

## Summary of Clinical Trial Results

### A study to look at whether tiragolumab with atezolizumab and chemotherapy worked and was safe in people with 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
- People who took part in the study

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

The study started in February 2020 . This summary includes results that were collected and analysed in February 2022 and final results that were collected in September 2022. At the time of writing this summary, the study is still happening – study doctors are still collecting information; however, the main analysis of results is complete.

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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#### Glossary

- ES-SCLC = extensive-stage small-cell lung cancer

#### 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 extensive-stage small-cell lung cancer (ES-SCLC) and the medicines studied – 'tiragolumab' and 'atezolizumab'.

## Key information about this study

- This study was done to see if tiragolumab combined with atezolizumab and chemotherapy worked better than atezolizumab and chemotherapy alone for treating extensive-stage SCLC (ES-SCLC) . Researchers also looked at how many people had side effects and how serious they were when receiving treatment.
- Tiragolumab and atezolizumab are types of drugs that help the patients' own immune system seek out and fight cancer cells (known as 'immunotherapies').
- In this study, people were given either the medicine being studied (called tiragolumab) with an existing treatment (atezolizumab and chemotherapy) or a placebo with the existing treatment – it was decided by chance which treatment each person was given. Neither the people taking part in the study, or the study doctors knew which of the study medicines people were taking.
- This study included 490 people in 23 countries.
- The main finding was that combining tiragolumab with the existing treatment did not affect how long it took for peoples' cancer to progress (approximately 5½ months in both treatment groups) or how long people survived (approximately 13 months in both treatment groups).
- Around 45% of people (108 out of 239 people) taking tiragolumab with atezolizumab and chemotherapy had serious side effects, compared to around 42% of people (104 out of 246 people) taking placebo with atezolizumab and chemotherapy.

## 1. General information about this study

### Why was this study done?

Small-cell lung cancer (or SCLC) is a very fast-growing type of lung cancer and is typically caused by smoking. Around 1 out of every 10 lung cancers diagnosed are SCLC. Extensive-stage SCLC (ES-SCLC) describes SCLC that has spread to the other lung or to other parts of the body. The main treatment for extensive stage disease is chemotherapy with immunotherapy.

Although chemotherapy can be effective, it can cause lots of harmful side effects and can stop working after time (people become 'resistant') and the cancer can return. Therefore, other treatments are being developed.

Immunotherapy uses the body's immune system to destroy cancerous cells and has been used with chemotherapy to treat ES-SCLC. A new combination of immunotherapy treatments with chemotherapy were looked at in this study to see how safe it is and if it may provide better health outcomes for people with ES-SCLC.

### What were the study medicines?

This study looked at 3 types of treatment:

- Atezolizumab and chemotherapy – existing medicines.

- Tiragolumab – the medicine that was studied (with existing medicine).

**Atezolizumab** (Tecentriq™) is an existing medicine which is approved by the Food and Drug Administration (FDA) in the United States and by the European Medicines Agency (EMA) for the treatment of ES-SCLC when used with chemotherapy.

- You say this as ‘a – teh – zoh –LIZ – yoo – mab’.
- Atezolizumab is a type of immunotherapy medicine. It blocks a protein called PD-L1, which can be found in some cancers. PD-L1 ‘hides’ the cancer from the immune system. Blocking it gives a signal to the body’s immune system to attack the cancer cells.

**Chemotherapy** is an existing medicine which is approved by the Food and Drug Administration (FDA) in the United States and by the European Medicines Agency (EMA) for the treatment of ES-SCLC when used with atezolizumab.

- There are many different types of chemotherapy, but they all work in a similar way by stopping cancer cells growing and spreading to other parts of the body.

**Tiragolumab** was the focus of this study.

- You say this as ‘tih – ruh – GOL – u - mab’.
- Tiragolumab works by blocking a protein called TIGIT. Like PD-L1, TIGIT ‘hides’ the cancer from the immune system. Blocking it gives a signal to the body’s immune system to attack the cancer cells.
- Researchers compared tiragolumab with atezolizumab and chemotherapy to a ‘placebo’ with atezolizumab and chemotherapy.
- You say this as ‘plah – see – bo’.
- The placebo looked the same as tiragolumab but did not contain any real medicine. This means it had no medicine-related effect on the body.
- A placebo was used in this study so that study doctors could show which benefits or side effects were caused by tiragolumab, rather than the other drugs being taken.

## What did researchers want to find out?

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

They also wanted to find out how safe tiragolumab was when given with atezolizumab and chemotherapy – by checking how many people had side effects and seeing how serious they were (see section 5 “What were the side effects?”).

