ForPatients
by Roche

Cervical Cancer

Safety and Efficacy of Bevacizumab in Combination With Carboplatin and Paclitaxel for Metastatic, Recurrent or Persistent Cervical Cancer

Trial Status	Trial Runs In	Trial Identifier
Completed	18 Countries	NCT02467907 2014-005491-28 MO29594

The source of the below information is the publicly available website ClinicalTrials.gov. It has been summarised and edited into simpler language.

Trial Summary:

This study is to assess safety as defined by the frequency and severity of gastrointestinal (GI) perforation/fistula, GI-vaginal fistula and genitourinary (GU) fistula in participants treated with bevacizumab 15 milligrams per kilogram (mg/kg) in combination with paclitaxel and carboplatin, all repeated every 3 weeks, for recurrent, persistent or metastatic cervical cancer. In addition, this study will include evaluation of the overall safety profile of bevacizumab in combination with paclitaxel and carboplatin in this setting, assessment of GI perforation/fistula, GI-vaginal fistula and GU fistula events over time, and evaluation of efficacy.

Hoffmann-La Roche	**Phase 2**
Sponsor	Phase

NCT02467907 2014-005491-28 MO29594
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
Female	>=18 Years	No

About this summary

This is a summary of the results of a study in women with advanced cervical cancer – written for:

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

This summary is based on final results and information known at the time it was written (April 2020). More information may now be known.

One study can't tell us everything about how safe a medicine is and how well it works. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from results from 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.**

Key information about this study

- This study was done to find out what effects, good or bad, a medicine called bevacizumab had on women with advanced cervical cancer when given with other cancer drugs called carboplatin and paclitaxel. This study included:
    - Women who had not responded to previous treatment for cervical cancer
    - Women whose cancer had come back after treatment
    - Women whose cancer had spread to other areas of the body
- The researchers looked at the safety of the study treatments by monitoring how many women developed abnormal openings (called 'perforations') or abnormal connections (called 'fistulas') in the following areas:
    - In the stomach or intestine
    - Between the intestine and vagina
    - Between the genital parts of the body (uterus, vagina, or cervix) and urinary parts (bladder, tubes that connect the kidneys and bladder, or tubes that carry urine outside the body)
- The study also looked at how well the study treatments worked
- In this study, 150 women in 18 countries received the study medicine (called 'bevacizumab') along with other cancer treatments (chemotherapy drugs called carboplatin and paclitaxel).
- The main finding was that 17 women (11%) developed a perforation or fistula. This was around the same percentage of women who developed perforations/fistulas in another study in which bevacizumab was given with different cancer treatments.
- Around 17% of women (25 out of 150 women) in this study had serious side effects.
- In this study of women with advanced cervical cancer, bevacizumab when given with carboplatin and paclitaxel worked as well as what has been seen in similar studies.

1. General information about this study

Why was this study done?

Women with cancer of the cervix (also called 'cervical cancer') are normally treated with surgery or radiation plus a medicine that kills cancer cells (called 'chemoradiotherapy').

Some women's cervical cancer may keep getting worse after these treatments – meaning that the surgery or chemoradiotherapy did not work (called 'persistent disease'). Some women's cervical cancer comes back after treatment (called 'recurrent disease'). When cervical cancer is persistent or recurrent, or if it has spread to other parts of the body (called 'metastatic disease'), doctors may use a different type of cancer drug called bevacizumab.

Studies have already shown that the study medicine, bevacizumab, is safe and works well in people with different types of tumours. Researchers have studied the use of bevacizumab plus 2 existing cancer treatments (or 'chemotherapy') called carboplatin and paclitaxel in people with ovarian cancer and in people with a type of lung cancer called 'non-small cell lung cancer'.

A previous study looked at women with cervical cancer that was persistent, recurrent, or metastatic (also called ' **advanced cervical cancer**'). The women who took **bevacizumab** plus 2 chemotherapy drugs called **cisplatin and paclitaxel** lived longer and had smaller tumours after treatment than women who took only **cisplatin and paclitaxel**. However, a different combination of chemotherapy drugs, **carboplatin plus paclitaxel**, is used more often than cisplatin plus paclitaxel to treat women with advanced cervical cancer in some countries. This means it is important to look at the safety of **bevacizumab** when given with **carboplatin and paclitaxel** to women with advanced cervical 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 in combination with other cancer treatments is already given to people with the following types of cancer:

- Colorectal cancer (also known as bowel cancer) that has spread to other parts of the body
- Non-small cell lung cancer
- Glioblastoma (a type of brain tumour)
- Kidney cancer that has spread to other parts of the body
- Ovarian cancer
- Breast cancer

- Cervical cancer

Carboplatin is a chemotherapy used to treat different type of cancers. It damages the genetic material inside the cells and makes it hard for cells to fix the damage. This can slow or stop the tumour from growing.

