Summary of Clinical Trial Results

A study of atezolizumab with or without tiragolumab in people with cervical cancer, whose tumor cells have the protein PD-L1 and who have been treated in the past with chemotherapy

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:

- People who are taking part in the study, and
- Members of the public.

This summary is based on information known at the time of writing (August 2024).

The study started in June 2020, and this summary includes the complete results that were collected and analyzed until December 2021. At the time of writing this summary, this study is still happening—this summary presents the complete results for one part of the study.

No single study can tell us everything about the risks and benefits of a medication. 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 other studies with the same medication.

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

Contents of the summary

Glossary

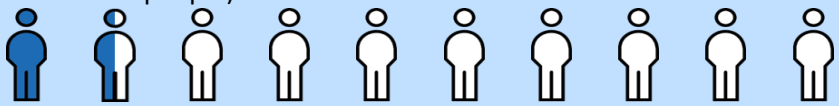
Programmed death-ligand 1 (PD-L1): a protein that normally stops the immune system from attacking good cells. In cancer, tumor cells can use PD-L1 to hide from the immune system.

Thank you to the people who are taking part in this study

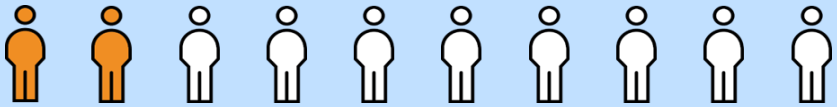
The people who are taking part in the study have helped researchers answer important questions about cervical cancer and the medications studied: "atezolizumab" and "tiragolumab".

Key information about this study

- This study is being done to find out if atezolizumab with or without tiragolumab can make cervical cancer tumors smaller or completely disappear and what the side effects are.
- In this study, people with cervical cancer, whose tumor cells have the protein PD-L1 and who have previously had chemotherapy, were selected by chance to get one of two treatments, atezolizumab or atezolizumab plus tiragolumab.
- This study includes 171 people in 17 countries.
- The main findings were that:
  - The cervical cancer tumors got smaller or disappeared completely in 16% of people (seven out of 45 people) who took atezolizumab alone.



  - The cervical cancer tumors got smaller or disappeared completely in 19% of people (24 out of 126 people) who took atezolizumab plus tiragolumab.



  - However, we do not know if this is a real difference or if it could have happened by chance.
  - During this study, 51% of people (23 out of 45 people) taking atezolizumab alone and 66% of people (83 out of 126 people) taking atezolizumab plus tiragolumab had treatment-related side effects. Only 9% of people (four out of 45 people) taking atezolizumab alone and 13% of people (17 out of 126 people) taking atezolizumab plus tiragolumab had severe side effects that may have required medical intervention or hospitalization. No people died because of side effects related to treatment.
- This study is expected to close within a few months' time. At the time of writing this summary, a few patients are still in the study, so they can continue to take their medication until they are able to receive it outside of the study.

1. General information about this study

Why is this study being done?

This study is being done to learn how best to treat people with cervical cancer whose tumor cells have the protein PD-L1, where available treatment options such as chemotherapy no longer work. The cervix is the lower part of the uterus or womb, opening into the vagina, which plays an important part in the passage of blood during menstruation and the birth of a baby. Cervical cancer occurs when the cells lining the cervix begin to grow uncontrollably. The cancer can also spread to other parts of the body. The main cause of cervical cancer is a persistent human papillomavirus (HPV) infection of the cervix. HPV causes 95% of cervical cancer cases and increases the expression of the PD-L1 protein on cervical cancer cells.

The treatment for cervical cancer is influenced by a number of factors, such as the size, shape, and stage of the tumor, as well as the person's health, age, and interest in having children. Many people with cervical cancer are treated with chemotherapy, a type of medication which kills cancer cells. However, chemotherapy may stop working, meaning that the cancer may return or start to grow again. Because of this, people with cervical cancer who are given chemotherapy and still have cancer or whose cancer has come back may need new medications to reduce the size of their tumors. If their tumors are smaller, people might find it easier to control their cancer.

In this study, researchers are testing a new way of trying to treat people with cervical cancer that has spread or come back. These people had received up to two types of chemotherapy, but the treatment was no longer making their tumors smaller. Researchers wanted to see if taking atezolizumab with or without tiragolumab could reduce the size of people's tumors or make them completely disappear. Atezolizumab is a type of "immunotherapy" that encourages the body's own immune system to attack cancer cells. Tiragolumab helps boost the body's immune system to stop or reverse the growth of cancer cells. Researchers think that combining these two medications may make tumors smaller than if the medications were used on their own. The study also looked at whether these medications were safe, that is, whether they caused any new side effects or any more side effects than previous treatments.

What are the study medications?

