Exploring the Safety of Combining Afatinib with Standard Treatments for Glioblastoma Multiforme (GBM)

This is a summary of a clinical study in brain 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 brain cancer.

What was this study about?

This study looked at the safety, effectiveness, and maximum tolerated dose of a medicine called afatinib. It was combined with the standard treatment for glioblastoma multiforme (GBM). GBM is a form of brain cancer that is difficult to treat. Standard treatment for GBM usually includes surgery followed by radiotherapy. Most patients also take a medicine called temozolomide while doing radiotherapy.

Researchers wanted to know the best dose of afatinib to combine with treatments for patients with GBM. Researchers also wanted to study health problems the patients had during treatment.

This study started in November 2009 and finished in September 2017.

Why was the study needed?

Treatment options for patients with GBM are limited. New treatments are needed. Not all patients benefit from taking temozolomide. Previous studies have shown that afatinib is effective in treating some forms of cancer (for example, lung cancer). Afatinib can slow the growth and spread of tumours, either by itself or combined with other treatments.

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. One of these is a protein called epidermal growth factor receptor (EGFR). Afatinib is taken as a tablet by mouth.

A combination of radiotherapy and temozolomide is the standard treatment for newly diagnosed GBM. Temozolomide is a medicine that helps to stop cancer from growing and spreading. It is given as a capsule by mouth. Radiotherapy is treatment with x-rays or other high-energy rays to control or kill cancer cells.

Who participated in the study?

Adult patients with newly diagnosed GBM took part in this study. Most patients had surgery prior to the trial. None of the patients had been treated with chemotherapy or radiotherapy before starting the study.

A total of 36 patients were treated in the study. This included 25 men and 11 women. The average age was 53 years. The youngest patient was 25 years old. The oldest patient was 68 years old. All patients were from the United Kingdom.

How was this study done?

The patients were divided into 2 groups. The patients were divided based on the results of genetic tests of their tumours.

One group of patients received afatinib plus radiotherapy and temozolomide. This was Regimen M. The type of tumour they had showed a benefit from receiving temozolomide in previous studies.

The other group received afatinib plus radiotherapy only. This was Regimen U. The type of tumour they had did not show a benefit from receiving temozolomide in previous studies.

This study had 2 parts.

In Part 1 of the study, researchers studied dosing. They wanted to know the highest dose of afatinib that patients assigned to Regimen M or U could tolerate. They wanted to know how much afatinib to give to patients on radiotherapy.

To find this dose, doctors gave increasing doses of afatinib to small groups of patients. They checked each patient for certain severe health problems that the doctors thought were caused by afatinib. They determined the dose at which no more than 1 out of 6 patients had such health problems. This dose was the maximum tolerated dose.

There were 3 different doses of afatinib being considered in Part 1 of this study. The doses were 20 mg, 30 mg, and 40 mg. Each patient was assigned to one of these doses. Both the study doctor and the patients knew what dose the patients were getting. Patients were treated for 6 weeks. Afatinib was taken daily. Temozolomide (75 mg per square metre of body surface area) was taken daily by patients assigned to Regimen M. The radiotherapy (total dose 60 Gy) was given 5 days a week to all patients.

After 6 weeks, patients entered Part 2 of the study. In this part, the patients no longer received radiotherapy. All patients took afatinib daily at a dose of 40 mg.

The patients assigned to Regimen M stopped taking temozolomide for 4 weeks. After that, patients took temozolomide for 6 (28-day) cycles. In each cycle, patients took temozolomide for 5 days followed by 23 days off. For Cycle 1, the dose was 150 mg per square metre body surface area. For Cycles 2 – 6, the dose was 200 mg per square metre body surface area if tolerated.

Patients could receive the study medicines until their cancer symptoms got worse, or until patients had a side effect they could not tolerate.

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

What were the results of this study?

For patients who received afatinib plus radiotherapy and temozolomide (Regimen M), the maximum tolerated dose was 30 mg of afatinib. For patients who received afatinib plus radiotherapy (Regimen U), the maximum tolerated dose was 40 mg of afatinib.

This study also examined all health problems patients had during the study. Health problems included those caused by GBM, other diseases, radiotherapy, and study or other medicines. Unwanted effects of afatinib are described in a separate section below.

All 20 patients in Regimen M had health problems. Of these patients, 9 (45%) had to stop taking afatinib because of health problems. Also, 3 patients (15%) had to stop taking temozolomide because of health problems.

All 16 patients in Regimen U had health problems. Of these patients, 10 (63%) had to stop taking afatinib because of health problems.

Health problems were serious for many reasons. Serious health problems included complications that required a visit to or longer stay in hospital. Serious health problems could also be life-threatening, fatal, or lead to disability. In addition, doctors could list health problems as serious for any other reason. For Regimen M, 12 patients (60%) had serious health problems. For Regimen U, 12 patients (75%) had serious health problems. In Regimen U, 3 patients (19%) died. None of these deaths were related to treatment.

Were there any unwanted effects?

Unwanted effects are any health problems that the doctors thought were caused by the study medicines. For Regimen M, 19 out of 20 patients (95%) had unwanted effects. For Regimen U, 15 out of 16 patients (94%) had unwanted effects. The most common unwanted effects seen in either regimen are shown in the table below.

	Regimen M Afatinib plus radiotherapy and temozolomide (20 patients)	**Regimen U Afatinib plus radiotherapy (16 patients)**
Patients with any unwanted effect	19 patients (95%)	15 patients (94%)
Diarrhoea	16 patients (80%)	13 patients (81%)
Rash	13 patients (65%)	12 patients (75%)
Fatigue	9 patients (45%)	6 patients (38%)
Nausea	9 patients (45%)	2 patients (13%)

Some unwanted effects were serious. Serious health problems are defined in the previous section. Serious unwanted effects are serious health problems the doctors thought were caused by the study drug. For Regimen M, 6 patients (30%) had serious unwanted effects. For Regimen U, 1 patient (6%) had serious unwanted effects.

Are there follow-up studies?

No follow-up studies are currently planned. 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: afatinib, BIBW 2992.

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: 1200.38
www.clinicaltrialsregister.eu/ctr-search	search for the EudraCT number: 2008-007284-17
www.clinicaltrials.gov	search for the NCT number: NCT00977431

The sponsor of this study was Boehringer Ingelheim.

The full title of the study is:

'Phase I, open label trial to explore safety of combining BIBW 2992 and radiotherapy with or without temozolomide in newly diagnosed GBM'.

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.