, and HER2 negative advanced unresectable metastatic left breast cancer (T4bN2M1) on Study Day − 23.

At screening sites of disease involvement included left breast (skin thickening and side quadrant), lymph node (left medial axillary), and lung (right apical segment).

No past cancer treatment was reported.

No medical history/surgical history was reported. No concurrent condition was reported.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 was reported.

Event: Diarrhea

Prior to the event of diarrhea, the most recent dose of atezolizumab was administered on Study Day 281, paclitaxel on Study Day 288, and ipatasertib on Study Day 291 (400 mg).

On Study Day 292, the patient experienced non-serious Grade 3 diarrhea. No relevant diagnostic test was performed. No treatment was given for the event. Later, on the same day (Study Day 292), the event of diarrhea was considered resolved.

Loperamide treatment details:

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	4	PO	1	39
Diarrhea	2	PO	41	49

Indication	Total daily dose (Units: mg)	Route	Start day	Stop day
Diarrhea	2	PO	57	57
Diarrhea	2	PO	85	91
Diarrhea	4	PO	92	105
Diarrhea	2	PO	113	133
Diarrhea	2	PO	141	161
Diarrhea	2	PO	169	189

Due to the event of diarrhea, there was no change in the study treatment with atezolizumab and paclitaxel; however treatment with ipatasertib was interrupted after Study Day 291 and was later never resumed due to symptomatic deterioration (see narrative below).

The Investigator considered diarrhea to be related to atezolizumab, ipatasertib and paclitaxel.

On Study Day 316, symptomatic deterioration assessment showed clinical progression in left breast lesion.

On Study Day 323, study treatment was permanently discontinued due to symptomatic deterioration with the last dose of ipatasertib administered on Study Day 291, paclitaxel, and atezolizumab on Study Day 295. The patient then entered the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Surgery (Tumor related orthopedic intervention)	456	NA
Surgery (left other)	489	NA

On Study Day 643, the patient was discontinued from the study as long-term follow-up was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious/ Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Nausea	1	Non-serious	37	39	Related	Related	Related
Paraesthesia	1	Non-serious	43	59	Related	Related	Related
Edema	1	Non-serious	50	60	Related	Related	Related
Diarrhea	1	Non-serious	92	96	Related	Related	Related
Anemia	1	Non-serious	98	119	Related	Related	Related
Asthenia	1	Non-serious	187	192	Related	Related	Related
Generalized edema	1	Non-serious	187	192	Related	Related	Related
Arthralgia	1	Non-serious	187	192	Related	Related	Related
Diarrhea	1	Non-serious	197	197	Related	Related	Related
Injury	1	Non-serious	248	Resolving	Unrelated	Unrelated	Unrelated
Rash	1	Non-serious	276	288	Related	Related	Related
Influenza	2	Non-serious	302	Resolving	Unrelated	Unrelated	Unrelated

1.8 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥2 COLITIS/ENTEROCOLITIS

No patient experienced Grade ≥ 2 Colitis/Enterocolitis during the protocol defined study period.

1.9 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥3 RASH

Study Number/CRTN:	CO40016/304448	Patient number	3012
Demographics:	58-year-old Asian female		

Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)
Cohort:	Cohort C
Event 1 (PT) Category:	Rash maculo-papular Grade ≥ 3 rash
Event 2 (PT) Category:	Hyperglycemia (First episode) Grade ≥ 3 hyperglycemia
Event 3 (PT) Category:	Hyperglycemia (Second episode) Grade ≥ 3 hyperglycemia
Event 4 (PT) Categories:	Hyperglycemia (Third episode) AE leading to study treatment discontinuation, Grade ≥ 3 hyperglycemia
Event 5 (PT) Categories:	Diabetic ketoacidosis SAE, AE leading to study treatment discontinuation, Grade ≥ 3 hyperglycemia
Event 6 (PT) Category:	Hyperglycemia (Fourth episode) Grade ≥ 3 hyperglycemia
Event 7 (PT) Categories:	Hyperglycemia (Fifth episode) AE leading to study treatment discontinuation, Grade ≥ 3 hyperglycemia

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304663	Patient number	3013
Demographics:	64-year-old female (Race unknown)		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Rash (First episode) Grade ≥ 3 rash		
Event 2 (PT)	Rash (Second episode)		

Category:	Grade ≥ 3 rash

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER 2 negative, left breast cancer (TXN2MX) on Study Day -105.

On Study Day −71, the patient was diagnosed with locally advanced unresectable disease with ER/PR and HER2 negative. At screening sites of disease involvement included lymph nodes (left axillary node, inferior).

No past cancer treatment was reported.

No medical history or surgical history was reported. Concurrent condition included glaucoma.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

Concomitant medication ongoing at Study Day 1 included latanoprost/timolol.

Event 1: Rash (First episode)

Prior to the event of rash (first episode), the most recent dose of atezolizumab was administered on Study Day 1, paclitaxel on Study Day 8, and ipatasertib (400 mg) on Study Day 10.

On Study Day 11, the patient experienced flare, non-serious Grade 1 (initial intensity) rash and Grade 3 pruritus (non-serious, related to ipatasertib and atezolizumab) spreading over her back. She received treatment with prednisone and betamethasone. On Study Day 28, the event of rash worsened to Grade 3. On Study Day 36, the events of rash and pruritis improved to Grade 1. On Study Day 40, the event of pruritus was considered resolved. On Study Day 55, the event of rash (first episode) was considered resolved.

Due to the event of rash (first episode), study treatment with paclitaxel and atezolizumab was interrupted and the next dose was administered on Study Day 57. Dose of ipatasertib was reduced to 300 mg from 400 mg on Study Day 58.

The Investigator considered rash (first episode), to be related to ipatasertib and atezolizumab, and unrelated to paclitaxel.

Event 2: Rash (Second episode)

Prior to the event of rash (second episode), the most recent dose of atezolizumab and paclitaxel was administered on Study Day 113, and ipatasertib (300 mg) on Study Day 114.

On Study Day 115, the patient experienced itchy non-serious Grade 3 skin rash (second episode, site not specified). She received treatment with prednisone for the event of rash. On Study Day 120, the event of rash improved to Grade 1. On Study Day 127, the event of rash was considered resolved.

Due to the event of rash (second episode), there was no change in study treatment with paclitaxel, however, study treatment with ipatasertib and atezolizumab was interrupted. The next dose of ipatasertib was administered on Study Day 168; however, atezolizumab was never resumed as patient withdrew the consent (see narrative below).

The Investigator considered rash (second episode), to be related to ipatasertib and atezolizumab, and unrelated to paclitaxel.

On Study Day 204, the patient withdrew consent from the study. The last dose of atezolizumab was administered on Study Day 113, paclitaxel on Study Day 169 and ipatasertib on Study Day 175.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Diarrhea	1	Non-serious	6	6	Yes	No	—
Pneumonitis	1	Non-serious	109	Unresolved	Yes	Yes	Yes
Rash	1	Non-serious	168	182	Yes	No	NA

Study Number/CRTN:	CO40016/304332	Patient number	3022
Demographics:	57-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Rash papular Grade ≥ 3 rash		
Event 2 (PT) Category:	Autoimmune hepatitis AE leading to study treatment discontinuation		
Event 3 (PT) Category:	Aspartate aminotransferase increased AE leading to study treatment discontinuation		

A narrative for this patient is available in Section 1.4 Narratives for patients who discontinued study treatment due to an adverse event.

