

Summary of Clinical Trial Results

A study to compare atezolizumab plus carboplatin and etoposide with placebo plus carboplatin and etoposide in people with a type of lung cancer called ‘extensive-stage small-cell lung cancer’

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 and
- People who took part in the study.

This summary is based on information known at the time of writing.

The study started in June 2016 and will end in March 2021. This summary includes the results that were analysed in January 2019. At the time of writing this summary, the study is still ongoing – study doctors are still collecting information.

One study can’t tell us everything about how safe a medicine is and how well it works. The results from this study are based on the investigations and observations made in the specific people involved. More studies in more people will help to expand the knowledge of a drug. Therefore, 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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Glossary

- PD-L1 = programmed death-ligand 1.

Thank you to the people who took part in this study

The people who took part helped researchers to answer important questions about a type of lung cancer called ‘extensive-stage small-cell lung cancer’ and the medicines being studied – ‘atezolizumab’, ‘carboplatin’, and ‘etoposide’.

Key information about this study

- This study was done to look at the effects of atezolizumab (a type of immunotherapy) given in combination with two chemotherapy medicines – carboplatin and etoposide - in people with a type of lung cancer called ‘extensive-stage small-cell lung cancer’.
- In this study, people were given either atezolizumab (plus carboplatin and etoposide) or a placebo, which does not have any real medicine (plus carboplatin and etoposide) – it was decided by chance which treatment each person was given.
- This study included 403 people (called the ‘**total population**’ in this summary) in 21 countries.
- So far, information collected by researchers over 23 months has shown that atezolizumab plus carboplatin and etoposide can help people to live longer than placebo plus carboplatin and etoposide.
 - In the **total population**, people who took atezolizumab plus carboplatin and etoposide lived for about 12 months, and people who took placebo plus carboplatin and etoposide lived for about 10 months.
 - Out of the total population, 394 people took at least one dose of the study medicines. These people make up the ‘**safety population**’.
 - In the **safety population**, about 39% of people (77 out of 198 people) taking atezolizumab plus carboplatin and etoposide had serious side effects, compared to around 35% of people (69 out of 196 people) taking placebo plus carboplatin and etoposide.
 - At the time of writing this summary, the study is still happening. It will end in March 2021.

1. General information about this study

Why was this study done?

People with a type of lung cancer called ‘extensive-stage small-cell lung cancer’ are usually given medicines that will help improve the burden of their disease. A type of medicine often given to people with this type of cancer is called ‘platinum-based chemotherapy’. Two types of platinum-based chemotherapy that are used regularly are called ‘carboplatin’ and ‘cisplatin’. These are given with a different type of chemotherapy medicine called ‘etoposide’.

Platinum-based chemotherapy does not work in everyone, or it may work for only a short time and then the cancer gets worse again. These people are sometimes given a treatment called immunotherapy, which is a medicine that helps a person’s own immune system to attack malignant tumours (that is, cancer that grows and spreads to other parts of the body). Immunotherapy medicines can help some people with extensive-stage small-cell lung cancer improve the burden of their disease and live longer, but these medicines do not cure cancer. Some immunotherapy medicines target a protein called ‘programmed death-ligand 1’ or **PD-L1**. Everyone has PD-L1 in their bodies. Normally, PD-L1 helps to stop a person’s immune system from attacking good cells. When PD-L1 is in cancer cells, it stops the immune system from killing the cancer. Some immunotherapy medicines can block (stop) PD-L1 so the immune system can attack the tumour.

In this study, researchers wanted to see if adding an immunotherapy that blocks PD-L1 to an existing treatment (carboplatin and etoposide) would help people with extensive-stage small-cell lung cancer live longer than people treated with carboplatin and etoposide given with a placebo (which does not have any real medicine).

Researchers also wanted to see if the combination of these medicines led to any side effects (that is, they were safe for people to take). The people in the study had extensive-stage small-cell lung cancer that had not been treated with chemotherapy before.

