

A study to look at the safety of a drug called bevacizumab given to people with different types of cancer over a long period of time

See the end of the summary for the full title of the study.

Thank you!

Thank you for taking part in this global clinical trial (called a 'study' in this document). Your generous participation is helping researchers to answer important health questions about the study drug, called bevacizumab. This study, AVALTE, looked at the safety of bevacizumab in people with cancer when given alone or when given with other cancer treatments.

We hope this summary helps you to understand the results of this study and how they will be used to improve the care of people with tumours caused by several different types of cancers. If you have any questions about these results, please speak with your study doctor.

About this summary

This is a summary of the results of a study in people with tumours caused by several different types of cancers – written for:

- People who took part in the study
- Members of the public

Contents of the summary

- 1.** General information about this study
- 2.** Who took part in this study?
- 3.** What happened during the study?
- 4.** What were the results of the study?
- 5.** How has this study helped research?

The study started in July 2012 and ended in September 2019. This summary is based on final results and information known at the time it was written (June 2020). More information may now be known.

One study can't tell us everything about how safe a medicine is. It takes a lot of people in many studies to find out everything we need to know. The results from this study may be different from the results of other studies of the same medicine. **This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.**

6. Are there plans for other studies?
7. Where can I find more information?

Key information about this study

- This study was done to find out what effects, good or bad, a medicine called bevacizumab (the ‘study medicine’) has on people with cancer.
- People who participated in this study had these types of cancer:
 - Breast cancer
 - Ovarian cancer
 - Peritoneal carcinoma (a cancer that develops in the tissue that lines the abdomen)
 - Renal cell carcinoma (also known as kidney cancer)
 - Colorectal cancer (also known as bowel cancer)
 - Lung cancer
 - Glioblastoma multiforme (a type of brain cancer)
- This study was a type of study called an extension study. That means people had taken bevacizumab (alone or in combination with other medicines) in an earlier study and benefitted from taking it. After the previous study had finished, they continued taking bevacizumab in this extension study.
- The researchers wanted to look at how safe treatment with bevacizumab was over a long (‘extended’) period of time.
- This study included 95 people in 21 countries.
- The main finding was that 17 out of the 95 people (18%) had at least one serious medical problem (a life-threatening problem or one that required hospitalisation) that may or may not have been related to bevacizumab.
- Four people died during the study.
- A total of 21 people out of the 95 in the study (22%) had severe side effects (also known as severe ‘adverse reactions’) thought to be related to bevacizumab.

1. General information about this study

Why was this study done?

Many studies have looked at the effects of a drug called bevacizumab in people who have different types of cancer. At the end of those studies, some people were still taking bevacizumab and could benefit from continuing to take bevacizumab because their cancer had not gotten worse.

This study was set up so that people could continue to take bevacizumab after the first study (also called a ‘parent study’) had ended. Researchers could also look at the effects of bevacizumab, good or bad, over a long period of time.

People participated in a number of different studies of bevacizumab (given alone or in combination with other medicines) before starting this extension study and were being treated for different types of cancer.

What are the study medicines?

This study looked at a medicine called ‘bevacizumab’ (known by its brand name, Avastin®). Bevacizumab works by starving a tumour of the blood it needs to grow (this is called ‘anti-angiogenic’ therapy). When a person has cancer, cancer treatments such as chemotherapy are often used because they attack fast-growing cells in the body, including cancer cells. Bevacizumab works differently. It blocks the blood supply that feeds the tumour by blocking a protein called vascular endothelial growth factor, or VEGF. Normal cells make VEGF, but some cancer cells make too much VEGF. Blocking VEGF may stop the growth of new blood vessels, including normal blood vessels and blood vessels that feed tumours. This can stop the tumour from growing. Bevacizumab also has effects on the way the body responds to a tumour. Blocking VEGF may lead to changes inside the tumour to make it easier for the immune system to attack the cancer.