Paclitaxel is a chemotherapy used to treat different types of cancers. It interferes with the ability of cancer cells to divide. This can slow or stop the tumour from growing.

The women in this study all took **bevacizumab plus carboplatin and paclitaxel**.

What did researchers want to find out?

Researchers wanted to look at the effects of bevacizumab when given with carboplatin and paclitaxel. They focused on safety (see section 4 'What were the results of the study?' and section 5 'What were the side effects?') and how well the treatments worked (see section 4 'What were the results of the study?')

The main questions that researchers wanted to answer were:

1. How many women developed an abnormal opening ('perforation') or connection ('fistula') in the stomach and intestines or the genital and urinary parts of the body?
2. Where in the body was the perforation or fistula?

Other questions that researchers wanted to answer were:

3. How long was the time between the start of the study and the cancer getting worse?4. How long did the women in this study live?

What kind of study was this?

This study was a ' **Phase 2**' study. This means that bevacizumab had been tested in some women with cervical cancer before this study. In this study, researchers wanted to look at how safe bevacizumab is for women with advanced cervical cancer when taken with other cancer treatments – carboplatin and paclitaxel.

This study was ' **single arm**'. This means that all women started out receiving the same treatment.

This study was ' **open label**'. This means that the women taking part in the study and the study doctors knew which study medicines the women were taking.

When and where did the study take place?

This summary was written after the study had ended.

The study took place at 39 study centres in 18 countries in Africa, Central America, 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, 150 women with advanced cervical cancer received the study medicines.

Women who took part in the study were between 24 and 80 years old. The average age of women in the study was 50 years, and most women (87%) were younger than 65 years.

Women could take part in the study if they:

- Were 18 years old or older
- Had persistent, recurrent, or metastatic cervical cancer that could not be treated
- with surgery or radiation therapy
- Had recovered from previous treatments for their cancer, including surgery,
- radiation, and medicine to treat the cancer (called ‘chemotherapy’)
- Had normal ‘blood clotting,’ which is the body’s ability to stop bleeding
- Had kidneys and a liver that were working normally

Women could not take part in the study if they:

- Were pregnant or breastfeeding
- Had a history of fistula or stomach/intestinal perforation
- Had a type of cancer other than cervical cancer in the past 5 years
- Had disease of the bladder or rectum (lower bowel)
- Had chemotherapy before for their advanced cervical cancer
- Had untreated tumours in the nervous system, including the brain or spinal cord
- Had any other serious health problems, such as serious infections, uncontrolled HIV, heart problems, uncontrolled high blood pressure, or blood vessel disease

3. What happened during the study?

At the start of the study, 152 women were selected to take part, but only 150 women received the study drugs (1 woman died before taking the study drugs, and 1 woman developed a blood clot that made her unable to receive the study drugs). The study ended 2 years after the last woman in the study received her first dose of study medicine.

All 150 women in the study were given bevacizumab plus carboplatin and paclitaxel.

This picture shows what happened in the study.

* It was recommended to continue giving carboplatin and paclitaxel for at least 6 treatments (or 'cycles') if possible. Women in the study took the study drugs until their disease got worse, they developed a serious side effect of the treatment (also known as an 'adverse reaction'), or the doctor or the woman taking part decided to stop treatment.

† After they stopped the study treatment, the women who took part were asked to go back to their study centre for more visits (follow-up phase)– to check for potential problems related to the study treatment.

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 8).

Question 1: How many women developed an abnormal opening ('perforation') or connection ('fistula') in the stomach and intestines or the genital and urinary parts of the body?

Overall, 17 out of the 150 women in the study (11%) developed a perforation or fistula.

Question 2: Where in the body was the perforation or fistula?

The researchers looked at where the perforations and fistulas were in the body during the study:

- 7 women (5%) had a perforation (abnormal opening) or fistula (abnormal connection) in the stomach or intestine (called a 'gastrointestinal perforation/fistula').
- 6 women (4%) had a fistula between the intestine and vagina (called a 'gastrointestinal-vaginal fistula').
- 7 women (5%) had a fistula between the genital parts of the body (uterus, vagina, or cervix) and urinary parts of the body (bladder, urethra, or ureters; called a 'genitourinary fistula').