What are the study medicines?

A medicine called ‘atezolizumab’ (known by its brand name, Tecentriq®) was the focus of this study.

- You say ‘atezolizumab’ as ‘a – teh – zo – liz – oo – mab’.
- You say ‘Tecentriq’ as ‘teh – sen – trik’.
- The body’s immune system fights diseases like cancer. However, cancer cells containing PD-L1 can block (stop) the immune system from attacking the cancer. Atezolizumab releases this blockage by stopping PD-L1 from working – meaning that the immune system is able to fight the cancer cells.
- When people take atezolizumab, their tumour (cancer) may get smaller.
- This medicine is a type of immunotherapy.

Atezolizumab plus carboplatin and etoposide was compared to carboplatin and etoposide given with a 'placebo'.

- You say this as 'plah – see – bo'
- The placebo looked the same as atezolizumab but did not contain any real medicine. This means it had no medicine-related effect on the body.
- Carboplatin is a chemotherapy medicine that kills cancer cells by preventing them from dividing into new cancer cells.
- Etoposide is a chemotherapy medicine that kills cancer cells by causing the genetic material in the cancer cells to break.
- Researchers gave one group of people carboplatin and etoposide plus atezolizumab. They gave another group carboplatin and etoposide plus a placebo. This let researchers see what benefits or side effects are actually caused by adding atezolizumab to carboplatin and etoposide.

What did researchers want to find out?

- Researchers did this study to look at whether adding atezolizumab to 2 existing medicines (carboplatin and etoposide) worked better than the 2 existing medicines alone. The existing medicines were given for 4 cycles. Atezolizumab was given with the existing medicines for 4 cycles and then given alone afterwards (see section 4 "What were the results of the study?").
- They also wanted to find out how safe these medicines were for the people in the study – by checking if there were any side effects and how serious these side effects were (see section 5 "What were the side effects?").

The main questions that researchers wanted to answer were:

1. How long did people live (during the study)?
2. How much time was there between the start of the study and people's cancer getting worse?

Other questions that researchers wanted to answer included:

3. How many people had smaller tumours after taking their medicine?
4. For people whose tumours got smaller during the study, how much time was there until their cancer then got worse?

What kind of study was this?

The first part of this study was a 'Phase 1' study, which means that this was one of the first studies of atezolizumab in people with extensive-stage small-cell lung cancer. A small number of people with extensive-stage small-cell lung cancer took either atezolizumab or placebo in combination with carboplatin and etoposide. An independent group of researchers and doctors checked these people to find out whether atezolizumab in combination with carboplatin and etoposide led to any side effects.

The second part of this study was a 'Phase 3' study. In this part of the study, a larger number of people with extensive-stage small-cell lung cancer took either atezolizumab or a placebo – both were given with carboplatin and etoposide. This was to find out if atezolizumab helped people with extensive-stage small-cell lung cancer live longer.

The study was ‘randomised’. This means that it was decided by chance which of the medicines people in the study would have – like tossing a coin. Randomly choosing which medicine people take (that is, which study arm they in), makes it more likely that the types of people in both groups (for example, age, race) will be a similar mix. Other than the exact medicines being tested in each group, all other aspects of care were planned to be the same between the groups.

The study was a ‘double-blind’ study. This means that neither the people taking part in the study or the study doctors knew which of the study medicines people were taking.

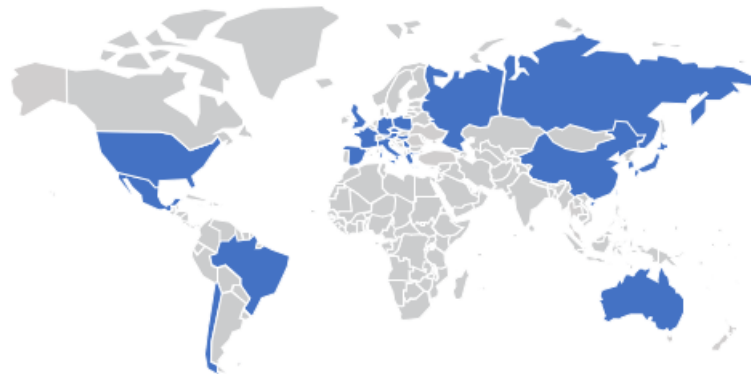
‘Blinding’ of a study is done so that any effect seen from the medicine is not due to something people expected to happen – if they had known which medicine they were taking.