Study Number/CRTN:	CO40016/318721	Patient number	3067
Demographics:	58-year-old female (Unknown race)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle)+Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Rash pruritic Grade ≥ 3 rash		
Event 2 (PT) Category:	General physical health deterioration SAE		
Event 3 (PT) Categories:	Covid-19 SAE, COVID-19 SAE		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304792	Patient number	3091
Demographics:	51-year-old Black or African American female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Categories:	Rash SAE, Grade ≥ 3 rash		
Event 2 (PT) Categories:	Hypersensitivity SAE, AE leading to study treatment discontinuation		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

1.10 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥2 PNEUMONITIS

Study Number/CRTN:	CO40016/318263	Patient number	3004
Demographics:	63-year-old Asian female		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Hyperglycemia Grade ≥ 3 hyperglycemia		
Event 2 (PT) Category:	Lymphoedema SAE		
Event 3 (PT) Category:	Urinary tract infection SAE		
Event 4 (PT) Category:	Febrile neutropenia SAE		
Event 5 (PT) Categories:	Pneumonitis SAE, Grade ≥ 2 pneumonitis		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/305145	Patient number	3008
Demographics:	46-year-old Black or African American female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Pneumonitis Grade ≥ 2 pneumonitis		
Event 2 (PT) Category:	Musculoskeletal chest pain SAE		
Event 3 (PT) Category:	Cholecystitis SAE		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/318144	Patient number	3047
Demographics:	83-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Categories:	Diarrhea SAE, Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Gamma-glutamyl transferase increased Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Category:	Nausea SAE		
Event 4 (PT) Categories:	Pneumonitis SAE, AE leading to study treatment discontinuation, Grade ≥ 2 pneumonitis		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304680	Patient number	3081
Demographics:	65-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Blood alkaline phosphatase increased Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Categories:	Immune-mediated lung disease SAE, Grade ≥ 2 pneumonitis		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

1.11 NARRATIVES FOR PATIENTS WHO EXPERIENCED GRADE ≥3 HEPATOTOXICITY

Study Number/CRTN:	CO40016/319067	Patient number	3001
Demographics:	55-year-old female (race unknown)		
Study treatment (Dosage Regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Categories:	Dystonia SAE, AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Mixed connective tissue disease AE leading to study treatment discontinuation		
Event 3 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 4 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 5 (PT) Category:	Skin infection SAE		
Event 6 (PT) Category:	Vomiting SAE		

Event 7 (PT) Categories:	Alanine aminotransferase increased SAE, Grade ≥ 3 hepatotoxicity
Event 8 (PT) Categories:	Aspartate aminotransferase increased SAE, Grade ≥ 3 hepatotoxicity

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304880	Patient number	3014
Demographics:	65-year-old Asian female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Peripheral sensory neuropathy AE leading to study treatment discontinuation		
Event 2 (PT) Category:	Hyperglycemia Grade ≥ 3 hyperglycemia		
Event 3 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		

A narrative for this patient is available in Section 1.4 Narratives for patients who discontinued study treatment due to an adverse event.

Study Number/CRTN:	CO40016/305639	Patient number	3016
Demographics:	62-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea		
Event 2 (PT) Category:	Peripheral motor neuropathy AE leading to study treatment discontinuation		

Event 3 (PT) Category:	Fatigue AE leading to study treatment discontinuation
Event 4 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity
Event 5 (PT) Categories:	Cardiac arrest Death due to adverse event, SAE

A narrative for this patient is available in Section 1.1 Narratives for patients who died due to an adverse event(s).

Study Number/CRTN:	CO40016/306603	Patient number	3024
Demographics:	49-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Gastroenteritis norovirus SAE		
Event 2 (PT) Category:	Aspartate aminotransferase increased Grade ≥3 hepatotoxicity		
Event 3 (PT) Category:	Diarrhea Grade ≥3 diarrhea		
Event 4 (PT) Category:	Pyrexia SAE		
Event 5 (PT) Category:	Hypertransaminasaemia SAE		
Event 6 (PT) Category:	Fatigue SAE		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304331	Patient number	3031
Demographics:	40-year-old White female		

Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)
Cohort:	Cohort C
Event (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity

The patient was randomized on Study Day −1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR and HER 2 negative, left breast cancer (T2N1M0) on Study Day −581 following biopsy of left breast on the same day.

On Study Day −82, the patient was diagnosed with metastatic disease with ER/PR and HER 2 negative in metastatic tissues. At screening sites of disease involvement included lungs (left subpleural lesion, S7 left side, right lung, S10 and S3) and soft tissue (thickening of skin fold in left breast).

Past cancer treatments are listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Epirubicin, paclitaxel and cyclophosphamide	-558	-452
Surgery	Curative	Radical mastectomy of left breast	-420	NA
Radiotherapy	Adjuvant	Breast (left breast; dose: 5000 cGy and 25 fractions) (tumor bed; 1600 cGy and 8 fractions)	-376	-329

The patient′s medical history included Grade 2 neuropathy peripheral and Grade 1 fibroadenoma of right breast. Surgical history included caesarean section. Concurrent conditions included Grade 2 myopia, Grade 1 radiation fibrosis (left lung), Grade 2 autonomic nervous system imbalance, Grade 1 venous angioma of brain, Grade 1 cholecystitis chronic and Grade 1 goiter.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with ipatasertib, paclitaxel and atezolizumab.

No concomitant medication ongoing at Study Day 1 was reported.

Event: Alanine aminotransferase increased (Increased ALT level)

Prior to the event of alanine aminotransferase increased, the most recent dose of paclitaxel and atezolizumab was administered on Study Day 266 and ipatasertib (400 mg) on Study Day 270.

On Study Day 273, the patient′s laboratory work-up showed ALT 182 U/L (normal range: 4-33 U/L) and AST 87 U/L (normal range: 5-32 U/L). She was diagnosed with non-serious Grade 3 alanine aminotransferase increased and Grade 1 aspartate aminotransferase increased (non-serious, related). She received treatment with ademetionine, arginine citrate/betaine/betaine hydrochloride and polymethylsiloxane polyhydrate. On Study Day 278, the event of alanine aminotransferase increased improved to Grade 1 and the event of aspartate aminotransferase increased was considered resolved. On Study Day 337, the event of alanine aminotransferase increased was considered resolved.

Due to the event of alanine aminotransferase increased, Cycle 11 Day 1 of paclitaxel and atezolizumab was delayed and treatment with ipatasertib was interrupted on Study Day 271. The next dose was administered on Study Day 282.

The Investigator considered alanine aminotransferase increased, to be related to ipatasertib, paclitaxel, atezolizumab and other cause (unspecified).

Relevant laboratory work-up:

Study Day	**AST** Normal range 5-34 U/L	**ALT** Normal range 4-36 U/L	**Total bilirubin** Normal range: 3.4-20.4 μmol/L	**ALP** Normal range: 35-123 U/L
Screening	16	16	12.3	66
273	87[*]	182[@]	8.30[$]	87[^]
278	23[*]	70[@]	4.10[$]	95[^]
282	14[#]	36[#]	8.0[a]	104[b]
290	36[#]	54[#]	6.1[a]	118[b]
296	33[#]	87[#]	7.1[a]	116[b]

Study Day	AST Normal range 5-34 U/L	ALT Normal range 4-36 U/L	Total bilirubin Normal range: 3.4-20.4 μmol/L	ALP Normal range: 35-123 U/L
309	35[#]	58[#]	7.0[a]	114[b]
315	27[#]	75[#]	7.6[a]	146[b]
323	45[#]	88[#]	12.6[a]	196[b]
337	24[#]	30[#]	12.4[%]	114[b]

[*]Normal range: 5-32 U/L, [#]normal range: 0-31 U/L, [@]normal range: 4-33 U/L, [$]normal range: 3.4-21 μmol/L, [a]normal range: 5-21 μmol/L, [^]normal range: 35-104 U/L, [b]normal range: 35-123 U/L

Study treatment with paclitaxel was permanently discontinued as per physician decision (for patient safety to reduce the risk of minimization) last dose of paclitaxel administered on Study Day 381.

On Study Day 673, a radiographic response assessment showed disease progression with new lesions in left lung (S1).

On Study Day 729, study treatment was permanently discontinued due to disease progression with the last dose of atezolizumab and ipatasertib administered on Study Day 659 and Study Day 666, respectively. The patient entered into long term follow-up.