Bevacizumab in combination with other cancer treatments is given to people with these types of cancer:

- Colorectal cancer (also known as bowel cancer)
- Non-small cell lung cancer
- Glioblastoma (a type of brain cancer)
- Kidney cancer
- Ovarian cancer
- Breast cancer
- Cervical cancer

All of the people who took part in this study were treated with bevacizumab. Some were treated with bevacizumab only, and others were treated with bevacizumab combined with other cancer treatments. People kept taking the same treatments they had been given in their previous study. For example, if a person took only bevacizumab in their previous study, they took only bevacizumab in this extension study.

What did researchers want to find out?

Researchers did this study to find out how safe bevacizumab was over a long period of time by checking how many people had medical problems (called side effects) during the study.

The questions that researchers looked at were:

1. How many people had medical problems (that may or may not have been related to bevacizumab) during the study?
2. How many people had serious medical problems (that may or may not have been related to bevacizumab) during the study?
3. How many people died during the study?
4. How many people had side effects related to bevacizumab treatment?
5. How many people had severe side effects (side effects with a higher degree of severity) related to bevacizumab treatment?

What kind of study was this?

This study was a **'Phase 3b/4'** study. This means that the study was done after bevacizumab had been approved for doctors to give to people.

This study was **'single arm'**. This means that everyone in this study was treated with bevacizumab (alone or in combination with other drugs).

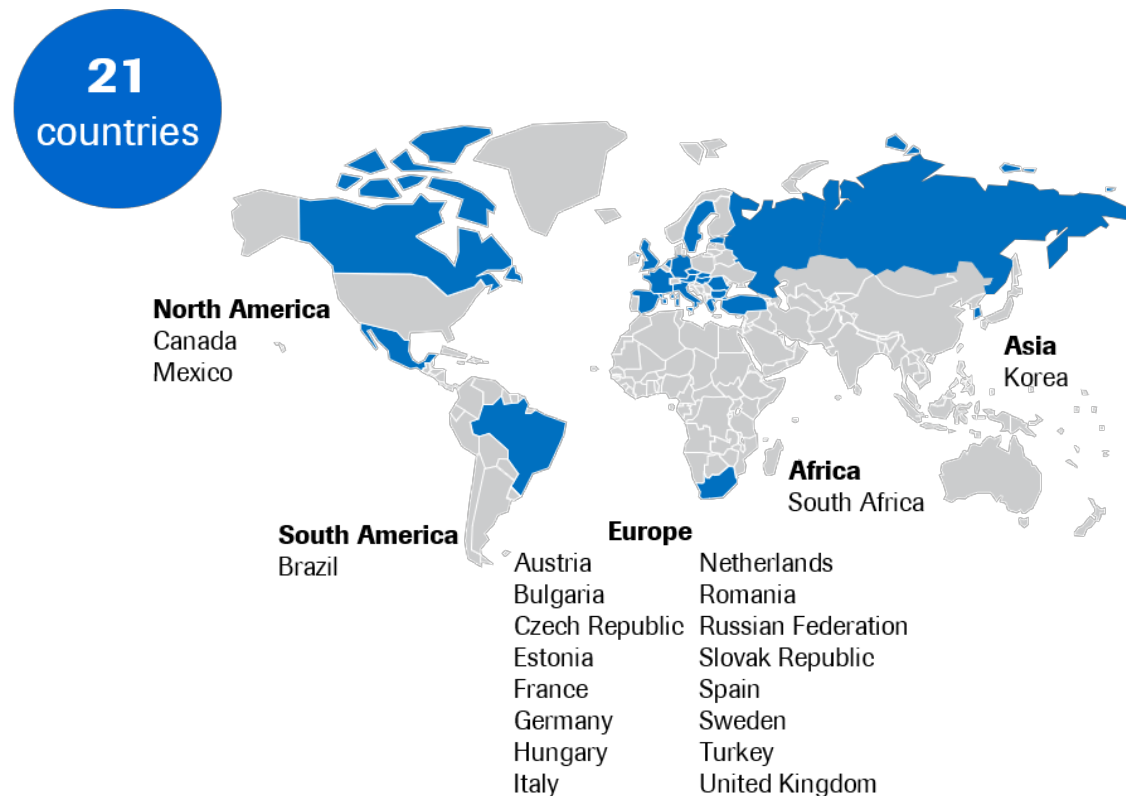
This study was **'open label'**. This means that both the people taking part in the study and the study doctors knew what study medicines people were taking.

