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Plain language summary: clinical trial of BI 1015550 as a potential treatment for idiopathic pulmonary fibrosis

Luca Richeldi[1], Arata Azuma[2], Vincent Cottin[3], Christian Hesslinger[4], Susanne Stowasser[5], Claudia Valenzuela[6], Marlies S Wijsenbeek[7], Donald F Zoz[8], Florian Voss[9] & Toby M Maher[10]

[1]Unità Operativa Complessa di Pneumologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy; [2]Pulmonary Medicine and Oncology, Nippon Medical School, Tokyo, Japan; [3]Hôpital Louis Pradel, Centre Coordonnateur National de Référence des Maladies Pulmonaires Rares, Hospices Civils de Lyon, Université Claude Bernard Lyon 1, Lyon, France, [4]Translational Medicine + Clinical Pharmacology, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany; [5]TA Inflammation Med, Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; [6]ILD Unit, Pulmonology Department, Hospital Universitario de la Princesa, University Autonoma de Madrid, Madrid, Spain; [7]Department of Respiratory Medicine, Erasmus Medical Center, Rotterdam, The Netherlands; [8]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; [9]Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim am Rhein, Germany; [10]Keck Medicine of USC, Los Angeles, CA, USA

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Summary

What is this summary about?

This plain language summary describes the main findings from a trial in people with idiopathic pulmonary fibrosis (also called IPF) that was recently published in the *New England Journal of Medicine*. IPF is a rare disease, where the lungs become more and more scarred, with breathing and oxygen uptake becoming increasingly difficult.

This trial looked at the medication BI 1015550 as a potential treatment for IPF. It compared BI 1015550 to placebo (a dummy drug that does not contain any active ingredients) to investigate the effectiveness of the drug in treating people with IPF. The study also looked at the additional medical issues (referred to as adverse events) reported during the study. Some participants took approved treatments to reduce scarring (nintedanib or pirfenidone), and some did not.

What were the results?

Overall, 147 people with IPF from 22 countries took part in the trial. The results showed that BI 1015550 prevented lung function from decreasing in people with IPF. There was no difference in the percentage of patients with medical issues rated as severe by the study physician with BI 1015550 or placebo. However, more people treated with BI 1015550 had diarrhoea. Among those treated with BI 1015550, 13 participants stopped their treatment due to medical issues, whereas treatment was not stopped due to medical issues for any participants treated with placebo.

What do the results mean?

These results provide evidence that BI 1015550 prevents lung function from worsening in people with IPF. Further clinical studies will be conducted in the future to test BI 1015550 in a larger group of people with IPF and other forms of lung scarring that get worse over time, and for a longer time period.

How to say medical terms used in this summary (double click on the sound icon to play the sound)

Antifibrotics: an-tee-fie-broht-iks

Idiopathic pulmonary fibrosis: id-i-uh-path-ik pul-muh-nuh-ree fie-broh-sis

Interstitial lung disease: in-tuh-stish-uhl luhng di-zeez

Nintedanib: nin-ted-a-nib

Pirfenidone: pir-fen-i-dun

Phosphodiesterase: fos-foe-die-est-er-ase

Placebo: pluh-see-boh

Becaris PUBLISHING

An Animated Video describing this study is available online alongside this article. Scan the QR code or click on this link to watch the video:
https://www.globalmedcomms.com/respiratory/PhaseII_PLSP/Richeldi

Where can I find the original article on which this summary is based?

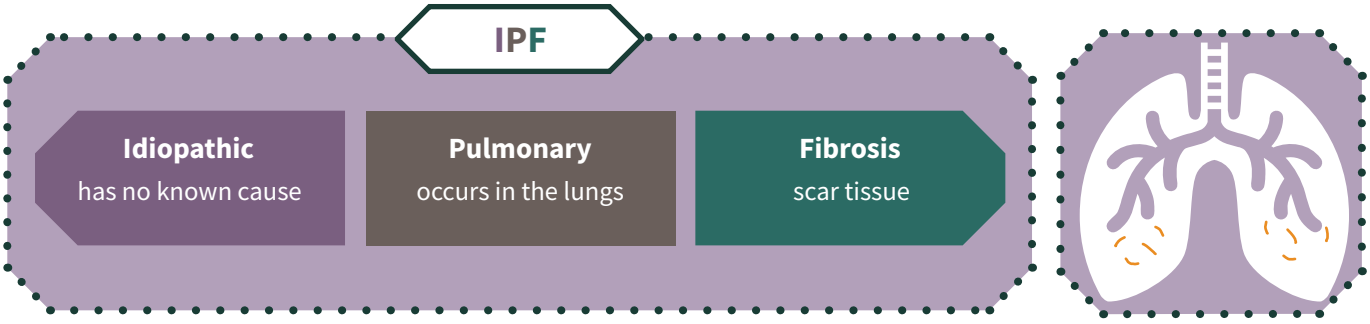
You can read the original article published in *New England Journal of Medicine* at:
https://www.nejm.org/doi/full/10.1056/NEJMoa2201737

Who is this article for?

