A study to find the best dose of afatinib in children with different types of cancer with ErbB pathway deregulation

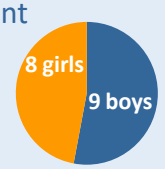
Boehringer Ingelheim

Afatinib is used to treat certain **types of lung cancer** in adults. It works by blocking signals that tell cancer to grow.

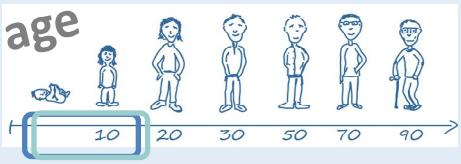
This **study** was to find out:

- **Part** 1 **:** What is the **best dose** of **afatinib** for children with cancer?
- **Part** 2 **:** Does **afatinib help** children who have cancer with ErbB pathway deregulation?

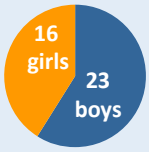
1 **Children** had cancer and the cancer had to have worsened or spread after treatment



There were **17 children** from **Europe.**



2 **Children** had cancer with ErbB pathway deregulation and the cancer had to have worsened or spread after treatment



There were **39 children** from **Europe, North America** and **Australia.**

Each child took afatinib as a tablet or dissolved in a drink. The exact amount of afatinib each child took was adjusted for their body size.

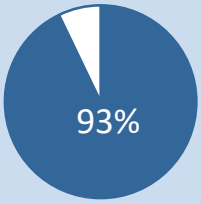
1 The children took either a **low** dose **or** a **high** dose of **afatinib** once a day.

2 The children took a **low** dose of **afatinib** once a day.

93% of children who took afatinib had **unwanted effects.**

1 & 2

afatinib



Diarrhoea was the most common unwanted effect. 73% of children who took afatinib had this unwanted effect.

RESULTS

1 We found the **highest** dose of afatinib the children could tolerate was **the low dose.**

2 The number and size of tumours **decreased** for 1 participant out of 39 (3%).

Study: 1200-0120

A study to find the best dose of afatinib in children with different types of cancer with ErbB pathway deregulation

This is a summary of results from 1 clinical study.

We thank all study participants and their families. You helped us to answer important questions about afatinib and the treatment of cancer.

What was this study about?

This study tested a medicine called afatinib in children with certain types of cancer. Afatinib is already used to treat some types of lung cancer in adults. Afatinib works by blocking signals that tell cancer to grow (scientists call this type of cancer growth 'ErbB pathway deregulation'). We wanted to see if using afatinib helps children who have cancer with ErbB pathway deregulation. This type of cancer is difficult to treat. Additionally, children are often less able to tolerate therapies than adults. That is why new cancer treatments for children are needed.

This study had 2 parts. The purpose of Part 1 was to find the best dose for children with cancer. The purpose of Part 2 was to find out if afatinib helps children who have cancer with ErbB pathway deregulation. Each part is described separately in most of the following sections.

Who took part in this study?

Part 1

Children could be in this part of the study if they had certain types of cancer. The cancer had to have worsened or spread after the children had already received treatment.

17 children were in this part of the study. 9 were boys and 8 were girls. The youngest participant was 2 years old and the oldest participant was 17 years old. The average age was 10 years.

The children were from Denmark, France, and the United Kingdom.

Part 2

Children could be in this part of the study if they had cancer with ErbB pathway deregulation. The cancer had to have worsened or spread after the children had already received treatment.

39 children were in this part of the study. 23 were boys and 16 were girls. The youngest participant was 3 years old and the oldest participant was 18 years old. The average age was 11 years.

The following table shows the numbers of children in the study in different regions.

Region	Countries	Number of Participants
Europe	Austria, Denmark, France, Germany, Italy, Spain, United Kingdom	28
North America	Canada, United States	8
Other	Australia	3

How was this study done?

Part 1

For this part of the study, we wanted to find out the highest dose of afatinib the participants could tolerate. The dose determined from this part would be used for Part 2 of the study.

