

Clinical Trial Results – Layperson Summary

A study to look at tiragolumab with atezolizumab compared with placebo with atezolizumab – in people with PD-L1-positive non-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 (August 2022). More information may now be known.

The study started in August 2018. This summary includes the results up until August 2021. At the time of writing this summary, the study is ongoing (as people are continuing to benefit from the study medicines) – this summary presents the complete results from one part of the study.

No single 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. 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 a type of lung cancer called non-small cell lung cancer (NSCLC) and helped us to learn more about the study medicines, tiragolumab and atezolizumab.

Key information about this study

- This study was done to test whether the combination of tiragolumab + atezolizumab could be safe and effective for people with PD-L1-positive NSCLC tumours who have not received previous treatment for their cancer.
- In this study, people were given either the study medicine, tiragolumab + atezolizumab or placebo + atezolizumab. It was decided by chance which treatment each person was given.
- This study included 135 people from 41 study centres in Europe, Asia and the USA.
- So far, the study has shown that tiragolumab + atezolizumab has an acceptable safety profile, similar to atezolizumab alone, and improves outcomes in people with PD-L1-positive NSCLC compared with placebo + atezolizumab.
- 21% of people (14 out of 67) taking tiragolumab + atezolizumab had serious side effects compared with 18% of people (12 out of 68) taking placebo + atezolizumab.
- At the time of writing this summary, the study is still happening. The study was expected to end in October 2022; however, this may be extended to follow those people in the study doing well.

1. General information about this study

Why was this study done?

NSCLC is the most common type of lung cancer – about 80% of people with lung cancer will have NSCLC. Various factors increase the chance of a person developing NSCLC. These include being over the age of 65 years, smoking or having smoked in the past.

Although NSCLC is serious, different treatments are available for different NSCLC types, which aim to make you feel better and stop the cancer from getting worse. In the past, chemotherapy was a common treatment option for people with NSCLC. Chemotherapy can cause a lot of harmful side effects so other treatments are being developed.

One type of treatment is called immunotherapy. In immunotherapy, medicines are given to encourage the body's immune system (the cells in our body that keep us well and fight off infection when we become poorly) to attack the cancer cells. One type of immunotherapy targets a protein called PD-L1, found on the surface of some NSCLC tumour cells. People who participated in this study had NSCLC tumours that were positive for PD-L1. This means some of their tumour cells had the PD-L1 protein on their surface.

Current immunotherapy treatments only work for around half of people with advanced NSCLC that cannot be removed by surgery. New therapies that combine two or more treatments are being developed as an alternative for people whose cancer is not improved by current treatment options.

What were the study medicines?

Atezolizumab is an existing immunotherapy medicine that helps to shrink tumours so people with NSCLC can live longer. Atezolizumab works by allowing your immune cells to fight the cancer cells and is approved for the treatment of NSCLC.

In this study, a new immunotherapy medicine called tiragolumab was studied in combination with atezolizumab. Everyone in the study received atezolizumab, but only half of people received tiragolumab. Tiragolumab works in a similar way to atezolizumab – it helps the body's immune system to attack the tumour. The combination of tiragolumab + atezolizumab was compared with a substance with no active ingredients (known as a placebo) + atezolizumab. The placebo appeared similar to tiragolumab but did not contain any medicine. This means it did not have any medicine-related effects on the body.

What did researchers want to find out?

Researchers did this study to see if tiragolumab + atezolizumab worked better than standard treatment with atezolizumab alone (see section 4 “What were the results of the study?”).

They also wanted to find out how safe the combination of tiragolumab + atezolizumab was. They did this 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 questions that researchers wanted to answer were:

1. How many people's cancer reduced or shrank when taking tiragolumab + atezolizumab compared with placebo + atezolizumab?
2. How long were people able to live without their cancer increasing when taking tiragolumab + atezolizumab compared with placebo + atezolizumab?

