A study of atezolizumab (immunotherapy: a medicine that helps a person's own immune system attack their cancer) compared with single-agent chemotherapy for people with a type of lung cancer called '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
- People who took part in the study and other patients

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

The study **started in September 2017 and ended in October 2023**. This summary includes the results that were collected through April 2022. The summary was written after the study ended.

The results from this study may be different from other studies of the same medicine. 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.

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

- NSCLC = non-small cell lung cancer

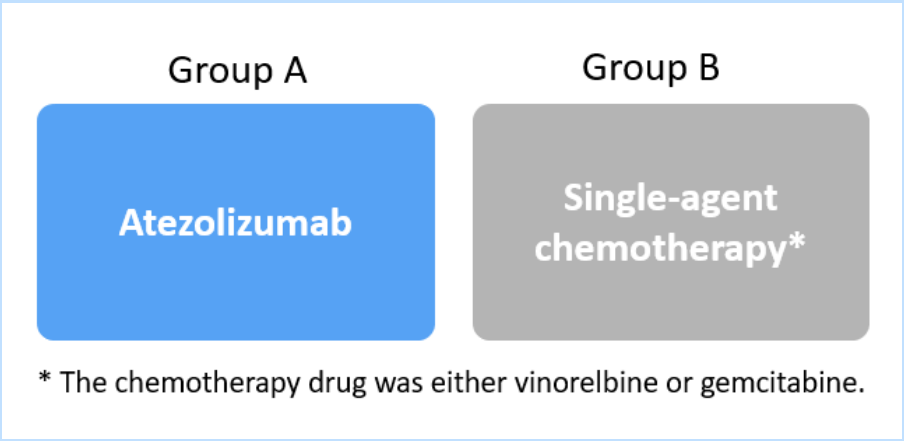
Thank you to the people who took part in this study

The people who took part in this study have helped researchers answer important questions about a type of lung cancer called 'non-small cell lung cancer' (NSCLC) and the medicine being studied – 'atezolizumab'. Atezolizumab was compared with single-agent chemotherapy for patients with NSCLC who could not receive platinum-based chemotherapy based on a decision by their doctor.

Key information about this study

Why was this study done?

- This study was done to compare how a drug called '**atezolizumab'** works compared with a type of chemotherapy (called **single-agent chemotherapy)** in a group of patients with NSCLC who could not receive platinum-based chemotherapy, which is a combination of 2 drugs. A patient's doctor decided that they could not receive platinum-based chemotherapy because they were either too frail or were at least 70 years old and had other medical conditions that could make the platinum-based chemotherapy unsafe for them.
- 453 people from 91 different centres in 23 countries or regions joined the study.
- People were divided into 2 study groups as shown here.



What were the results?

- The main findings were that:
  - People in the atezolizumab group lived about 10.3 months after starting treatment, compared with about 9.2 months for people in the single-agent chemotherapy group.
    - After 1 year, 44% of people in the atezolizumab group and 39% of people in the chemotherapy group were still alive.
    - After 2 years, 24% of people in the atezolizumab group and 12% of people in the chemotherapy group were still alive.
  - People in the atezolizumab group lived about 4.2 months after starting treatment without their cancer getting worse compared with 4.0 months for people in the chemotherapy group.
  - In the atezolizumab group, 17% of people had their cancer shrink or disappear after starting treatment compared with 8% of people in the chemotherapy group.
    - For these people, the cancer stayed smaller or stayed away for an average of 14.0 months in the atezolizumab group and 7.8 months in the chemotherapy group.

- People in the atezolizumab group rated themselves better on some of the quality-of-life questions than people in the single-agent chemotherapy group. We do not know if this is a real difference between groups.

How many people had side effects?

Some people may have started the study, but then left the study before getting at least one dose of their study medicine. While those people were still included in the study of how the drug worked, only people who got at least one dose of their assigned study drug were included in the study of side effects. Researchers looked at side effects in 300 people in the atezolizumab group and 147 people in the chemotherapy group.