To make sure that the children in the study got the right amount of study drug, we based the amount on their body size. This helped account for the differences in sizes among children.

There were 2 dose levels tested:

- The high dose was the same as the approved adult dose when adjusted for each child's body size.
- The low dose was 80% of the approved adult dose when adjusted for each child's body size.

We also measured the amount of afatinib in the blood when the participants took 1 dose of afatinib per day. We wanted to compare the amount of afatinib in the blood in children with the amount in adults.

Part 2

For this part of the study, we tested whether the dose of afatinib determined in Part 1 helped children with cancer with ErbB pathway deregulation. The amount of afatinib given still depended on the body size of each child. The doctors looked at the size and number of tumours every 8 weeks to see if the treatment helped.

Parts 1 and 2

In both parts of the study, all participants in the study took afatinib once a day. The children either took afatinib as a tablet or dissolved in a drink. The participants and doctors knew which dose each participant was receiving.

Participants visited the doctors regularly. During these visits, the doctors collected information about the participants' health.

Participants could continue to receive the medicine as long as it was safe, and their cancer was not becoming worse.

What were the results of this study?

Part 1

We found the highest dose of afatinib the participants could tolerate when taken every day was the low dose. In addition, the concentration of afatinib in the blood was similar to the amount in adults when children took the low dose.

Part 2

In this part of the study, the number and size of tumours decreased for only 1 participant out of 39 (3%).

Did participants have any unwanted effects?

Yes, participants had unwanted effects. Unwanted effects are health problems that the doctors think were caused by afatinib. In this study, 52 out of 56 participants (93%) had unwanted effects. In this section of the document, we are showing all results together instead of splitting them by part.

The table below shows the most common unwanted effects. The table also shows how many participants had each of these unwanted effects.

Type of unwanted effect	**Afatinib** **56 participants were in this group**	
Diarrhoea	41 participants (73%)	
Dry skin	14 participants (25%)	
Inflamed and sore mouth (stomatitis)	14 participants (25%)	
Vomiting	13 participants (23%)	
Abdominal pain	11 participants (20%)	
Fingernail or toenail infection (paronychia)	11 participants (20%)	

Some unwanted effects were serious because they required a stay in hospital, a longer stay in hospital, or were life-threatening. Unwanted effects were also serious if the doctor thought they were serious for any other reason. In this study, 10 participants (18%) had serious unwanted effects.

Where can I find more information about this study?

You can find further information about this study at these websites:

1. Go to http://www.mystudywindow.com and search for the study number 1200.120.
2. Go to www.clinicaltrialsregister.eu/ctr-search and search for the EudraCT number 2014-002123-10.
3. Go to www.clinicaltrials.gov and search for the NCT number NCT02372006.

Boehringer Ingelheim sponsored this study.

The full title of the study is: 'Phase I/II open label, dose escalation trial to determine the MTD, safety, PK and efficacy of afatinib monotherapy in children aged ≥1 year to <18 years with recurrent/refractory neuroectodermal tumours, rhabdomyosarcoma and/or other solid tumours with known ErbB pathway deregulation regardless of tumour histology'.

This study started in May 2015 and finished in August 2020.

Are there additional studies?

Because the results of this study were not promising, no other studies of afatinib for children are planned. If we do more clinical studies with afatinib, you will find them on the websites listed above. To search for these studies, use the word afatinib.

Important notice

This lay summary is provided as part of Boehringer Ingelheim's commitment to publicly share clinical study results.

This summary shows only the results from one study and may not represent all of the knowledge about the medicine studied. Other studies may have different results. Usually, more than one study is carried out to find out how well a medicine works and to determine the side effects of a medicine.

This lay summary may include uses, formulations, or treatment regimens for the medicine studied that may be approved or not approved in your country. This lay summary is not intended to promote any product or indication, to guide treatment decisions, or to replace the advice of a healthcare professional.

You should not change your therapy based on the results of this study. Always consult with your treating physician about your therapy.