Clinical Trial Results – Layperson Summary

A study to look at whether pirfenidone worked in people with unclassifiable interstitial lung disease – and how safe this medicine was

See the end of the summary for the full title of the study.

Contents of the summary

About this summary

This is a summary of the results of a clinical trial (called a 'study' in this document) – written for:

Members of the public and
People who took part in the study.

This summary is based on information known at the time of writing (September-2019). More information may now be known.

The study started in May 2017 and will end in January 2020. This study has two parts. The first part of the study looked at how well the study medicine worked – and how safe this medicine was. The second part of the study will focus on how safe this medicine is.

This summary includes the results up until November 2018. This summary presents the complete results from the first part of the study. At the time of writing this summary, the second part of the study is still taking place.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.

Thank you to the people who are taking part in this study

The people who are taking part in this study are helping researchers to answer important questions about unclassifiable interstitial lung disease and pirfenidone.

Key information about this study

- This study was done to compare pirfenidone (the 'study medicine') to a placebo in people with unclassifiable interstitial lung disease
- In this study, people were given either:
  - 801 mg of pirfenidone taken by mouth three times a day
  - A placebo
- It was decided randomly which treatment each person was given
- This study has two parts. The first part looked at how well pirfenidone worked – and how safe it was. The second part will focus on how safe pirfenidone is
  - This summary presents results from the first part of the study. At the time of writing, the second part of the study is still taking place
- This study included 253 people in 14 countries
- This study tested a new way of measuring lung function by asking people to measure their own lung function at home every day
- This study also measured lung function during hospital visits
- The devices that people took home to measure their lung function were set-up to work best if three measurements were performed each day. In this trial, people measured their lung function once a day, so the spirometer could not warn them if they made a mistake
  - This meant that the spirometers recorded some impossible lung function values and researchers could not get the information they needed to find out if pirfenidone had an effect on lung function when it was measured at home
- The lung function tests done at the hospital worked as expected and showed that the lungs of people who took placebo got worse over 6 months compared with people who took pirfenidone
- Less than 1% of people (1 out of 127 people) taking pirfenidone had serious side effects. Less than 1% of people (1 out of 124 people) taking the placebo had serious side effects

1. General information about this study

Why was this study done?

Interstitial lung diseases (ILDs) are illnesses where the lungs become scarred and breathing becomes difficult. There are lots of different types of ILD. Unclassifiable ILD (uILD) is when the doctors cannot be confident what type of ILD a person has.

There are no medicines to treat people with uILD.

The medicine 'pirfenidone' helps people with a type of ILD called idiopathic pulmonary fibrosis (IPF). IPF and some types of uILD are similar in many ways. Researchers wanted to learn more about whether pirfenidone could also help people with uILD.

What was the study medicine?

A medicine called 'pirfenidone' (Esbriet®) was the focus of this study.

- Pirfenidone works by slowing down scarring – fibrosis – of the lungs in people with IPF.
- This may mean that pirfenidone can also slow down scarring of the lungs in people with uILD.

Pirfenidone was compared with a 'placebo'.

- You say this as 'plah – see – bo'.
- The placebo capsule looked the same as the pirfenidone capsule but did not contain any real medicine. This means it had no medical effect on the body.
- Researchers compared pirfenidone with a placebo so they could show which benefits or side effects are actually caused by pirfenidone.

What did researchers want to find out?

- Researchers did this study to compare pirfenidone with a placebo – to see how well the study medicine worked (see section 4 "What were the results of the study?").
- They also wanted to find out how safe the medicine was – by checking how many people had side effects when taking pirfenidone or a placebo during this study (see section 5 "What were the side effects?").

The main question that researchers wanted to answer was:

1. Does pirfenidone have an effect on lung function decline over 6 months when measured at home every day?

Other questions that researchers wanted to answer included:

2. Does pirfenidone have an effect on lung function decline over 6 months when measured at hospital visits?
3. Does pirfenidone have an effect on how far people in the study could walk in 6 minutes?
4. Did people in the study feel like pirfenidone reduced their symptoms?

What kind of study was this?

This study was a 'Phase 2' study. This means that pirfenidone had been tested in a number of people before this study – but this was the first study in people with uILD.

The study was ‘randomised’. This means that it was decided by chance which of the people in the study would receive pirfenidone – like tossing a coin. In this study, people with uILD took either pirfenidone or a placebo.

This was a ‘double-blind’ study. This means that neither the people taking part in the study nor the study doctors knew which people were taking pirfenidone.

‘Blinding’ of a study is done so that any effect seen from the medicine is not due to something people expected to happen – if they had known which medicine they were taking.