When and where did the study take place?

The study started in June 2016 and will end in March 2021. This summary includes the results up until January 2019. At the time of writing this summary, the study is still happening – study doctors are still collecting information.

The study took place at 106 study centres – across 21 countries in Australia, Asia, Europe, and North and South America. The following map shows the countries where this study took place.

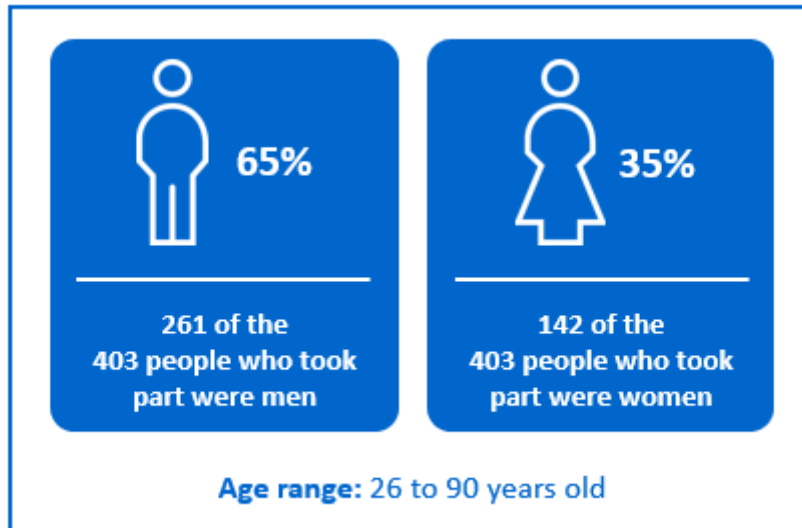
- Australia
- Austria
- Brazil
- Chile
- China
- Czechia
- France
- Germany
- Greece
- Hungary
- Italy
- Japan
- Korea, Republic of
- Mexico
- Poland
- Russian Federation
- Serbia
- Spain
- Taiwan
- United Kingdom
- USA



2. Who took part in this study?

In this study, 403 people with extensive-stage small-cell lung cancer took part.

Here is more information on the people who took part.



People could take part in the study if they:

- Had a type of lung cancer called extensive-stage small-cell lung cancer.
- Were able to do activities or were able to do light activity as well as they could before they got cancer.

People could not take part in the study if they:

- Had been given chemotherapy before for their extensive-stage small-cell lung cancer.
- Had untreated cancer that had spread to the brain or spinal cord.

3. What happened during the study?

During the study, people with extensive-stage small-cell lung cancer were selected by chance to get one of two treatments. The treatments were selected at random – by a computer.

The treatment groups were either:

- **Atezolizumab** – injected into a vein once every 3 weeks.
- **Placebo** – injected into a vein once every 3 weeks.