On Study Day 804, the patient was discontinued from the study as long-term follow-up was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Alanine aminotransferase increased	1	Non-serious	15	29	Related	Related	Related
Alopecia	2	Non-serious	18	631	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	23	24	Related	Unrelated	Unrelated
Peripheral sensory neuropathy	1	Non-serious	29	Unresolved	Unrelated	Related	Related

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Alanine aminotransferase increased	1	Non-serious	36	43	Related	Related	Related
Vomiting	1	Non-serious	40	40	Related	Related	Unrelated
Neutropenia	1	Non-serious	43	57	Related	Related	Unrelated
Hyperbilirubinemia	1	Non-serious	64	71	Related	Related	Related
Nasopharyngitis	2	Non-serious	92	99	Unrelated	Unrelated	Unrelated
Hyperbilirubinemia	1	Non-serious	92	99	Related	Related	Related
Alanine aminotransferase increased	1	Non-serious	92	113	Related	Related	Related
Insomnia	1	Non-serious	96	104	Unrelated	Unrelated	Related
Neutropenia	1	Non-serious	99	113	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	123	125	Related	Unrelated	Unrelated
Vomiting	1	Non-serious	131	131	Related	Related	Unrelated
Nausea	2	Non-serious	132	132	Related	Unrelated	Unrelated
Neutropenia	1	Non-serious	148	176	Unrelated	Related	Unrelated
Leukopenia	1	Non-serious	148	204	Unrelated	Related	Unrelated
Diarrhea	1	Non-serious	149	157	Related	Unrelated	Related
Ligament sprain	2	Non-serious	167	190	Unrelated	Unrelated	Unrelated
Hyperkalemia	2	Non-serious	176	183	Related	Related	Unrelated
Neutropenia	1	Non-serious	183	197	Unrelated	Related	Unrelated
Leukopenia	1	Non-serious	224	240	Unrelated	Related	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Alanine aminotransferase increased	1	Non-serious	224	240	Related	Related	Related
Hyperbilirubinemia	1	Non-serious	250	255	Related	Related	Related
Leukopenia	2	Non-serious	255	266	Unrelated	Related	Unrelated
Neutropenia	2	Non-serious	273	278	Unrelated	Related	Unrelated
Leukopenia	2	Non-serious	273	278	Unrelated	Related	Unrelated
Leukopenia	1	Non-serious	296	309	Unrelated	Related	Unrelated
Neutropenia	1	Non-serious	296	309	Unrelated	Related	Unrelated
Leukopenia	2	Non-serious	315	394	Unrelated	Related	Unrelated
Neutropenia	1	Non-serious	315	337	Unrelated	Related	Unrelated
Hypercreatinaemia	1	Non-serious	344	365	Related	Related	Related
Neutropenia	1	Non-serious	351	365	Unrelated	Related	Unrelated
Alanine aminotransferase increased	2	Non-serious	365	407	Related	Related	Unrelated
Weight increased	1	Non-serious	365	Unresolved	Unrelated	Unrelated	Unrelated
Neutropenia	1	Non-serious	371	394	Unrelated	Related	Unrelated
Aspartate aminotransferase increased	2	Non-serious	394	397	Related	Related	Related
Lipase increased	2	Non-serious	394	397	Related	Related	Related
Neutropenia	2	Non-serious	407	450	Unrelated	Related	Unrelated
Leukopenia	2	Non-serious	407	450	Unrelated	Related	Unrelated
Hyperbilirubinemia	1	Non-serious	407	421	Related	Unrelated	Unrelated

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Seborrheic dermatitis	1	Non-serious	439	519	Related	NA	Related
Alanine aminotransferase increased	1	Non-serious	450	476	Related	NA	Related
Aspartate aminotransferase increased	1	Non-serious	450	463	Related	NA	Related
Hyperbilirubinemia	1	Non-serious	463	476	Related	NA	Related
Leukopenia	2	Non-serious	476	505	Related	NA	Unrelated
Neutropenia	2	Non-serious	476	505	Related	NA	Unrelated
Leukopenia	1	Non-serious	519	533	Related	NA	Unrelated
Neutropenia	1	Non-serious	519	533	Related	NA	Unrelated
Leukopenia	1	Non-serious	547	561	Related	NA	Unrelated
Neutropenia	2	Non-serious	547	561	Related	NA	Unrelated
Alanine aminotransferase increased	1	Non-serious	547	591	Related	NA	Related
Hypercreatinaemia	1	Non-serious	547	561	Related	NA	Related
Neutropenia	2	Non-serious	575	591	Related	NA	Unrelated
Leukopenia	2	Non-serious	575	617	Related	NA	Unrelated
Thoracic radiculopathy	1	Non-serious	586	Unresolved	Unrelated	NA	Unrelated
Neutropenia	1	Non-serious	604	617	Related	NA	Unrelated
Alanine aminotransferase increased	1	Non-serious	617	631	Related	NA	Related
Aspartate aminotransferase increased	1	Non-serious	617	631	Related	NA	Related

Event	Most extreme grade	Serious / Non-serious	Onset day	Resolution day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Hypercreatinaemia	1	Non-serious	617	631	Unrelated	NA	Related
Alanine aminotransferase increased	1	Non-serious	646	659	Related	NA	Related
Leukopenia	1	Non-serious	659	674	Related	NA	Unrelated
Neutropenia	2	Non-serious	659	674	Related	NA	Unrelated

Study Number/CRTN:	CO40016/304331	Patient number	3043
Demographics:	47-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Category:	Alanine aminotransferase increased Grade $\geq$ 3 hepatotoxicity		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with advanced unresectable poorly differentiated, ER/PR negative and HER2 negative left breast cancer (T4N1M0) (histological subtype: other), on Study Day −67 followed by left breast biopsy performed on the same day.

At screening, sites of disease involvement included formation in left breast.

No past cancer treatments were reported.

No medical/surgical history was reported. The patient′s concurrent conditions included renal cyst (left), uterine leiomyoma, ovarian cyst (right) and cholecystitis chronic.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 was reported.

On Study Day 266, the patient was noted with Grade 1 aspartate aminotransferase increased (AST: 79 U/L; normal range: 0-31 U/L), Grade 2 alanine aminotransferase increased (ALT: 127 U/L; normal range: 0-31 U/L), and Grade 1 blood alkaline phosphatase increased (ALP: 275 U/L normal range: 35-123 U/L) (all non-serious, related to paclitaxel and atezolizumab). She received treatment with ademetionine and calcium chloride/magnesium chloride/potassium chloride/sodium chloride/sodium lactate/sorbitol. On Study Day 273, the events of aspartate aminotransferase increased, and alanine aminotransferase increased were considered resolved. On Study Day 280, the event of blood alkaline phosphatase increased was considered resolved.

Event: Alanine aminotransferase increased (Increased ALT count)

Prior to the event of alanine aminotransferase increased, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 287 and ipatasertib (400 mg) on Study Day 293.

On Study Day 294, a laboratory work-up showed ALT 275 U/L (normal range: 35-123 U/L) and ALP 275 U/L (normal range: 0-31 U/L) and the patient was diagnosed with non-serious Grade 3 alanine aminotransferase increased and Grade 1 blood alkaline phosphatase increased (non-serious, related to paclitaxel and atezolizumab). She received treatment with ademetionine, calcium chloride dihydrate/potassium chloride/sodium chloride/sodium lactate, ascorbic acid and pyridoxine. On Study Day 301, the event of alanine aminotransferase increased was considered resolved. On Study Day 343, the event of blood alkaline phosphatase increased was considered resolved.

Relevant laboratory values listed in the table below:

Study Day	**AST** (normal range: 5-31 U/L)	**ALT** (normal range: 0-31 U/L)	**ALP** (normal range: 35-123 U/L)	**Total bilirubin** (normal range: 5-21 μmol/L)
-1	17*	14**	79	10.3@
266	79	127	275	23.9
269	35	81	198	9.7
273	13	17	143	8.5
280	20	33	116	9.9
287	24	23	87	11.6
294	59	275	275	10.4

301	27	57	171	11.2
308	58	137	189	12
315	20	60	131	12.8
322	55	40	224	8.2
329	22	36	187	11
343	14	31	112	11.9

*normal range: 5-43 U/L, **normal range: 4-36 U/L, @ normal range: 3.4-20.4 μmol/L

Due to this event, there was no change in the study treatment with atezolizumab and ipatasertib; however, study treatment with paclitaxel was delayed and the next dose was given at a reduced dose of 65 mg/m^2 from 80 mg/m^2 on Study Day 301.

