

Summary of Clinical Trial Results

A study to compare atezolizumab with platinum-based chemotherapy in people with a type of lung cancer called ‘non-small cell lung cancer’ (NSCLC)

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 on July 21, 2015, and will end in May 2021. This summary includes the results based on data collected up to September 10, 2018. At the time of writing this summary, the study is still going on – study doctors are still collecting information.

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

- **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

- NSCLC = ‘non-small cell lung cancer’
- PD-L1 = ‘programmed death-ligand 1’

Thank you to the people who took part in this study

The people who took part have helped researchers answer important questions about a type of lung cancer called ‘non-small cell lung cancer’ (NSCLC) and the new medicine being studied – ‘atezolizumab’, a type of immunotherapy.

Key information about this study

- This study was done to compare the medicine being studied (called 'atezolizumab') with an existing medicine (called 'platinum-based chemotherapy') in people with a type of lung cancer called 'non-small cell lung cancer'.
- In this study, it was decided by chance which treatment each person was given (atezolizumab or platinum-based chemotherapy).
- This study included 572 people in 19 countries.
- People who took part in the study all had a protein called 'programmed death-ligand 1' in their tumours (called the '**any PD-L1** group' in this summary) and were divided into subgroups based on how much PD-L1 protein they had (people with a high amount of PD-L1 were in the **high PD-L1** group, and people with a medium or high amount were in the **medium-high PD-L1** group).
- So far, the study has shown that in the **high PD-L1** group, atezolizumab worked better than platinum-based chemotherapy. Within this group (at the time the results were collected, September 10, 2018):
 - People taking atezolizumab lived for about 20 months on average, and people taking platinum-based chemotherapy lived for about 13 months.
 - People's cancer got worse about 8 months after starting atezolizumab, and about 5 months after starting platinum-based chemotherapy.
 - Tumours got smaller in 41 out of 107 people (38%) who took atezolizumab and in 28 out of 98 people (29%) who took platinum-based chemotherapy.
 - For the people whose tumours got smaller during the study, 28 out of 41 (68%) people taking atezolizumab and 10 out of 28 (36%) people taking platinum-based chemotherapy had their tumours remain smaller.
- About 28% of people (81 out of 286 people) taking atezolizumab had serious side effects, compared with about 29% of people (75 out of 263 people) taking platinum-based chemotherapy. In people taking atezolizumab, 8% (24 out of 286) had a serious side effect that was considered to be related to the treatment. In people taking platinum-based chemotherapy, 16% (41 out of 263) had a serious side effect that was considered to be related to the treatment.
- At the time of writing this summary, the study is still going on. It will end in May 2021.

1. General information about this study

Why was this study done?

People with non-small cell lung cancer that has spread to other parts of the body are sometimes given a treatment called immunotherapy—a medicine that helps a person’s own immune system attack tumours (cancer).

Immunotherapy medicines work better in some people with non-small cell lung cancer, such as people with tumours that contain 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 a tumour, it stops the immune system from killing the cancer. Immunotherapy medicines can block (stop) PD-L1, so the immune system can attack the tumour.

In this study, researchers wanted to compare a medicine called atezolizumab – an immunotherapy medicine that blocks PD-L1 – with ‘platinum-based chemotherapy’ – an existing treatment that is often given to people with non-small cell lung cancer. These medicines were given to people with non-small cell lung cancer who had different levels of PD-L1 protein in their tumours. Researchers wanted to see:

- If atezolizumab helped these people to live longer.
- If the immunotherapy medicine is safe for people to take.

The people in the study had non-small cell lung cancer that had not been treated with chemotherapy for their metastatic disease before.

What are the study medicines?

This study looked at 2 medicines:

- **Atezolizumab**– the medicine that was studied.
- **Platinum-based chemotherapy** – an existing medicine.

Atezolizumab’ (known by its brand name, Tecentriq®) is the new medicine that was studied – it works in a different way than platinum-based chemotherapy.

- You say this as ‘a – teh – zo – liz – oo – mab’.
- Atezolizumab works by stopping PD-L1 from working. This can help the immune system fight the cancer cells.
- When people take atezolizumab, their tumour (cancer) may get smaller. This medicine is a type of immunotherapy.

‘Platinum-based chemotherapy’ is an existing medicine given to people with non-small cell lung cancer.

- Platinum-based chemotherapy includes a medicine containing the metal called platinum. This medicine kills cancer cells by blocking (stopping) cancer cells from dividing and making more cancer cells.

What did researchers want to find out?

