This is a summary of a clinical study in patients with idiopathic pulmonary fibrosis, a rare type of lung disease. It is written for the general reader and uses language that is easy to understand. It includes information about how researchers did the study and what the results were. The simplified title for the study is: 'A study of nintedanib in patients with idiopathic pulmonary fibrosis'.

We thank all patients who took part in this study. Through your participation, you helped researchers answer important questions about nintedanib and the treatment of idiopathic pulmonary fibrosis.

## What was this study about?

The purpose of this study was to find out if a medicine called nintedanib helps patients with idiopathic pulmonary fibrosis (IPF). During the study, researchers also collected information on side effects of nintedanib.

This study started in May 2011 and finished in October 2013. The sponsor of this study was Boehringer Ingelheim.

## Why was the study needed?

New medicines are needed to treat patients with IPF, a rare disease of the lung. Idiopathic pulmonary fibrosis causes scarring of the tissue inside the lungs. The lungs become thick and stiff (fibrotic). This makes breathing difficult. The word 'idiopathic' means that doctors do not know the cause of the lung scarring. Common symptoms of IPF are shortness of breath, persistent dry cough, and enlargement (clubbing) of fingertips. Currently, there is no cure for IPF, and there are very few treatments for patients with IPF. The disease worsens over time and will eventually lead to death.

## Which medicines were studied?

Researchers studied the medicine nintedanib (also known as BIBF 1120). Researchers think that nintedanib blocks biological signals that take place in the lung-scarring process. Nintedanib had already been tested in clinical studies in patients with IPF and in patients with various types of cancer. Nintedanib is given as a capsule taken by mouth.

Some patients in the study were treated with nintedanib, and the others were treated with placebo. The placebo capsules looked just like the nintedanib capsules, but did not contain any medicine.

## Who participated in the study?

Patients who had been diagnosed with IPF within the last 5 years could take part in this study. They had to be at least 40 years old.

A total of 513 patients were treated with nintedanib or placebo in the study. A total of 414 patients were men and 99 were women. The average age was 68 years. The youngest patient was 42 years old, and the oldest patient was 87 years old. Many patients were from the European Union (288 patients from Belgium, Czech Republic, France, Germany, Ireland, Italy, and UK). Some patients were from Asia (103 patients from China, India, and Japan). Other patients were from Australia (33 patients), Israel (19 patients), and the United States (70 patients).

## How was this study done?

The researchers wanted to know if patients who took nintedanib did better in lung function tests than patients who took placebo. To test this, the patients were divided into 2 groups. It was decided by chance who got into which group. One group of 309 patients was given nintedanib, and the other group of 204 patients was given placebo. Patients did not know if they were taking nintedanib or placebo. The doctors also did not know it.

Patients took nintedanib capsules or placebo capsules twice a day. Patients in the nintedanib group were started on a dose of 150 milligrams (mg) twice a day. If patients had side effects that they could not tolerate, the doctors could lower the dose to 100 mg twice a day. Patients could also stop taking nintedanib for a while. If patients taking placebo had side effects that they could not tolerate, the doctors could also ‘lower the dose’, or patients could stop taking the capsules for a while.

It was planned for patients to be treated in the study for 1 year. During their time in the study, all patients followed the same procedures:

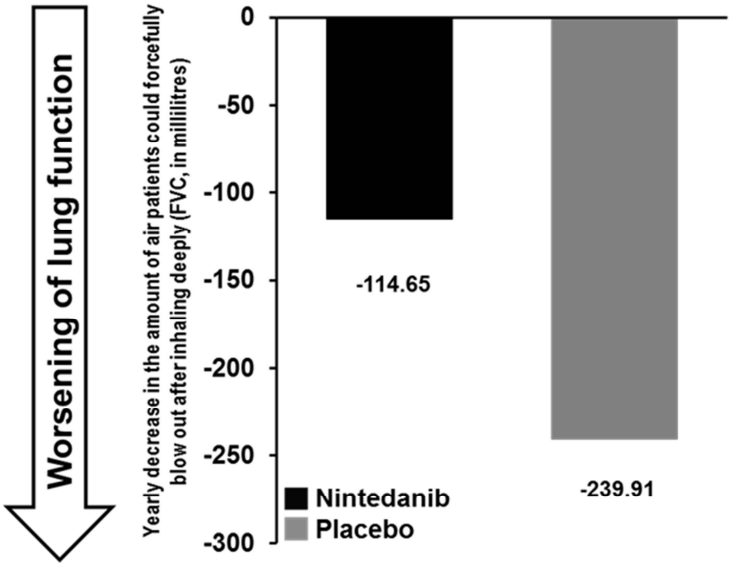
- The patients visited the doctor every 2 weeks for the first 6 weeks of the study. After this, they visited the doctor every 6 weeks.
- The patients took lung function tests.
- The patients answered questions about their health and quality of life.
- The patients had blood tests to check their health.
- The doctors collected information on side effects.