In 9 out of the 17 women with perforations or fistulas, the perforation/fistula was either severe or life-threatening (8 women) or resulted in death (1 woman).

Question 4: How long was the time between the start of the study and the cancer getting worse?

Researchers also looked at how much time it took for the women's cancer to get worse – this information was collected from the start of the study treatment until the end of the study (December 2018).

- In the women in the study, the cancer got worse around 11 months after the start of study treatment. This is the median length of time (or middle number – half of the women's cancer got worse before 11 months and half after 11 months)

Question 5: How long did women in this study live?

Researchers wanted to know how long women in this study lived after start of study treatment.

- Around 78% of the women were still alive 1 year after the start of study treatment.
- Around 52% of the women were still alive 2 years after the start of study

  treatment.

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.

- They are described in this summary because the study doctor believes the side effects were related to the drugs used in the study.
- Not all of the women in this study had all of the side effects.

Common and serious side effects related to bevacizumab and to carboplatin and/or paclitaxel are listed in the following sections.

Most common side effects

During this study, 108 out of the 150 women (72%) had a side effect related to bevacizumab.

This table shows the most common side effects related to bevacizumab – 10% or more of the women in the study had these side effects.

During this study, 143 out of 150 women (95%) had a side effect related to carboplatin and/or paclitaxel.

The most common side effects related to carboplatin and/or paclitaxel are shown in the following table –10% or more of the women in the study had these side effects.

Serious side effects

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

During this study, 25 out of the 150 women (17%) had at least one serious side effect thought to be related to bevacizumab.

A total of 89 serious side effects happened during the study. Of these 89 serious side effects:

- 35 were thought to be related to bevacizumab; the most common were genital tract fistula (5 events), bleeding from the rectum (3 events), urogenital fistula (3 events), vaginal bleeding (2 events), and blood in the urine (2 events).
- 15 were thought to be related to carboplatin and/or paclitaxel; the most common carboplatin/paclitaxel-related side effects were low level of red blood cells (4 events) and 2 events each of fever with low levels of a type of white blood cell called neutrophils, low blood pressure, low level of platelets, and vomiting.
- 10 were thought to be related to all 3 study treatments (bevacizumab, carboplatin, and paclitaxel); the most common of these side effects were low levels of red blood cells, white blood cells, and platelets (2 events each).

Out of the 150 women who were given the study treatment, 74 women died.

Most of the deaths happened because the women’s cervical cancer got worse. In any study looking at treatment for advanced cervical cancer, some women will probably die during the study because of cervical cancer. It is important to collect information about women who died during the study to understand whether the treatments were linked with any of the deaths.

Eight women out of the 150 in the study (5%) died from side effects that may or may not have been related to one of the study medicines.

During the study, some women stopped taking their medicine because of side effects:

- 48 out of 150 women (32%) stopped taking bevacizumab because of side effects.

- 42 out of 150 women (28%) stopped taking carboplatin or paclitaxel because of 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 8.

6. How has this study helped research?

The information in this summary is from one study of 150 women with persistent, recurrent, or metastatic cervical cancer. These results helped researchers learn more about women with advanced cervical cancer who were treated with bevacizumab plus carboplatin and paclitaxel.

The number of perforations and fistulas in the women in this study (treated with bevacizumab plus carboplatin and paclitaxel) was similar to the number of perforations and fistulas in women in another study (treated with bevacizumab plus cisplatin and paclitaxel). Bevacizumab plus carboplatin and paclitaxel worked as well in this study as it did in other similar studies when bevacizumab was given with different chemotherapy treatments.

The results of this study suggest that treating women who have advanced cervical cancer with bevacizumab plus carboplatin and paclitaxel leads to similar results as treating them with bevacizumab plus cisplatin and paclitaxel.

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.

7. 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 for women with advanced cervical cancer.

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/NCT02467907

https://www.clinicaltrialsregister.eu/ctr-search/trial/2014-005491-28/results

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

If you have any more questions after reading this summary:

- 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 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 Multicentre Open-Label Single-Arm Phase II Study Evaluating the Safety and Efficacy of Bevacizumab in Combination with Carboplatin and Paclitaxel in Patients with Metastatic, Recurrent or Persistent Cervical Cancer’.

The study is known as ‘CECILIA’.

- The protocol number for this study is: MO29594.
- The ClinicalTrials.gov identifier for this study is: NCT02467907.
- The EudraCT number for this study is: 2014-005491-28.