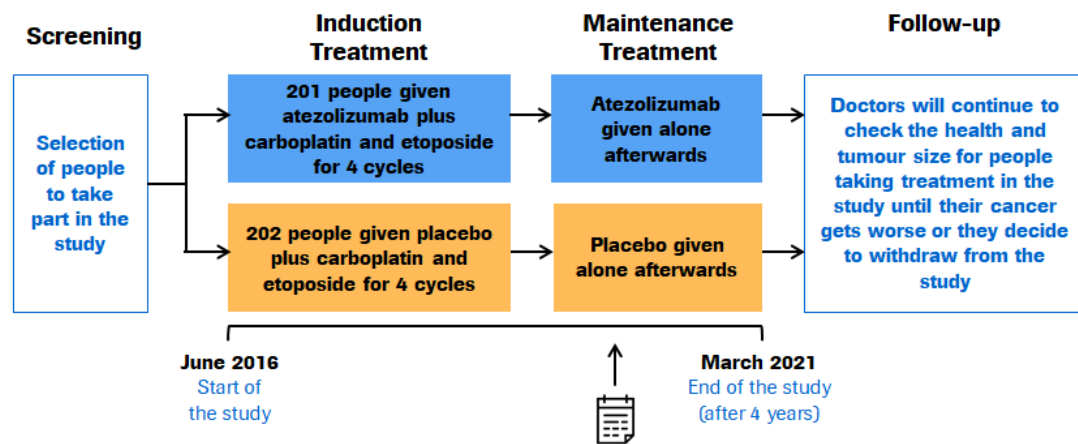
Both groups also received both:

- **Carboplatin** – injected into a vein once every 3 weeks.
- **Etoposide** – injected into a vein up to 3 times every 3 weeks.

Carboplatin with etoposide was given for 4 cycles. Atezolizumab or placebo was each given with carboplatin and etoposide for 4 cycles and alone afterwards.

When the study started, 201 people were chosen to get atezolizumab plus carboplatin and etoposide, and 202 people were chosen to get placebo plus carboplatin and etoposide. This is called the ‘total population’.

This study is still happening, so some people are still being treated with the study medicines. When the study ends, the people who took part will be asked to go back to their study centre for more visits – to check their health. Here is more information about what has happened in the study so far – and what the next steps are.



This study is still happening, so the symbol on the timeline (📅) shows when the information shown in this summary was analysed (January 2019) – 2.5 years from the start of the study in 2016.

4. What were the results of the study?

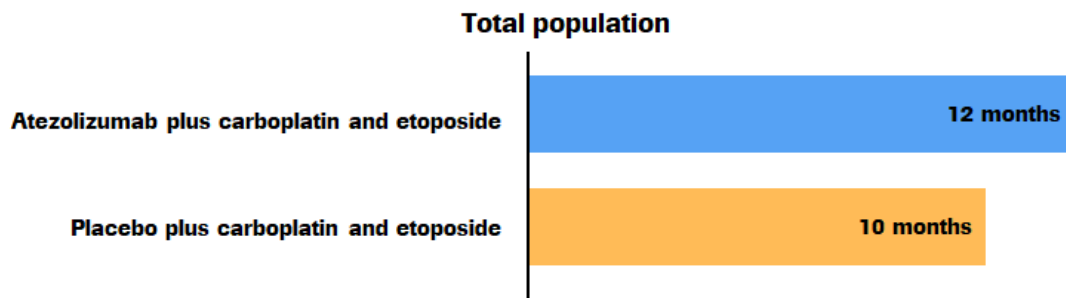
Question 1: How long did people live (during the study)?

Researchers looked at how long people in the study lived on average – this was compared between the people who took atezolizumab plus carboplatin and etoposide and the people who took placebo plus carboplatin and etoposide. Researchers collected information for around 23 months after people in the study started taking the medicines.

- In the **total population**, people who took atezolizumab plus carboplatin and etoposide lived for around 12 months, and people who took placebo plus carboplatin and etoposide lived for around 10 months.

These numbers are averages – that means that some people died sooner and some people lived longer. The study is still ongoing, so some of the people who participated in it are still alive and are still being checked by investigators.

On average, how long did people in each group live?



Out of the 403 people who took medicine in this study, 302 people had died at the time the information in this summary was collected (January 2019).

In a study like this looking at a new treatment option for extensive-stage small-cell lung cancer, the goal is for the medicine to help provide some relief to the people participating in the study and help them to live longer. Some people are still likely to die from their lung cancer during the study. It is important to collect this information to understand whether the treatments were linked with any of the deaths.

