The LUME Lung 1 study of nintedanib with docetaxel compared to docetaxel in patients with lung cancer that has returned or spread

This is a summary of a clinical study in lung cancer. It is written for the general public. It includes information about how researchers did the study and what the results were.

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 lung cancer.

What was this study about?

Patients in this study had non-small cell lung cancer (NSCLC). They had previously received therapy, but their cancer had returned or spread to other parts of their body (metastasised).

During this study, researchers compared 2 different treatments for NSCLC. One treatment was a combination of nintedanib and docetaxel. The other treatment was docetaxel alone (docetaxel and placebo). They wanted to find out if the combination was more effective than docetaxel alone in preventing further growth of NSCLC. Researchers also wanted to find out which patients would benefit most from this treatment combination.

This study started in December 2008 and finished in November 2017.

Why was the study needed?

NSCLC is the most common type of lung cancer. Unfortunately, NSCLC is often diagnosed late. This means that surgery is no longer possible. The cancer has already spread into other parts of the body (metastasised) and is considered 'advanced'. There are several treatments for advanced NSCLC. Sometimes these treatments make patients feel sick. Sometimes the treatments don't stop the cancer from growing. Therefore, new medicines are needed to treat NSCLC.

Which medicines were studied?

Nintedanib is a medicine that helps to stop cancer from growing and spreading. Nintedanib blocks the development of new blood vessels in growing tumours. It is used to treat a certain type of lung cancer in combination with chemotherapy (docetaxel). Nintedanib is taken as a capsule by mouth.

Docetaxel is used as standard treatment for patients with NSCLC that has returned or spread after initial treatment. It is a type of chemotherapy and given by infusion into a vein. This means it is dripped into a vein through a plastic tube and needle.

Who participated in the study?

All patients in this study were adults with NSCLC. They had already received treatment when they entered the study. The cancer had returned or spread after that initial treatment. Overall, 1314 patients took part in the study. The study included 955 men and 359 women. The average age was 60 years. The youngest patient was 26 years old. The oldest patient was 84 years old.

The table below shows the number of patients by geographical region and country.

Geographical Region	Countries	Number of Patients
Europe	Austria, Belarus, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, France, Georgian Republic, Germany, Greece, Israel, Italy, Lithuania, Poland, Portugal, Romania, Russia, Slovakia, Spain, Switzerland, Ukraine, United Kingdom	985 patients
Asia	China, India, South Korea	308 patients
South Africa	South Africa	21 patients

How was this study done?

The patients were divided into 2 groups. Every patient had an equal chance of being in either group. One group received nintedanib and docetaxel. The other group received placebo and docetaxel, or in other words, docetaxel alone. The placebo capsules looked just like the nintedanib capsules, but did not contain any medicine. In this way, the patients did not know which treatment they were taking. The doctors did not know either.

Patients in the nintedanib and docetaxel group started on a nintedanib dose of 200 milligrams (mg) twice a day. The doctors decreased the dose if the patients had health problems that they could not tolerate. Patients in the placebo and docetaxel group took placebo capsules twice a day.

All patients began at a dose of docetaxel based on their body size. They were given 75 mg per square metre of body surface area once every 3 weeks. The doctors decreased the dose if the patients had side effects that they could not tolerate.

To compare nintedanib and docetaxel with docetaxel alone, the researchers measured 'progression-free survival'. This is the time from starting the study medicines until the cancer grew or the patient died. Researchers also measured the time from starting the medicines until the patients died from cancer or from any other cause. This is called 'overall survival'.

Researchers also wanted to know which patients could be helped the most by addition of nintedanib to docetaxel. They looked at progression-free survival and overall survival of:

- All patients, and
- Patients with a special type of NSCLC called adenocarcinoma

Patients visited their doctor regularly. During the visits, the doctors collected information on each patient's health.

What were the results of this study?

For all patients, the progression-free survival was 3.4 months on average for patients who took nintedanib and docetaxel. It was 2.7 months for patients who took docetaxel alone.