The Investigator considered alanine aminotransferase increased to be unrelated to ipatasertib and related to paclitaxel and atezolizumab.

On Study Day 424, the patient withdrew consent from the study treatment with the last dose of atezolizumab and paclitaxel given on Study Day 413 and ipatasertib on Study Day 419. The patient then entered the long-term follow-up phase.

The patient received follow-up anti-cancer therapy as listed in table below:

Treatments	**Start Day**	**Stop Day**
Radiotherapy to left breast, left axillary area, cervico-supraclavicular, parasternal area (dose:5000 cGy) and tumor bed (dose:6000 cGy)	484	518

On Study Day 785, the patient was discontinued from the study as the study was terminated by the Sponsor.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Atezolizumab)	Causality (Paclitaxel)
Alopecia	2	Non-serious	26	364	Unrelated	Unrelated	Related
Alanine aminotransferase increased	1	Non-serious	35	42	Related	Related	Related
Aspartate aminotransferase increased	1	Non-serious	35	42	Related	Related	Related
Breast pain	2	Non-serious	81	87	Unrelated	Unrelated	Unrelated
Alanine aminotransferase increased	2	Non-serious	182	196	Unrelated	Related	Related
Vascular access site inflammation	2	Non-serious	240	247	Unrelated	Unrelated	Unrelated
Scar pain	2	Non-serious	247	256	Unrelated	Unrelated	Unrelated
Alanine aminotransferase increased	2	Non-serious	308	315	Related	Related	Related
Blood alkaline phosphatase increased	1	Non-serious	350	371	Unrelated	Unrelated	Related
Alanine aminotransferase increased	2	Non-serious	378	385	Unrelated	Related	Related

Study Number/CRTN:	CO40016/318144	Patient number	3047
Demographics:	83-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Categories:	Diarrhea SAE, Grade $\geq$ 3 diarrhea		
Event 2 (PT) Category:	Gamma-glutamyl transferase increased Grade $\geq$ 3 hepatotoxicity		

Event 3 (PT) Category:	Nausea SAE
Event 4 (PT) Categories:	Pneumonitis SAE, AE leading to study treatment discontinuation, Grade ≥ 2 pneumonitis

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/318813	Patient number	3050
Demographics:	45-year-old White and American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		

The patient was randomized on Study Day 1.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR negative and HER2 negative left breast cancer (T3N2aM0) on Study Day – 76.

The patient was diagnosed with metastatic disease on an unknown day with ER /PR negative and HER2 negative disease in metastatic tissue. At screening, sites of disease involvement included lymph node (left axillary and retro pectoral).

No past cancer treatment was reported.

No medical/surgical history was reported. The patient′s concurrent condition included anemia.

At screening, the patient′s ECOG Performance Status was 0.

On Study Day 1, the patient received her first study treatment with ipatasertib, atezolizumab and paclitaxel.

No concomitant medications ongoing at Study Day 1 was reported.

On Study Day 57, a laboratory work-up AST 103 U/L (normal range: 0-32 U/L) and ALT 148 U/L (normal range: 0-32 U/L). The patient was diagnosed with Grade 2 aspartate aminotransferase increased and Grade 2 alanine aminotransferase increased (both non-serious, unrelated). No treatment was reported for these events. On Study Day 64, the event of aspartate aminotransferase increased was considered resolved. On Study Day 71, the event of alanine aminotransferase increased was considered resolved.

Event 1: Alanine aminotransferase increased (ALT elevation)

Event 2: Aspartate aminotransferase increased (AST elevation)

Prior to the events of alanine aminotransferase increased and aspartate aminotransferase increased, the most recent dose of atezolizumab and paclitaxel was administered on Study Day 71 and ipatasertib (400 mg) on Study Day 77.

On Study Day 85, Cycle 4 laboratory work-up showed ALT 303 U/L (normal range: 0-33 U/L) and AST 169 U/L (normal range: 0-32 U/L). The patient was diagnosed with non-serious Grade 3 alanine aminotransferase increased and Grade 3 aspartate aminotransferase increased without clinical implications. No treatment was reported for these events. On Study Day 92, the event of aspartate aminotransferase increased was considered resolved. On Study Day 99, the event of alanine aminotransferase increased was considered resolved.

Relevant laboratory values listed in the table below:

Study Day	**AST** (normal range: 0-32 U/L)	**ALT** (normal range: 0-33 U/L)	**ALP** (normal range: 35-104 U/L)	**Total bilirubin** (normal range: 0.1-1 mg/dL)
-10	17	17	127	0.22
57	103	148	165	0.46
64	25	48	148	0.47
71	21	27	119	0.33
85	169	303	193	0.53
92	26	87	140	0.51
99	21	30	117	0.46

There was no change in the study treatment due to the events of alanine aminotransferase increased and aspartate aminotransferase increased.

The Investigator considered alanine aminotransferase increased and aspartate aminotransferase increased to be unrelated to atezolizumab, paclitaxel and ipatasertib and related to other causes (unspecified).

On Study Day 220, an overall response assessment showed disease progression.

On Study Day 246, study treatment was permanently discontinued due to disease progression with the last dose of atezolizumab and paclitaxel given on Study Day 212, and ipatasertib on Study Day 218. The patient entered into the long-term follow-up.

The patient received follow-up anti-cancer therapies as listed in table below:

Treatments	Start Day	Stop Day
Doxorubicin and cyclophosphamide (5 cycles each)	345	Ongoing
Surgery of left breast	679	–

On Study Day 805, the patient died due to disease progression. An autopsy was not performed.

Other AEs experienced by the patient during the study:

Event	Most extreme grade	Serious / non-serious	Onset Day	Resolution Day / Outcome	Causality (Ipatasertib)	Causality (Paclitaxel)	Causality (Atezolizumab)
Epigastric discomfort	1	Non-serious	69	74	Unrelated	Unrelated	Unrelated
Dry mouth	1	Non-serious	69	74	Unrelated	Unrelated	Unrelated
Alanine aminotransferase increased	1	Non-serious	113	120	Unrelated	Unrelated	Unrelated
Aspartate aminotransferase increased	1	Non-serious	113	120	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	127	130	Unrelated	Unrelated	Unrelated

Study Number/CRTN:	CO40016/304787	Patient number	3052
Demographics:	59-year-old White female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		

Cohort:	Cohort C
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea
Event 2 (PT) Category:	Diarrhea (second episode) Grade ≥ 3 diarrhea
Event 3 (PT) Category:	Hyperglycemia Grade ≥ 3 hyperglycemia
Event 4 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity

A narrative for this patient is available in Section 1.6 narratives for patients who experienced Grade ≥ 3 hyperglycemia.

Study Number/CRTN:	CO40016/304787	Patient number	3061
Demographics:	75-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Category:	Hyperbilirubinemia Grade ≥ 3 hepatotoxicity		
Event 4 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity		
Event 5 (PT) Categories:	Alanine aminotransferase increased AE leading to study treatment discontinuation, Grade ≥ 3 hepatotoxicity		

Event 6 (PT) Category:	Aspartate aminotransferase increased Grade ≥ 3 hepatotoxicity
Event 7 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity
Event 8 (PT) Categories:	Aspartate aminotransferase increased AE leading to study treatment discontinuation, Grade ≥ 3 hepatotoxicity

A narrative for this patient is available in Section 1.4 Narratives for patients who discontinued study treatment due to an adverse event.

Study Number/CRTN:	CO40016/305948	Patient number	3070
Demographics:	53-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Category:	Blood alkaline phosphatase increased Grade ≥ 3 hepatotoxicity		

The patient was randomized on Study Day – 3.