- Researchers did this study to compare atezolizumab with an existing medicine (platinum-based chemotherapy)– to see how well atezolizumab worked (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 and seeing how serious they were, 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 people live (during the study)?

Other questions that researchers wanted to answer included:

2. How much time was there between the start of the study and people’s cancer getting worse?
3. How many people had smaller tumours after getting their medicine?
4. For people whose tumours got smaller during the study, how many people had their tumours remain smaller?

What kind of study is this?

This study is a ‘Phase 3’ study. This means that atezolizumab had been tested in a smaller number of people with non-small cell lung cancer before this study. In this study, a larger number of people with non-small cell lung cancer took either atezolizumab or platinum-based chemotherapy– this was to find out if atezolizumab worked to help people with non-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 get. Randomly choosing which medicine people take, makes it more likely that the types of people in both groups will be a similar mix of, for example, different age ranges or different races. Apart from the exact medicines being tested in each group, all other aspects of care were the same between the groups.

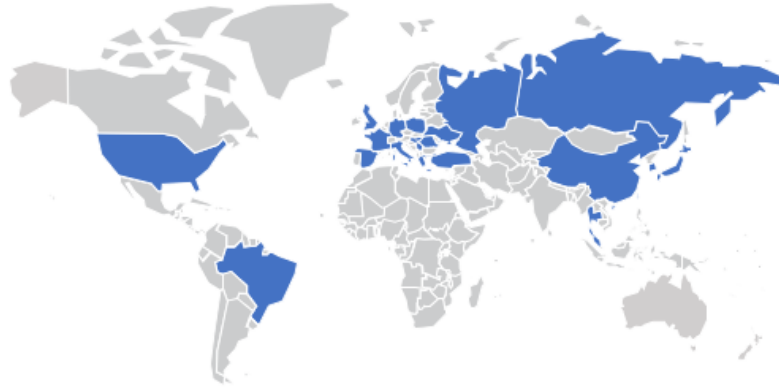
This is an ‘open label’ study. This means that both the people taking part in the study and the study doctors knew which of the study medicines people were taking.

When and where did the study take place?

The study started in July 2015 and will end in May 2021. This summary includes the results up until September 2018. At the time of writing this summary, the study is still going on – study doctors are still collecting information.

The study took place at 144 study centres – in 19 countries in Asia, Europe and North and South America. This map shows the countries where this study took place.

- Brazil
- China
- France
- Germany
- Greece
- Hungary
- Italy
- Japan
- Korea, Republic of
- Poland
- Romania
- Russian Federation
- Serbia
- Spain
- Thailand
- Turkey
- Ukraine
- United Kingdom
- USA

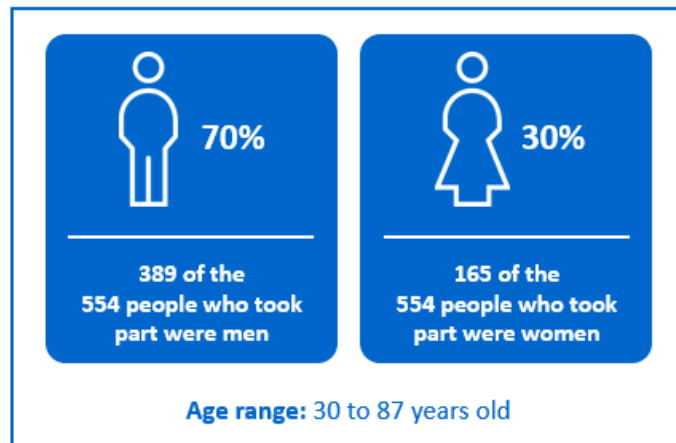


2. Who took part in this study?

In this study, 572 people with non-small cell lung cancer took part.

Eighteen of the 572 people had tumours with changes in the *EGFR* and *ALK* genes. These 18 people were not included in the part of the study results that looked at how well atezolizumab worked. This is because immunotherapy on its own has been shown to not work well in people who have tumours with these changes.

Here is more information about the 554 people in the study who had tumours without changes in the *EGFR* or *ALK* genes.



People could take part in the study if they:

- Were 18 years of age or older
- Had advanced non-small cell lung cancer that had spread to other parts of the body
- Had the PD-L1 protein in their tumour
- Were able to perform activities as well or almost as well as they could before they got cancer

People could not take part in the study if they:

- Had been given chemotherapy before
- Had untreated cancer that had spread to the brain or spinal cord

3. What happened during the study?

During the study, people with non-small cell lung cancer and PD-L1 protein in their tumours were selected by chance to get one of two treatments. The treatments were selected at random – by a computer.