Researchers calculated the risk of the cancer growing or the patient dying. It was 21% lower for patients who took nintedanib and docetaxel than for patients who took docetaxel alone. Researchers used statistical tests on the results to check if the results were reliable. They found that this difference in progression-free survival was not likely due to chance.

These results were based on an analysis conducted while the study was still in progress during 2010. A follow-up analysis in 2013 also confirmed these results.

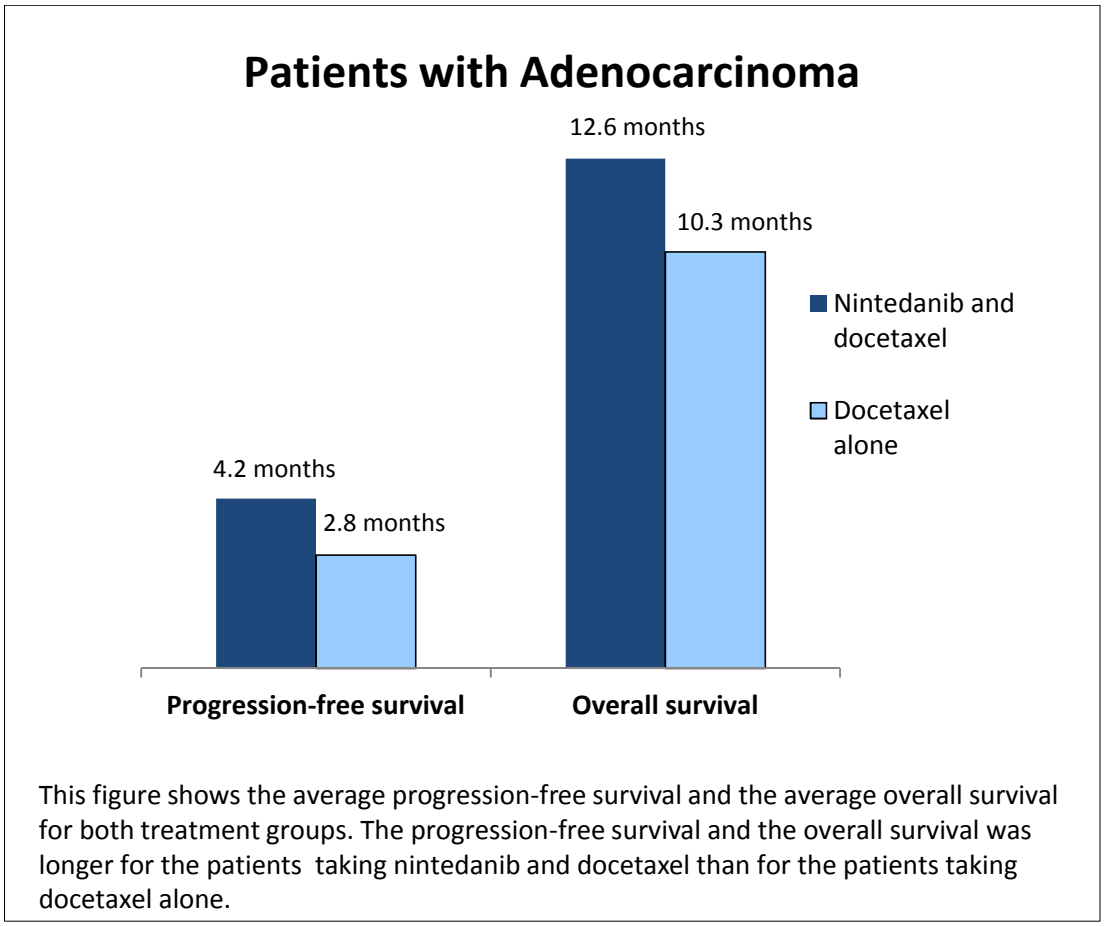
From the follow-up analysis, researchers found there was a small difference in overall survival between treatments when all patients were compared. The average overall survival was 10.1 months for all patients who took nintedanib and docetaxel. It was 9.1 months for all patients who took docetaxel alone. Researchers did statistical tests on the results. They found that this difference in overall survival was likely due to chance. This means it was probably not caused by nintedanib.