How many people had a *serious* side effect related to their treatment? (A serious side effect was one that caused lasting problems, required hospitalization, was life-threatening, or caused death.)

- Group A (atezolizumab): 35 out of 300 people (12%) had a *serious* side effect related to their treatment.
- Group B (single-agent chemotherapy): 23 out of 147 people (16%) had a *serious* side effect related to their treatment.

How many people had a *severe* side effect related to their treatment? (A severe side effect was one that was considered intense or medically important by a person's doctor. A severe side effect may have overlapped with a serious side effect if it caused disability or death. Or it may not have been life-threatening, but it may have been severe in intensity, such as a bad headache or rash, that required some medical care.)

- Group A (atezolizumab): 52 out of 300 people (17%) had a *severe* side effect related to their treatment.
- Group B (single-agent chemotherapy): 53 out of 147 people (36%) had a *severe* side effect related to their treatment.

This summary includes all data collected through April 2022. The study ended in October 2023.

1. General information about this study

Why was this study done?

People who have cancer that spread to other parts of the body can have locally advanced disease (meaning the cancer spread to nearby areas in the chest) or metastatic disease (meaning the cancer spread far away from where it started). For both of these groups, people often become very ill and may not live very long. Often, they are given a medicine called platinum-based chemotherapy to try to kill the cancer cells or stop the cancer cells from growing more. However, platinum-based chemotherapy also kills healthy cells, so it can make people feel very sick.

For people with NSCLC who are physically frail or are at least 70 years old and have other health conditions, their doctors may decide that platinum-based chemotherapy would make them too ill. Doctors may give these people a different type of medicine called single-agent chemotherapy, which might not make them as sick as the platinum-based chemotherapy

would. However, single-agent chemotherapy doesn't always work as well at killing the cancer, and people still may feel very sick from taking the medicine. Therefore, other medicines are needed to help people live longer with better quality of life.

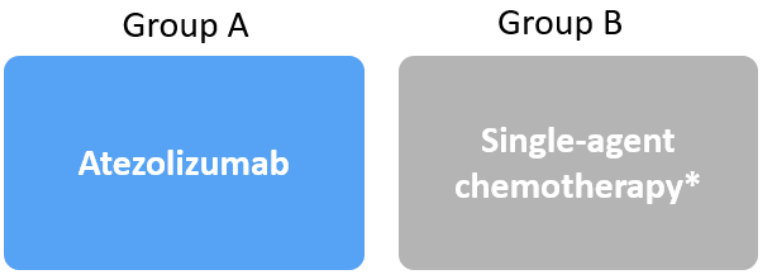
'Immunotherapy' is a different type of medicine that helps the person's own immune system attack their cancer (tumour). A type of immunotherapy called an 'immune checkpoint inhibitor' works by blocking proteins called 'checkpoint proteins'. Normally, these proteins stop a person's immune system from attacking healthy cells, but they can also stop the immune system from killing the cancer cells. Immune checkpoint inhibitors block these proteins, which allows the immune system to attack the cancer. One checkpoint protein that can be blocked in this way is called 'programmed death-ligand 1' or 'PD-L1'. Atezolizumab is a medicine that blocks PD-L1.

Researchers wanted to see whether atezolizumab would help people live longer than chemotherapy. They also wanted to compare how long people in each group lived without their cancer getting worse, how many people in each group had their cancer shrink or disappear, and how long people's cancer stayed smaller or stayed away before it came back. And they looked at whether atezolizumab or single-agent chemotherapy would help people have a higher quality of life while taking the medicine and which medicine had fewer side effects.

What were the treatments being studied?

This study compared people with NSCLC who were given atezolizumab (Group A) or single-agent chemotherapy (vinorelbine or gemcitabine) (Group B).

- **Group A: atezolizumab**
- **Group B: single-agent chemotherapy (vinorelbine or gemcitabine)**



* The chemotherapy drug was either vinorelbine or gemcitabine.