The treatment groups were:

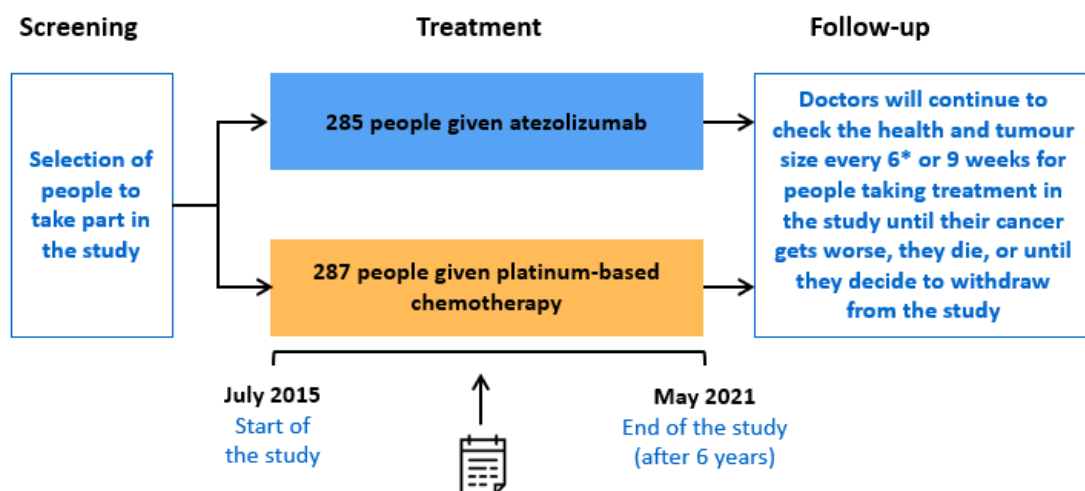
- **Atezolizumab** – injected into a vein once every 3 weeks.
- **Platinum-based chemotherapy** – injected into a vein once every 3 weeks.

When the study started, 285 people were chosen to get atezolizumab and 287 people were chosen to get platinum-based chemotherapy.

During the study:

- Only people without *EGFR* or *ALK* gene changes in their tumours were included in the part of the study results that looked at how well atezolizumab worked (277 out of the 285 who took atezolizumab and 277 out of the 287 people who took platinum-based chemotherapy).
 - These people all had the PD-L1 protein in their tumours (called the '**any PD-L1**' group in this summary). They were divided into subgroups by how much PD-L1 protein they had in their tumours – people with a lot of PD-L1 were in the '**high PD-L1**' group and people with a medium or high amount were in the '**medium-high PD-L1**' group.
- All 572 people in the study were included in the part of the study results that looked at how safe the study medicines were – whether their tumours had changes in *EGFR* or *ALK* genes or not.

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



* For the first 48 weeks of the study.

This study is still happening, so the symbol on the timeline (📅) shows when the information shown in this summary was collected – after 3 years (September 2018).