For patients with adenocarcinoma who took nintedanib and docetaxel, the average progression-free survival was 4.2 months. It was 2.8 months for patients with adenocarcinoma who took docetaxel alone.

Researchers calculated the risk of the cancer growing or the patient dying for patients with adenocarcinoma. It was 16% lower for patients who took nintedanib and docetaxel than for patients who took docetaxel alone. Researchers used statistical tests on the results to check if the results were reliable. They found that this difference in progression-free survival was not likely due to chance.

Researchers also looked at overall survival in patients with adenocarcinoma. The average overall survival was 12.6 months for patients in this group who took nintedanib and docetaxel. It was 10.3 months for patients in this group who took docetaxel alone. The risk of dying was 17% lower for patients who took nintedanib and docetaxel than for patients who took docetaxel alone. Researchers did statistical tests on the results. They found that this difference in overall survival was not likely due to chance.

These results for progression-free survival and overall survival in patients with adenocarcinoma are shown in the picture below.



This figure shows the average progression-free survival and the average overall survival for both treatment groups. The progression-free survival and the overall survival was longer for the patients taking nintedanib and docetaxel than for the patients taking docetaxel alone.

The final results of the study were published in 2013. At that time, 11 patients were still in the study. Now, these last patients have left the study.

Were there any unwanted effects?

Unwanted effects are any health problems that the doctors thought were caused by the study medicines. In this study, 498 patients out of 652 patients (76%) in the nintedanib and docetaxel group had unwanted effects. In the placebo and docetaxel group, 446 out of 655 patients (68%) had unwanted effects.

The most common unwanted effects seen in at least 15% of patients in either group are shown in the table below.

	Nintedanib and docetaxel (652 patients)	Placebo and docetaxel (655 patients)
Patients with any unwanted effect	498 patients (76%)	446 patients (68%)
Diarrhoea	217 patients (33%)	99 patients (15%)
Reduced number of a type of white blood cells (neutrophil count decreased)	192 patients (29%)	183 patients (28%)
Increase in a liver enzyme (ALT increased)	152 patients (23%)	42 patients (6%)
Increase in a liver enzyme (AST increased)	126 patients (19%)	30 patients (5%)
Reduced number of all white blood cells (WBC count decreased)	122 patients (19%)	119 patients (18%)
Nausea	112 patients (17%)	78 patients (12%)
Feeling tired (fatigue)	104 patients (16%)	100 patients (15%)

Some unwanted effects were serious because they required a visit to hospital or a longer stay in hospital. Some led to disability or were life-threatening or fatal. Some the doctor thought were serious for other reasons. In this study, 95 patients (15%) in the nintedanib and docetaxel group had serious unwanted effects. In the placebo and docetaxel group, 74 patients (11%) had serious unwanted effects. This included patients who died from unwanted effects. In the nintedanib and docetaxel group, 11 patients (2%) died from unwanted effects. In the placebo and docetaxel group, 6 patients (1%) died from unwanted effects.

Are there follow-up studies?

No follow-up study is planned.

If more clinical studies with nintedanib are done, they may be found on the public websites listed in the section below. To search for these studies, use the following names: BIBF 1120, nintedanib.

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: 1199.13
www.clinicaltrialsregister.eu/ctr-search	search for the EudraCT number: 2007-004803-36
www.clinicaltrials.gov	search for the NCT number: NCT00805194

The sponsor of this study was Boehringer Ingelheim.

The full title of the study is:

'Multicentre, Randomised, Double-blind, Phase III Trial to Investigate the Efficacy and Safety of Oral BIBF 1120 Plus Standard Docetaxel Therapy Compared to Placebo Plus Standard Docetaxel Therapy in Patients With Stage IIIB/IV or Recurrent Non-Small Cell Lung Cancer After Failure of First Line Chemotherapy'.

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.