The patient was initially diagnosed with ductal, poorly differentiated, ER/PR negative and HER2 negative left breast cancer (T3N0M0) approximately 4 years and 5 months prior to study entry followed by left simple mastectomy performed on the same day.

On Study Day – 84, the patient was diagnosed with locally recurrent and metastatic disease with ER/PR negative and HER2 negative in metastatic tissue. At screening, sites of disease involvement included chest (left chest wall tumor mass), lung (left lower lobe lung metastasis and right middle lobe lung metastasis and bilateral), and lymph node (left hilar and left mediastinal).

Past cancer treatment is listed in the table below:

Type of treatment	Therapy Setting/Intent	Treatments details	Start Day	Stop Day
Cancer therapy	Neoadjuvant	Fluorouracil, epirubicin, cyclophosphamide and docetaxel	Approximately 4 years 7 months prior to study entry	Approximately 4 years 5 months prior to study entry

No medical/surgical history was reported. The patient′s concurrent conditions included back pain and arthralgia.

At screening, the patient′s ECOG Performance Status was 1.

On Study Day 1, the patient received her first study treatment with atezolizumab, ipatasertib and paclitaxel.

No concomitant medications ongoing at Study Day 1 was reported.

On Study Day 279, a laboratory work-up showed ALT 126 U/L (normal range: 0-49.99 U/L) and AST 97 U/L (normal range: 0-39.99 U/L). The patient as diagnosed with Grade 1 alanine aminotransferase increased and Grade 2 aspartate aminotransferase increased (both non-serious, related to paclitaxel). No treatment was reported for this event. The events of alanine aminotransferase increased, and aspartate aminotransferase increased remained unresolved at the time of patient′s death (see narrative below).

Event: Blood alkaline phosphatase increased (Elevated alkaline phosphatase)

Prior to the event of blood alkaline phosphatase increased, the most recent dose of atezolizumab was given on Study Day 281, paclitaxel on Study Day 288 and ipatasertib (400 mg) on Study Day 290.

On Study Day 291, the patient was diagnosed with non-serious Grade 3 blood alkaline phosphatase increased (ALP not reported for this day; initial intensity Grade 2). No treatment was reported for this event. On Study Day 293, the event of blood alkaline phosphatase increased was considered resolved with sequelae (unspecified).

Relevant laboratory values listed in the table below:

Study Day	**AST** (normal range: 0-39.99 U/L)	**ALT** (normal range: 0-49.99 U/L)	**ALP** (normal range: 30-150 U/L)	**Total bilirubin** (normal range: 0-20.99 μmol/L)
-16	83	96	126	7
279	97	126	800	6
286	64	95	626	11
293	55	72	705	12
307	75	85	558	6

314	71	91	543	13
321	90	107	695	12
335	99	119	738	6

There was no change in the study treatment due to the event of blood alkaline phosphatase increased.

The Investigator considered blood alkaline phosphatase increased to be related to paclitaxel and unrelated to ipatasertib and atezolizumab.

On Study Day 329, an overall response assessment showed disease progression.

On Study Day 335, the patient was discontinued from the study treatment due to disease progression with the last dose of atezolizumab and paclitaxel was given on Study Day 323 and ipatasertib on Study Day 329. The patient then entered the long-term follow-up.

On Study Day 695, per the death by public records the patient died due to disease progression. No information regarding autopsy was reported.

Other AEs experienced by the patient during the study:

Event	**Most extreme grade**	**Serious / non-serious**	**Onset Day**	**Resolution Day / Outcome**	**Causality (Ipatasertib)**	**Causality (Atezolizumab)**	**Causality (Paclitaxel)**
Diarrhea	1	Non-serious	1	8	Related	Unrelated	Related
Vomiting	1	Non-serious	1	1	Related	Unrelated	Related
Taste disorder	1	Non-serious	1	Unresolved	Unrelated	Unrelated	Related
Neuropathy peripheral	1	Non-serious	5	Unresolved	NA	Unrelated	Related
Urinary tract infection	2	Non-serious	16	21	Unrelated	Unrelated	Unrelated
Diarrhea	1	Non-serious	19	26	Unrelated	Unrelated	Related
Epistaxis	1	Non-serious	27	Unresolved	Unrelated	Unrelated	Related
Urinary tract infection	1	Non-serious	53	62	NA	Unrelated	Unrelated
Fatigue	1	Non-serious	97	174	Unrelated	Unrelated	Related
Cough	1	Non-serious	97	Unresolved	Unrelated	Unrelated	Unrelated

Foreign body sensation in eyes	1	Non-serious	103	Unresolved	Unrelated	Unrelated	Related
Rash	1	Non-serious	139	242	NA	Related	Unrelated
Muscle spasms	1	Non-serious	143	Unresolved	Unrelated	Unrelated	Related
Alopecia	2	Non-serious	146	Unresolved	Unrelated	Unrelated	Related
Nausea	1	Non-serious	167	174	Related	—	Related
Pleuritic pain	1	Non-serious	174	Unresolved	Unrelated	Unrelated	Unrelated
Decreased appetite	1	Non-serious	181	Unresolved	Unrelated	Unrelated	Related
Fatigue	1	Non-serious	181	Unresolved	Unrelated	Unrelated	Related
Chills	1	Non-serious	235	Unresolved	Unrelated	—	Unrelated
Anemia	1	Non-serious	251	Unresolved	Unrelated	Unrelated	Related
Dysphonia	1	Non-serious	273	Unresolved	Unrelated	—	Unrelated
Fatigue	3	Non-serious	293	Unresolved	Related	Unrelated	Related
Perioral dermatitis	1	Non-serious	321	Unresolved	Unrelated	—	Unrelated

Study Number/CRTN:	CO40016/304680	Patient number	3081
Demographics:	65-year-old White female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Blood alkaline phosphatase increased Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Categories:	Immune-mediated lung disease SAE, Grade ≥ 2 pneumonitis		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/304785	Patient number	3088

Demographics:	51-year-old White female
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)
Cohort:	Cohort C
Event 1 (PT) Category:	Diarrhea Grade ≥ 3 diarrhea
Event 2 (PT) Category:	Alanine aminotransferase increased Grade ≥ 3 hepatotoxicity
Event 3 (PT) Categories:	Aspartate aminotransferase increased AE leading to study treatment discontinuation, Grade ≥ 3 hepatotoxicity
Event 4 (PT) Categories:	Alanine aminotransferase increased (Second episode) AE leading to study treatment discontinuation, Grade ≥ 3 hepatotoxicity

A narrative for this patient is available in Section 1.4 Narratives for patients who discontinued study treatment due to an adverse event.

Study Number/CRTN:	CO40016/318813	Patient number	3101
Demographics:	38-year-old American Indian or Alaska Native female		
Study treatment/Dosage Regimen	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m^2 IV weekly: D1, D8 and D15 of 28 days cycle) + Atezolizumab (840 mg IV D1 and D15 of 28 days cycles)		
Cohort:	Cohort C		
Event 1 (PT) Categories:	Alanine aminotransferase increased AE leading to study treatment discontinuation, AESI: Grade ≥ 3 hepatotoxicity		
Event 2 (PT) Categories:	Aspartate aminotransferase increased AE leading to study treatment discontinuation, AESI: Grade ≥ 3 hepatotoxicity		
Event 3 (PT) Categories:	Blood alkaline phosphatase increased AE leading to study treatment discontinuation, AESI: Grade ≥ 3 hepatotoxicity		

A narrative for this patient is available in Section 1.4 Narratives for patients who discontinued study treatment due to an adverse event.

1.12 NARRATIVES FOR PATIENTS WHO EXPERIENCED POTENTIAL DRUG INDUCED LIVER INJURY AS DEFINED BY HY′S LAW

No patient experienced drug induced liver injury during the protocol defined study period.