This article may be useful for people with IPF, their families and caregivers. Patient advocates and healthcare professionals may also find it useful.

What is idiopathic pulmonary fibrosis?

Idiopathic pulmonary fibrosis, also known as IPF, is a severe type of lung disease where scarring of the lungs will continue to get worse over time.



The scar tissue cannot be repaired by the body, and this scarring will continue to worsen over time. This causes the lungs to become stiff and decreases their volume, which makes it more difficult for people with IPF to breathe and get oxygen into their bloodstream.

Common symptoms of IPF include breathlessness and cough.

Two **antifibrotic treatments**, nintedanib and pirfenidone, have been **approved** to treat IPF.

Antifibrotic treatment: Drugs that reduce but do not stop scarring in the lungs of people with IPF.

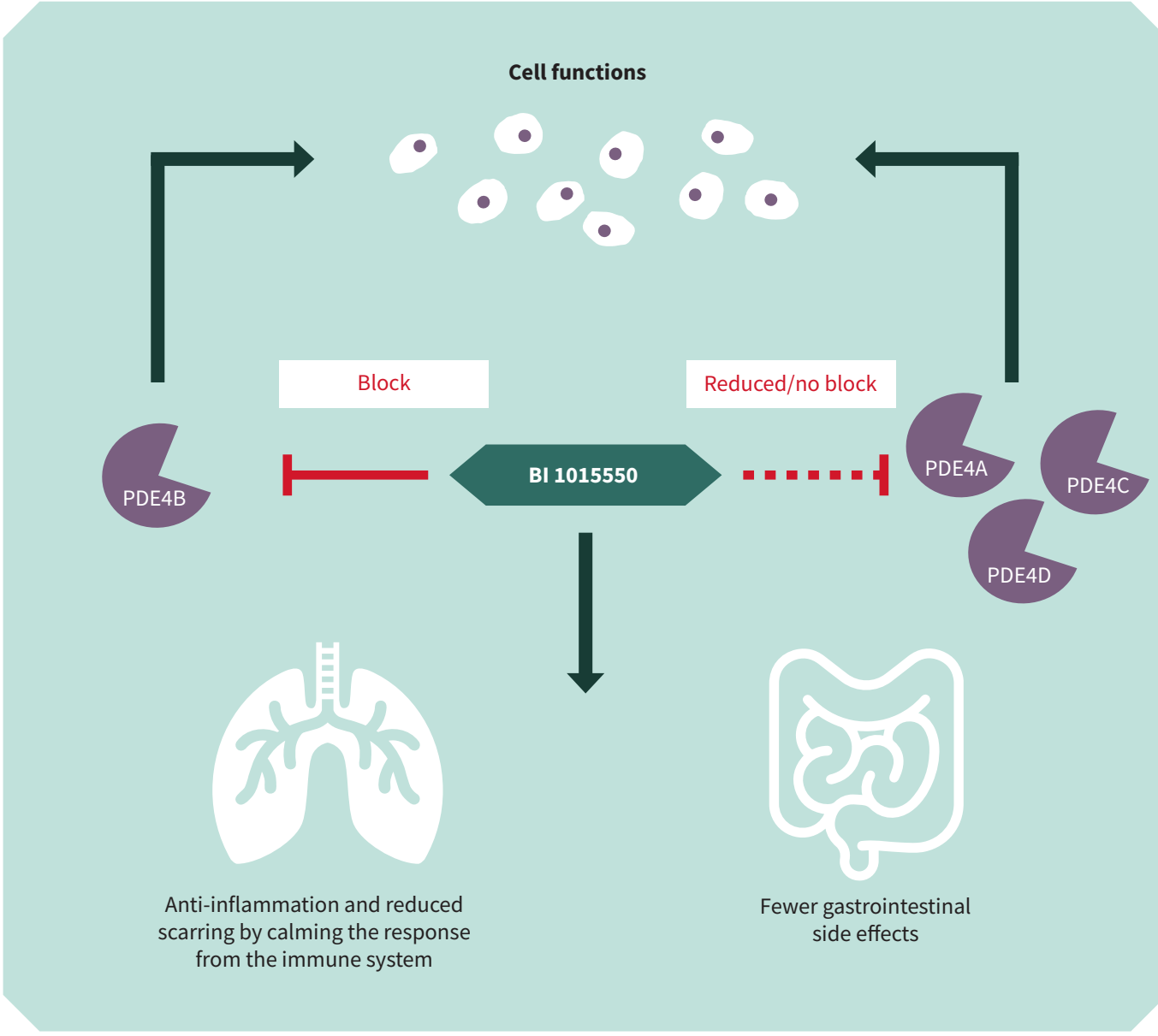
Approved means that the treatment has been reviewed by the appropriate regulatory authorities and they have determined that the benefits of this drug outweigh its known potential risks. A treatment that is approved means it can be prescribed to patients.