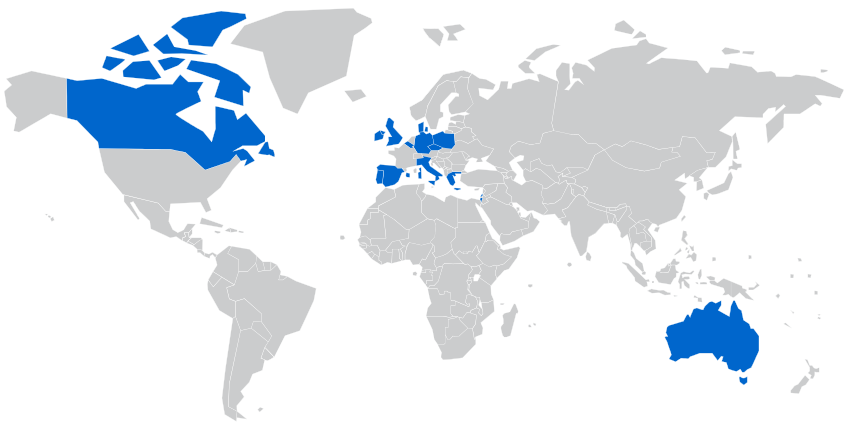
When and where did the study take place?

The study started in May 2017 and will end in January 2020. This study has two parts. The first part of the study looked at how well the study medicine worked – and how safe this medicine was. The second part of the study will focus on how safe this medicine is.

This summary includes the results up until November 2018. This summary presents the complete results from the first part of the study. At the time of writing this summary, the second part of the study is still taking place.

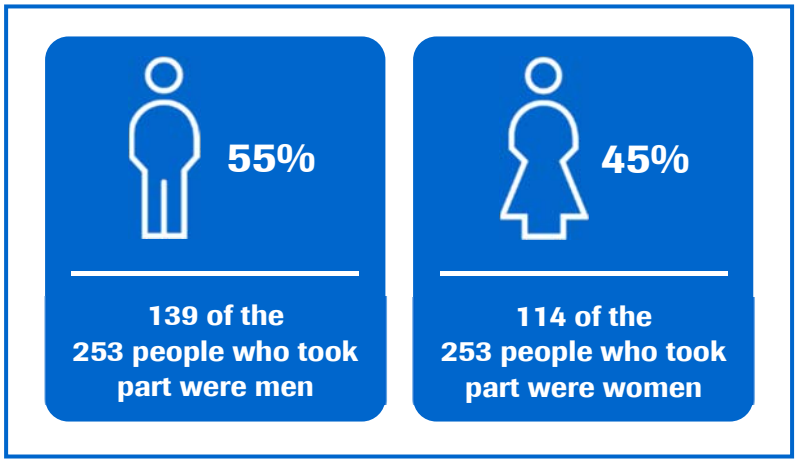
The study took place at 70 study centres – across 14 countries. The following map shows the countries where this study took place.

- Australia
- Belgium
- Canada
- Czech Republic
- Denmark
- Germany
- Greece
- Ireland
- Israel
- Italy
- Poland
- Portugal
- Spain
- UK



2. Who took part in this study?

253 adults with uILD took part in this study.



People could take part in the study if they met these criteria:

- They had uILD that was getting worse.
- More than 10% of their lung tissue showed scarring – fibrosis.
- They had at least 45% of the lung function that you would expect for a healthy person of the same age and sex.

People could not take part in the study if they met these criteria:

- They had any other serious health problems.
- They were taking certain medicines.
- They smoked or had only stopped smoking in the last 3 months.

3. What happened during the study?

During the study, people were selected by chance to get one of two treatments. The treatments were selected at random by a computer.

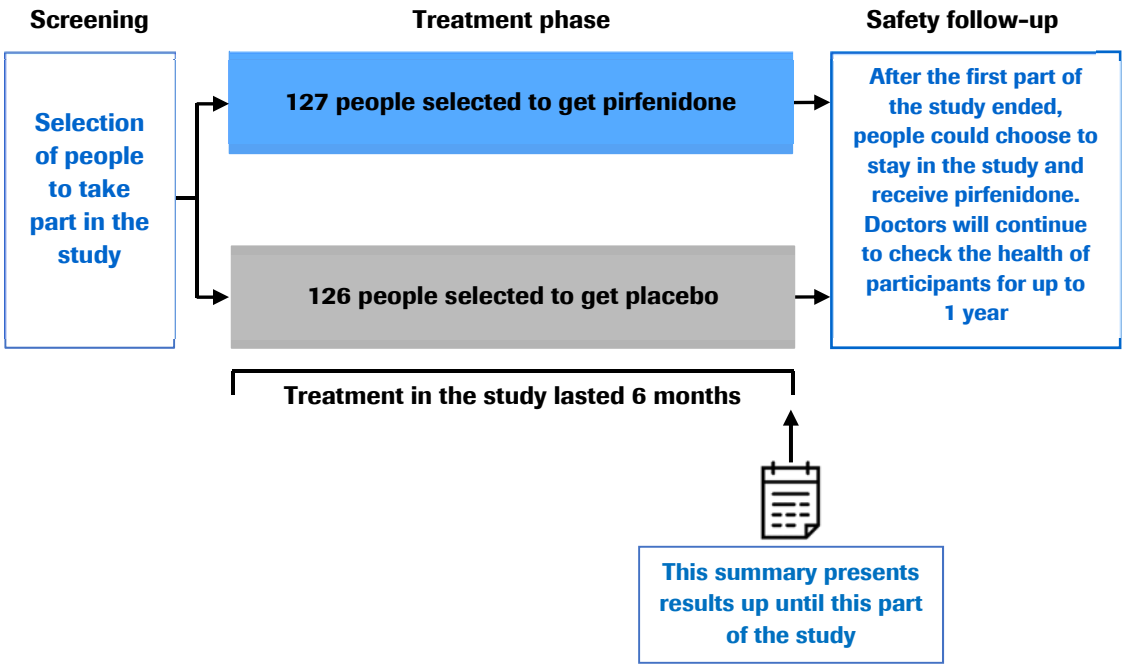
People in the study took the treatments for 6 months. People visited the hospital once every month for 6 months while they were taking the treatment. This part of the study is called the treatment phase.