Another question that researchers wanted to answer was:

3. How long did people in the study live?

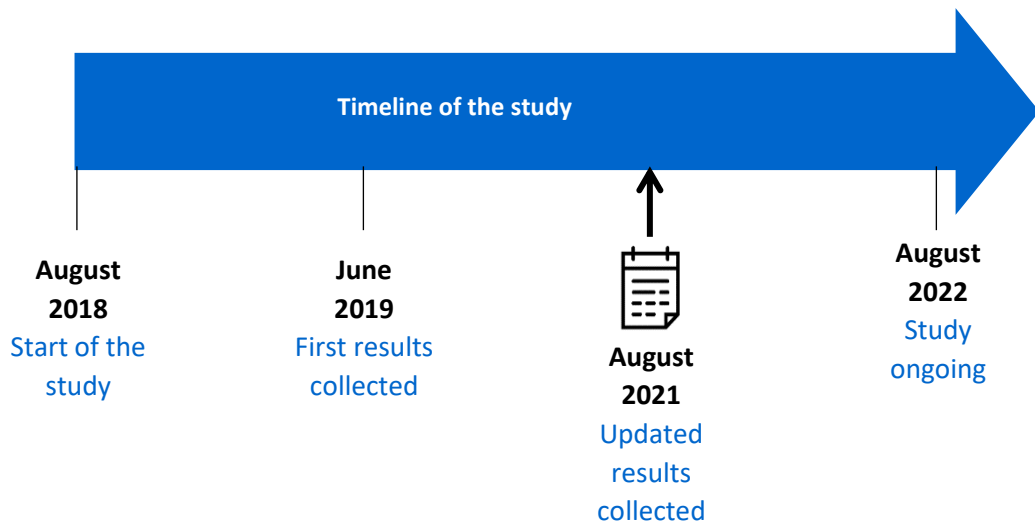
What kind of study was this?

This study was a 'Phase 2' study. This means that tiragolumab had been tested in a number of people with advanced cancer before this study.

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.

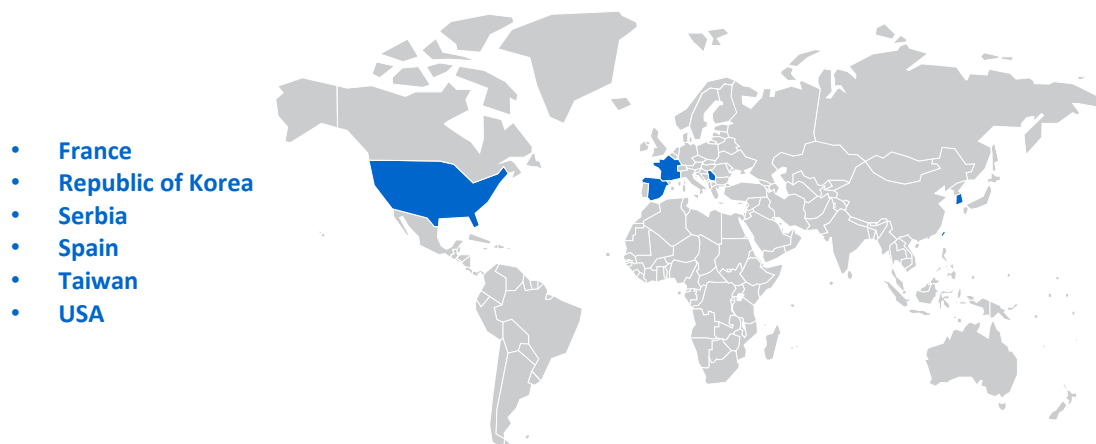
When and where did the study take place?

The study began in August 2018 and is ongoing. This summary includes the results up until August 2021.



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

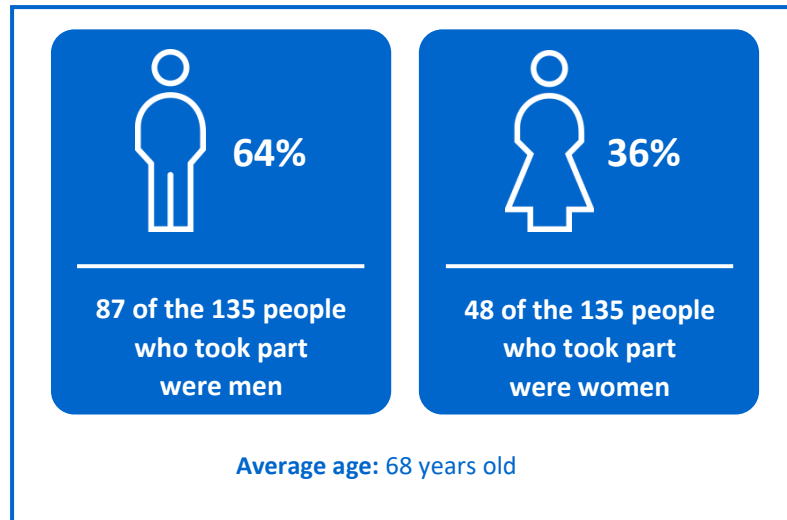
The study took place at 41 study centres across Europe, Asia and the USA. The following map shows the countries where this study took place.



