A study of afatinib compared with methotrexate in patients with cancer of the head and neck that has returned or spread

This is a summary of a clinical study in patients with head and neck 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 afatinib and the treatment of head and neck cancer.

What was this study about?

The patients in this study had a type of cancer known as 'head and neck squamous cell carcinoma'. This is a type of cancer of the mouth and throat. Furthermore, the patients had already been treated, but their cancer returned or spread. The standard treatment for this type of cancer that has returned or spread includes platinum-based chemotherapy. However, in many patients the cancer returns again, despite treatment with chemotherapy. The purpose of this study was to test how treatment with afatinib compared with methotrexate could help prevent further growth of cancer in patients whose cancer had returned after chemotherapy. During the study, researchers also collected information on side effects of afatinib and methotrexate.

This study started in January 2012 and finished in December 2016.

Why was the study needed?

New treatments for squamous cell carcinoma of the head and neck are needed. This type of cancer can grow and spread quickly. Head and neck squamous cell carcinoma is a major cause of cancer-related illness and death. Each year, more than 600,000 cases of head and neck squamous cell carcinoma are diagnosed worldwide. The standard treatment includes surgery, radiotherapy, or chemotherapy. Although some patients are free of disease after treatment, there is a risk that some cancer cells are left in the body and that tumours return. More than half of patients treated with chemotherapy, radiotherapy, or surgery will have their cancer return or spread to other parts of the body.

Afatinib is being studied to see if it can prevent the tumours from growing further in patients with head and neck squamous cell carcinoma. In this study, patients had been treated with chemotherapy but their cancer still grew. Methotrexate is a medicine approved for use in these patients. It is used after the first attempts at treatment fail and cancer returns or spreads. Researchers wanted to compare afatinib with methotrexate as treatments for squamous cell carcinoma of the head and neck.

Which medicines were studied?

Afatinib (also known as BIBW 2992) is a medicine that helps to stop cancer from growing and spreading. Afatinib permanently blocks several growth factor signals (including a protein called EGFR). It is used in certain types of lung cancer that grow because of EGFR mutations. Afatinib is taken as a tablet by mouth.

Methotrexate is another medicine that can prevent tumours from growing and spreading. Methotrexate is used to treat cancer, including head and neck cancer. It is also used to treat other diseases such as rheumatoid arthritis and severe cases of psoriasis. Methotrexate is given by intravenous injection. 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 head and neck squamous cell carcinoma. Patients with cancer of the nasopharynx (upper throat behind the nose), sinuses, or salivary glands could not participate in the study. Patients in the study had cancer that had returned or spread to other parts of their body. They had already received platinum-based chemotherapy, but the disease had continued to spread. They had tumours that could not be removed by surgery.

Overall, 483 patients took part in the study, including 412 men and 71 women. The average age was 60 years. The youngest patient was 32 years old and the oldest patient was 88 years old. Of these patients, 480 received either afatinib or methotrexate in the study. Three patients did not receive any study medicine.

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, Czech Republic, Denmark, France, Germany, Greece, Italy, Russia, Spain, Sweden, Switzerland	369
North/Latin America	Argentina, Brazil, Mexico, United States	60
Asia	Japan	43
Other	Israel, South Africa	11

How was this study done?

About two-thirds of the patients (320 patients) in this study were treated with afatinib and the other 160 patients were treated with methotrexate. It was decided by chance who got which treatment. Patients and doctors knew if the patients were taking afatinib or methotrexate.

Patients in the afatinib group began with a dose of 40 milligrams (mg) once a day. Patients in the methotrexate group began at a dose based on their body size (40 mg per square metre of body surface area, or m^2) once a week. Doses of each treatment could be increased or decreased depending on whether the patients had side effects that they could not tolerate.

Patients were to take afatinib tablets or receive methotrexate injections until their cancer grew further or until they had side effects that they could not tolerate.

All patients in the study followed the same procedures:

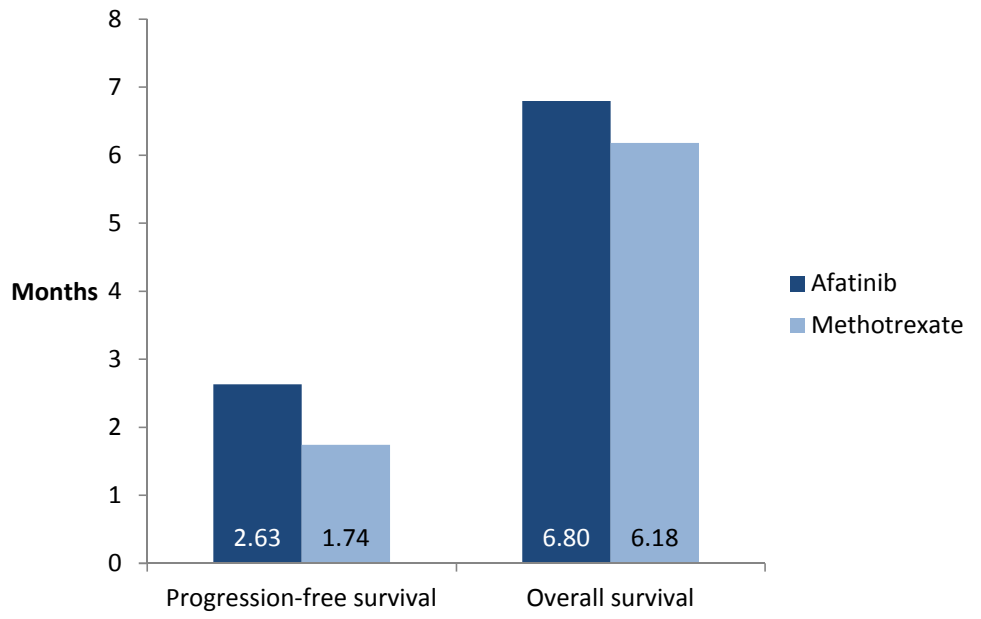
- The patients visited the doctor about once a week while they received study medicine.
- At these visits, the patients answered questions about their health.
- At some visits, tests were done to check if the patient's cancer had grown or if any new tumours had formed. Other assessments were also done to check the patient's health.
- At all visits, the doctors collected information on side effects.

To see if afatinib or methotrexate could prevent the cancer from growing further, the researchers measured the time from starting the medicines 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?

The average progression-free survival was longer for patients who got afatinib than for patients who got methotrexate. The average progression-free survival was 2.63 months for patients who got afatinib and 1.74 months for patients who got methotrexate. These results are shown in the picture on the next page. The risk of the cancer growing further or the patient dying was 20% lower for patients in the afatinib group than for patients in the methotrexate group. 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. Overall, 85.4% of patients in the afatinib group and 83.9% of patients in the methotrexate group had their cancer grow further or died.

Researchers also looked at overall survival. They found that there was no difference in average overall survival between patients who got afatinib and patients who got methotrexate. The average overall survival was 6.80 months in the afatinib group and 6.18 months in the methotrexate group. The risk of dying was about the same in both groups. Researchers used statistical tests on the results. They found that this difference in overall survival was likely due to chance. These results are shown in the picture on the next page. Overall, 68.3% of patients in the afatinib group and 70.8% of patients in the methotrexate group died during the study.



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). The results for patients getting afatinib are shown in dark blue bars and results for those getting methotrexate are shown in light blue bars.

The results described above were based on an analysis conducted while the study was still in progress during 2014. Once the study was completed, a final analysis confirmed these results.

Were there any unwanted effects?

Unwanted effects are any health problems that the doctors thought were caused by the study medicines. In this study, 303 out of 320 patients (95%) in the afatinib group and 137 out of 160 patients (86%) in the methotrexate group had unwanted effects.

The most common unwanted effects are shown in the table on the next page.

	Afatinib (320 Patients)	Methotrexate (160 Patients)
Patients with any unwanted effect	303 patients (95%)	137 patients (86%)
Diarrhoea	231 patients (72%)	19 patients (12%)
Rash	127 patients (40%)	9 patients (6%)
Mouth sores (stomatitis)	68 patients (21%)	28 patients (18%)
Acne-like skin (dermatitis acneiform)	65 patients (20%)	4 patients (3%)
Swelling of the mucous linings (mucosal inflammation)	65 patients (20%)	40 patients (25%)
Nausea	64 patients (20%)	36 patients (23%)

Some unwanted effects were serious. They required a visit to hospital or a longer stay in hospital, needed a doctor's immediate attention, or were life-threatening or fatal.

In this study, 44 patients (13.8%) in the afatinib group and 18 patients (11.3%) in the methotrexate group had serious unwanted effects. This included 2 patients (0.6%) in the afatinib group and 5 patients (3.1%) in the methotrexate group who died from unwanted effects.

Are there follow-up studies?

If more clinical studies with afatinib are done, they may be found on the public websites listed in the section below. To search for these studies, use the following names: BIBW 2992, afatinib.

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: 1200.43
www.clinicaltrialsregister.eu	search for the EudraCT number: 2011-000391-34
www.clinicaltrials.gov	search for the NCT number: NCT01345682

The sponsor of this study was Boehringer Ingelheim.

The full title of the study is:

'LUX-Head & Neck 1: A randomised, open-label, phase III study to evaluate the efficacy and safety of oral afatinib (BIBW 2992) versus intravenous methotrexate in patients with recurrent and/or metastatic head and neck squamous cell carcinoma who have progressed after platinum-based therapy'.

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.