**The main questions that researchers wanted to answer were:**

1. How long does tiragolumab, given in combination with atezolizumab and chemotherapy, prevent cancer progression in people with ES-SCLC?
2. How long did people live in this study when taking tiragolumab with atezolizumab and chemotherapy compared with placebo with atezolizumab and chemotherapy?

**Other questions that researchers wanted to answer included:**

3. How safe was tiragolumab, given in combination with atezolizumab and chemotherapy, for people with ES-SCLC?

**What kind of study was this?**

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This study was a ‘Phase 3’ study. In this study, a larger number of people with ES-SCLC were given tiragolumab with atezolizumab and chemotherapy (an existing treatment for ES-SCLC) or placebo with atezolizumab and chemotherapy.

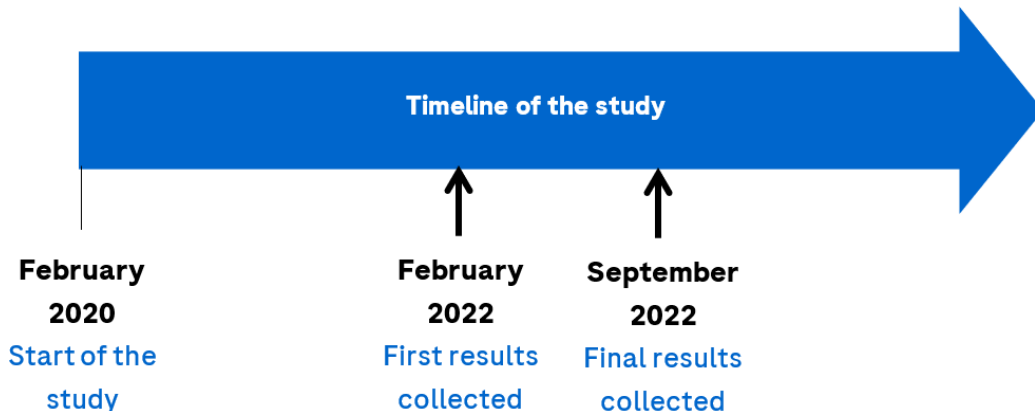
The study was ‘randomised’. This means that it was decided by chance which of the treatments people in the study would have – like tossing a coin. Randomly choosing which medicine people take makes it more likely that the types of people (for example, age, race) in both groups will be a similar mix.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

This 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.

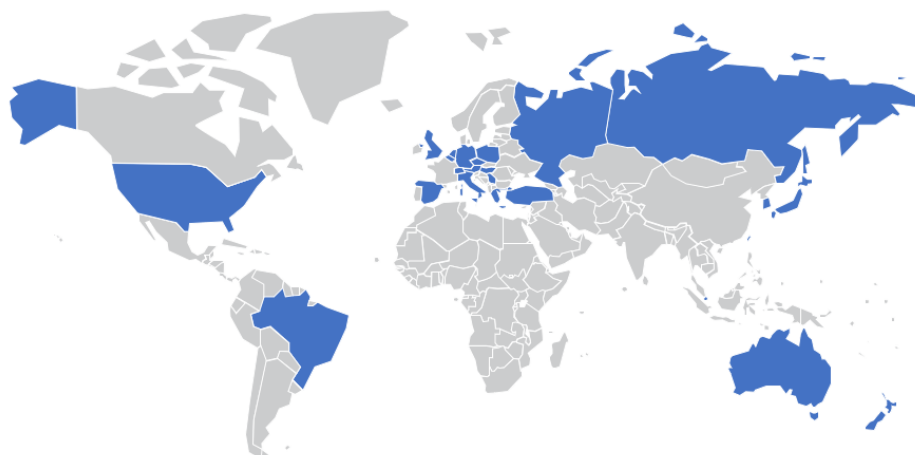
**When and where did the study take place?**

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The study started in February 2020. At the time of writing this summary, the study is still happening – study doctors are still collecting information; however, the main analysis of results (collected in September 2022) is complete.



The study took place at 121 study centres – across 23 countries across the USA, Europe, Asia, South America and Oceania. The following map shows the countries where this study took place.