2. Who took part in this study?

In this study, 135 people with NSCLC took part.

People who took part in the study were on average 68 years of age. 87 of the 135 people (64%) were male and 48 of the 135 people (36%) were female.



People could take part in the study if they:

- Were over 18 years old
- Had been diagnosed with PD-L1-positive NSCLC
- Were fully physically active or were restricted in physically strenuous activity only (ECOG PS 0–1)
- Had not received any chemotherapy treatment or cancer immunotherapy treatment for their advanced cancer

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

- Cancer that had spread to the brain and spinal cord and was causing symptoms, was untreated, or was getting worse
- Any changes to the *EGFR* or *ALK* genes in their tumours
- A history of allergic reactions to the same type of medicines that were used in the study
- Were pregnant or breastfeeding

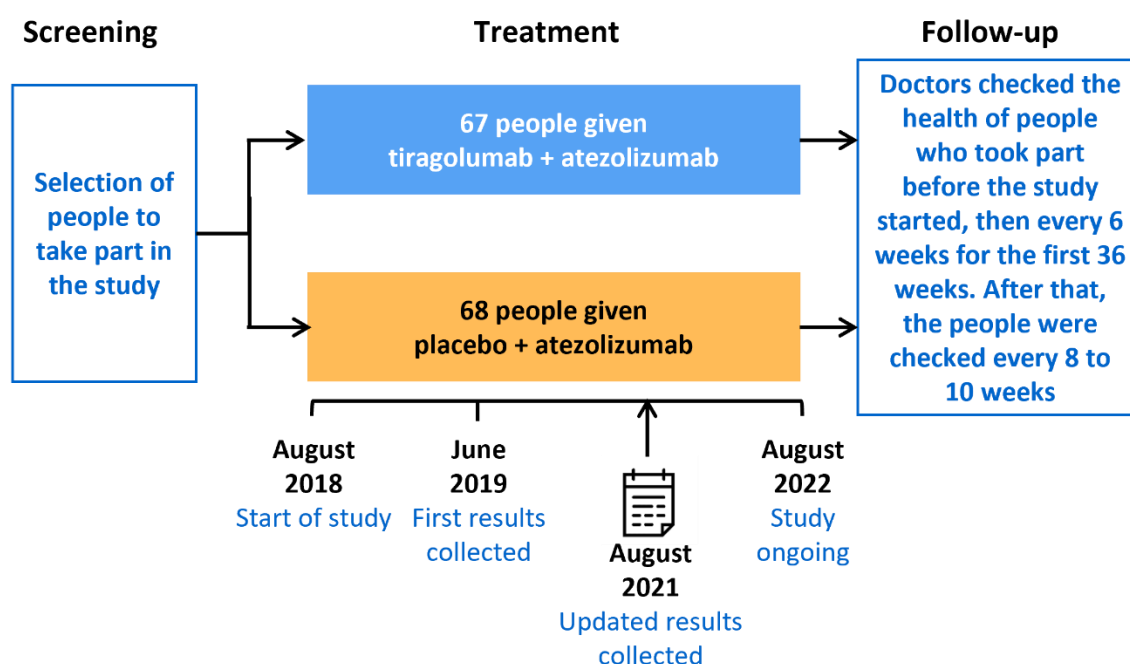
3. What happened during the study?

During the study, people were selected randomly to a treatment group (known as “randomisation”). This means that it was decided by chance which of the medicines people in the study would have – like tossing a coin.

The treatment groups were:

- **Tiragolumab + atezolizumab** – tiragolumab 600 mg and atezolizumab 1200 mg were both injected into a vein (sometimes called an IV injection) once every 3 weeks
- **Placebo + atezolizumab** – placebo + atezolizumab 1200 mg were both injected into a vein once every 3 weeks

The study flowchart shows all planned stages and treatment groups of the study.



