INSTAGE®: A study to test nintedanib alone or in combination with sildenafil in patients with advanced IPF (1199.36)

Boehringer Ingelheim

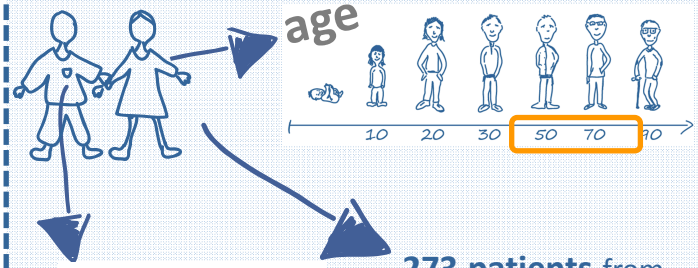
Idiopathic pulmonary fibrosis is a rare disease leading to loss of lung function. This leads to a **reduced quality of life** of the patients.

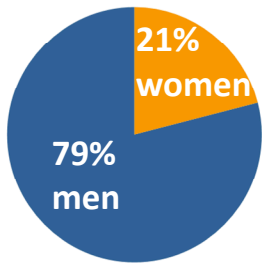
This **study** wanted to find out:

Does the **addition of sildenafil to nintedanib** help patients with IPF and advanced lung impairment more than nintedanib alone?

Patients who took part

had IPF with advanced lung impairment





273 patients from **13 countries** in Europe, North America, Asia and Australia took part.

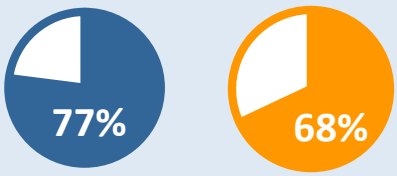
Each patient took per day

2 150 mg nintedanib and
3 20 mg sildenafil

or

2 150 mg nintedanib and
3 Placebo, *which looked like sildenafil capsules but didn't contain any medicine*

77% of patients who took nintedanib and sildenafil and 68% of patients who took nintedanib alone had **unwanted effects**.



RESULTS

We found that **adding sildenafil** to treatment with nintedanib **did not improve patients' quality of life** after 12 weeks of treatment.

A study to test nintedanib alone or in combination with sildenafil in patients with advanced IPF

This is a summary of a clinical study about idiopathic pulmonary fibrosis (IPF). This summary describes the results of the study.

We thank all patients who took part in this study. You helped to answer important questions about nintedanib and the treatment of IPF.

What was this study about?

The purpose of this study was to find out whether adding a medicine called sildenafil to treatment with a medicine called nintedanib helps patients with advanced IPF more than nintedanib alone.

Why was this study needed?

In IPF, the lungs become scarred and stiff. This makes breathing difficult. A medicine called nintedanib is used to treat IPF. We wanted to check if adding another medicine that works in a different way than nintedanib helps patients more than nintedanib alone.

Which medicines were studied?

We studied the combination of 2 medicines called nintedanib and sildenafil.

Nintedanib can help to slow down the worsening of IPF. Nintedanib is taken as a capsule that patients swallow.

Sildenafil is a medicine used to treat pulmonary arterial hypertension and other conditions. It works by increasing blood flow. Another study showed that sildenafil may help patients with advanced IPF feel better. Sildenafil is taken as a capsule that patients swallow.

Who took part in this study?

Patients 40 years old and older who had advanced IPF could participate in this study.

Overall, 273 patients took part in the study. 216 patients (79%) were men and 57 patients (21%) were women. The average age was 70 years. The youngest patient was 40 years old and the oldest patient was 86 years old.

This study was done in Europe, North America, Asia, and Australia. The table below shows the countries that the study was done in.

Region	Countries	Number of Patients
Europe	Belgium, France, Germany, Italy, Spain, United Kingdom	135
North America	Canada, Mexico, United States	64
Asia	India, Japan, Korea	67
Australia	Australia	7

How was this study done?

The patients were divided into 2 groups of almost equal size. Patients in one group took nintedanib and sildenafil. Patients in the other group took only nintedanib. Every patient had an equal chance of being in either group.