The immunotherapy medicine used in this study is called '**atezolizumab**' (known by its brand name, Tecentriq®).

- You say '**atezolizumab'** as 'a – teh – zo – li – zoo – mab'.
- You say '**Tecentriq'** as 'tee – sen – trik'.

The body's immune system can fight diseases like cancer. However, PD-L1 in cancer cells can stop the immune system from attacking the cancer. Atezolizumab helps the immune system attack the cancer cells by stopping PD-L1 from working. This may make the cancer (tumour) get smaller.

What did researchers want to find out?

- Researchers wanted to see how well **atezolizumab** (**Group A**) and **single-agent chemotherapy** (**Group B**) worked (see section 4 "What were the results of the study?").
- They also wanted to find out how safe the treatments were by checking how many people had side effects related to their treatment and seeing how serious or severe they were (see section 5 "What were the side effects?").

The main questions that researchers wanted to answer were:

- How long did people in each group live after starting treatment, and how many people in each group were still alive 1 and 2 years after starting treatment?
- How long did people live without their cancer getting worse after starting treatment?
- How many people in each group had their cancer shrink or disappear, and for those that did, how long did the cancer stay smaller or stay away?
- How did people rate their quality of life while taking each treatment?
- How safe were the treatments?

What kind of study was this?

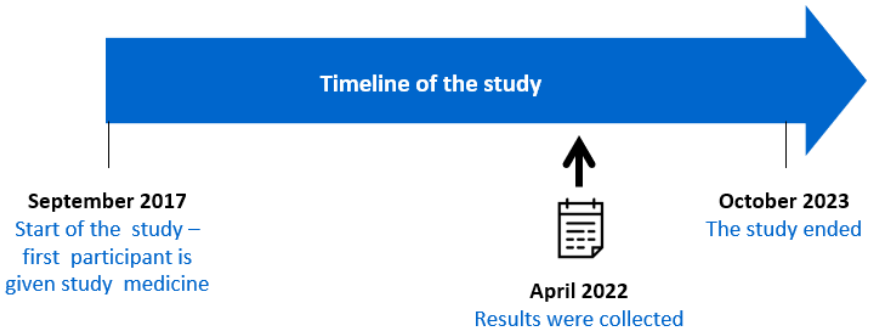
This study was a '**Phase 3**' study. Phase 3 studies are done in a large number of people to see if a drug works better than the usual treatment and is safe enough for it to be 'approved' as a treatment that can be prescribed by your doctor.

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 the study groups will be a similar mix (for example, similar ages, similar races). Other than the different medicines being given to people in each group, all other care was the same.

This was an '**open label**' study. This means that both the people taking part in the study and the study doctors knew which group the people were in.

When and where did the study take place?

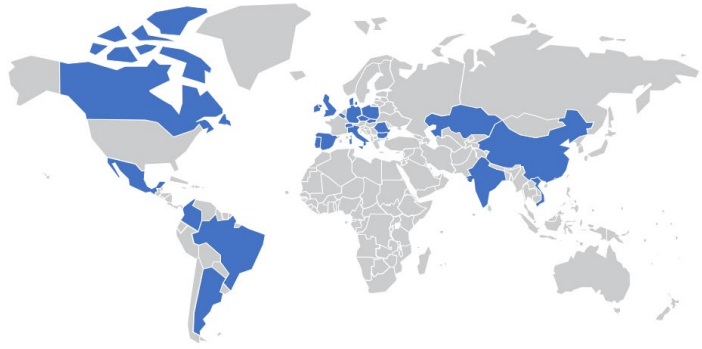
The study started in September 2017 and ended in October 2023. This summary includes the results collected through April 2022. This summary was written after the study ended.



The symbol on the timeline ( ) shows when the information reported in this summary was collected (April 2022 – about 5 years after the study started).

This study took place at 91 hospitals and clinics in 23 countries or regions across Asia, Europe, North America, and South America.