This study is still happening so some people are still being treated with the study medicines. The symbol on the timeline (📅) shows when the information shown in this summary was collected. 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.

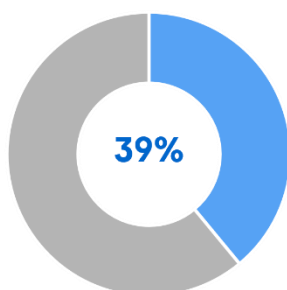
4. What were the results of the study?

Question 1: How many people's cancer reduced or shrank when taking tiragolumab + atezolizumab compared with placebo + atezolizumab?

Researchers looked for response to treatment in each person— this could either be a complete or partial response. A complete response meant that there was no more detectable cancer left in the person. A partial response meant that the cancer had reduced (for example it shrank) but was still present.

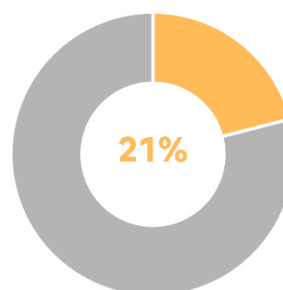
26 people (39%) in the tiragolumab + atezolizumab group showed improvement. This was higher than in the placebo + atezolizumab group, where 14 people (21%) showed improvement.

How many people recorded responses in the tiragolumab + atezolizumab group?



26 out of 67 people recorded either partial or complete responses

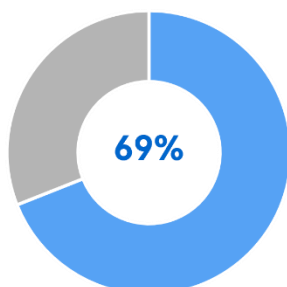
How many people recorded responses in the placebo + atezolizumab group?



14 out of 68 people recorded either partial or complete responses

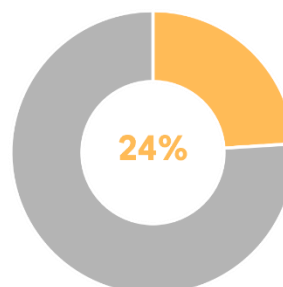
Researchers also looked at response to treatment in people who had more than 50% of their tumour cells covered with the PD-L1 protein (these people were also known as the PD-L1-high population). Among these individuals, 20 people (69%) in the tiragolumab + atezolizumab group recorded responses. This was higher than in the placebo + atezolizumab group, where 7 people (24%) recorded responses.

How many people with high levels of PD-L1 recorded responses in the tiragolumab + atezolizumab group?



20 out of 29 people recorded either partial or complete responses

How many people with high levels of PD-L1 recorded responses in the placebo + atezolizumab group?



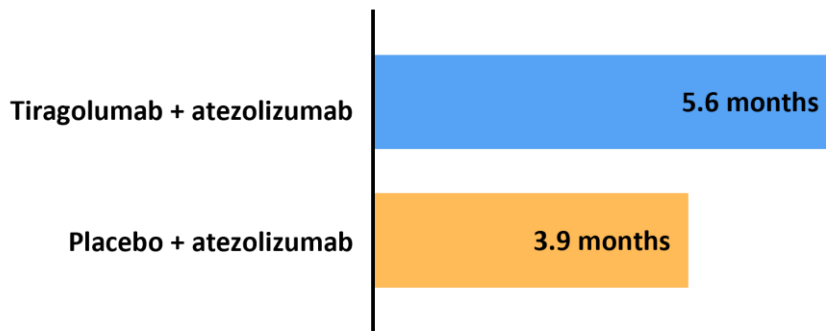
7 out of 29 people recorded either partial or complete responses

Question 2: How long were people able to live without their cancer increasing when taking tiragolumab + atezolizumab compared with placebo + atezolizumab?

Researchers looked at how much time passed from the start of the study until cancer began to get worse or the person died (known as ‘progression-free survival’).