This study was an **'extension study'**. This means that people who had previously taken part in a study of bevacizumab kept taking bevacizumab after the previous study ('parent study') had ended.

When and where did the study take place?

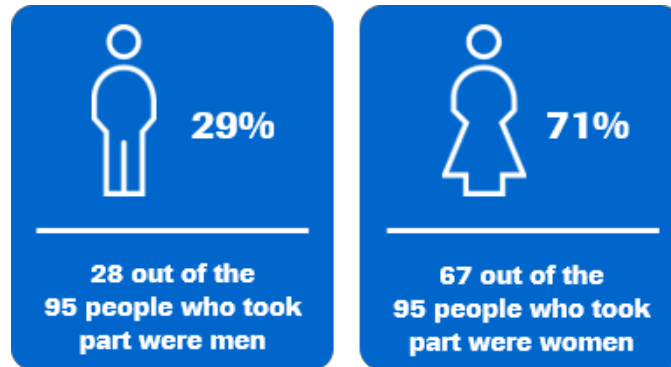
The study started in July 2012 and ended in September 2019. This summary was written after the study had ended.

The study took place at 67 study centres in 21 countries in Africa, Asia, Europe, North America, and South America. This map shows the countries where this study took place.



2. Who took part in this study?

In this study, 95 people with cancer took bevacizumab. Here is more information about the people who took part in the study.



Age range: 23 to 81 years old

The 95 people in this study had been in previous studies where they took bevacizumab. When people finished their first bevacizumab study, they started this extension study.

People could take part in this study if they:

- Had cancer that did not get worse after treatment with bevacizumab (as the only treatment or when given with another anti-cancer treatment) in their first study.
 - People in this study had the following types of cancer:
 - 11 people had breast cancer
 - 41 people had ovarian cancer or peritoneal cancer (a cancer in the tissue that lines the abdomen)
 - 7 people had colorectal cancer (also known as bowel cancer)
 - 6 people had renal cell carcinoma (also known as kidney cancer)
 - 16 people had non-small cell lung cancer
 - 14 people had glioblastoma multiforme (a type of brain cancer)

People could not take part in the study if they:

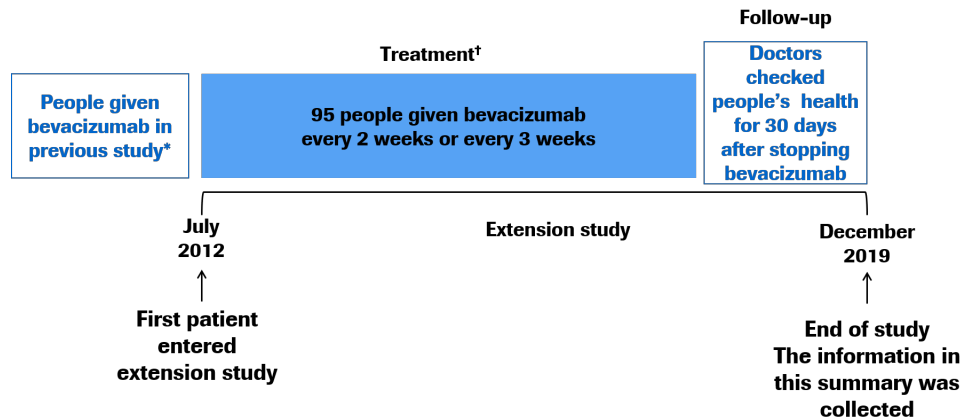
- Had cancer that got worse after treatment with bevacizumab in the first study.
- Had a medical problem in the first study that may have been related to bevacizumab, and researchers recommended that they stop taking bevacizumab.