The treatment groups were:

- **Pirfenidone** (the study medicine) – 801 milligrams (801 mg), taken by mouth three times a day.
- **Placebo** – taken by mouth three times a day.

After 6 months, people in the study found out if they had been taking pirfenidone or placebo during the treatment phase. People could choose to take part in the second part of the study. The second part of the study is called the safety follow-up. People who took pirfenidone in the treatment phase kept taking it in the safety follow-up. People who took placebo in the treatment phase were switched to pirfenidone for the safety follow-up. The safety follow-up is still taking place so some people are still being treated with pirfenidone.

This summary presents results from the treatment phase of the study. Look below to see more information about what happened in the study.



4. What were the results of the study?

Question 1: Does pirfenidone have an effect on lung function decline over 6 months when measured at home every day?

People in this study were given a device – a spirometer – to take home. The spirometer measured how much air they could breathe out after taking as big a breath as possible – forced vital capacity. Each person measured their forced vital capacity every day at home.

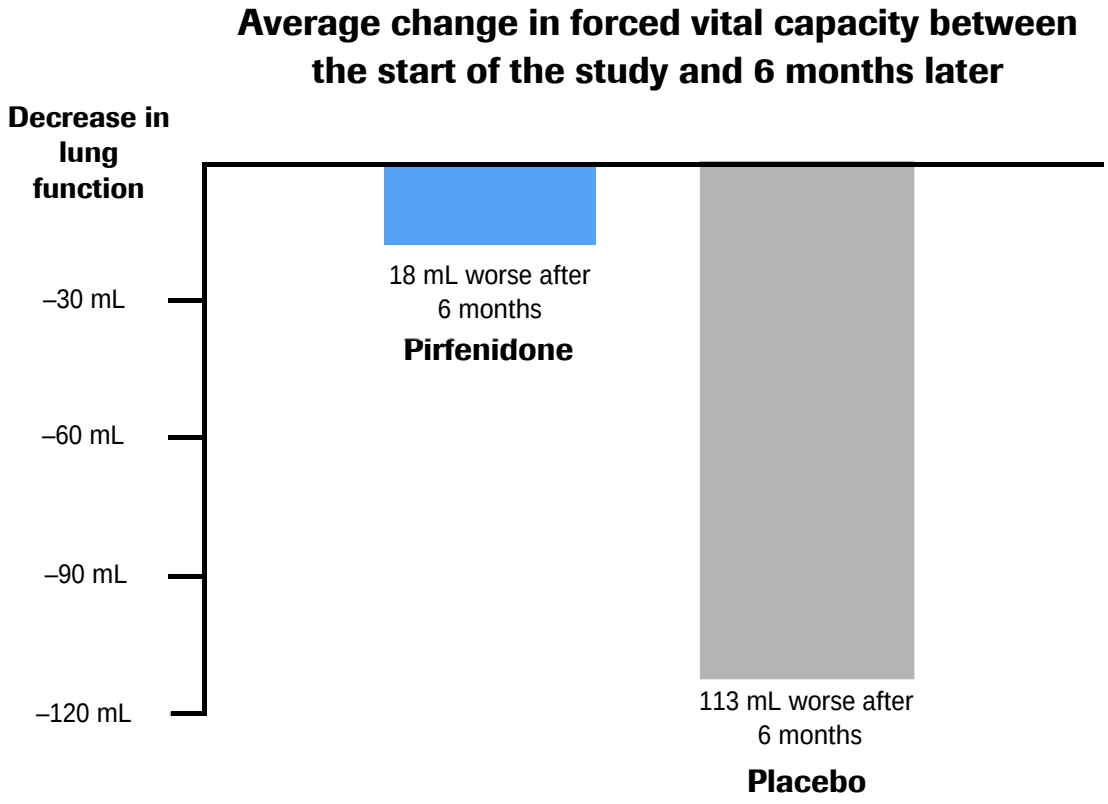
- The devices that people took home to measure their lung function were set up to work best if three measurements were performed each day. In this trial, people measured their lung function once a day, so the spirometer could not warn them if they made a mistake.
- This meant that the spirometers recorded some impossible lung function values and researchers could not get the information they needed to find out if pirfenidone had an effect on lung function when it was measured at home.

Question 2: Does pirfenidone have an effect on lung function decline over 6 months when measured at hospital visits?

Researchers also used the traditional method to measure lung function – forced vital capacity measured at the hospital. People went to the hospital once every month for 6 months to have their lung function measured.

Researchers wanted to know how much forced vital capacity changed between the start of the study and after 6 months. They compared the changes in the pirfenidone and placebo groups to see if there was a difference.

