This is a summary of a clinical study in patients with cancer. 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 treating patients with metastatic or advanced colorectal cancer'.

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 cancer.

What was this study about?

The purpose of this study was to test how well nintedanib worked in patients who had colorectal cancer that could not be cured (advanced disease) or had spread to other parts of the body (metastatic disease). During the study, researchers also collected information on side effects of nintedanib.

This study started in October 2014 and finished in August 2016. The sponsor of this study was Boehringer Ingelheim.

Why was the study needed?

Colorectal cancer is difficult to treat. About half of patients with colorectal cancer eventually develop metastatic disease. In most patients with advanced or metastatic colorectal cancer, the standard treatments that are available will stop working sooner or later. New treatment options are needed for patients with colorectal cancer who have stopped responding to the available standard treatments or who cannot tolerate these treatments.

Which medicines were studied?

Nintedanib (also known as BIBF 1120) is a medicine that helps to slow the growth and spread of certain types of cancer. Nintedanib blocks the activity of a group of proteins which are involved in the development of new blood vessels that cancer cells need to supply them with food and oxygen. By blocking the activity of these proteins, nintedanib can help stop the growth and spread of the cancer. Nintedanib is taken as a capsule by mouth.

About half of the patients in the study were treated with nintedanib and the other half were treated with placebo. The placebo capsules looked just like the nintedanib capsules, but did not contain any medicine. Researchers use a placebo to see if the study medicine works better or causes more side effects than not taking anything.

Who participated in the study?

All patients were adults with metastatic or advanced colorectal cancer. All patients in this study had stopped responding to the available standard cancer treatments or they could no longer tolerate taking them. The only remaining therapy available to the patients was 'best supportive care'. Best supportive care is therapy that does not target the cancer but rather helps to make the patient feel more comfortable and improves the patient's quality of life.

Best supportive care treatments may include medicines to help with pain, nausea and vomiting, or bacterial infections. These treatments may also include surgery, blood transfusions, or nutritional treatments.

Overall, 768 patients took part in the study, including 454 men and 314 women. The average age was 61 years. The youngest patient was 22 years old and the oldest patient was 85 years old.

The table below shows the number of patients in different geographical regions and countries who took part in the study.

Geographical Region	Countries	Number of Patients
Western Europe	Austria, Belgium, Denmark, France, Germany, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden, United Kingdom	369 patients
Asia	Hong-Kong, Japan, Korea, Taiwan	193 patients
North America	Canada, United States of America	63 patients
Australia	Australia	26 patients
Rest of the World	Argentina, Czech Republic, Israel, Mexico, Poland, Russia, Turkey	117 patients

How was this study done?

Patients were divided into 2 groups of similar size. It was decided by chance who got into which group. One group of patients was given nintedanib (plus best supportive care) and the other group of patients was given placebo (plus best supportive care). Patients and doctors did not know if they were taking nintedanib or placebo.

Patients took nintedanib capsules or placebo capsules by mouth, twice a day. Patients in the nintedanib group were started on a dose of 200 milligrams (mg) twice a day. If patients experienced side effects that they could not tolerate, the dose was decreased to 150 mg twice a day, or further decreased to 100 mg twice a day.

Patients continued treatment with nintedanib or placebo until their cancer got worse, or until they had side effects that they could not tolerate and a further dose reduction was not possible.

All patients in the study followed the same procedures:

- The patients visited the doctor about once every 3 weeks.
- At these visits, the patients answered questions about their health.
- At some visits, the size of their tumour was measured and their blood was tested to check their health.
- At all visits, the doctors collected information on side effects.

In order to measure the effectiveness of nintedanib in patients with colorectal cancer, the researchers measured the following:

- The time from starting study treatment (nintedanib or placebo) until the cancer got worse or the patient died (this was called 'progression-free survival').
- The time from starting study treatment (nintedanib or placebo) until the patient died (this was called 'overall survival').

What were the results of this study?

In this study, there was a difference in progression-free survival between patients who took nintedanib and patients who took placebo. At the time the results were analysed, 350 patients in the nintedanib group and 337 patients in the placebo group had their cancer get worse or had died. The average (median) time it took from starting study treatment until the cancer got worse or the patient died was 1.51 months for patients who took nintedanib and 1.38 months for patients who took placebo. The risk of the cancer getting worse or the patient dying over time was lower for patients in the nintedanib group than for patients in the placebo group. Researchers used statistical tests on the results. They found that this difference in progression-free survival was not likely due to chance.

In this study, there was no meaningful difference in overall survival between patients who took nintedanib and patients who took placebo. At the time the results were analysed, 318 patients in the nintedanib group and 295 patients in the placebo group had died. The average (median) time it took from starting study treatment until the patient died was 6.44 months for patients who took nintedanib and 6.05 months for patients who took placebo. Researchers used statistical tests on the results. They found that the difference in overall survival between the treatment groups was likely due to chance.

What side effects did patients have?

In this study, 291 patients (76%) in the nintedanib group and 195 patients (51%) in the placebo group had side effects that doctors thought were caused by the study medicines.

The most common side effects that were reported in at least 5% of patients in either group are shown in the table below.

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.

Side Effects Related to Study Medicines	Nintedanib Group (384 patients)	Placebo Group (381 patients)
Patients who had side effects related to the study medicines	291 patients (76%)	195 patients (51%)
Diarrhoea	135 patients (35%)	36 patients (9%)
Nausea	120 patients (31%)	61 patients (16%)
Vomiting	103 patients (27%)	30 patients (8%)
Feeling tired (fatigue)	73 patients (19%)	39 patients (10%)
Increase in liver enzymes (alanine aminotransferase increased)	70 patients (18%)	12 patients (3%)
Increase in liver enzymes (aspartate aminotransferase increased)	67 patients (17%)	14 patients (4%)
Decreased appetite	64 patients (17%)	39 patients (10%)
Loss of energy (asthenia)	29 patients (8%)	19 patients (5%)
Abdominal pain	22 patients (6%)	10 patients (3%)
Abnormally high levels of protein in the urine (proteinuria)	22 patients (6%)	5 patients (1%)
High blood pressure (hypertension)	21 patients (6%)	7 patients (2%)

A total of 30 patients (8%) in the nintedanib group and 16 patients (4%) in the placebo group had a serious side effect that doctors thought were caused by the study medicines.

A total of 55 patients (14%) in the nintedanib group and 51 patients (13%) in the placebo group died due to side effects that occurred during the study. Most patients died due to their cancer getting worse. One patient in the nintedanib group and 2 patients in the placebo group died due to side effects that the doctors thought were caused by the study medicines. The patient in the nintedanib group died due to liver failure.

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?

No follow-up studies are planned.

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: 1199.52
www.clinicaltrialsregister.eu	search for the EudraCT number: 2012-000095-42
www.clinicaltrials.gov	search for the NCT number: NCT02149108

The full title of the study is:

'A double-blind, randomised, placebo controlled Phase III study of nintedanib plus best supportive care (BSC) versus placebo plus BSC in patients with colorectal cancer refractory to standard therapies'.

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.