This map shows the countries/regions where this study took place.

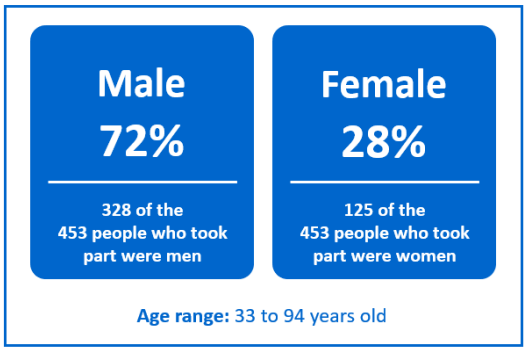


- Argentina
- Belgium
- Brazil
- Bulgaria
- Canada
- China
- Colombia
- Czech Republic
- Denmark
- Germany
- India
- Ireland
- Italy
- Kazakhstan
- Mexico
- Poland
- Portugal
- Romania
- Slovakia
- Spain
- Switzerland
- United Kingdom
- Vietnam

2. Who took part in this study?

In this study, 453 people with NSCLC took part.

This picture shows more information about the people who took part.



People in the study had NSCLC that was locally advanced (spread throughout the lungs and to lymph nodes) or metastatic (spread to other parts of the body).

- People could take part in this study if their doctor decided that they could not receive platinum-based chemotherapy for one of these reasons:
  - They were too physically frail, or
  - They were at least 70 years old and had medical conditions that their doctor felt made it unsafe for them to get the platinum-based chemotherapy.

People could not take part in the study if:

- They had changes in the genes called *EGFR* or *ALK*
- They had already received treatment for their lung cancer (after the cancer had spread)
- Their cancer could be removed by surgery.

These are just some of the requirements that people had to meet to be in this study.

3. What happened during the study?

During the study, people were selected at random by a computer to get one of two treatments. Twice as many people were put into Group A (atezolizumab) as in Group B (single-agent chemotherapy).

The treatment groups were:

- **Group A:** atezolizumab
- **Group B:** single-agent chemotherapy (vinorelbine or gemcitabine)

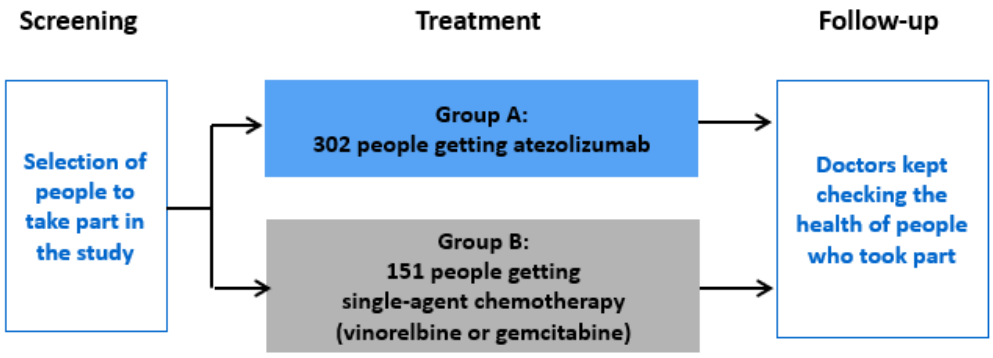
This table shows how many people took each study treatment and how often the drugs were taken.

	Group A Atezolizumab	**Group B Single-agent chemotherapy (vinorelbine or gemcitabine)**
Number of people who got the treatment	302	151
How the drug was given	Infused into a vein	Vinorelbine: taken by mouth or infused into a vein Gemcitabine: infused into a vein
How often the drug was given	Once every 3 weeks	As described in local Prescribing Information

In the single-agent chemotherapy group, 84 people got vinorelbine and 63 got gemcitabine. Four people in the chemotherapy group and two people in the atezolizumab group did not receive any study drug, but they are still included in the analysis comparing how the drugs worked.