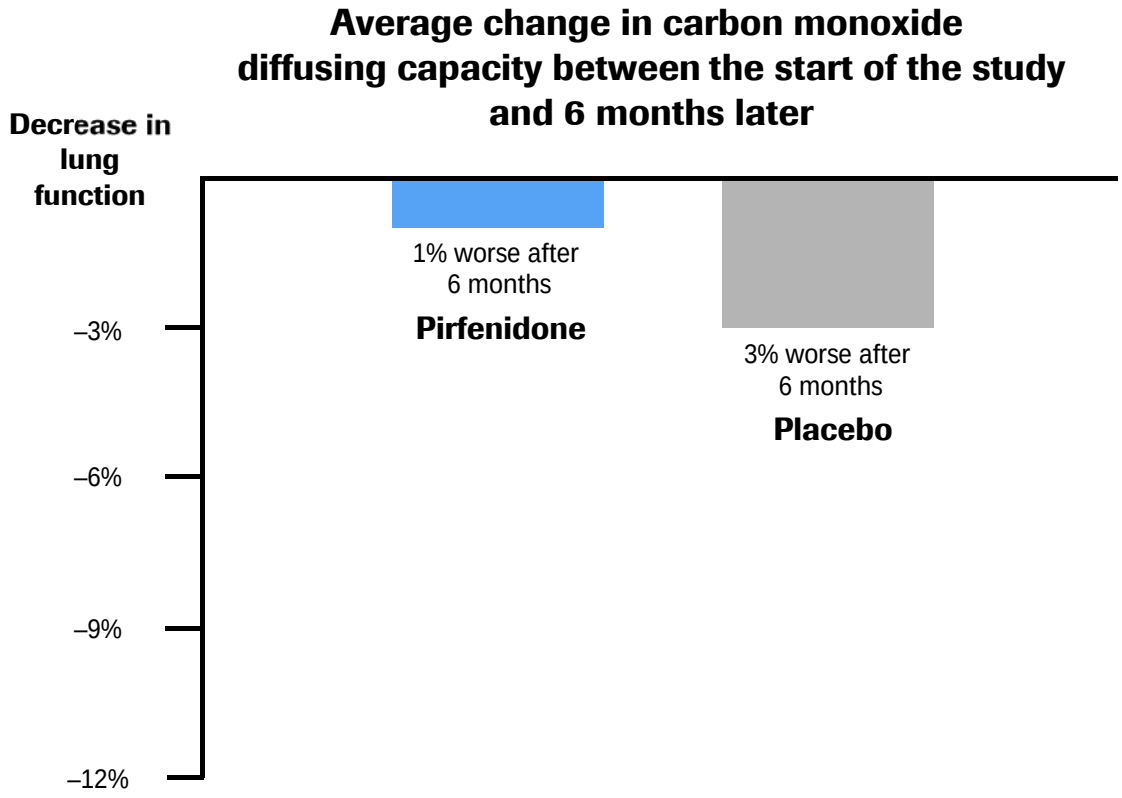
- Lung function got worse in both groups.
- Lung function worsened more in the group of people taking placebo compared with the group of people taking pirfenidone.



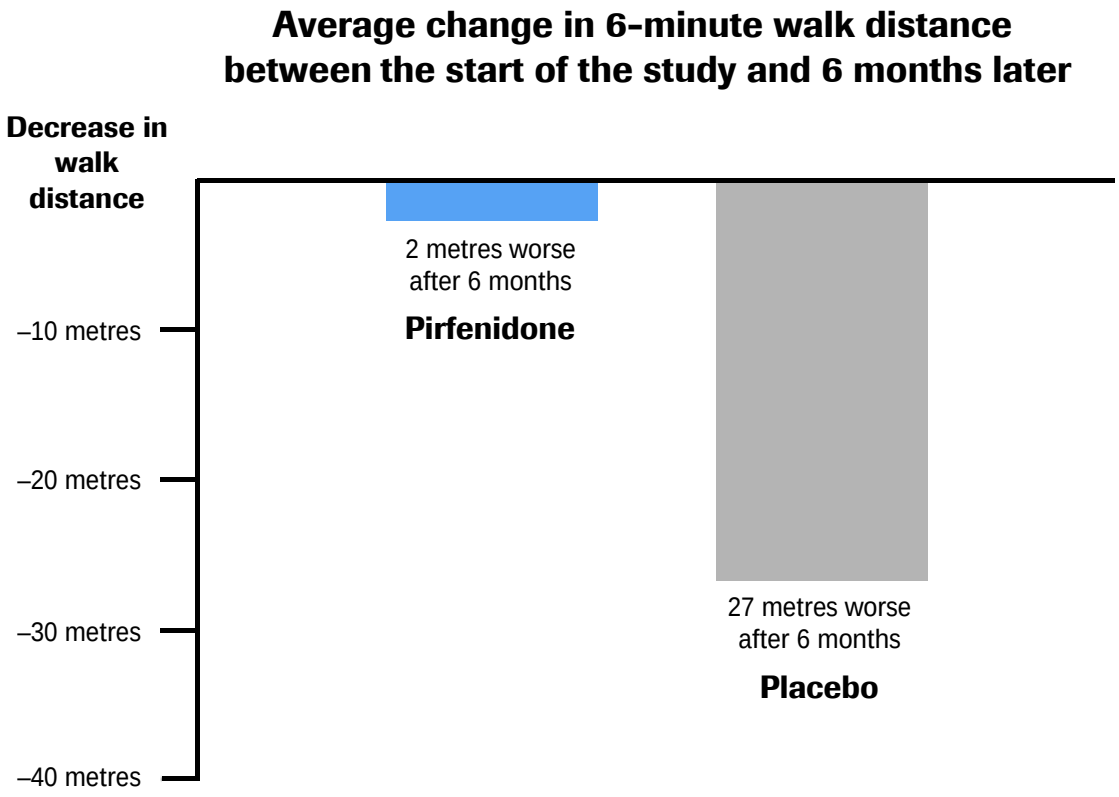
Forced vital capacity is not the only way to measure lung function. The researchers measured how well people's lungs moved oxygen into the blood – carbon monoxide diffusing capacity. The results were presented as a percentage of the value that you would expect for a healthy person of the same age and sex. For example, if the lungs of a person with uILD moved oxygen half as well as those of a person without uILD, they would have a carbon monoxide diffusing capacity of 50%.