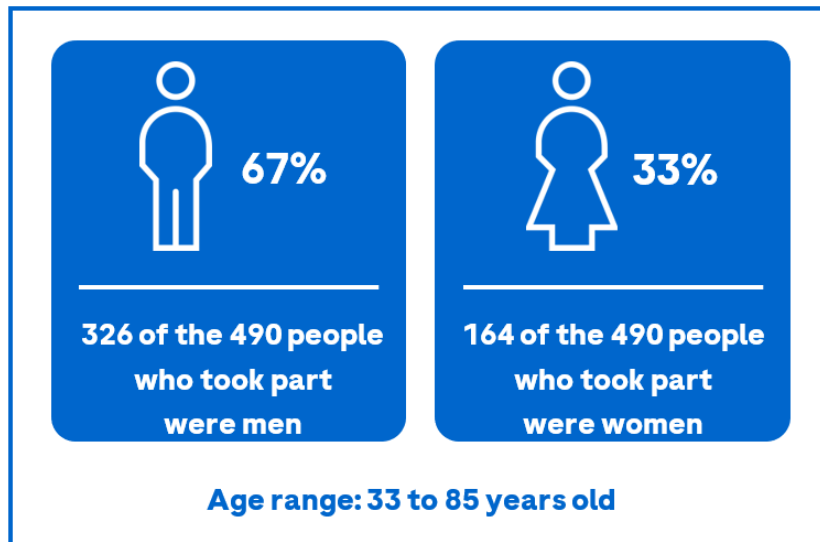


- Australia
- Austria
- Belgium
- Brazil
- Czechia
- Germany
- Greece
- Hungary
- Italy
- Japan
- Netherlands
- New Zealand
- Poland
- Russian Federation
- Serbia
- Singapore
- Spain
- Switzerland
- Taiwan
- Turkey
- UK
- USA

## 2. Who took part in this study?

In this study, 490 people with ES-SCLC took part. The results shown on this page are for the people who didn't have cancer that had spread to the brain when they joined this study (which is 397 people). However, similar results were seen in patients who did have cancer that had spread to the brain.

More information on the people who took part is given below.



People could take part in the study if they:

- Were over 18 years old.
- Had been diagnosed with ES-SCLC.
- Did not have any treatment for ES-SCLC before.
- Were able to perform activities - such as walking or going to work - as well or almost as well as they could before they had the illness.

People could not take part in the study if they:

- Had cancer that had spread to the brain causing symptoms.
- Had certain other medical conditions including conditions where a person's immune system attacks their own body (autoimmune diseases) or when a person's immune system does not work like it should (immune-deficiency).
- Were pregnant or breastfeeding.
- Had a history of allergic reactions to the same type of medicines that were used in the study.

### 3. What happened during the study?

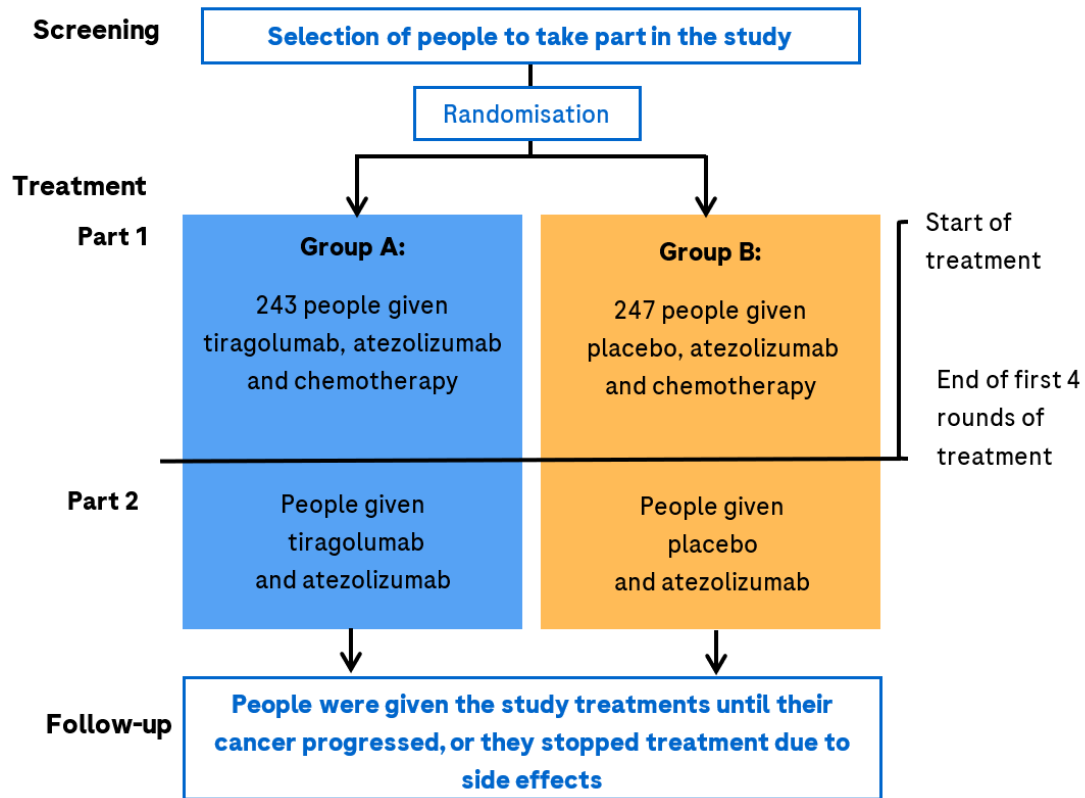
During the study, people were placed into treatment groups (Group A or Group B) at random. This means that it was decided by chance which of the medicines people in the study would have – like tossing a coin.