What is BI 1015550?

BI 1015550 is a type of drug called a phosphodiesterase 4 inhibitor. Phosphodiesterase 4, also known as PDE4, is a group of proteins that have important roles in human cells. Previous studies in animals or with human cells have shown that drugs that block the activity of PDE4 reduce inflammation and scarring.

There are four types of PDE4 molecules: PDE4A, PDE4B, PDE4C and PDE4D.

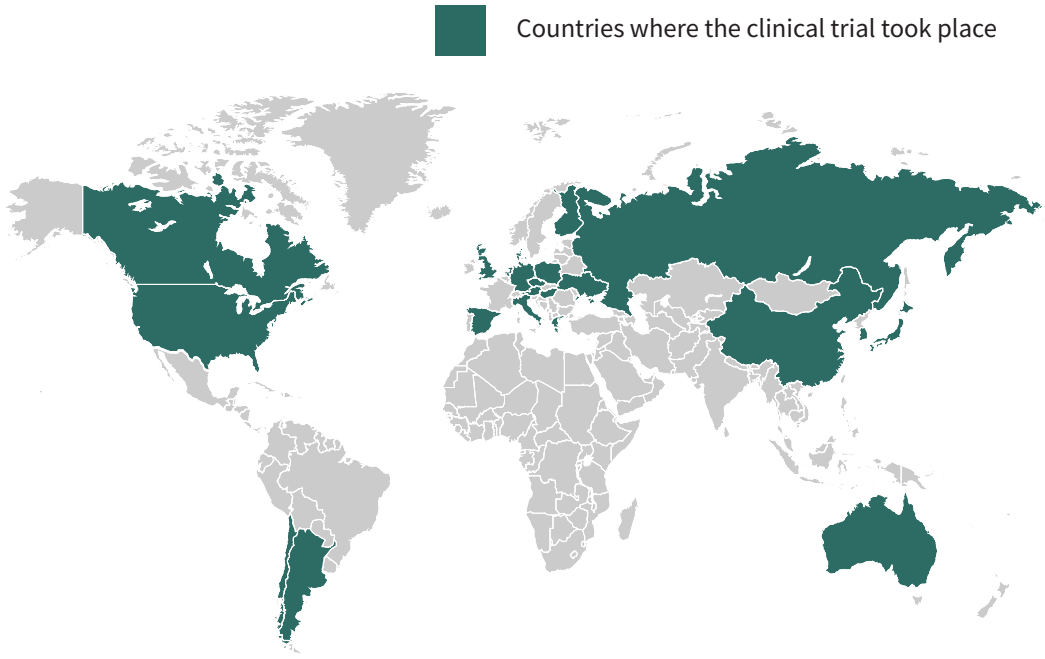
BI 1015550 is a new drug that blocks the activity of PDE4B. Since PDE4 proteins have different functions, blocking all types could lead to unwanted side effects elsewhere in the body. BI 1015550 mainly targets PDE4B, and researchers hope this will make side effects less likely.



Who took part in the trial?

147 participants from **22 countries** took part in this study.