Researchers wanted to know how much the carbon monoxide diffusing capacity changed between the start of the study and after 6 months. They compared the changes in the pirfenidone and placebo groups to see if there was a difference.

- Carbon monoxide diffusing capacity got worse in both groups.
- The differences between the two groups were too small to tell if pirfenidone had an effect on carbon monoxide diffusing capacity.



Question 3: Does pirfenidone have an effect on how far people in the study could walk in 6 minutes?



Researchers also looked at how far people in the study could walk in 6 minutes – 6-minute walk distance. They looked at 6-minute walk distance because people with ILD can get out of breath easily and can struggle to walk as far as they used to.

Researchers wanted to know how much 6-minute walk distance changed between the start of the study and after 6 months. They compared the changes in the pirfenidone and placebo groups to see if there was a difference.

- 6-minute walk distance got worse in both groups.
- 6-minute walk distance worsened more in the group of people taking placebo compared with the group of people taking pirfenidone.

Question 4: Do people with uILD feel like pirfenidone reduced their symptoms?

The symptoms of uILD cannot be eliminated but some treatments can help reduce the impact of symptoms on everyday life. The researchers asked people in the study to complete a number of surveys that asked about their breathlessness and cough. The researchers also asked people about their general well-being – quality of life. The researchers asked about well-being because people with ILD can feel depressed or limited by their symptoms.

- People in the pirfenidone and placebo groups provided similar answers to the surveys.
- The differences between the two groups were too small to tell if pirfenidone had an effect on breathlessness, cough or quality of life.

5. What were the side effects?

Side effects – also known as 'adverse reactions' – are unwanted medical problems (such as a headache) that happen during the study.

- They are described in this summary because the study doctor believes the side effects were related to the treatments in the study (pirfenidone or placebo). Side effects could be considered related to placebo because study doctors did not know if people were taking pirfenidone or placebo.
- Not all of the people in this study had all of the side effects.

Serious and common side effects are listed in the following sections.

Serious side effects

A side effect is considered 'serious' if it is life threatening, needs hospital care or causes lasting problems.

During this study, less than 1 in every 100 people (less than 1%) had at least one serious side effect. Less than 1% of people taking pirfenidone had a serious side effect. Less than 1% of people taking placebo had a serious side effect.

Two serious side effects were reported in this study. One happened in someone taking pirfenidone and the other happened in someone taking placebo.

	People taking pirfenidone (127 people total)	**People taking placebo** (124 people total)
Serious side effects reported in this study	Feeling less hungry Less than 1% (1 out of 127 people)	Liver problems Less than 1% (1 out of 124 people)

Nobody in this study died due to side effects that may have been related to one of the study medicines.