This study is looking at two medications:

- Atezolizumab received alone
- Atezolizumab received together with tiragolumab

These medications are new—they are not existing treatments for cervical cancer.
a
Atezolizumab is one of the medications being studied here.

● You say this as "a – teh – zo – liz – oo – mab".
● This is a type of cancer medication that is used to encourage the body's immune system to attack tumors. This type of treatment is called "cancer immunotherapy".
● The body's immune system fights diseases like cancer. However, cancer cells can block the immune system from attacking the cancer. Atezolizumab releases this block—meaning that the immune system is able to fight the cancer cells.

● When people take atezolizumab, their tumors may get smaller.

Tiragolumab is another one of the medications being studied here.
● You say this as “ti – ruh – gol – oo – mab”.
● This is a type of cancer immunotherapy medication that works by stopping cancer cells from blocking cells in the immune system, meaning the immune system can go back to attacking the cancer cells.
● When people take tiragolumab, tumors may get smaller.

What do researchers want to find out?

- Researchers are doing this study to see how well atezolizumab with or without tiragolumab works in people with cervical cancer (see section 4, “What were the results of the study?”).
- They also want to find out how safe atezolizumab with or without tiragolumab is, by checking how many people have side effects and seeing how severe they are, when taking each of the medications during this study (see section 5, “What were the side effects?”).

The main questions that researchers wanted to answer were:

1. Can taking atezolizumab with or without tiragolumab make the tumors of people with cervical cancer smaller or disappear completely?
2. How many people taking atezolizumab with or without tiragolumab experienced side effects caused by the treatments—and how severe were the side effects?

What kind of study is this?

This study is a “Phase II” study. This means that atezolizumab with or without tiragolumab has been tested in a number of people with cervical cancer before this study. In this study, people with cervical cancer are taking either atezolizumab alone or atezolizumab with tiragolumab to find out more about how well these medications work and how safe they are.

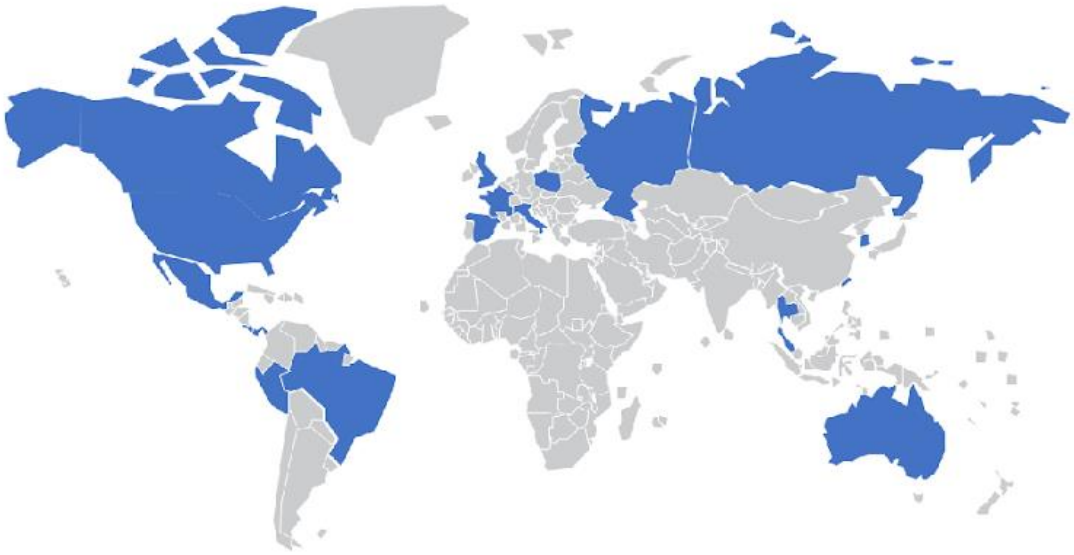
The study is “randomized”. This means that it was decided by chance, for example, by tossing a coin, which of the medications people in the study would have. Randomly choosing which medication people take makes it more likely that the types of people in both groups (for example, age, race) will be a similar mix. Apart from the exact medications being tested in each group, all other aspects of care were the same between the groups.

This study is “open label”. This means that both the researchers and people taking the medication know exactly what medications are being given to them.

When and where is the study taking place?

The study started in June 2020, and this summary includes the complete results until December 2021. This study is expected to close within a few months. At the time of writing this summary, a few patients remain in the study to continue taking their medication until they can receive it outside of the study.

The study is taking place at 59 study centers, across 17 countries in Asia, Australia, Europe, North America, and South America. The following map shows the countries where the study is taking place.