Argentina
Australia
Austria
Canada
Chile
China
Czech Republic
Denmark
Finland
Germany
Greece
Hungary
Italy
Japan
The Netherlands
Poland
Republic of Korea
Russian Federation
Spain
Ukraine
United Kingdom
United States



In order to take part, patients had to:

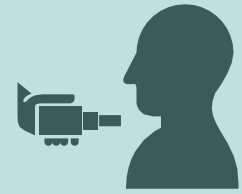
- Be aged 40 years or older with a diagnosis of IPF
- Have signs of lung scarring confirmed by a high-resolution computed tomography (an imaging technique) scan of the lungs
- Have lung test measures within a specific range:
  - Forced vital capacity (FVC) percent predicted ≥45% (normal range: 80–120%)
  - Diffusing capacity for carbon monoxide (DLco) percent predicted ≥25% to <80% (normal range: 75–140%)
- Have no evidence that there is any blockage of the airways
- Have no recent lung infections

Lung function tests

People with IPF undergo several tests, called lung function tests, to check if their disease if getting better or worse. These tests include:

Forced vital capacity (FVC): This is the total amount of air that can be blown out from the lungs. To measure this, a test is performed by a person blowing into a device called a spirometer. It measures the amount of air (in millilitres) a person can forcefully blow out after fully breathing in. It is used to show how well the lungs are working by testing the volume of the lungs. Since IPF causes lung function to get worse, FVC reduces over time.

A person with low FVC will have difficulty breathing and will have worse lung function.



Forced vital capacity (ml)

Diffusing capacity of the lung for carbon monoxide (DLco): DLco is a test to measure how much carbon monoxide from the air is taken up into the bloodstream in the lungs. It is measured by testing the amount of carbon monoxide breathed in and out by a person, and is used to indirectly measure how well the lungs can take up oxygen.

A person with low DLco is less able to take up oxygen into their body.

Percent predicted: Lung measures for FVC and DLco are sometimes expressed as a percentage of the average value that would be predicted for a person of that sex, height, age and race.

A person with a low FVC percent predicted or low DLco percent predicted has worse lung function.

What did the trial investigate?

This was a phase 2, randomised, double-blind, placebo-controlled trial

Phase 2

This is conducted after a phase 1 trial, which primarily tests the safety of the drug in healthy people. A phase 2 trial tests a drug in a small group of people with the disease to determine whether it is safe and whether it has any beneficial effects for treating the disease. If a treatment has been shown to work, a phase 3 trial will be conducted to test the safety and effects of the drug with more participants and over a longer period of time.

Randomised

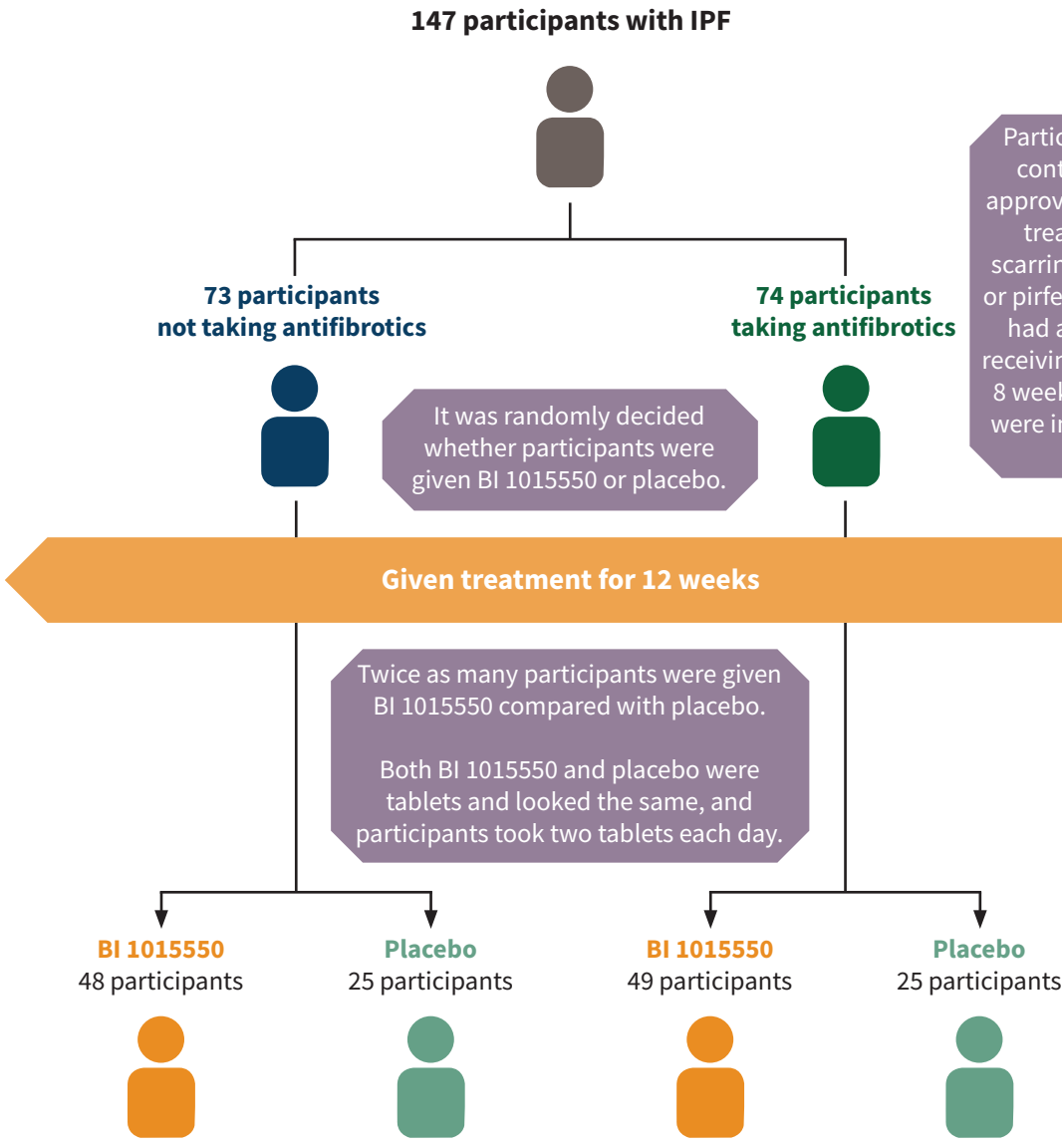
Participants were randomly assigned treatment. Distributing participants randomly between treatment groups means that any difference in outcomes is likely to be due to the treatment the participants received rather than any patient characteristics.