1.13 NARRATIVES FOR PATIENTS WHO EXPERIENCED SUSPECTED TRANSMISSION OF AN INFECTIOUS AGENT BY THE STUDY DRUG

No patient experienced suspected transmission of an infectious agent by the study drug during the protocol defined study period.

1.14 NARRATIVES FOR PATIENTS WHO EXPERIENCED COVID-19 SAEs

Study Number/CRTN:	CO40016/318721	Patient number	3067
Demographics:	58-year-old female (Unknown race)		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event 1 (PT) Category:	Rash pruritic Grade ≥ 3 rash		
Event 2 (PT) Category:	General physical health deterioration SAE		
Event 3 (PT) Categories:	Covid-19 SAE, COVID-19 SAE		

A narrative for this patient is available in Section 1.3 Narratives for patients who experienced serious adverse events.

Study Number/CRTN:	CO40016/305629	Patient number	3090
Demographics:	54-year-old American Indian or Alaska Native female		
Study treatment (Dosage regimen)	Ipatasertib (400 mg PO QD: D1-D21 of 28 days cycle) + Paclitaxel (80 mg/m2 IV weekly: D1, D8 and D15 of 28 days cycle) +Atezolizumab (840mg IV D1 and D15 of 28 days cycles)		
Cohort	Cohort C		
Event (PT) Categories:	Suspected COVID-19 Death due to AE, SAE, AE leading to study treatment discontinuation, COVID-19 SAE		

A narrative for this patient is available in Section 1.1 Narratives for patients who died due to an adverse event(s).

Appendix to CSR: Summary Impact of COVID-19 on Data Collection, Reporting and Analysis

TABLE OF CONTENTS

1. INTRODUCTION

On March 11, 2020, the World Health Organization (WHO) characterized the outbreak of Coronavirus Disease 2019 (COVID-19), caused by the novel coronavirus SARS-CoV-2, as a pandemic. Government restrictions on the population were implemented to varying degrees globally in response to the COVID-19 pandemic. Measures, such as restrictions of movement and travel and, therefore, visits to healthcare facilities, as well as the increased demands on the health service due to the pandemic and changes to study staff availability pose various challenges to the conduct of clinical studies. In addition, participants may have been required to self-isolate, which introduces difficulties for Investigators to maintain their medical oversight. Therefore, the COVID-19 pandemic may have had an impact on the conduct of clinical studies of medical products, on study participants, and on the collection and analysis of clinical study data.

It is difficult to determine the start of the COVID-19 outbreak and the Sponsor decided to use 1 December 2019 based on early cases reported in Mainland China. Study CO40016 began with first patient in (FPI) on 6 January 2018 and the CCOD for the study was 30 October 2021 for efficacy analyses. A snapshot date of 21 March 2023 was utilized for non-efficacy analyses. The last patient last visit (LPLV) for this study took place on 4 January 2023, which included the period during which the COVID-19 pandemic was occurring globally.

At the time of the primary analyses for Cohort A (Report No. 1101889) and Cohort B (Report No. 1100941) the COVID-19 pandemic had a minor impact on the study conduct, study patients, and data collection

The objective of this appendix is to document the impact of the COVID-19 pandemic up until the final snapshot for non-efficacy analyses (21 March 2023) on the study patients, study conduct, data collection and reporting, data analysis, and study results and conclusion. Overall, there has been minimal impact since the initial assessments for Cohort A and Cohort B.

2. METHODOLOGY

2.1 MITIGATION MEASURES IMPLEMENTED

2.1.1 Adjustments in Study Procedures

The Sponsor performed a comprehensive risk assessment to identify and document any specific COVID-19 pandemic risks relating to trial disruption and corresponding mitigation actions, for the defined critical variables (data and processes) of the study, which could ultimately impact patient safety and/or data integrity.

Disruptions as a result of the pandemic, including travel restrictions, quarantine, self-isolation and/or precaution measures, meant that some patients were unable to visit investigational sites for protocol-specified visits and undertake required clinical study

activities, or receive treatment. Alternative methods for assessments (e.g., remote visits, such as via telephone or virtual meetings, alternative location for assessment, including local labs or imaging centers) were initiated and implemented by investigator sites when necessary and feasible. Every effort was made to ensure safety information was reported as per protocol-required timelines, acknowledging that there could be some delays as a result of the pandemic.

Additional general guidance regarding reporting and actions in case of suspected/confirmed COVID-19 infections was also communicated via the Country Study Managers in line with Sponsor company-wide guidance.

No changes were made to the protocol due to the COVID-19 pandemic.

For some cases in which patients were unable to attend sites due to high numbers of positive cases at site clinics, arrangements were made for the IMP to be delivered directly to the patient's home, either by an approved courier service (ipatasertib only) or by qualified trial personnel, to ensure continuity of treatment, according to standard operating procedures (SOPs) and applicable local regulations. This was implemented for 8 patients at 7 sites in France, Peru, Russia, Turkey, and the UK. If, despite best efforts, the dose of study treatment could not be administered as defined in the protocol (see Protocol, Appendix 1 and Appendix 2, Schedule of Activities), this was recorded. If more than 3 doses of paclitaxel and/or 21 days of ipatasertib within any 28-day cycle were missed, this was also documented as a major protocol deviation.

The COVID-19 pandemic did not result in any site closures, but some patients were routed to other locations for patient safety, due to large number of COVID-19 cases at some sites. The patients at these sites attended visits at alternative sites or at home as described below for study assessments and in some cases, preparation and administration of study treatment. Visits, which occurred at alternative sites/patient's home, were documented in source notes. For 2 patients in Cohort A, visits to a medical facility were not feasible and, therefore, to ensure patient safety, remote visits were performed at the patient's home by qualified trial personnel according to SOPs and applicable regulations (refer to major protocol deviations in the final CSR Section 4.3.1). If visits to a site/home were not feasible, then the medical evaluation of safety and disease took place by telemedicine using secure video conferences, phone calls, or a web portal and/or mobile application for communicating with and monitoring the patient's progress.

For any of the mitigating actions mentioned above, the patients were informed of the proposal and any potential risks associated with the specific scenario and signed a revised ICF addendum, if required. Institutional Review Board/Independent Ethics Committee (IRB/IEC) were informed and/or approved of this procedural change.

The trial investigator was responsible for ensuring that the identification, management, and reporting of adverse events (AEs) and serious AEs (SAEs) was completed in accordance with the protocol and applicable regulations. AEs were reported by patients to the investigator/trial team or identified by the trial team during interactions with the patients via telemedicine. In addition, home health nurses may have identified AEs and reported them to the investigator for evaluation. Additional AEs may have been identified from laboratory reports, imaging or electrocardiogram (ECG) reports, or other records of trial procedures that were conducted at alternative locations due to the COVID-19 pandemic. As determined by the investigator, the appropriate medical intervention, therapeutic intervention, and/or support measures were instituted, as necessary.

Per protocol, local laboratories were used for routine monitoring, if needed this could be conducted at local laboratories closer to the patients. The Principal Investigator (PI) would need to do a timely review of the laboratory results to assess AEs and would report them in patients' eCRF. Laboratory certifications and reference ranges of the local labs would need to be collected by the sites. In addition, 2 patients in Cohort A located in Turkey had tumor assessments conducted at alternative imaging centers close to the patient's homes, due to COVID-19 restrictions. In these cases, the new facility was identified by the investigator who informed the Sponsor. In all instances, the alternate location met International Council for Harmonisation Good Clinical Practice/Good Laboratory Practice (ICH GCP/GLP) requirements and was well equipped to perform trial procedures and covered by adequate insurance. The investigator maintained sufficient oversight to ensure that the staff at the alternate location were trained to perform trial procedures.

2.1.2 Monitoring

Risk-based monitoring activities, including remote monitoring activities, were initiated as standard, at the beginning of the study. To mitigate any identified COVID-19 specific risks, that were related to site monitoring activities, the Sponsor evaluated and implemented alternative remote monitoring strategies as necessary, to maintain oversight and ensure the rights, safety and well-being of participants in the study, as well as the integrity of the study and study data.

