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: 'The LUX-Lung 3 study compares treatment with afatinib to chemotherapy in patients with lung adenocarcinoma that involves a mutated EGFR protein.'

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

What was this study about?

The patients in this study had a type of non-small cell lung cancer (NSCLC) called adenocarcinoma. Lung cancer is called adenocarcinoma if it starts in the tube-like airways in the lung. The type of adenocarcinoma that the patients had in this study involved a protein called EGFR that was abnormally changed (this is called mutated). This mutated EGFR protein acts as a switch that can turn lung cancer cells on so that they grow out of control.

The purpose of this study was to compare afatinib with chemotherapy as first therapy for patients with advanced adenocarcinoma with EGFR mutations. During the study, researchers also collected information on side effects of afatinib.

This study started in August 2009 and finished in March 2017. The sponsor of this study was Boehringer Ingelheim.

Why was the study needed?

Lung cancer is the leading cause of cancer deaths in the world and it is difficult to treat. In the past, patients with this type of cancer have taken chemotherapy as first therapy. But in many patients the cancer continues to grow and chemotherapy does not help all of them to live longer. Therefore researchers developed new treatments that block the mutated EGFR proteins. One of these treatments is afatinib, which had already been shown in preliminary studies to help patients with NSCLC with EGFR mutations.

Which medicines were studied?

About two-thirds of the patients in this study were treated with afatinib (also known as BIBW 2992) and the other patients were treated with chemotherapy.

Afatinib is a medicine that helps to stop cancer from growing and spreading. Afatinib permanently blocks several growth factor signals (including EGFR). It is used in certain types of lung cancer that grow because of EGFR mutations. Afatinib is taken as a tablet by mouth.

Chemotherapy is also used to help stop cancer cells from growing and spreading in the body. In this study, the chemotherapy was a combination of 2 medicines called pemetrexed and cisplatin. The combination was 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 lung adenocarcinomas with EGFR mutations. They had not had any prior treatment for their advanced cancer. Overall, 345 patients took part in the study, including 224 women and 121 men. The average age was 60 years. The youngest patient was 28 years old and the oldest patient was 86 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
Europe	Austria, Belgium, France, Germany, Hungary, Ireland, Italy, Romania, Russia, Ukraine, United Kingdom	74 patients
Asia	Hong Kong, Japan, Korea, Malaysia, Philippines, Taiwan, Thailand	243 patients
North America	Canada, United States	2 patients
Other	Argentina, Australia, Brazil, Chile, Peru	26 patients

How was this study done?

A total of 229 patients were treated with afatinib and 111 patients were treated with chemotherapy. It was decided by chance who got which treatment. Patients and doctors knew if the patients were taking afatinib or chemotherapy.

Patients in the afatinib group were started on a dose of 40 milligrams (mg) once a day. This dose could be increased or decreased depending on whether the patients had side effects that they could not tolerate.

Patients in the chemotherapy group received infusions into a vein once every 3 weeks. The infusions contained 2 medicines at the standard approved doses, which were pemetrexed at a dose of 500 mg per square metre (m^2) of body surface area and cisplatin at a dose of 75 mg/m^2. This means that the dose depended on the size of the patient's body.

Patients were to take afatinib until their cancer grew or they could not tolerate the medicine. It was planned that patients would receive up to 6 courses of chemotherapy, which would last about 5 months. Some patients had to stop treatment early because their cancer grew or because they had side effects that they could not tolerate.

All patients in the study followed the same procedures:

- Patients had to visit the doctor twice to see whether they could take part in the study.
- Each treatment course took 3 weeks. During the first 2 treatment courses, patients had to visit their doctor twice. After that, patients visited their doctor once during each treatment course.
- At each visit, the patients answered questions about their health.
- At some visits, the doctors measured the size of the tumours and checked if any new tumours had formed. Other assessments were also done to check the patient's health.
- At all visits, the doctors collected information on side effects.

The doctors looked after each patient and checked their test results. The doctors did more medical tests when needed.