Double-blind

Neither investigators nor participants knew which treatment a participant was going to take. Not knowing which treatment is being taken decreases the chance of bias in the results.

Placebo-controlled

A non-active substance (dummy drug) that looks the same as the study drug. In clinical trials, people given the active study drug are compared against people given the inactive placebo to test if the active drug has any beneficial or harmful effects.



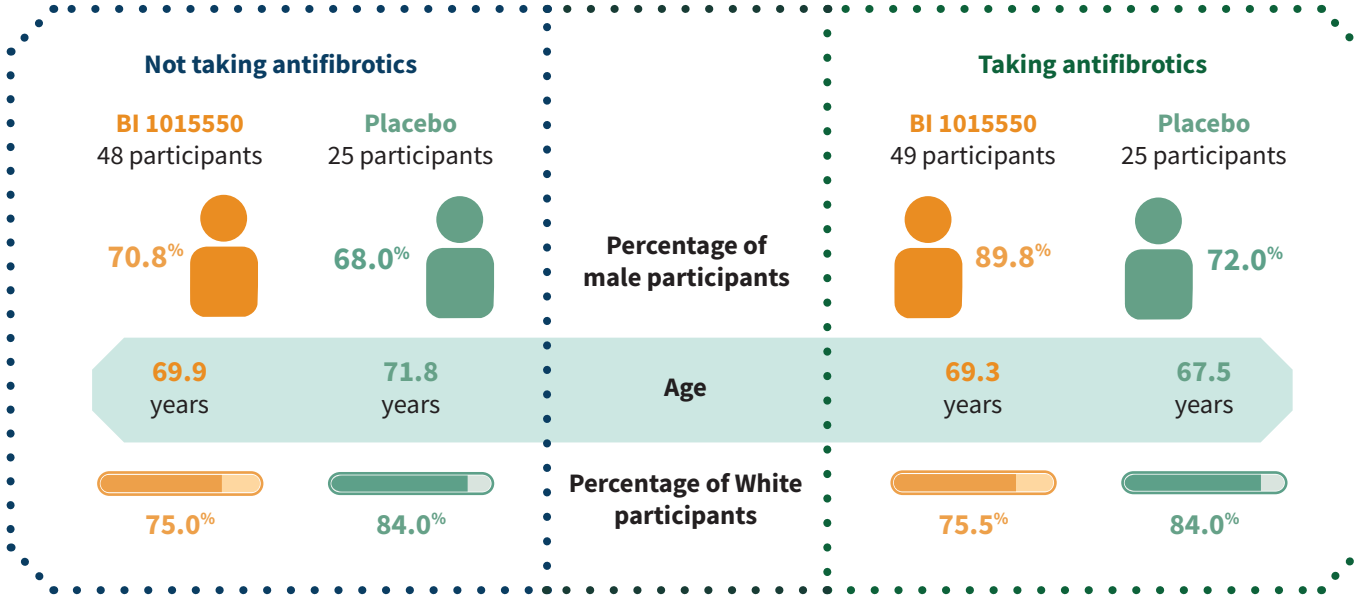
The participants' doctors measured their FVC over 12 weeks and also checked whether they had **adverse events**.