3. What happened during the study?

A total of 95 people had finished their previous study and were included in this extension study.

All 95 people kept taking bevacizumab as their only cancer treatment or in combination with other cancer treatments.

This picture shows what happened in the study.



* People were in one of 17 different studies before starting this extension study. In those studies, people took bevacizumab every 2 weeks or every 3 weeks.

† People took the same dose of bevacizumab as in their previous study. People in this extension study took bevacizumab until one of three things happened: their disease got worse, they developed a serious side effect of the treatment (also known as an 'adverse reaction') that made it unacceptable to continue treatment, or they or the doctor decided to stop treatment.

In this study, half of the people took bevacizumab for less than 15 months (1¼ years) and half took bevacizumab for more than 15 months. When the time they took bevacizumab in their first study was added in, half of the people took bevacizumab for less than 57 months (4¾ years) and half of the people took bevacizumab for more than 57 months. Three people took bevacizumab for more than 10 years (these people had breast cancer).

4. What were the results of the study?

This section shows only the main results from the study. You can find information about all other results on the websites at the end of this summary (see section 7).

Here, we talk about all medical problems that the people had during the study.

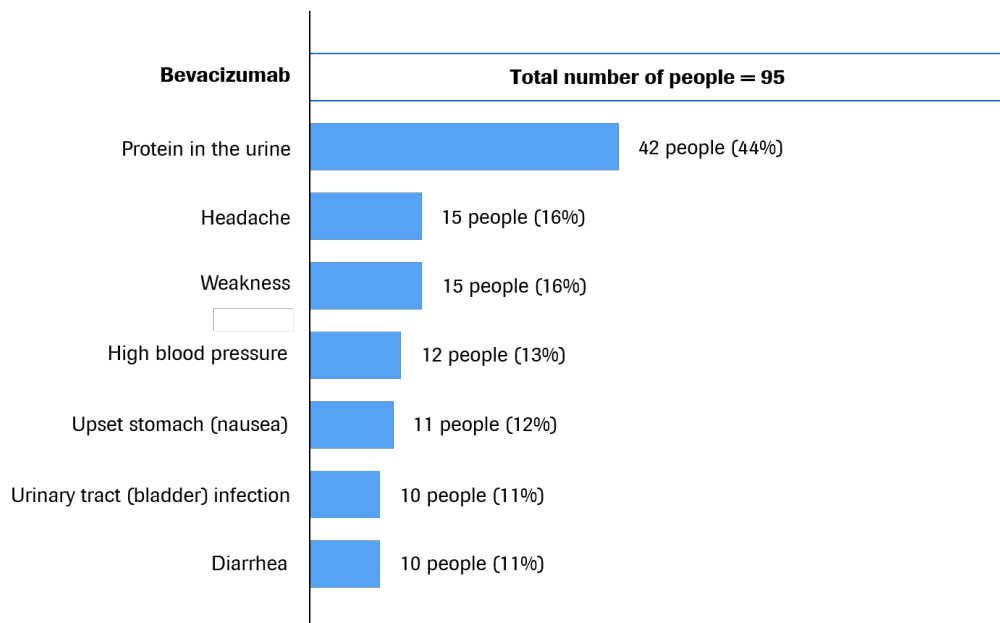
Questions 1 and 2 are about medical problems that may or may not have been related to bevacizumab. **Question 3** is about patients who died during the study. **Questions 4 and 5** are about side effects, which are medical problems thought to be related to bevacizumab.

Question 1: How many people had medical problems (that may or may not have been related to bevacizumab) during the study?

Overall, 79 out of the 95 people in the study (83%) had at least one medical problem that may or may not have been related to bevacizumab during the study. Some people in this study did not have any of the medical problems.

This picture shows the most common medical problems that happened during the study – 10% or more of the people in the study had these medical problems. The most common medical problem was **protein in the urine** – a sign of possible damage to the kidneys.