The doctors looked after each patient and checked results. They also discussed any health problems with the patients and did further medical tests when needed.

To see if nintedanib could slow down the worsening of lung function, the researchers used a special lung function test. This test measured how much air patients could forcefully blow out after inhaling deeply. Researchers call this measurement ‘Forced Vital Capacity’ or ‘FVC’. The researchers measured how much FVC changed over 1 year. A greater decrease in FVC over 1 year meant a faster worsening of lung function.

## What were the results of this study?

On average, the lung function in patients who took nintedanib worsened less over 1 year compared with patients who took placebo. In the nintedanib group, the yearly decrease in FVC, or the amount of air patients could forcefully blow out after inhaling deeply, was about half of the decrease in the placebo group. This is shown in the figure below. To be sure that the results were reliable, researchers used statistical tests. They found that it was very unlikely that the results came about by chance.




This picture shows the average yearly decrease in the amount of air patients could forcefully blow out after inhaling deeply (FVC). The black bar shows the decrease in the nintedanib group, and the grey bar shows the decrease in the placebo group. On average, lung function worsened less over the year for patients in the nintedanib group than for patients in the placebo group.

## What side effects did patients have?

More patients in the nintedanib group (74%) than in the placebo group (31%) had side effects.

The most common side effects affected the digestive system. These side effects were more common in patients who took nintedanib than in patients who took placebo.

Side effects that were seen in at least 5% of patients in either treatment group are shown in the table on the next page.

Doctors keep track of all health problems patients have during a study. Some of these health problems might be caused by the study medicines, and some by other medicines taken by the patient. Others might be caused by the disease, and some have yet a different cause. Here we describe health problems that the doctors thought were caused by the study medicines. These health problems are called side effects.

| | Nintedanib Group (309 patients) | Placebo Group (204 patients) |
|---|---|---|
| Patients who had side effects related to the study medicines | 228 patients (74%) | 64 patients (31%) |
| Frequent, loose bowel movements (diarrhoea) | 165 patients (53%) | 25 patients (12%) |
| Feeling sick (nausea) | 55 patients (18%) | 9 patients (4%) |
| Decreased appetite | 25 patients (8%) | 7 patients (3%) |
| Vomiting | 21 patients (7%) | 2 patients (1%) |
| Stomach pain (abdominal pain) | 17 patients (6%) | 0 patients |

Some patients stopped taking the study medicines and others lowered their dose of study medicine because of side effects. More patients in the nintedanib group (42 patients, 14%) than in the placebo group (6 patients, 3%) stopped taking study medicines because of side effects. Also, more patients in the nintedanib group (52 patients, 17%) than in the placebo group (2 patients, 1%) lowered their dose of study medicine because of side effects.

A total of 14 patients (5%) in the nintedanib group and 6 patients (3%) in the placebo group had at least 1 serious side effect during the study.

A total of 12 patients (4%) in the nintedanib group and 10 patients (5%) in the placebo group died during the study. Most of these patients died due to their lung disease. The doctors did not think any of the deaths in the nintedanib group were caused by the study medicine. One patient in the placebo group died due to a side effect that the doctor thought was related to the study medicine (placebo).

Some patients in the study had serious side effects. A side effect was serious if it caused the patient to go to the hospital or stay longer in the hospital. Or if it needed a doctor's immediate attention, was life-threatening, or caused death.

## Are there follow-up studies?

Patients who completed this study could participate in a follow-up study 1199.33. This study is still ongoing.

## Where can I find more information?

You can find the scientific summaries of the study results at these websites:

| | |
|---|---|
| www.trials.boehringer-ingelheim.com | search for the study number: 1199.32 |
| www.clinicaltrialsregister.eu | search for the EudraCT number: 2010-024251-87 |
| www.clinicaltrials.gov | search for the NCT number: NCT01335464 |

The full title of the study is:

'A 52 weeks, double blind, randomized, placebo-controlled trial evaluating the effect of oral BIBF 1120, 150 mg twice daily, on annual Forced Vital Capacity decline, in patients with Idiopathic Pulmonary Fibrosis (IPF)'.

## Important notice

This summary shows only the results from one study and may not represent all of the knowledge about the medicine studied. Usually, more than one study is done to find out how well a medicine works and the side effects of the medicine. Other studies may have different results.

You should consult the prescribing information for your country to get more information on the medicine studied, or ask your physician about the medicine. You should not change your therapy based on the results of this study without first talking to your physician. Always consult your physician about your specific therapy.

Boehringer Ingelheim has provided this lay summary in accordance with transparency obligations. This lay summary is intended for audiences located within the European Union.