Adverse events are new medical issues that the patient has reported after taking the study drug or placebo. These may occur during the study and the study physician may decide they are related or not related to the study drug.

If these **adverse events** are caused by the study drug, they are called side effects.

Participant characteristics

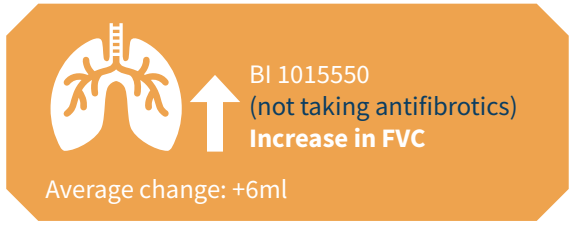
At the start of the study, participant characteristics were similar between participant groups.

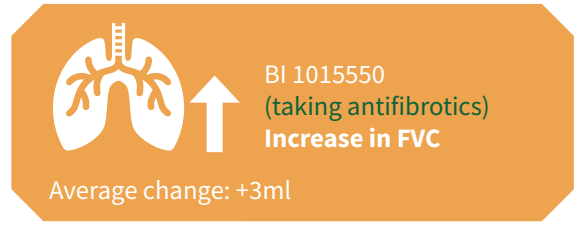


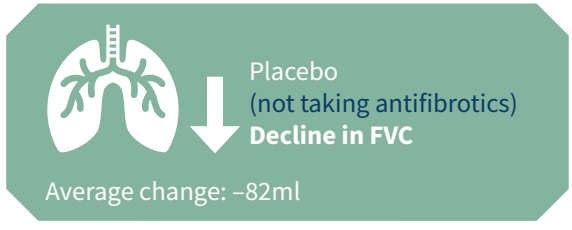
What were the results of the study?

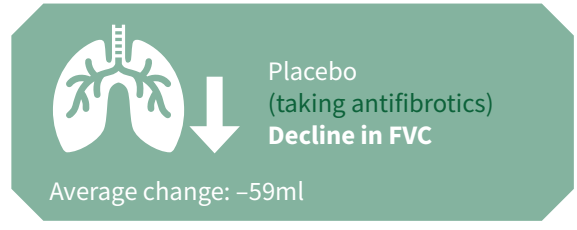
BI 1015550 prevented a decrease in lung function (measured by FVC) after 12 weeks, both in participants using antifibrotic treatment and those not using antifibrotic treatment.

In contrast, in participants treated with placebo, FVC continued to decrease, suggesting that their lung function worsened after 12 weeks.









How many participants have adverse events?

The most common adverse event with BI 1015550 was diarrhoea, which was mostly mild.

- Among participants taking BI 1015550 who stopped their treatment because of adverse events:

20% were taking antifibrotics

6% were not taking antifibrotics

In comparison, no participants taking placebo stopped their treatment

Similar proportions of participants had serious and severe adverse events, whether they were taking BI 1015550 or placebo.

The study physician may rate an adverse event as mild, moderate or severe.

Adverse events are considered serious if they are life-threatening or lead to death, disability or hospitalisation

Is this treatment available yet? What is the next step?

A larger and longer trial needs to take place to test the effectiveness and safety of BI 1015550 in people with IPF, before the treatment can be made available.

Researchers are looking to understand the effects of BI 1015550 in people with IPF and other forms of lung scarring that get worse over time.

What do the results of the study mean?

BI 1015550 prevented lung function from getting worse over the 12-week treatment period in people with IPF.

The main adverse event with BI 1015550 was diarrhoea, which was mostly mild.

Who sponsored this study?

The study was sponsored by a pharmaceutical company called Boehringer Ingelheim.

Where can readers find out more information on this study?

The full title of the original publication is 'Trial of a Preferential Phosphodiesterase 4B Inhibitor for Idiopathic Pulmonary Fibrosis' and was published in *New England Journal of Medicine*.

You can read the abstract of the original article here:
https://www.nejm.org/doi/full/10.1056/NEJMoa2201737

You can read more about the study on the following website:
https://www.clinicaltrials.gov/ct2/show/NCT04419506

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