Clinical trial results – layperson summary

A study to look at the effectiveness of chemotherapy plus bevacizumab compared with chemotherapy alone in children and adolescents with metastatic soft tissue sarcoma (STS)

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

About this summary

This is a summary of the results of a clinical trial (called a 'study' in this document) – written for:

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

This summary is based on information known at the time of writing. More information may now be available.

The study started in July 2008 and finished in April 2019. This summary was written after the study had ended.

No single study can tell us everything about the risks and benefits of a medicine. It takes many people in many studies to find out everything we need to know. The results from this study may be different from other studies with 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

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Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about children and adolescents with cancer of connective, muscle and nervous tissues and the study medicine.

Key information about this study

- This study was done to investigate the addition of bevacizumab to chemotherapy for treating metastatic soft tissue sarcomas (STSs)
- In this study, children and adolescents with metastatic STS were given chemotherapy plus bevacizumab, or chemotherapy alone. It was decided by chance which treatment each person was given
- This study included 154 people
- The study found no statistical difference in the effect of chemotherapy plus bevacizumab on the length of time patients were free from signs and symptoms of their STS, compared with chemotherapy alone
- All patients experienced at least one side effect and similar numbers of patients experienced serious side effects

1. General information about this study

Why was this study done?

STSs are a group of rare cancers affecting the tissues that connect, support and surround other body structures and organs. Tissues that can be affected by this type of cancer include fat, muscle, blood vessels, tendons and ligaments. Patients with STS may have one or several tumours that have spread to different parts of the body – called 'metastatic' STS.

Treatment for STS includes medicines called chemotherapy, and also procedures such as surgery and radiotherapy. However, new and effective treatments are urgently needed. This study was done to investigate whether a drug called bevacizumab could improve outcomes for children and adolescents with metastatic STS when given with standard chemotherapy.

What was the study medicine?

'Bevacizumab' is the medicine that was being studied here – it works in a different way to chemotherapy:

- Bevacizumab cuts off the blood supply to the tumour and stops the growth of new blood vessels
- This may mean that tumour cells may decrease in size

What did researchers want to find out?

- Researchers did this study to see if adding bevacizumab to standard chemotherapy worked better than standard chemotherapy alone (see section 4 "What were the results of the study?")
- They also wanted to find out how safe the medicine was – by checking how many people had side effects when taking each of the medicines during this study (see section 5 "What were the side effects?")

The main question that researchers wanted to answer was:

1. How long did patients stay free of any signs and symptoms of their STS when taking chemotherapy plus bevacizumab, compared with chemotherapy alone?

What kind of study was this?

This study was a 'Phase 2' study. This means that bevacizumab has been tested in a number of people before this study.

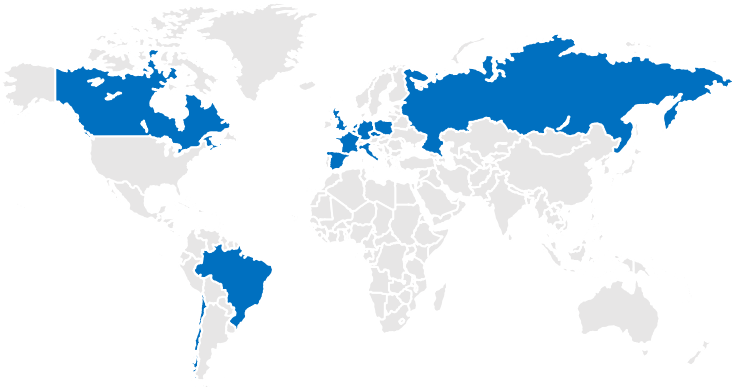
The study was 'randomised'. This means that patients were split into treatment groups by chance – like tossing a coin.

The study was 'open label'. This means that both the researchers and the participants in the study knew what treatment was being given.

When and where did the study take place?

The study started in July 2008 and finished in April 2019. This summary was written after the study had ended.

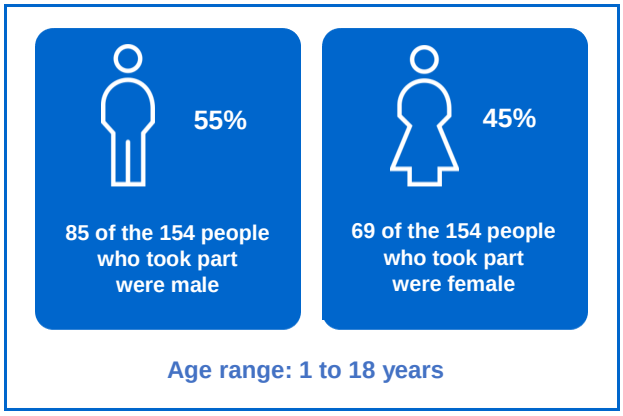
The study took place at 61 study centres – across 14 countries. The following map shows the countries where this study took place.



- Belgium
- Brazil
- Canada (Ontario, Quebec)
- Chile
- Czechia
- France
- Germany
- Israel
- Italy
- Netherlands
- Poland
- Russian Federation
- Spain
- United Kingdom

2. Who took part in this study?

In this study, 154 patients with STS took part.