4. What were the results of the study?

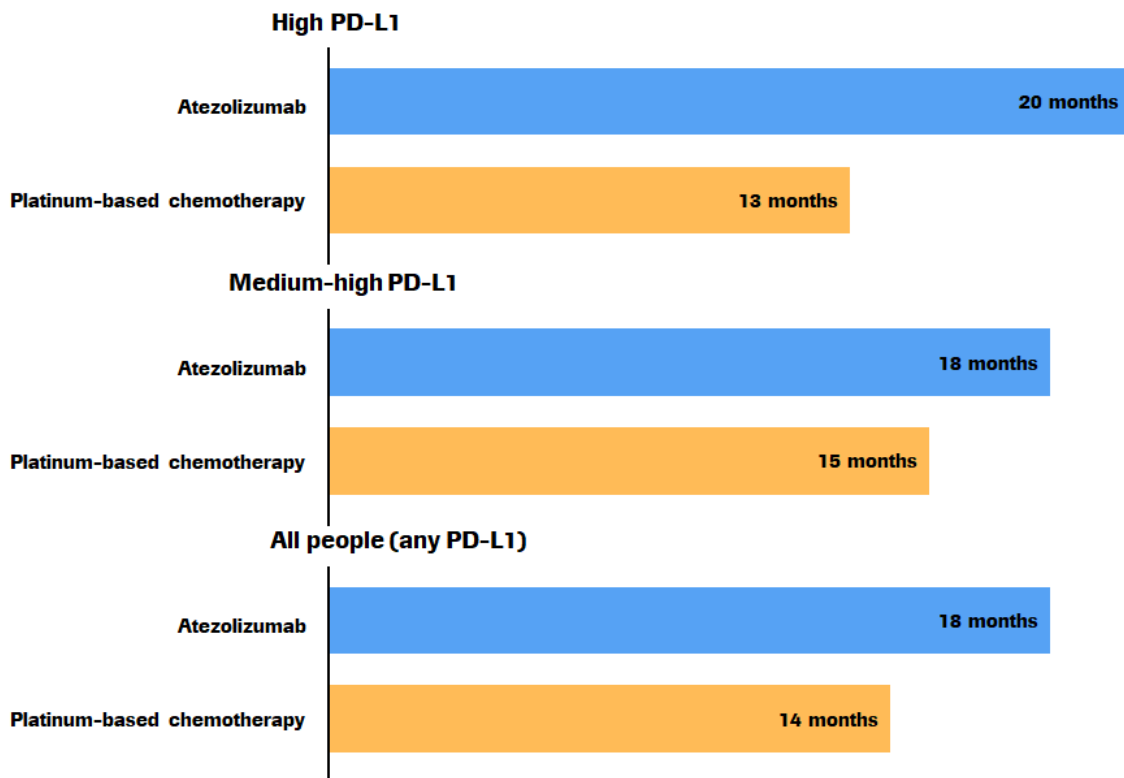
Question 1: How long did people live (during the study)?

Researchers looked at how long people lived on average during this study – this was compared between the people who took atezolizumab and the people who took platinum-based chemotherapy. Researchers collected information for about 16 months after people in the study started getting the medicines.

- In the **high PD-L1** group, people who took atezolizumab lived for about 20 months, and people who took platinum-based chemotherapy lived for about 13 months.
- In the **any PD-L1** and **medium-high PD-L1** groups, people who took atezolizumab lived for about 18 months, and people who took platinum-based chemotherapy lived for 14 to 15 months.

These numbers are averages – that means that some people died sooner, and some people lived longer.

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



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

Researchers also looked at how much time there was before people’s cancer got worse – this information was collected from the start of the study until September 2018.

- In the **high PD-L1** group, people’s cancer got worse about 8 months after they started atezolizumab and about 5 months after they started platinum-based chemotherapy.
- In the **any PD-L1** group, people’s cancer got worse about 6 months after they started atezolizumab or after they started platinum-based chemotherapy.
- In the **medium-high PD-L1** group, people’s cancer got worse about 7 months after they started atezolizumab and about 6 months after they started platinum-based chemotherapy.

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

Researchers looked at how many people had smaller tumours after they started atezolizumab or platinum-based chemotherapy – this information was collected from the start of the study until September 2018.

- In the **high PD-L1** group, tumours got smaller in 41 out of 107 people (38%) taking atezolizumab and in 28 out of 98 people (29%) taking platinum-based chemotherapy.

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- In the **any PD-L1** and **medium-high PD-L1** groups, about the same number of people who took atezolizumab and people who took platinum-based chemotherapy had their tumours get smaller:
 - In the **any PD-L1** group, tumours got smaller in 81 out of 277 people taking atezolizumab (29%) and 88 out of 277 people taking platinum-based chemotherapy (32%).
 - In the **medium-high PD-L1** group, tumours got smaller in 51 out of 166 people taking atezolizumab (31%) and 52 out of 162 people taking platinum-based chemotherapy (32%).

Question 4: For people whose tumours got smaller during the study, how many people had their tumours remain small?

Researchers looked at people whose tumours got smaller during the study and recorded how many people had their tumours remain smaller. This information was collected from the start of the study until September 2018.

- In the **high PD-L1** group, 28 out of 41 (68%) people taking atezolizumab and 10 out of 28 (36%) people taking platinum-based chemotherapy had their tumours remain smaller.
- In the **any PD-L1** group, 57 out of 81 (70%) people taking atezolizumab and 29 out of 88 (33%) people taking platinum-based chemotherapy had their tumours remain smaller.
- In the **medium-high PD-L1** group, 36 out of 51 (70%) people taking atezolizumab and 18 out of 52 (35%) people taking platinum-based chemotherapy had their tumours remain smaller.

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 can happen during the study.

- Not all of the people in this study 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 on 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, causes lasting problems, or leads to death.