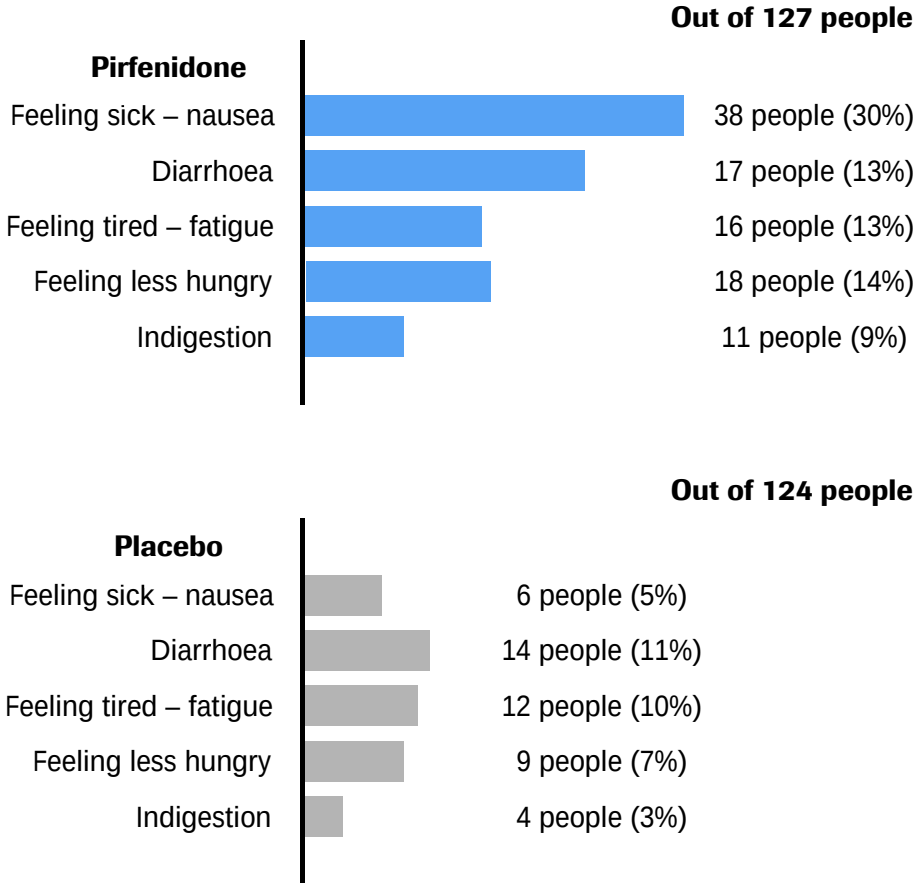
During the study, some people decided to stop taking their medicine:

- In the pirfenidone group, 25 out of 127 people (20%) stopped taking their medicine; in 16 out of 127 people (13%), this was due to a side effect related to the medicine.
- In the placebo group, 10 out of 124 people (8%) stopped taking their medicine; in 1 out of 124 people (less than 1%), this was due to a side effect related to the medicine.

Most common side effects

During this study, nearly 60 out of every 100 people (59%) had a side effect. Around 71% of people taking pirfenidone had a side effect, compared with 46% of people taking a placebo.

The most common side effects are shown in the following visual – these were the five most common side effects among all the people who took part in the study.



Other side effects

You can find information about other side effects – not shown in the sections above – on the websites listed at the end of this summary – see section 8.

6. How has this study helped research?

The information presented here is from a single study of 253 people with uILD. These results helped researchers learn more about uILD and pirfenidone.

This study tested a new way of measuring lung function by asking people to measure their own lung function at home every day. However, the devices that people took home to measure their lung function were set up to work best if three measurements were performed each day. In this trial, people measured their lung function once a day, so the spirometer could not warn them if they made a mistake. This meant that the spirometers recorded some impossible lung function values and researchers could not get the information they needed to find out if pirfenidone had an effect on lung function when it was measured at home. Researchers will need to find out how to set up the devices so that clinical studies in the future do not have the same problem.

People in the study also attended visits at the hospital to have their lung function and 6-minute walk distance measured. Although forced vital capacity and 6-minute walk distance got worse in both the pirfenidone and placebo groups, people who took placebo worsened more than people who took pirfenidone.

Researchers also measured how well people's lungs moved oxygen into the blood – carbon monoxide diffusing capacity. Carbon monoxide diffusing capacity got worse in both treatment groups. The differences between the two groups were too small to tell if pirfenidone had an effect on carbon monoxide diffusing capacity.

People in the study completed surveys on their breathlessness, cough and general well-being – quality of life. People in the pirfenidone and placebo groups provided similar answers to the survey. The differences between the two groups were too small to tell if pirfenidone had an effect on breathlessness, cough or quality of life.

Researchers also looked at medical problems people had during the study. Less than 1% of people who took pirfenidone had a serious side effect. Around 71% of people who took pirfenidone had a side effect compared with 46% of people who took placebo.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.

7. Are there plans for other studies?

At the time of writing this summary, no more studies looking at pirfenidone in uILD are planned.

The study started in May 2017 and will end in January 2020. This study has two parts. The first part of the study looked at how well the study medicine worked – and how safe this medicine was. The second part of the study will focus on how safe this medicine is.

This summary includes the results up until November 2018. This summary presents the complete results from the first part of the study. At the time of writing this summary, the second part of the study is still taking place.

8. Where can I find more information?

You can find more information about this study on the websites listed below:

- https://clinicaltrials.gov/ct2/show/results/NCT03099187
- https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-002744-17
- https://forpatients.roche.com/en/trials/respiratory-disorder/a-study-of-pirfenidone-in-patients-with-unclassifiable--64703.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: "Pirfenidone in patients with unclassifiable progressive fibrosing interstitial lung disease: a double-blind, randomised, placebo-controlled, phase 2 trial". The authors of the scientific paper are: T.M. Maher, T.J. Corte, A. Fischer, M. Kreuter, D.J. Lederer and others. The paper is published in the journal '*Lancet Respiratory Medicine*'.

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – https://forpatients.roche.com/en/trials/respiratory-disorder/a-study-of-pirfenidone-in-patients-with-unclassifiable--64703.html
- Contact a representative at your local Roche office.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

Who organised and paid for this study?