This study ended in October 2023. The results shown here are based on data collected up until April 2022.

This picture shows more information about what happened in the study. People kept taking atezolizumab or chemotherapy for as long as it was helping them. They stopped taking the medicine if their cancer got worse or they were having serious side effects. Doctors kept checking people's health even after they stopped taking the medicine.

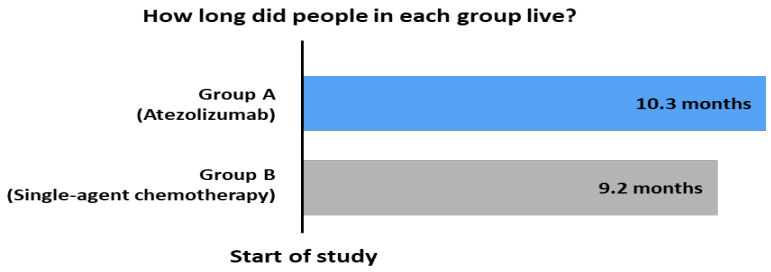


4. What were the results of the study?

Question 1: How long did people in this study live?

Researchers wanted to know how long people lived after they started treatment.

- People who got **atezolizumab** lived about **10.3 months** after starting the medicine.
- People who got **single-agent chemotherapy** lived for about **9.2 months** after starting the medicine.



Out of the 453 people who were treated in this study, 379 people died during the study.

- In **Group A (atezolizumab)**, 249 out of 302 people (82%) died. Of these people, 180 (72%) died because their cancer got worse.
- In **Group B (single-agent chemotherapy)**, 130 out of 151 people (86%) died. Of these people, 103 (79%) died because their cancer got worse.

After 1 year, the percentage of people who were still alive was similar in both groups.

- After 1 year, 44% of people in the atezolizumab group were still alive.
- After 1 year, 39% of people in the chemotherapy group were still alive.

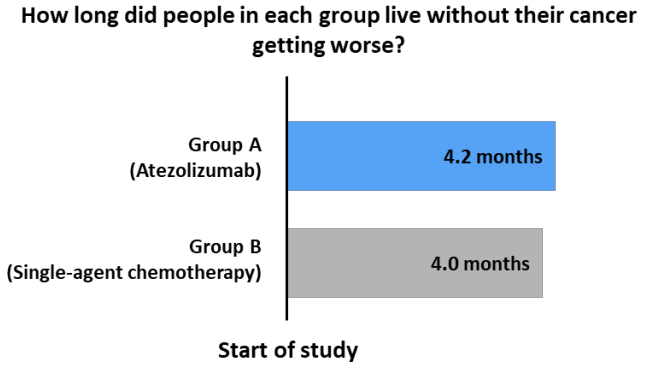
After 2 years, the percentage of people who were still alive was twice as high in the atezolizumab group as in the chemotherapy group.

- After 2 years, 24% of people in the atezolizumab group were still alive.
- After 2 years, 12% of people in the chemotherapy group were still alive.

Question 2. How long did people in each group live without their cancer getting worse?

Researchers wanted to know how long people in both groups lived after starting treatment without their cancer getting worse.

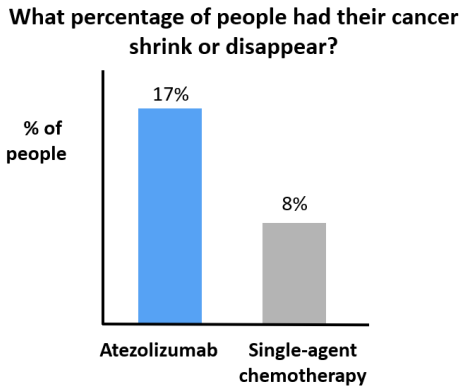
- People who got **atezolizumab** lived for about **4.2 months** without their cancer getting worse.
- People who got **single-agent chemotherapy** lived for about **4.0 months** without their cancer getting worse.



Question 3: How many people in each group had their cancer shrink or disappear?