What were the most common medical problems during the study?

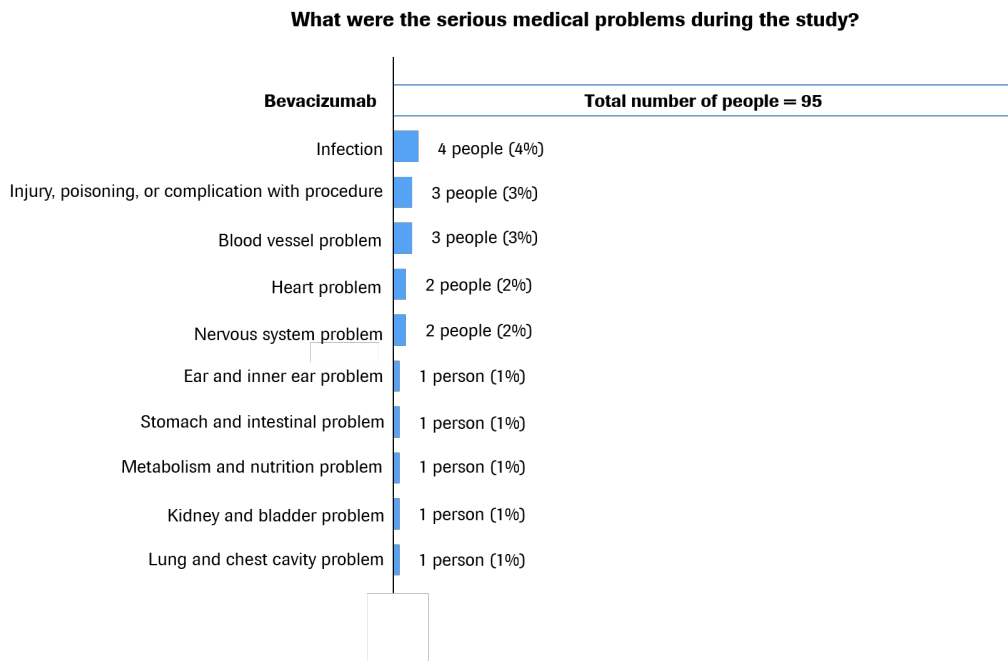


Question 2: How many people had serious medical problems (that may or may not have been related to bevacizumab) during the study?

A medical problem is considered 'serious' if it is life-threatening, needs hospital care, or causes lasting problems.

During this study, 17 out of the 95 people (18%) had at least one serious medical problem that may or may not have been related to bevacizumab.

This picture shows the serious medical problems that happened during the study.



During the study, some people stopped taking bevacizumab because of medical problems that may or may not have been related to bevacizumab:

- 23 out of 95 people (24%) stopped taking bevacizumab due to medical problems
 - The most common reason was for protein in the urine – a sign of possible damage to the kidneys – 13 out of 95 people (14%) stopped taking bevacizumab because of protein in the urine

Question 3: How many people died during the study?

Out of the 95 people who took bevacizumab during this extension study, 4 people died.

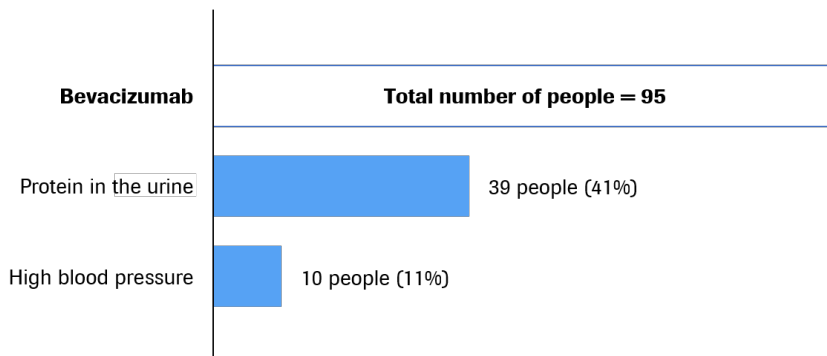
- Three people (3%) died because their cancer got worse. In studies that look at treatments for cancer, some people are likely to die of their cancer during the study. It is important to collect information about people who died during the study to understand whether the treatments were linked with any of the deaths.
- One person (1%) died due to a medical problem that was not related to bevacizumab treatment.