In most countries and sites (based on-site and/or country policy), on-site monitoring visits were not permitted at some point prior to the final analysis. In these cases, remote monitoring was employed, where permissible per local regulations. Remote monitoring consisted of remote data review (RDR) and remote site contact, such as telephone / email. Where RDR was employed, the Monitor was to ensure data appeared reasonable and logical according to protocol requirements. The Monitor was to check for safety reporting to the Sponsor (and IRB/IEC as required) during the remote contact. If any issues were identified, the Monitor should follow up with the site via telephone conversation or video call. Remote site contact with site staff could help assess that

critical processes were being followed and data obtained. The study management team also evaluated all source data verification (SDV) data fields per the trial monitoring plan (TMP) and tiered all fields in terms of importance for analysis to ensure in case of any resource/time/on-site visit constraints a clear prioritization and to ensure the priority fields were reviewed. As per standard practice, Monitors were also directed to pay specific attention to aspects of site trial management susceptible to the pandemic challenges such as resourcing, investigator oversight, and delegation of duties.

Remote SDV, whereby the Monitor obtained remote access to source data (e.g. via access to Electronic Health Records Systems, video conferencing, or discussed via telephone conference call), could be considered under the COVID-19 pandemic situation. Where on-site monitoring visits could not be conducted per the TMP, this was recorded in the clinical trial management system (CTMS), including the specific reason imposed by COVID-19. These were annotated with the specific tag “COVID-19” in the free-text description field.

At three sites in Peru, monitoring could not be completed on-site or remotely due to institutional rules and regulations. For final analysis, data from these sites underwent centralized monitoring review or RDR, and the monitors followed the Sponsor’s SOP.

2.2 DATA CAPTURE AND REPORTING

For all non-adherence to protocol-specified approaches due to COVID-19 pandemic, a specific protocol deviation was recorded, with an option to report the associated reason imposed by COVID-19 (e.g., Subject Movement Restricted due to Pandemic, Confirmed or Suspected Infection, etc.) and with the specific tag “COVID-19” in the description field. “Confirmed or suspected infection” was utilized if the patient’s infection caused by COVID-19 had been confirmed by a diagnostic test, or a patient had symptoms compatible with COVID-19, that had not been confirmed by a diagnostic test.

The Sponsor’s definition of a protocol deviation (i.e., major vs. minor) remained unchanged during the pandemic (See Section 4.3.1 of CO40016 Final CSR). However, due to the increased likelihood of protocol deviations occurring during the COVID-19 pandemic, the Sponsor study team reassessed, as appropriate, the original protocol deviation classifications in the TMP of major and minor deviations to ensure the changes imposed by COVID-19 were categorized properly. The Protocol Deviation Management System (PDMS) captured all major protocol deviations including the ones which were titled COVID-19, so that protocol deviations caused by COVID-19 pandemic could be consistently reported. After evaluation, the Sponsor considered that, at this time, the categories in place were adequate, and no updates to the protocol deviation classifications in the TMP were deemed necessary.

Safety Data Reporting: See Section 2.1 for mitigation measures to ensure timely reporting of safety information. With the onset of the COVID-19 pandemic (1 December 2019) until the final snapshot for non-efficacy analyses (21 March 2023) being about 3.5

years, the Sponsor considers the additional time taken was sufficient and had made every possible effort during this time to capture delayed reporting of events that occurred prior to CCOD.

In order to assess the impact of COVID-19 illness and the pandemic disruption on the safety reporting, the Sponsor developed safety analyses concepts to capture COVID-19 associated AEs. These are defined in Section 2.3.

2.3 ADDITIONAL ANALYSES PERFORMED

2.3.1 Statistical Considerations

No changes to the Statistical Analysis Plan were made as a result of COVID-19 impact.

2.3.2 Additional Safety Analyses

Based on the first reports of COVID-19 infection globally, the Sponsor determined that the window for all analyses of COVID-19 associated events would start from 1 December 2019, until the final snapshot for non-efficacy analyses (21 March 2023).

The Sponsor utilized the standardized narrow Medical Dictionary for Regulatory Activities (MedDRA) COVID-19 Standard MedDRA Query (SMQ) identified by Maintenance and Support Services Organization (MSSO) to identify AEs of a confirmed or suspected COVID-19 infection. All analyses used the most current version of the SMQ.

The search identified AEs of a confirmed or suspected COVID-19 infection, and for patients with confirmed or suspected COVID-19 infections the following listings were generated as follows:

- A listing of confirmed or suspected COVID-19 AEs
- A listing of patients who died for reasons related to COVID-19 outside per protocol AE reportable window, identified via manual review of the free-text field associated with reason for death as “other”.

In addition, the Sponsor developed a broad search strategy for AEs associated with COVID-19 infection to further evaluate the confirmed events of COVID-19 and reported AEs that could be considered complications of the disease. This search strategy included both the PTs of a confirmed or suspected COVID-19 infection and any AEs considered associated with COVID-19 (temporally reported around PTs for confirmed or suspected COVID-19 infection). As causality to COVID-19 was not collected on the standard eCRFs, the Sponsor identified associated AEs as those reported ≤7 days before and ≤30 days after any reported AE suggesting a confirmed COVID-19 infection.

For patients identified from the search as having COVID-19 associated AEs, listings and tables to evaluate these safety events were produced as follows:

- Listings and tables of COVID-19 Associated Events: including the AEs of a confirmed or suspected COVID-19 infection plus, for those patients with confirmed

COVID-19 infection or positive PCR test, any other AEs occurring within ≤7 days before and ≤30 days after start date of all the confirmed COVID-19 events.

Determining whether the AE led to discontinuations from treatment and/or study relies on the study AE eCRF already containing fields to collect these data. In addition, discontinuations from treatment and/or study due to indirect COVID-19 pandemic-related aspects (e.g., patients leaving the study due to fear of going to the site during the pandemic) were assessed by manual review of the additional information reported on the disposition or study treatment discontinuation eCRF free-text fields.

Patient narratives are included for patients with confirmed/suspected COVID-19 SAEs in the active arm.

3. IMPACT ASSESSMENT

3.1 IMPACT OVERVIEW

The CCOD for the final efficacy and safety analysis for Study CO40016 occurred on 30 October 2021 and 21 March 2023, respectively. The overall impact of COVID-19 on the study was assessed as follows:

- The impact of COVID-19 on study conduct was minor. A low proportion of study visits and/or data collected were impacted by site closures, travel restrictions and requirements for remote activities.
- Contingency measures, which modified the trial conduct and administration of trial procedures, were implemented to allow patients to continue in the trial despite the challenging circumstances (see Section 2.1).
- No protocol or SAP amendment due to COVID-19 was required (up to the CCOD), however, a COVID-19 specific update to the ICF (COVID-19 ICF addendum) was implemented to capture the written consent of any patients needing to implement any mitigation measures as a result of COVID-19 restriction or safety concerns.
- Eight major protocol deviations due to COVID-19 were reported and none of these resulted in missing data (Section 3.4).
- There was no significant impact on data collection for assessment of primary and key secondary efficacy endpoints, as no patient missed two or more efficacy assessments.
- 17 patients with confirmed or suspected COVID-19 were reported (Section 3.6.2).
- Minimal impact on safety analyses, patient safety was monitored and managed, and the safety results still hold scientific validity.

3.2 DISPOSITION

3.2.1 Study Status

When the pandemic disruption occurred, enrollment in the trial was almost complete, and as such, the impact was minimal. The trial was completed despite the disruption that occurred, and the primary and key secondary objectives were achieved.

The study's Independent Data Monitoring Committee (iDMC) continued review of collected safety data at an interval pre-specified in the iDMC's charter.

3.2.2 Patients Discontinued from Treatment Due to Reasons Related to COVID-19 Pandemic

Two patients discontinued from treatment for reasons related to COVID-19 infection or study disruption: one in Cohort B and one in Cohort C (l_ae_COV_A_SE, l_ae_COV_B_SE, l_ae_COV_C_SE).