Patients and doctors did not know in which group the patients were.

During treatment, all patients took 2 capsules of nintedanib every day. Each capsule contained 150 milligrams (mg) of nintedanib. Patients in the nintedanib and sildenafil group also took 3 capsules of sildenafil every day. Each tablet contained 20 mg of sildenafil. To make sure that nobody knew who took which medicines, patients in the nintedanib group also took 3 placebo capsules every day. The placebo capsules looked like the sildenafil capsules but did not contain any medicine.

Patients visited the doctors regularly. During these visits, the doctors collected information about the patients' health.

We wanted to know how the patients' quality of life related to health changed after 12 weeks of treatment. For this, patients answered a set of questions called the St. George's Respiratory Questionnaire (SGRQ). Patients answered questions about how their breathing problems were troubling them and how this affected their lives. We used the answers of each patient to calculate the SGRQ score. We compared the patients' SGRQ score after 12 weeks of treatment with the results before treatment.

Patients took the study drugs for 24 weeks so that we could also study unwanted effects. Unwanted effects are health problems that the doctors think were caused by the study medicines.

What were the results of this study?

We found that adding sildenafil to treatment with nintedanib did not improve the SGRQ score.

Did patients have any unwanted effects?

Yes, patients in both groups had unwanted effects. 106 out of 137 patients (77%) who took nintedanib and sildenafil had unwanted effects. 96 out of 136 patients (68%) who took nintedanib alone had unwanted effects.

The table below shows the most common unwanted effects.

Unwanted effect	**Nintedanib and Sildenafil (137 patients)** 	**Nintedanib (136 patients)** 
Diarrhoea	73 patients (53%) 	59 patients (43%) 
Nausea	20 patients (15%) 	9 patients (7%) 
Decreased appetite	16 patients (12%) 	16 patients (12%) 
Vomiting	13 patients (10%) 	7 patients (5%) 
Indigestion (dyspepsia)	9 patients (7%) 	2 patients (2%) 
Headache	9 patients (7%) 	1 patient (1%) 
Increase in an enzyme that may indicate problems with your liver (alanine aminotransferase)	7 patients (5%) 	7 patients (5%) 

Some unwanted effects were serious because they required a visit to hospital, were life-threatening, or fatal. Unwanted effects were also serious if the doctor thought they were serious for any other reason. In this study, 25 patients (18%) who took nintedanib and sildenafil had serious unwanted effects. 30 patients (22%) who took nintedanib alone had serious unwanted effects. There were also some deaths from unwanted effects. 1 patient in the nintedanib and sildenafil group died from IPF. In the nintedanib only group, 1 patient died from reduced blood flow to the intestines (intestinal ischaemia), 1 patient died from a combination of pneumonia and septic shock, and 1 patient died suddenly.

Where can I find more information about this study?

You can find further information about the study at these websites:

1. Go to http://www.trials.boehringer-ingelheim.com/ and search for the study number **BI 1199.36.**
2. Go to www.clinicaltrialsregister.eu/ctr-search and search for the EudraCT number **2015-002619-14**.
3. Go to www.clinicaltrials.gov and search for the NCT number **NCT02802345.**

Boehringer Ingelheim sponsored this study.

The full title of the study is: 'INSTAGE®: A 24-week, double-blind, randomized, parallel-group study evaluating the efficacy and safety of oral nintedanib co-administered with oral sildenafil, compared to treatment with nintedanib alone, in patients with idiopathic pulmonary fibrosis (IPF) and advanced lung function impairment'.

This was a Phase III study. This study started in July 2016 and finished in April 2018.

Are there additional studies?

If we do more clinical studies with nintedanib, you will find them on the websites listed above. To search for these studies, use the word nintedanib.

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 carried out in order to find out how well a medicine works and the side effects of the medicine. Other studies may have different results.

You should not change your therapy based on the results of this study without first talking to your treating physician. Always consult your treating physician about your specific therapy.

Boehringer Ingelheim has provided this lay summary in accordance with European Union transparency obligations.