The treatment groups were:

- **Group A: Tiragolumab with atezolizumab and chemotherapy** – tiragolumab with atezolizumab and chemotherapy were given as an infusion (into the vein) once every 3 weeks, 4 times. After this, only tiragolumab and atezolizumab were given as an infusion, once every 3 weeks for as long as the treatment helped them.

- **Group B: Placebo with atezolizumab and chemotherapy** – placebo with atezolizumab and chemotherapy were given as an infusion (into the vein) once every 3 weeks, 4 times. After this, only placebo and atezolizumab were given, once every 3 weeks for as long as the treatment helped them.

Look below to see more information about what happened in the study.



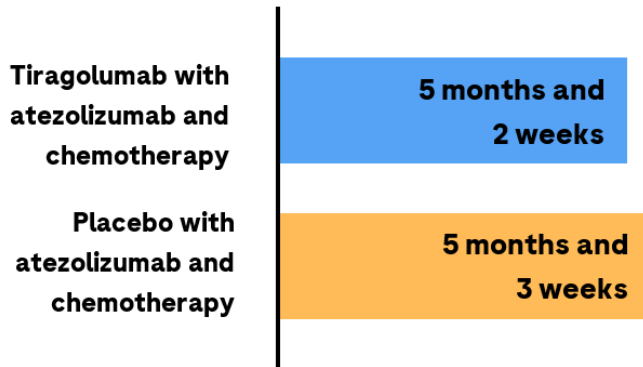
## 4. What were the results of the study?

**Question 1:** How long does tiragolumab, given in combination with atezolizumab and chemotherapy, prevent cancer progression in people with ES-SCLC?

This question was looked at in 397 people in the study who didn't have cancer that had spread to the brain. However, similar results were seen in patients who did have cancer that had spread to the brain. Researchers looked at how much time passed from the start of the study until a person's cancer began to progress (known as 'progression-free survival'). These results were collected in February 2022.

Across both treatment groups, approximately 5 ½ months (22 weeks) had passed before people’s cancer began to progress in both treatment groups.

**On average, how long did it take for people’s cancer to progress in the two groups?**



**Question 2: How long did people live in this study when taking tiragolumab with atezolizumab and chemotherapy compared with placebo with atezolizumab and chemotherapy?**

Another piece of information that researchers collected was how long people in the study lived for when/after receiving treatment (known as overall survival). This question was looked at in 397 people in the study who didn’t have cancer that had spread to the brain. These results were collected in September 2022. On average, people lived for about a year (13 months) in both treatment groups.

**On average, how long people in each treatment group live?**



**Question 3: How safe was tiragolumab, given in combination with atezolizumab and chemotherapy, for people with ES-SCLC?**

Side effects are medical problems (such as feeling dizzy) that can happen during the study, which may or may not be directly related to the treatments in the study.

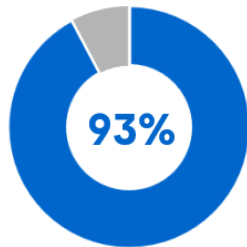
- Not all the people in this study had all of the side effects.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflets.
- Side effects can vary from mild to very serious and may vary from person to person.

Out of all the 490 patients in the study, 485 received at least one dose of treatment, therefore, any side effects that they had were looked at. During this study, around 93 out of every 100 people (93%) had a side effect that the study doctor believed was related to the



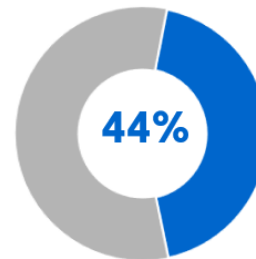
treatments in the study, and approximately 44 in every 100 people (44%) had at least one serious side effect which may or may not have been directly related to the treatments in the study.