This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland. This study was initially developed as part of an NIHR-funded Clinician Scientist Fellowship awarded to Professor Toby M. Maher (NIHR Ref: CS-2013-13-017) and subsequently adapted following discussions with F. Hoffmann-La Roche, Ltd.

Full title of the study and other identifying information

The full title of this study is: "Multicenter, International, Double-Blind, Two-Arm, Randomized, Placebo-Controlled Phase II Trial of Pirfenidone in Patients with Unclassifiable Progressive Fibrosing ILD".

- The protocol number for this study is: MA39189.
- The ClinicalTrials.gov identifier for this study is: NCT03099187.
- The EudraCT number for this study is: 2016-002744-17.

9. Glossary

6-minute walk distance	How far a person can walk in 6 minutes on a flat surface
Carbon monoxide diffusing capacity	How well a person's lungs move oxygen from the air into the blood
Clinical trial	A clinical trial – or study – is when researchers give a group of people a medicine The researchers regularly follow-up with the people taking the medicine and perform medical tests Clinical trials aim to find out if a new medicine is safe, has side effects, works better than the medicine currently used and if it helps people feel better
Double-blind	Some clinical trials include more than one treatment that researchers want to compare. For example, a lot of clinical trials include: • A study medicine • A placebo A 'double-blind' study means that neither the people taking part in the trial nor the study doctors know which people are taking the study medicine and which people are taking the placebo
Fatigue	Feeling tired
Fibrosis	Scarring
Forced vital capacity	How much air a person can breathe out after taking as big a breath as possible
Idiopathic pulmonary fibrosis (IPF)	An illness where the lungs become scarred and breathing becomes difficult Idiopathic pulmonary fibrosis is a type of interstitial lung disease
Interstitial lung diseases (ILDs)	A group of illnesses where the lungs become scarred and breathing becomes difficult
Lung function	How well the lungs work
Nausea	Feeling sick

Pirfenidone (Esbriet®)	A medicine used to treat people with idiopathic pulmonary fibrosis Pirfenidone works by slowing down scarring of the lungs in people with idiopathic pulmonary fibrosis
Phase 2 study	Phase 2 studies take place after a medicine has been tested in people with no health problems A Phase 2 study aims to show that the medicine has a real benefit to people with a health problem
Placebo	A treatment in a clinical trial that does not contain any real medicine People who take part in a clinical trial are given either: • The real study medicine • A placebo that looks the same as the study medicine Placebos help researchers show which benefits or side effects are caused by the medicine
Quality of life	General well-being
Randomised	Some clinical trials include more than one treatment that researchers want to compare. For example, a lot of clinical trials include: • A study medicine • A placebo Randomised means that the treatment received by each person in the trial was selected at random by a computer
Serious side effect	A side effect that is life-threatening, needs hospital care or causes lasting problems
Side effects	Unwanted medical problems that happen after people take a medicine
Spirometer	A device that measures forced vital capacity – lung function
Unclassifiable interstitial lung disease (uILD)	When doctors cannot be confident what type of interstitial lung disease a person has

A study of pirfenidone in unclassifiable interstitial lung disease

This is a summary of the results of a clinical trial written in September 2019 for members of the public and people who took part in the study. No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine. This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment

Study summary

This study was done to find out if pirfenidone helps people with unclassifiable interstitial lung disease (uILD) by comparing the effects of pirfenidone with a placebo

Pirfenidone helps people with a type of ILD called idiopathic pulmonary fibrosis (IPF). IPF and some types of uILD are similar in many ways. Researchers wanted to learn more about whether pirfenidone could also help people with uILD

This study also tested a new way of measuring lung function by asking people to measure their own lung function at home every day. However, the devices that people took home to measure their lung function were set up to work best if three measurements were performed each day. In this trial, people measured their lung function once a day, so the spirometer could not warn them if they made a mistake.

This meant that the spirometers recorded some impossible lung function values and researchers could not get the information they needed to find out if pirfenidone had an effect on lung function when it was measured at home

Interstitial lung diseases (ILDs) are illnesses where the lungs become scarred and breathing becomes difficult. uILD is when the doctors cannot be confident what type of ILD a person has

People had their lung function measured at the hospital each month during the study – these tests showed that the lung function of people who took placebo got worse over 6 months compared with people who took pirfenidone

Less than 1% of people (1 out of 127 people) taking pirfenidone had serious side effects. Less than 1% of people (1 out of 124 people) taking the placebo had serious side effects

Detailed information about this study can be found at https://clinicaltrials.gov/ct2/show/study/NCT03099187

Who took part in the study?

What tests were used in the study?

Researchers wanted to know how much the results of the following tests changed between the start of the study and after 6 months

Lung Function

Forced vital capacity
how much air people can breathe out after taking as big a breath as possible

- Measured at home every day using handheld spirometers
- Measured at hospital once every month

Carbon monoxide diffusing capacity
measured how well peoples' lungs moved oxygen from the air and into the blood

Other Tests

6-minute walk distance
how far people could walk in 6 minutes

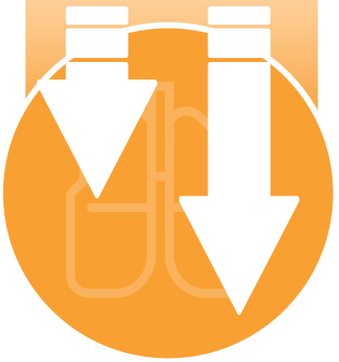
People filled out surveys to measure how they felt about their symptoms (shortness of breath and cough) and about their general well-being (quality of life)

What are the main results from the study?