Question 2: How much time was there between the start of the study and people's cancer getting worse?

Another piece of information that researchers collected was how much time there was before people's cancer got worse – this information was collected from the start of the study until January 2019.

- In the **total population**, people's cancer got worse around 5 months after they started taking atezolizumab plus carboplatin and etoposide and around 4 months after they started placebo plus carboplatin and etoposide.

These numbers are averages – that means some people's cancer got worse sooner than this and some people's cancer got worse after a longer time than this.

Question 3: How many people had smaller tumours after taking their medicine?

Researchers also looked at how many people had smaller tumours up to around 23 months after they started taking atezolizumab plus carboplatin and etoposide or placebo plus carboplatin and etoposide.

- The number of people whose tumours got smaller were similar among those taking atezolizumab plus carboplatin and etoposide and those taking placebo plus carboplatin and etoposide. In the **total population**, tumours got smaller in 60 out of 100 people (60%) taking atezolizumab plus carboplatin and etoposide and in 64 out of 100 people (64%) taking placebo plus carboplatin and etoposide.

Question 4: For people whose tumours got smaller during the study, how much time was there until their cancer then got worse again?

For people whose tumours got smaller during the study, researchers recorded how long it took for people's cancer to then get worse again. This information was collected from the start of the study until January 2019.

- In the **total population**, people whose tumours got smaller had their cancer get worse in around 4 months. This was true for both people taking atezolizumab plus carboplatin and etoposide and people taking placebo plus carboplatin and etoposide. Some people's tumours remained smaller for less time than this, and some people's tumours remained smaller for longer.

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.

- Every drug can cause serious side effects. During clinical studies, researchers investigate whether the benefits of taking a drug outweigh any potential side effects.
- During the study, researchers evaluated people who received at least one dose of the study medicines (called the **safety population**) to see if any of them had side effects.
 - The **safety population** included 198 people in the atezolizumab plus carboplatin and etoposide group and 196 people in the placebo plus carboplatin and etoposide group.
- Side effects in this summary are described because the study doctor believes they were related to the treatments in the study.
- Not all of the people in the **safety population** had all of the side effects.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the side effects reported here are from this one study. Therefore, the side effects shown here may be different from those seen in other studies or those that appear in the medicine leaflets.
- 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, the percentages of people who had a serious side effect were similar for those taking atezolizumab plus carboplatin and etoposide and those taking placebo plus carboplatin and etoposide. In the study, 77 out of 198 people (39%) taking atezolizumab plus carboplatin and etoposide and 69 out of 196 people (35%) taking placebo plus carboplatin and etoposide had a serious side effect.

Some people in the study died due to side effects that may have been related to one of the study medicines. In the **safety population**, a total of 6 out of 394 people died possibly due to serious side effects from one of the study medicines:

- 3 out of 198 people (1.5%) in the atezolizumab plus carboplatin and etoposide group.
- 3 out of 196 people (1.5%) in the placebo plus carboplatin and etoposide group.

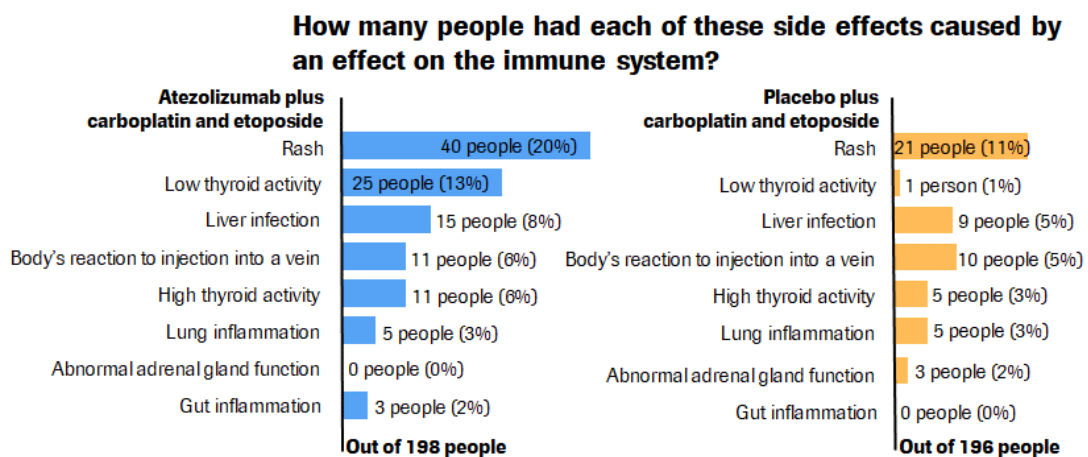
During this study, some people decided to stop taking their medicine because of side effects:

- In the atezolizumab plus carboplatin and etoposide group, 24 out of 198 people (12%) stopped taking their medicine.
- In the placebo plus carboplatin and etoposide group, 6 out of 196 people (3%) stopped taking their medicine.

Most common side effects

During this study, about 9 to 10 out of every 10 people in the **safety population** (98%) had a side effect of any severity due to any cause. About 100% of people taking atezolizumab plus carboplatin and etoposide and about 96% of people taking placebo plus carboplatin and etoposide had a side effect of any severity due to any cause.

This picture shows the most common side effects caused by the medicines' effect on the immune system – these are the 8 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 bar in the picture.



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 403 people with extensive-stage small-cell lung cancer. The study is still happening. These results helped researchers learn more about extensive-stage small-cell lung cancer and treatment with atezolizumab plus carboplatin and etoposide.

So far, information collected by researchers over 23 months has shown that atezolizumab plus carboplatin and etoposide has helped people to live longer than placebo plus carboplatin and etoposide.

- In the **total population**, people who took atezolizumab plus carboplatin and etoposide lived for around 12 months, and people who took placebo plus carboplatin and etoposide lived for around 10 months.

In the **safety population**, 77 out of 198 people (39%) taking atezolizumab plus carboplatin and etoposide had serious side effects.

No one study can 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 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?

Studies with atezolizumab are still happening, and more studies 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/NCT02763579>
- <https://www.clinicaltrialsregister.eu/ctr-search/trial/2015-004861-97/results>
- <https://forpatients.roche.com/en/trials/cancer/lung-cancer/a-study-of-carboplatin-plus-etoposide-with-or-without-atezolizum.html>

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “Updated overall survival and PD-L1 subgroup analysis of patients with extensive-stage small-cell lung cancer treated with atezolizumab, carboplatin and etoposide (IMpower133)”. The authors of the scientific paper are: Stephen V. Liu, Martin Reck, Aaron S. Mansfield, Tony Mok, Arnaud Scherpereel and others. The paper was published online on January 13, 2021 in the journal ‘Journal of Clinical Oncology’ and can be assessed by visiting: <https://ascopubs.org/doi/10.1200/JCO.20.01055>.

If you would like to find out about earlier results of this study (analysed in April 2018), the full title of the relevant scientific paper is: “First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer.” The authors of the paper are: Leora Horn, Aaron S. Mansfield, Aleksandra Szczesna, Libor Havel, Maciej Krzakowski and others. The paper is published in the journal ‘New England Journal of Medicine’, volume number 379, on pages 2220-2229.

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/lung-cancer/a-study-of-carboplatin-plus-etoposide-with-or-without-atezolizum.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: “A Study of Carboplatin Plus Etoposide With or Without Atezolizumab in Participants With Untreated Extensive-Stage (ES) Small Cell Lung Cancer (SCLC) (IMpower133)”.

The study is known as ‘IMpower133’.

- The protocol number for this study is: GO30081.
- The ClinicalTrials.gov identifier for this study is: NCT02763579.
- The EudraCT number for this study is: 2015-004861-97.