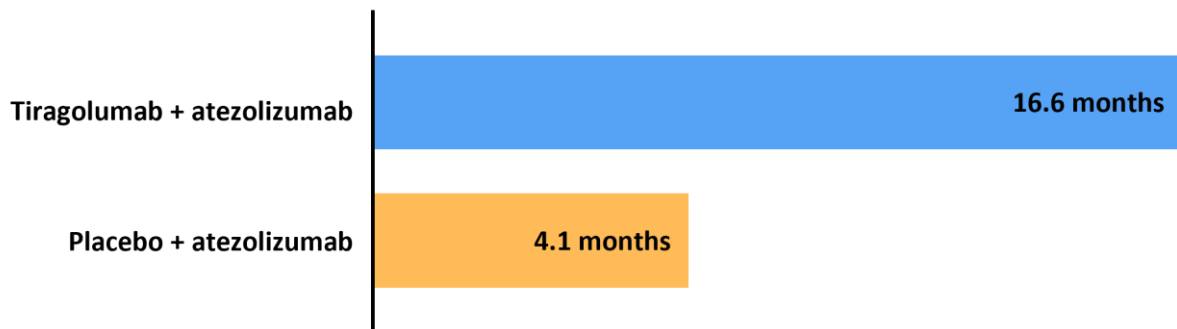
Overall, approximately 5 and a half months had passed before cancer began to get worse when people were given tiragolumab + atezolizumab. Approximately 4 months had passed before cancer began to get worse when people were given placebo + atezolizumab.

On average, how long did it take for the cancer to get worse in the two groups?



Researchers also looked at progression-free survival in people who had more than 50% of their tumour cells covered with the PD-L1 protein (high level of PD-L1). Here, more time passed before the cancer increased in the tiragolumab + atezolizumab group (16.6 months) compared with the placebo + atezolizumab group (4.1 months).

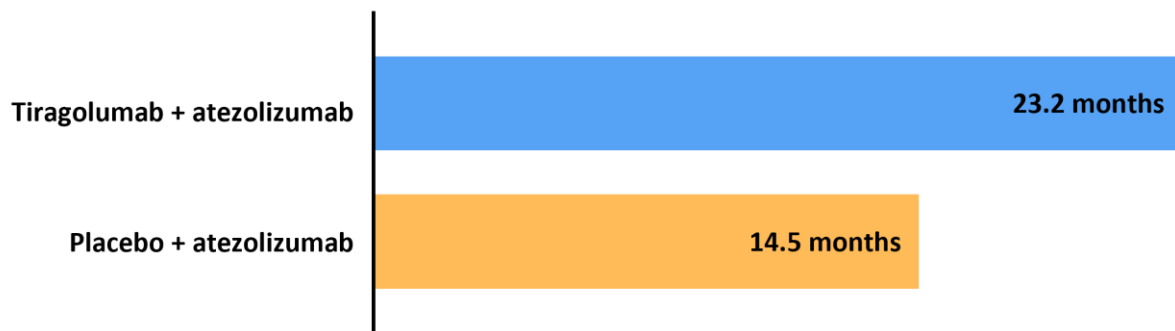
On average, how long did it take for the cancer to get worse in in people with high levels of PD-L1?



Question 3: How long did people in the study live for?

Researchers looked at how long people taking each type of treatment lived for. This is known as overall survival. The average overall survival in the tiragolumab + atezolizumab group was 23.2 months. This was longer than in the placebo + atezolizumab group, where the average overall survival was 14.5 months.

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



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 treatments in 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 and severe side effects

A side effect is considered 'serious' if it is life-threatening, needs hospital care, or causes lasting problems. During this study, approximately 2 in every 10 people (19%) had at least one serious side effect. Around 21% of people taking tiragolumab + atezolizumab had a serious side effect compared with around 18% of people taking placebo + atezolizumab.

Side effects are also ranked from Grade 1 (mild and generally not bothersome) to Grade 5 (resulting in death). 'Severe' side effects are those graded as 3–5.