The devices that people took home to measure their lung function were set up to work best if three measurements were performed each day. In this trial, people measured their lung function once a day, so the spirometer could not warn them if they made a mistake. This meant that the spirometers accepted some impossible lung function values and researchers could not get the information they needed to find out if pirfenidone had an effect on lung function when it was measured at home. However, the measurements taken at the hospital worked as expected:

Forced vital capacity

got worse in the people taking placebo compared with the people taking pirfenidone



pirfenidone **-18mL** placebo **-113mL**

Carbon monoxide diffusing capacity

The differences between the two groups were too small to tell if pirfenidone had an effect

pirfenidone **-1%** placebo **-3%**

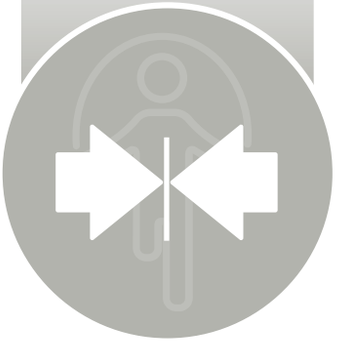
6-minute walk distance

got worse in the people taking placebo compared with the people taking pirfenidone

pirfenidone **-2m** placebo **-27m**

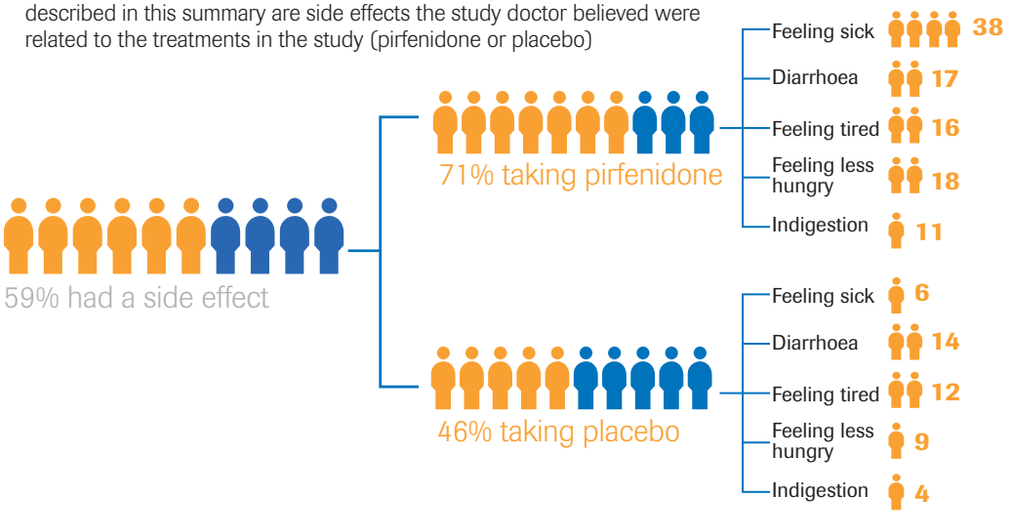
Shortness of breath, cough & quality of life

The differences between the two groups were too small to tell if pirfenidone had an effect



Were there any side effects?

Side effects – also known as 'adverse reactions' – are unwanted medical problems (such as a headache) that happen during the study. The side effects described in this summary are side effects the study doctor believed were related to the treatments in the study (pirfenidone or placebo)



Two serious side effects were reported in this study. One happened in someone taking pirfenidone (feeling less hungry) and the other happened in someone taking placebo (liver problems)

During the study, some people decided to stop taking their medicine

- In the pirfenidone group, 25 out of 127 people (20%) stopped taking their medicine; in 16 out of 127 people (13%) this was due to a side effect related to the medicine
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Visit the ForPatients platform and fill out the contact form: https://forpatients.roche.com/en/trials/respiratory-disorder/a-study-of-pirfenidone-in-patients-with-unclassifiable--64703.html

Or contact a representative at your local Roche office

If you took part in this study and have any questions about the results:

Speak with the study doctor or staff at the study hospital or clinic

If you have questions about your own treatment:

Speak to the doctor in charge of your treatment

Are there plans for other studies?

At the time of writing, no more studies looking at pirfenidone in uILD are planned

The study started in May 2017 and will end in January 2020. This study has two parts. The first part of the study looked at how well the study medicine worked – and how safe this medicine was. The second part of the study will focus on how safe this medicine is

This summary includes the results up until November 2018. This summary presents the complete results from the first part of the study. At the time of writing this summary, the second part of the study is still taking place

Who organised and paid for this study?

This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland. This study was initially developed as part of an NIHR-funded Clinician Scientist Fellowship awarded to Professor Toby M. Maher (NIHR Ref: CS-2013-13-017) and subsequently adapted following discussions with F. Hoffmann-La Roche, Ltd.