During this study, 81 out of 286 people (28%) taking atezolizumab had a serious side effect, compared with 75 out of 263 people (29%) taking platinum-based chemotherapy.

Researchers looked at how many people died due to side effects that may have been related to one of the study medicines. They found:

- 0 out of 286 people (0%) in the atezolizumab group.
- 1 out of 263 people (0.4%) in the platinum-based chemotherapy group.

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

- In the atezolizumab group, 18 out of 286 people (6%) stopped taking their medicine.
- In the platinum-based chemotherapy group, 43 out of 263 people (16%) stopped taking their medicine.

Most common side effects

During this study, 258 out of 286 people (90%) taking atezolizumab had a side effect that was not considered serious, compared with 249 out of 263 people (95%) taking platinum-based chemotherapy.

The most common side effects are shown in the following table – these are the eight 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 (in more than 10% of people in any treatment group)	People taking atezolizumab (286 people total*)	People taking platinum-based chemotherapy (263 people total)
Low level of red blood cells	15% (44 out of 286 people in this treatment group)	48% (125 out of 263 people in this treatment group)
Lack of appetite	15% (44 out of 286)	19% (50 out of 263)
Feeling sick (nausea)	14% (39 out of 286)	34% (89 out of 263)
Low energy levels	13% (37 out of 286)	18% (46 out of 263)
Feeling tired	13% (37 out of 286)	18% (46 out of 263)
Constipation	12% (35 out of 286)	22% (57 out of 263)
Low level of white blood cells	1% (4 out of 286)	28% (74 out of 263)
Low level of the pieces of blood cells that help blood to clot – called 'platelets'	2% (7 out of 286)	17% (44 out of 263)

* One person chosen by chance to get platinum-based chemotherapy was given atezolizumab and so was included in the atezolizumab group.

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 one study of 572 people with non-small cell lung cancer. The study is still going on. These results are helping researchers learn more about non-small cell lung cancer and treatment with atezolizumab.

So far, the study has shown that in the **high PD-L1** group, atezolizumab worked better than platinum-based chemotherapy. In the **high PD-L1** group:

- People who took atezolizumab lived for about 20 months on average, and people who took platinum-based chemotherapy lived for about 13 months.
- People's cancer got worse about 8 months after starting atezolizumab and about 5 months after starting platinum-based chemotherapy.
- Tumours got smaller in 41 out of 107 people (38%) who took atezolizumab and in 28 out of 98 people (29%) who took platinum-based chemotherapy.
- For people whose tumours got smaller during the study, 28 out of 41 (68%) taking atezolizumab and 10 out of 28 (36%) taking platinum-based chemotherapy had their tumours remain smaller.

In the **any PD-L1** and **medium-high PD-L1** groups, results with atezolizumab were not significantly different than results with platinum-based chemotherapy (meaning that the differences investigators saw could be due to chance), so researchers cannot conclude that atezolizumab worked better for people in those groups.

The side effects that people in this study had were similar to side effects seen in other studies in people getting either atezolizumab or chemotherapy.

7. Are there plans for other studies?

Studies with atezolizumab are still happening, and further 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/NCT02409342>
- <https://www.clinicaltrialsregister.eu/ctr-search/trial/2014-003083-21/results>
- <https://forpatients.roche.com/en/trials/cancer/lung-cancer/a-study-of-atezolizumab--mpdl3280a--compared-with-a-platinum-age.html>
- https://www.ema.europa.eu/en/documents/product-information/tecentriq-epar-product-information_en.pdf
- https://www.gene.com/download/pdf/tecentriq_prescribing.pdf

If you want to find out more about the results of this study, the full title of the relevant scientific paper is: “Atezolizumab for first-line treatment of PD-L1–selected patients with NSCLC”. The authors of the scientific paper are: R.S. Herbst, G. Giaccone, F. de Marinis, N. Reinmuth, A. Vergnenegre and others. The paper is published in the journal ‘New England Journal of Medicine’, volume number 383, on pages 1328-1339.

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-atezolizumab--mpdl3280a--compared-with-a-platinum-agent.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 Atezolizumab (MPDL3280A) Compared With a Platinum Agent (Cisplatin or Carboplatin) + (Pemetrexed or Gemcitabine) in Participants With Stage IV Non-Squamous or Squamous Non-Small Cell Lung Cancer (NSCLC)”.

The study is known as ‘IMpower110’.

- The protocol number for this study is: GO29431.
- The ClinicalTrials.gov identifier for this study is: NCT02409342.
- The EudraCT number for this study is: 2014-003083-21.