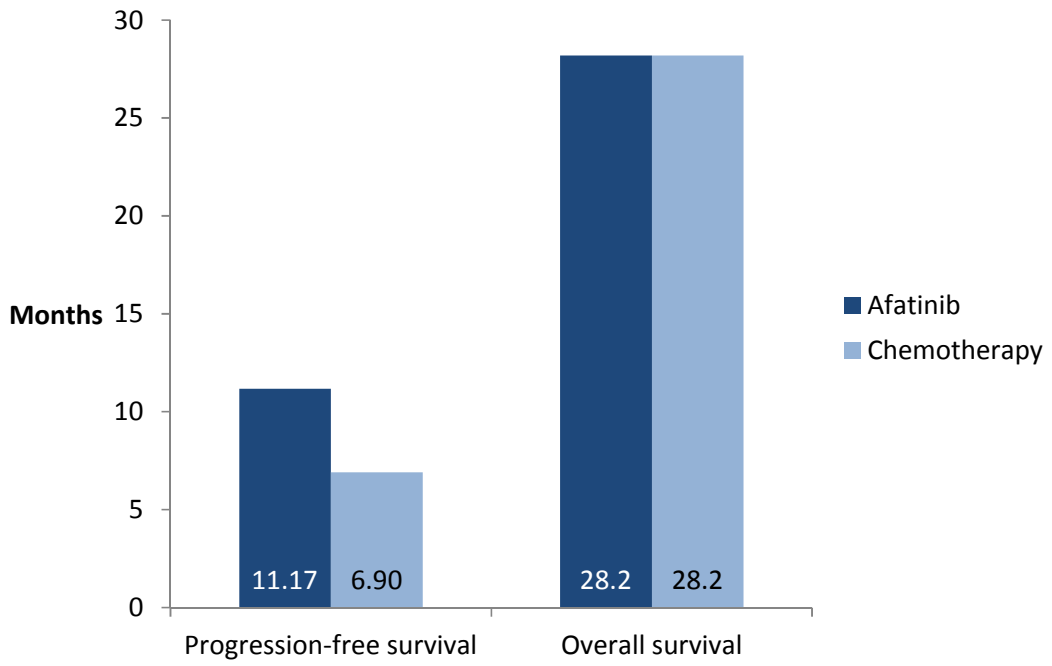
In order to compare how well afatinib and chemotherapy worked in these patients with lung cancer, the researchers measured the time from starting the study medicine (afatinib or chemotherapy) until the cancer grew further or the patient died. This is called 'progression-free survival'. Researchers also measured the time from starting the medicines until the patients died from cancer or from any other cause. This is called 'overall survival'.

What were the results of this study?

In this study, there was a difference in progression-free survival between patients who took afatinib and patients who received chemotherapy. The results were calculated 12 months after the last patient started treatment and then again at the end of the study. After the 12 months, the average progression-free survival was 11.17 months for patients who took afatinib and 6.90 months for patients who had chemotherapy. The risk of the cancer growing further or the patient dying during this time was 42% lower for patients in the afatinib group than for patients in the chemotherapy group. Overall, 48.1% of patients in the afatinib group and 22.0% of patients in the chemotherapy group had their cancer stop growing and were still alive after the 12 months. The results for progression-free survival calculated at the end of the study were similar to the results calculated after the 12 months.

Researchers used statistical tests on the results to check if the results were reliable. They found that the differences in progression-free survival were not likely due to chance.

At the end of the study, researchers found that there was no difference in overall survival between patients who got afatinib and patients who received chemotherapy. The average overall survival was 28.2 months for both groups.



This figure shows the average time it took from starting study treatment until the cancer grew again or the patient died (progression-free survival). The figure also shows the average time it took from starting study treatment until the patient died (overall survival). Results for patients getting afatinib are shown in dark blue bars and results for those getting chemotherapy are in light blue bars.

What side effects did patients have?

In this study, almost all patients had side effects: 228 patients out of 229 patients in the afatinib group and 106 patients out of 111 patients in the chemotherapy group.

For about half of the patients, these side effects were of mild or moderate intensity. The most common side effects seen in at least 20% of patients in either 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.

	Afatinib (229 patients)	Chemotherapy (111 patients)
Patients with any side effect	228 patients (more than 99%)	106 patients (96%)
Diarrhoea	218 patients (95%)	17 patients (15%)
Rash	142 patients (62%)	7 patients (6%)
Infection of the skin around the fingernails or toenails (paronychia)	132 patients (58%)	0 patients
Mouth sores (stomatitis)	87 patients (38%)	10 patients (9%)
Dry skin	69 patients (30%)	2 patients (2%)
Swelling of the mucous linings (mucosal inflammation)	68 patients (30%)	5 patients (5%)
Pimples (acne)	52 patients (23%)	0 patients
Decreased appetite	49 patients (21%)	59 patients (53%)
Itchy skin (pruritus)	46 patients (20%)	1 patient (less than 1%)
Nausea	43 patients (19%)	73 patients (66%)
Vomiting	42 patients (18%)	47 patients (42%)
Feeling tired (fatigue)	32 patients (14%)	38 patients (34%)
Reduced number of red blood cells (anaemia)	9 patients (4%)	31 patients (28%)
Reduced number of white blood cells (neutropenia)	2 patients (less than 1%)	35 patients (32%)

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. It was also serious if it needed a doctor's immediate attention, was life-threatening, or caused death.

A total of 33 out of 229 patients (14%) in the afatinib group and 15 out of 111 patients (14%) in the chemotherapy group had a serious side effect. The most common serious side effects were diarrhoea, vomiting, feeling tired (fatigue), and weakness (asthenia).

A total of 15 out of 229 patients (7%) in the afatinib group and 3 out of 111 patients (3%) in the chemotherapy group died during treatment in the study. For 4 patients in the afatinib group, the doctor thought that the death could have been caused by the study medicine. The causes of death for these 4 patients were reported as blood poisoning (sepsis), difficult breathing (dyspnoea), lungs filled with liquid (acute respiratory distress syndrome), and unexplained 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: 1200.32
www.clinicaltrialsregister.eu	search for the EudraCT number: 2008-005615-18
www.clinicaltrials.gov	search for the NCT number: NCT 00949650

The full title of the study is:

'LUX-Lung 3; A randomised, open-label, phase III study of BIBW 2992 versus chemotherapy as first-line treatment for patients with stage IIIB or IV adenocarcinoma of the lung harbouring an EGFR-activating mutation'.

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.