Severe side effects reported in this study	People taking tiragolumab + atezolizumab (67 people total)	People taking placebo + atezolizumab (68 people total)
Increased lipase (a substance that breaks down fat we eat)	9% 6 out of 67	3% 2 out of 68
Diabetes	3% 2 out of 67	1% 1 out of 68
Increased aspartate aminotransferase (a substance in the kidneys that helps to create sugar)	0	3% 2 out of 68
Increased amylase (a substance that breaks down the sugar we eat)	0	3% 2 out of 68

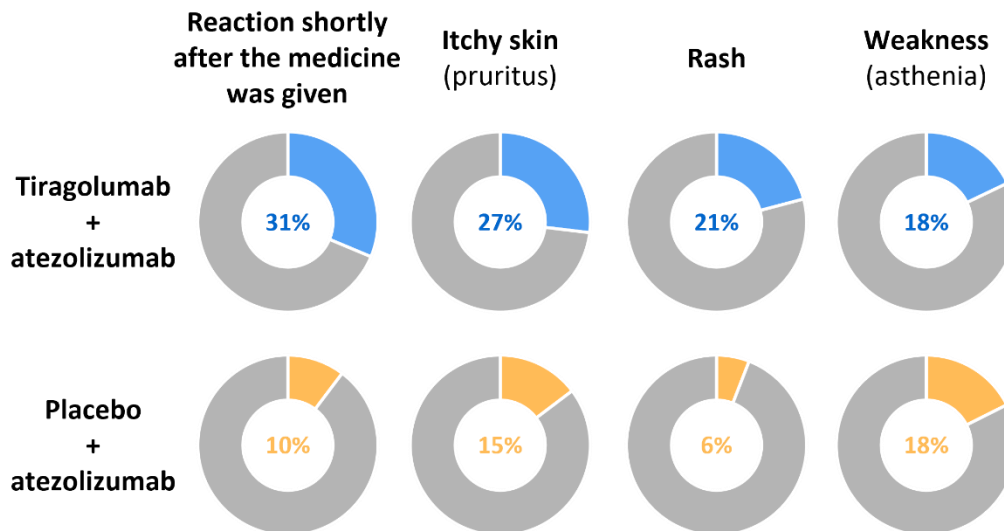
There were 2 people in the tiragolumab + atezolizumab group who died due to side effects related to one of the study medicines. These were due to fever (pyrexia) and infection. There were no deaths related to study medicines in the placebo + atezolizumab group.

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

- In the tiragolumab + atezolizumab group, 10 out of 67 people (15%) stopped taking their medicine
- In the placebo + atezolizumab group, 9 out of 68 people (13%) stopped taking their medicine

Most common side effects

During the study, around 8 in every 10 people (82%) in the tiragolumab + atezolizumab group and 7 in every 10 people (71%) in the placebo + atezolizumab group had side effects. The most common side effects were reactions that presented shortly after the medicine was given (infusion-related reactions), itchy skin, rashes and weakness.



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 135 people with a type of lung cancer called non-small cell lung cancer or NSCLC. These results helped researchers learn more about NSCLC and the effects and safety of combining tiragolumab + atezolizumab.

The combination of tiragolumab + atezolizumab was more effective in treating people with NSCLC than placebo + atezolizumab. In the study, tiragolumab + atezolizumab resulted in slower tumour/cancer progression than placebo + atezolizumab. Tiragolumab + atezolizumab showed an acceptable safety profile that was similar to placebo + atezolizumab.

These results are important as they help researchers learn more about tiragolumab + atezolizumab for the treatment of NSCLC.

No single 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. 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?

Other studies looking at the effects and safety of tiragolumab + atezolizumab on lung cancers and other cancers are taking place.

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/NCT03563716>
- <https://www.clinicaltrialsregister.eu/ctr-search/trial/2018-000280-81/results>

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “Tiragolumab plus atezolizumab versus placebo plus atezolizumab as a first-line treatment for PD-L1-selected non-small-cell lung cancer (CITYSCAPE): primary and follow-up analyses of a randomised, double-blind, phase 2 study”. The authors of the scientific paper are: Byoung Chul Cho, Delvys Rodriguez Abreu, Maen Hussein, Manuel Cobo, Anjan J Patel and others. The paper is published in the journal ‘Lancet Oncology’, volume number 23, on pages 781–792.

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

If you have any further 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 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: “Tiragolumab plus atezolizumab versus placebo plus atezolizumab as a first-line treatment for PD-L1-selected non-small-cell lung cancer (CITYSCAPE): primary and follow-up analyses of a randomised, double-blind, phase 2 study”.

The study is known as ‘CITYSCAPE’.

- The protocol number for this study is: GO40290.
- The ClinicalTrials.gov identifier for this study is: NCT03563716.
- The EudraCT number for this study is: 2018-000280-81.