Question 4: How many people had side effects related to bevacizumab treatment?

The researchers looked at side effects that were thought to be related to bevacizumab (also called ‘adverse reactions’). Side effects are medical problems believed to be caused by the study medicine.

A total of 54 people of the 95 in the study (57%) had a side effect thought to be related to bevacizumab. This picture shows the most common side effects that happened during the study – 10% or more of the people in the study had these side effects.

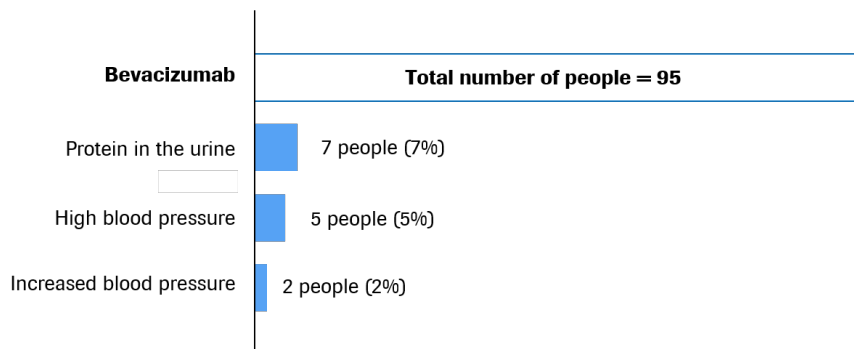
What were the most common side effects thought to be related to bevacizumab?



Question 5: How many people had severe side effects (side effects with a higher degree of severity) related to bevacizumab treatment?

A total of 21 people of the 95 people in the study (22%) had severe side effects (side effects with a higher degree of severity) thought to be related to bevacizumab. This picture shows side effects that happened in more than one person.

What were the most common severe side effects thought to be related to bevacizumab?



None of the side effects thought to be related to bevacizumab were life-threatening, and none of the people died from these side effects.

Other side effects

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see section 7.

5. How has this study helped research?

The information in this summary is from one study of 95 people with different types of cancer. These results helped researchers learn more about people with cancer who were treated with bevacizumab over a long period of time.

The safety results of this study were similar to other studies of bevacizumab. All of the medical problems in people who took bevacizumab in this study have been seen in other studies of bevacizumab. The most common medical problems (protein in the urine and high blood pressure) could be managed.

No one study can tell us everything about how safe a medicine is and how well it works. It takes a lot of people in many studies to find out everything we need to know. The results from this study may be different from other studies with bevacizumab.

- This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.

6. Are there plans for other studies?

Other studies are being done to look at the effects of bevacizumab in combination with other existing cancer treatments.

7. Where can I find more information?

You can find more information about this study on the websites listed below:

- <https://clinicaltrials.gov/ct2/show/NCT01588184>
- <https://www.clinicaltrialsregister.eu/ctr-search/trial/2011-002009-31/results>
- <https://forpatients.roche.com/>

Who can I contact if I have questions about this study?

If you have any more questions after reading this summary:

- Contact your local Roche office.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak with the doctor in charge of your treatment.

Who organised and paid for this study?

This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: 'A Single Arm, Open Label Multicentre Extension Study of Bevacizumab in Patients With Solid Tumours on Study Treatment With Bevacizumab, at the End of a F. Hoffmann-La Roche and/or Genentech Sponsored Study'.

The study is known as 'AVALTE'.

- The protocol number for this study is: MO25757.
- The ClinicalTrials.gov identifier for this study is: NCT01588184.
- The EudraCT number for this study is: 2011-002009-31.