3.2.3 Patients Discontinued from Study Due to Reasons Related to COVID-19

One patient in Cohort C discontinued from the study for reasons related to COVID-19 infection or study disruption (l_ae_COVAS_SDSC_A_SE, l_ae_COVAS_SDSC_B_SE, l_ae_COVAS_SDSC_C_SE).

3.3 STUDY POPULATION

Because recruitment and last patient in was completed shortly after the pandemic outbreak, analysis of subpopulations based on recruitment measures was not performed.

3.4 PROTOCOL DEVIATIONS

A summary of all major protocol deviations is provided in the final CSR Section 4.3.1, also including a summary of COVID-19 related major protocol deviations. Major protocol deviations related to COVID-19 were reported in 8 patients across all cohorts and are summarized below. No major protocol deviations in laboratory testing and data collection that may have impacted the safety reporting of the study were reported. Overall, COVID-19 pandemic disruption did not impact the frequency or nature of major protocol deviations and did not impact the overall quality of the study or the outcome of the study.

Cohort A

In Cohort A, four major protocol deviations were reported in 4 (1.6%) participants. Two participants missed more than 1 cycle of paclitaxel and 2 participants had study procedures performed at home visits.

Cohort B

In Cohort B, two major protocol deviations were reported in 2 (0.9%) participants, both participants missed more than 1 cycle of study treatment.

Cohort C

In Cohort C, two major protocol deviations were reported in 2 (2%) participants, one participant had study procedures performed at home visits and one participant did not discontinue study treatment per protocol.

A listing of patients who were reported to have major protocol deviations related to COVID-19 pandemic is provided (l_dv_reas_COVDV_A_IT, l_dv_reas_COVDV_B_IT, l_dv_reas_COVDV_C_IT).

3.5 EFFICACY

3.5.1 Exposure

The COVID-19 pandemic disruption led to missed or delayed dosing for some patients. Overall, major protocol deviations were reported for four patients who missed more than 1 cycle of study treatment due to COVID-19 (Section 3.4), which had no impact on efficacy.

3.5.2 Impact of COVID-19 Pandemic on Efficacy Analyses

Missing two consecutive tumor assessments was considered a major protocol deviation, and no deviations related to COVID-19 were reported under this category (l_dv_reas_COVDV_A_IT, l_dv_reas_COVDV_B_IT, l_dv_reas_COVDV_C_IT). As described in Section 2.1.1, the use of alternative imaging centers was implemented as a temporary change and tumor assessments for 2 patients in Cohort A were performed at an alternative center.

Overall, the impact of the COVID-19 pandemic disruption on efficacy analysis was minimal.

3.6 SAFETY

Overall, the COVID-19 pandemic did not significantly impact the ability to monitor and manage patient safety during the conduct of the study. In addition, COVID-19 disruption did not significantly impact the safety results of the study or the safety profile of the study treatment. The observed safety findings from the study are not confounded significantly by the pandemic and remain scientifically valid.

3.6.1 Impact of COVID-19 Pandemic on Adverse Event Reporting

Overall, the COVID-19 pandemic did not significantly impact the ability to monitor and manage patient safety during the conduct of the trial.

3.6.2 Confirmed or Suspected COVID-19 Infection

Seventeen patients (Cohort A, n=9; Cohort B=3; Cohort C, n=5) were reported to have confirmed or suspected COVID-19 infection AEs, as identified by the MedDRA COVID-19 SMQ (l_ae_COV_A_SE, l_ae_COV_B_SE, l_ae_COV_C_SE). See Section 3.6.3.1 below.

Patient narratives are provided for all patients with Confirmed/Suspected COVID-19 SAEs in each cohort (active arm only).

3.6.3 Impact of COVID-19 on Adverse Event Profile

3.6.3.1 Summary of COVID-19 Associated AEs

A total of 17 AEs associated with COVID-19 were reported across the three cohorts: 9 (5.4%) patients in Cohort A (all in the Ipat+Pac arm), 3 patients in Cohort B [2 (1.4%) in the Ipat+Pac arm) and 1 (1.3%) in the Pbo+Pac arm], and 5 (4.9%) patients in Cohort C. (l_ae_COVAS_A_SE, l_ae_COVAS_B_SE, l_ae_COVAS_C_SE, t_ae_COVAS_A_SE, t_ae_COVAS_B_SE, t_ae_COVAS_C_SE). Of these, 2 patients (1 in the Ipat+Pac arm in Cohort B and 1 in Cohort C) discontinued treatment due to confirmed or suspected COVID-19 infection (l_ae_COV_A_SE, l_ae_COV_B_SE, l_ae_COV_C_SE).

3.6.3.2 COVID-19 Associated Adverse Events Leading to Study or Study Treatment Discontinuation

Two patients across all cohorts discontinued study treatment due to COVID-19 associated AE: 1 patient in the Ipat+Pac arm in Cohort B and 1 patient in Cohort C (l_ae_COV_A_SE, l_ae_COV_B_SE, l_ae_COV_C_SE). Of these, the 1 patient in Cohort C also discontinued the study due to Grade 5 AE of suspected COVID-19. This was also assessed as a death related to COVID-19 by the investigator (l_ae_COVAS_SDSC_C_SE, l_dd_C_SE).

3.6.4 Impact of COVID-19 Pandemic on Laboratory Testing

Overall, the COVID-19 pandemic had a minor impact on the laboratory testing with no impact on the study safety results.

The use of local laboratories for hematology and biochemistry testing was implemented in Study CO40016 as part of the protocol schedule of activities. As described in Section 2.1.1, blood work could be conducted at local laboratories closer to the patients, if needed. If an alternate local laboratory was used for safety bloodwork, the results would have then been shared with the PI site. Despite having the laboratory samples collected at patients' homes, the overall laboratory results were not impacted.

4. INTERPRETATION OF FINDINGS

Study CO40016 began on 6 January 2018 (FPI) and ended on 4 January 2023 (LPLV). Before the pandemic, the study was nearly fully enrolled, and the protocol-defined primary analyses were completed soon after the pandemic onset. The CCOD for the study was 30 October 2021 for efficacy analyses. A snapshot date of 21 March 2023 was utilized for non-efficacy analyses. Some additional measures for safety data and protocol deviation collection due to COVID-19 were added to mitigate the impact on the study. Overall, 17 patients (2.96%) had a confirmed or suspected COVID-19 infection (all cohorts) and 8 major protocol deviations due to COVID-19 were reported in 8 patients (1.39%). However, their impact was minimal and did not affect the overall analyses. Despite the pandemic, every effort was made to report the safety events on time and no major safety concerns were observed. Therefore, the overall efficacy and safety data collected from the study still hold scientific validity.

5. CONCLUSION

The COVID-19 pandemic had minor impact on the study conduct and data collection. Data analysis has not been impacted:

- The study protocol or conduct has not been altered.
- The study had minimal missing data.
- The impact on safety data collection was minor. The observed overall safety findings from the study were not confounded by the pandemic, still hold scientific validity and are clinically meaningful.
- The risk/benefit ratio of ipatasertib remains unchanged, as both efficacy and safety results have not been impacted.

6. REFERENCES

Primary Clinical Study Report: Study CO40016, (Cohort A–Triple Negative Breast Cancer). A double-blind, placebo-controlled, randomized phase III study of ipatasertib in combination with paclitaxel as a treatment for patients with PIK3CA/AKT1/PTEN-altered, locally advanced or metastatic, triple-negative breast cancer or hormone receptor–positive, HER2-negative breast cancer. Report No 1101889. November 2020.

Primary Clinical Study Report: Study CO40016, (Cohort B-Hormone Receptor Positive, HER2-Negative Breast Cancer). A double-blind, placebo-controlled, randomized phase III study of ipatasertib in combination with paclitaxel as a treatment for patients with PIK3CA/AKT1/PTEN-altered, locally advanced or metastatic, triple-negative breast cancer or hormone receptor–positive, HER2-negative breast cancer. Report No 1100941. July, 2020.

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