- Australia
- Brazil
- Canada
- Costa Rica
- France
- Italy
- Mexico
- Panama
- Peru
- Poland
- Spain
- Taiwan
- Thailand
- Republic of Korea
- Russian federation
- United Kingdom
- United States

2. Who is taking part in this study?

In this study, 171 people with cervical cancer are taking part. All people taking part in this study are women, who are between 26 and 80 years of age. In this study, 107 out of the 171 people are white, 22 are Asian, six are American Indian/Alaska Native, two are Black or African American, and the race of 34 people is unknown. More information on the people who are taking part in the study is given below.

People could take part in the study if:

They were women who were 18 years of age or older

They still had cervical cancer despite taking up to two types of chemotherapy

They could perform activities as well or almost as well as they could before the illness

Their tumor had cells with the protein PD-L1

People could not take part in the study if:

They were being treated with anti-viral therapy for hepatitis B virus (HBV) or hepatitis C virus (HCV)

They had central nervous system (CNS) or brain tumors

They have or had diseases where the immune system did not function correctly or attacked their own bodies

They were previously treated with any medications that work in the same way as either atezolizumab or tiragolumab

3. What is happening during the study?

During the study, people were assigned by chance to get atezolizumab with or without tiragolumab. The choice of treatment combination was selected by a computer at random.

People are either given:

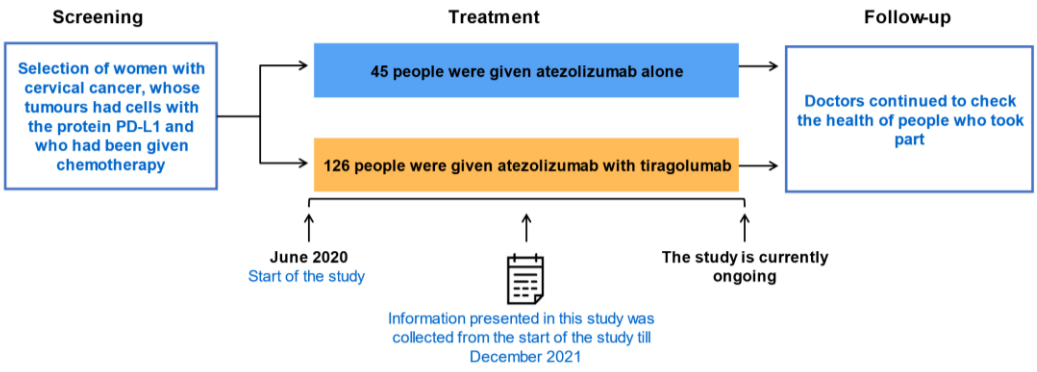
- Group one: atezolizumab alone
- Group two: atezolizumab with tiragolumab

The medications in this study are given to the people every three weeks until they stopped working, or the side effects become unmanageable.

This table shows the number of people who are taking each study treatment, and how often the medications are given.

	Atezolizumab alone	**Atezolizumab plus tiragolumab**
Number of people in each group	45	126
How the medications are received	1200 mg of atezolizumab is given by infusion	1200 mg of atezolizumab followed by 600 mg of tiragolumab is given by infusion
How often are the medications received	Every three weeks	Every three weeks

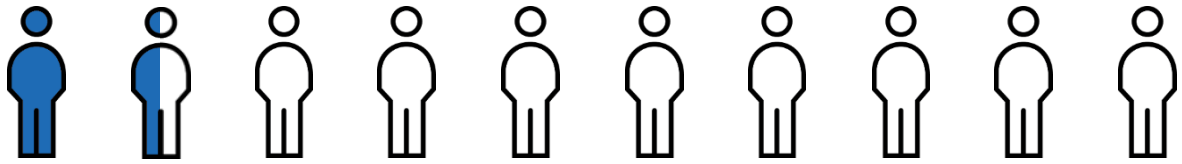
This picture shows what is happening in the study for each of the two groups. Once the people who are taking part in the study finish taking the medication, they are asked to go back to their study center for more visits to check their overall health. A few patients still remain in the study, so that they can continue to take their medication until they are able to receive it outside of the study.



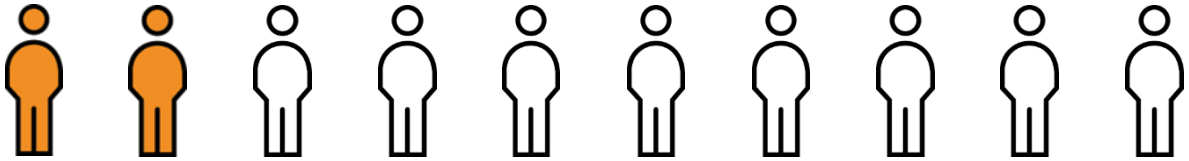
4. What were the results of the study?

Question one: Can taking atezolizumab with or without tiragolumab make the tumors of people with cervical cancer smaller or disappear completely?