Researchers wanted to know how many people in each group had their cancer shrink or disappear during treatment. The percentage of people whose cancer got smaller or went away was over twice as high in the atezolizumab group compared with the chemotherapy group.

- In the **atezolizumab** group, 17% of people had their cancer shrink or disappear while taking study medicine.
- In the **single-agent chemotherapy** group, 8% of people had their cancer shrink or disappear while getting study medicine.



For people whose cancer shrank or disappeared, researchers wanted to see how long the improvement lasted. The cancer stayed smaller or stayed away for almost twice as long in the atezolizumab group as in the chemotherapy group.

- In the **atezolizumab** group, the cancer stayed smaller or stayed away for an average of 14.0 months.
- In the **single-agent chemotherapy** group, the cancer stayed smaller or stayed away for an average of 7.8 months.

Question 4: How did people rate their quality of life while taking each medicine?

Researchers looked at how people in **Group A** and **Group B** rated their quality of life while taking the medicine. People filled out quality-of-life questionnaires at each study visit, with questions about their physical, emotional, and mental well-being. People were then scored in 25 categories related to quality of life.

- People in the atezolizumab group reported:
  - *Improvements* in 5 categories: cough, chest pain, constipation, difficulty breathing, and poor appetite
  - *No change* in the other 20 categories
- People in the chemotherapy group reported:
  - *Improvements* in 2 categories: trouble sleeping and generalized pain
  - *Worsening* in 6 categories: ability to think and remember, social functioning, ability to perform normal responsibilities, numbness in hands or feet, hair loss, and poor appetite
  - *Improvements* and *worsening* over time in 1 category: pain in body (outside of chest, arm, or shoulder)
  - *No change* in the 16 other categories

Researchers looked at how long after people started treatment until they had chest pain, a common lung cancer symptom.

- People in the atezolizumab group reported a longer time until they started to feel chest pain than people in the chemotherapy group.

This section only shows the main 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 or getting a rash) that may happen during the study.

- The study doctor decided if the side effects were related to the study treatment or not.
- Not all of the people in this study had all of the side effects.
- Side effects may be mild to very serious.
- Side effects 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.
- Side effects are described in the next sections.

The safety results shown in this section are for all the people who took the medicines in the study. Results were collected for 300 people who got atezolizumab and 147 people who got single-agent chemotherapy.

Serious side effects related to treatment

A side effect is considered '*serious*' if it causes lasting problems, requires hospital care, is life-threatening, or causes death.

- In the **atezolizumab** group, 35 out of 300 people (12%) had a *serious* side effect thought to be related to treatment.
- In the **single-agent chemotherapy** group, 23 out of 147 people (16%) had a *serious* side effect thought to be related to treatment.

Severe side effects related to treatment

A 'severe' side effect is one that is considered intense or medically important by a person's doctor. A severe side effect may overlap with a serious side effect if it causes disability or death. Or it may not be life-threatening, but it may be severe in intensity and require some medical care.

- In the **atezolizumab** group, 52 out of 300 people (17%) had a *severe* side effect thought to be related to treatment.
- In the **single-agent chemotherapy** group, 53 out of 147 people (36%) had a *severe* side effect thought to be related to treatment.

Most common side effects related to study medicine

This table shows the most common side effects related to the study medicines. These are the side effects reported by at least 10% of people (1 out of 10) in either group. Some people had more than 1 side effect.