People could take part in the study if they:

- Had metastatic STS
- Were between the ages of 6 months and 18 years old

People could not take part in the study if they had:

- Previously received any anti-tumour treatment
- Tumours affecting certain areas of the body such as the central nervous system or major blood vessels

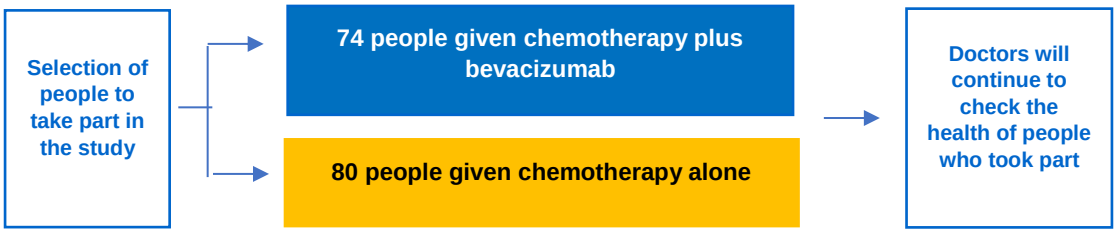
3. What happened during the study?

During the study, people were selected by chance to get one of two treatments. The treatments were selected at random by a computer.

The treatment groups were:

- **Chemotherapy plus bevacizumab**
  - Chemotherapy and bevacizumab every 3 weeks for 9 rounds, followed by
  - Chemotherapy and bevacizumab every 4 weeks for 12 rounds

- **Chemotherapy alone**
  - Chemotherapy every 3 weeks for 9 rounds, followed by
  - Chemotherapy every 4 weeks for 12 rounds



Four patients did not receive any treatment and are not included in these results.

4. What were the results of the study?

How long did patients stay free of any signs and symptoms of their STS when taking chemotherapy plus bevacizumab, compared with chemotherapy alone?

Researchers wanted to see if there were any differences between the two treatment groups in how long patients stayed free of any signs and symptoms of their STS.

People who were given chemotherapy plus bevacizumab had an average of 20.6 months before experiencing signs and symptoms of their STS. This compares with 14.9 months for people who were given chemotherapy alone.

14.9 months free of STS signs and symptoms (chemotherapy alone)

20.6 months free of STS signs and symptoms (chemotherapy plus bevacizumab)

Researchers use statistics to understand whether differences between groups are due to chance. In this study, although the results show an improvement for patients treated with chemotherapy plus bevacizumab, statistical analysis did not find any significant difference between the groups. This means that the improvement could just be down to chance.

5. What were the side effects?

Side effects (also known as 'adverse reactions') are unwanted medical problems (such as a headache) that happen during the study.

- Not all of the people in this study had all of the side effects

Serious and common side effects are listed in the following sections.

Serious side effects

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

During this study, 86% of patients receiving chemotherapy alone had a serious side effect, compared with 93% of patients receiving chemotherapy plus bevacizumab.

The following table shows the top five most common serious side effects, where there was a difference of at least 5% between the treatment groups:

Serious side effects reported in this study	**People receiving chemotherapy alone** (79 people total)	**People receiving chemotherapy plus bevacizumab** (71 people total)
Fever with low white blood cell count	78.5% (62 out of 79)	84.5% (60 out of 71)
Reduced white blood cell count	65.8% (52 out of 79)	76.1% (54 out of 71)

Reduced red blood cell count	54.4% (43 out of 79)	69.0% (49 out of 71)
Low blood platelet count	39.2% (31 out of 79)	33.8% (24 out of 71)
Inflammation of the mucosa (a membrane that lines various cavities in the body and covers the surface of internal organs)	16.5% (13 out of 79)	25.4% (18 out of 71)

During the study, some people decided to stop taking some or all of their treatments because of side effects:

- Six (7.6%) patients in the chemotherapy alone group stopped treatment due to side effects
- Eleven (15.5%) patients in the chemotherapy plus bevacizumab group stopped treatment due to side effects

Most common side effects

During this study, all patients had at least one side effect that was not considered serious. The most common of these side effects were anaemia (reduced red blood cell count), neutropenia (reduced white blood cell count), vomiting, constipation, back pain, cough, nose bleeds, headache, tears or sores around the anus, weakness or low energy, damage to nerves in the hands and feet, and reduced ability to make new blood cells in bone marrow.

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 8).

6. How has this study helped research?

The information presented here is from a single study of 154 people with STS. This study did not find any statistical difference between chemotherapy plus bevacizumab, and chemotherapy alone in affecting the length of time patients stayed free of any signs and symptoms of their STS. These results are important as they help researchers learn more about STS and the role of bevacizumab with chemotherapy.

No single study can tell us everything about the risks and benefits of a medicine. It takes many people in many studies to find out everything we need to know. The results from this study may be different from other studies with 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

7. Are there plans for other studies?

At the time of writing this summary, no more studies looking at chemotherapy plus bevacizumab in these patients are planned.

8. Where can I find more information?

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

- https://clinicaltrials.gov/ct2/show/results/NCT00643565
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2007-005017-19/results
- https://forpatients.roche.com/en/trials/cancer/a-study-of-avastin--bevacizumab--in-combination-with-st-82381.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: Open-label, multicentre, randomised, phase II study of the EpSSG and the ITCC evaluating the addition of bevacizumab to chemotherapy in childhood and adolescent patients with metastatic soft tissue sarcoma (the BERNIE study). The lead author of the scientific paper is Julia C. Chisholm. The paper is published in the journal *European Journal of Cancer*.

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

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – https://forpatients.roche.com/en/trials/cancer/a-study-of-avastin--bevacizumab--in-combination-with-st-82381.html
- Contact a representative at 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 to 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: An open-label, multi-center, randomized study of the safety and effect on event-free survival of bevacizumab in combination with standard chemotherapy in childhood and adolescent patients with metastatic rhabdomyosarcoma and non-rhabdomyosarcoma soft tissue sarcoma.

The study is known as 'BERNIE'.

- The protocol number for this study is: BO20924
- The ClinicalTrials.gov identifier for this study is: NCT00643565
- The EudraCT number for this study is: 2007-005017-19