Researchers looked at what had happened to the tumors of people with cervical cancer who took atezolizumab alone or with tiragolumab. The cervical cancer tumors got smaller or disappeared completely in 16% of people (seven out of 45 people) who took atezolizumab alone.



The cervical cancer tumors got smaller or disappeared completely in 19% of people (24 out of 126 people) who took atezolizumab plus tiragolumab.



However, we do not know if this is a real difference as it could have been caused by chance.

Question two: How many people taking atezolizumab with or without tiragolumab experienced side effects caused by the treatments—and how severe were the side effects?

Another piece of information that researchers collected was the side effects people experienced when taking atezolizumab alone or with tiragolumab.

- See section 5 for a summary of side effects.

This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see section 8).

5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happen during the study.

- They are described in this summary because the study doctor believes the side effects were related to the treatments in the study.
- Not all of the people in this study had all of the side effects.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medication guides.
- Side effects can vary from mild to severe and may vary from person to person.
- Severe and common side effects are listed in the following sections.

Side effects

During this study, 51% of people (23 out of 45 people) taking atezolizumab alone and 66% of people (83 out of 126 people) taking atezolizumab plus tiragolumab had treatment-related side effects. Only 9% of people (four out of 45 people) taking atezolizumab alone and 13% of people (17 out of 126 people) taking atezolizumab plus tiragolumab had severe side effects that may have required medical intervention or hospitalization.

No people in this study died because of side effects related to the treatment.

Most common side effects

The most common side effects are shown in the following table—these are the most common side effects across both treatment groups. Some people had more than one side effect—this means that they are included in more than one row in the table.

Most common side effects reported in this study	**People taking atezolizumab** (45 people in total)	**People taking atezolizumab plus tiragolumab** (126 people in total)
Low level of red blood cells (*anemia*)	24 (11 out of 45 people)	32 (40 out of 126 people)
Throwing up (*vomiting*)	16% (7 out of 45 people)	14% (18 out of 126 people)
Joint pain/stiffness (*arthralgia*)	16% (7 out of 45 people)	13% (16 out of 126 people)
Low energy levels (*asthenia*)	13% (6 out of 45 people)	17% (22 out of 126 people)
Fever (*pyrexia*)	13% (6 out of 45 people)	17% (21 out of 126 people)
Feeling nauseous (*nausea*)	11% (5 out of 45 people)	20% (25 out of 126 people)
Feeling tired (*fatigue*)	7% (3 out of 45 people)	17% (22 out of 126 people)
Lower appetite	7% (3 out of 45 people)	15% (19 out of 126 people)
Itchy skin (*pruritus*)	0% (0 out of 45 people)	18 (23 out of 126 people)

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 171 people with cervical cancer whose tumor cells have the protein PD-L1 and whose tumors continued to grow or had come back after being given chemotherapy. These results help researchers learn more about how well atezolizumab with or without tiragolumab works to treat this type of cancer, and how safe these cancer medications are.

Overall, this study showed that both atezolizumab alone and atezolizumab with tiragolumab made the tumors smaller or disappear completely in approximately 15 to 20 out of every 100 people. The people in this study did not have any new side effects that had not been seen before in people who took atezolizumab in other studies.

No single study can tell us everything about the risks and benefits of a medication. 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 other studies with the same medication.

- **This means that you should not make decisions based on this one summary—always talk 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 the combination of atezolizumab with tiragolumab treatment in cervical cancer 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/study/NCT04300647
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2019-004895-21/GB
- https://forpatients.roche.com/en/trials/cancer/cca/a-study-of-tiragolumab-plus-atezolizumab-and-atezolizum-32500.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “A non-comparative randomized phase II trial of atezolizumab or atezolizumab plus tiragolumab for programmed death-ligand 1-positive recurrent cervical cancer (SKYSCRAPER-04)”. The authors of the scientific paper are Ritu Salani, Mary McCormack, Yong-Man Kim, Sharad Ghamande, Shaundra L Hall, and others. The paper is published in the journal *International Journal of Gynaecologic Cancer*, DOI number is 10.1136/ijgc-2024-005588.

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/cca/a-study-of-tiragolumab-plus-atezolizumab-and-atezolizum-32500.html
- Contact a representative at your local Roche office.

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

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

If you have questions about your own treatment:

- Talk to the doctor in charge of your treatment.

Who organized and paid for this study?

This study was organized and paid for by F. Hoffmann-La Roche Ltd, which has its headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: “A Study of Tiragolumab Plus Atezolizumab and Atezolizumab Monotherapy in Participants with Metastatic and/or Recurrent PD-L1-Positive Cervical Cancer (SKYSCRAPER-04)”.

The study is known as “SKYSCRAPER-04”.

- The protocol number for this study is: WO42017.
- The ClinicalTrials.gov identifier for this study is: NCT04300647.
- The EudraCT number for this study is: 2019-004895-21.