Most common side effects related to study medicine	**Group A Atezolizumab** (300 people total)	**Group B Single-agent chemotherapy** (147 people total)
Low appetite	12% (36 out of 300)	15% (22 out of 147)
Fatigue (excessive tiredness)	10% (29 out of 300)	17% (25 out of 147)

Diarrhoea	7% (22 out of 300)	14% (21 out of 147)
Nausea	6% (17 out of 300)	22% (32 out of 147)
Low red blood cell count	5% (16 out of 300)	28% (41 out of 147)
Vomiting	3% (8 out of 300)	14% (21 out of 147)
Low neutrophil (type of white blood cell) count	1% (2 out of 300)	13% (19 out of 147)
Neutrophil (type of white blood cell) count decreased	0% (0 out of 300)	11% (16 out of 147)

- In the atezolizumab group, 39 out of 300 people (13%) decided to stop getting atezolizumab because of side effects.
- In the chemotherapy group, 20 out of 147 people (14%) decided to stop getting chemotherapy 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 presented here is from one study of 453 people with locally advanced or metastatic NSCLC. The people included in this study were considered by their doctor to be physically frail or ≥70 years old with other health conditions that made it unsafe for them to get platinum-based chemotherapy. These results helped researchers compare whether atezolizumab or single-agent chemotherapy would work better and be safer for this group of people.

Overall, this study showed that after starting treatment, the atezolizumab group (compared with the chemotherapy group):

1) Lived longer on average
2) Had a similar survival rate after 1 year and twice as high a survival rate after 2 years
3) Lived about the same amount of time without their cancer getting worse
4) Had twice the percentage of people whose cancer got smaller or went away while taking their medicine. For people whose cancer got smaller or went away, this improvement lasted for almost twice as long.
5) Rated themselves higher on some of the questions about their quality of life while taking the study medicine, including a longer time until they felt chest pain
6) Had a similar rate of serious side effects related to study medicine and half the rate of severe side effects related to the study medicine

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 talk to your doctor before making any decisions about your treatment.**

7. Are there plans for other studies?

Other studies looking at the safety and effects of atezolizumab are happening. These studies are looking at the use of atezolizumab in different situations, for example:

- In combination with other treatments
- Given before or after another treatment, to help that other treatment work better
- Given before and/or after surgery (for people diagnosed with lung cancer when it can still be removed with surgery)
- Given to people as the first treatment for lung cancer that spread to other parts of the body
- For other types of lung cancer

8. Where can I find more information?

You can learn more about this study on the websites listed below:

- https://classic.clinicaltrials.gov/ct2/show/NCT03191786
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2015-004105-16/results
- https://forpatients.roche.com/en/trials/cancer/lung-cancer/a-study-of-atezolizumab-compared-with-chemotherapy-in-treatment-.html

If you want to find out more about the results of this study, the full title of the paper we described here is:

- "First-line atezolizumab monotherapy versus single-agent chemotherapy in patients with non-small-cell lung cancer ineligible for treatment with a platinum-containing regimen (IPSOS): a phase 3, global, multicentre, open-label, randomised controlled study" by Siow Ming Lee, Christian Schulz, Kumar Prabhash, Dariusz Kowalski, Aleksandra Szczesna, Baohui Han, Achim Rittmeyer, Toby Talbot, David Vicente, Raffaele Califano, Diego Cortinovis, Anh Tuan Le, Dingzhi Huang, Geoffrey Liu, Federico Cappuzzo, Jessica Reyes Contreras, Martin Reck, Ramon Palmero, Milena Perez Mak, Solange Peters and others. This paper is published in the *Lancet* journal and can be accessed by visiting: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)00774-2/fulltext.

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

- If you have any questions after reading this summary, visit the ForPatients website and fill out the contact form: https://forpatients.roche.com/en/trials/cancer/lung-cancer/a-study-of-atezolizumab-compared-with-chemotherapy-in-treatment-.html.
- You can also 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 your 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 Phase III, open-label, multicenter, randomized study to investigate the efficacy and safety of atezolizumab compared with chemotherapy in patients with treatment-naïve advanced or recurrent (stage IIIB not amenable for multimodality treatment) or metastatic (stage IV) non-small cell lung cancer who are deemed unsuitable for platinum-containing therapy”.

The study is known as ‘IPSOS.’

- The protocol number for this study is: MO29872.
- The ClinicalTrials.gov identifier for this study is: NCT03191786.
- The EudraCT number for this study is: 2015-004105-16.