### How many people had side effects related to a study treatment?



**450 out of 485 people had a treatment-related side effect**

### How many people had serious side effects?



**212 out of 485 people had a serious side effect**

See Section 5 for more information about the type of side effects that people had.

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?

### Serious side effects

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

Out of all the 490 patients in the study, 485 received at least one dose of treatment, therefore, any side effects that they had were looked at. During this study, approximately 44 in every 100 people (44%) had at least one serious side effect which may or may not have been directly related to the treatments in the study. Out of the 239 people taking tiragolumab with atezolizumab and chemotherapy, 108 people had at least one serious side effect (45%), compared with around 104 out of 246 (42%) of people taking placebo with atezolizumab and chemotherapy.

The most common serious side effects are shown in the following table – these are the top 5 most common serious 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.

Serious side effects reported in this study	People taking tiragolumab with atezolizumab and chemotherapy (239 people total)	People taking placebo with atezolizumab and chemotherapy (246 people total)
Fever while having low levels of white blood cells called 'neutrophils' (febrile neutropenia)	7% (16 out of 239)	6% (14 out of 246)
Lung infection (pneumonia)	3% (7 out of 239)	5% (12 out of 246)
Low levels of red blood cells (anaemia)	4% (9 out of 239)	3% (8 out of 246)
COVID-19	3% (6 out of 239)	4% (9 out of 246)
Low levels of sodium in the blood (Hyponatremia)	4% (9 out of 239)	2% (4 out of 246)

There were some people in the study who died due to side effects related to tiragolumab with atezolizumab and chemotherapy or placebo with atezolizumab and chemotherapy. These included:

- 1 out of 239 people (less than 1%) in the tiragolumab group.
- 5 out of 246 people (2%) in the placebo group.

During the study, some people decided to stop taking their medicine because of side effects, which may or may not have been directly related to tiragolumab with atezolizumab and chemotherapy or placebo with atezolizumab and chemotherapy:

- In the tiragolumab group, 8 out of 100 people (8%) stopped taking their medicine.
- In the placebo group, 9 out of 100 people (9%) stopped taking their medicine.

### Most common side effects

During this study, around 93 out of every 100 people (93%) had a side effect that the study doctor believed were related to either of the treatments in the study (also known as treatment-related side effects). Out of the 239 people taking tiragolumab with atezolizumab and chemotherapy, 223 people had a treatment-related side effect (93%) compared with 227 out of 246 (92%) of people taking placebo with atezolizumab and chemotherapy.

The most common treatment-related side effects are shown in the following table – these are the top 5 most common side effects across both treatment groups. Some people had more than one side effect – this means that they are included in more than one row in the table.

Most common side effects reported in this study	People taking tiragolumab with atezolizumab and chemotherapy (239 people total)	People taking placebo with atezolizumab and chemotherapy (246 people total)
Low levels of red blood cells (anaemia)	36% (86 out of 239)	38% (93 out of 246)
Low levels of white blood cells called 'neutrophils' (neutropenia)	26% (62 out of 239)	30% (74 out of 246)
Low level of the blood cell fragments that help blood to clot – called 'platelets' (thrombocytopenia)	11% (27 out of 239)	11% (28 out of 246)
Fever while having low levels of white blood cells (febrile neutropenia)	7% (17 out of 239)	6% (15 out of 246)
Lower number of white blood cells than normal (leukopenia)	5% (12 out of 239)	5% (13 out of 246)

### 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 490 people with a type of lung cancer called extensive-stage small-cell lung cancer or ES-SCLC. These results helped researchers learn more about ES-SCLC and the effects and safety of combining tiragolumab, atezolizumab and chemotherapy.

The addition of tiragolumab with atezolizumab and chemotherapy did not improve how well people responded to atezolizumab and chemotherapy treatment. The results from people in Group A were similar to the results from people in Group B, so we cannot say that there was a benefit from the addition of tiragolumab. The safety of patients taking the combination of tiragolumab with atezolizumab and chemotherapy was similar to the safety of patients taking placebo with atezolizumab and chemotherapy. The results are important because they help researchers learn more about tiragolumab plus atezolizumab and chemotherapy for the treatment of ES-SCLC.

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 plus 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/NCT04256421>
- [https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract\\_number:2019-003301-97](https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2019-003301-97)
- <https://forpatients.roche.com/en/trials/cancer/lung-cancer/a-study-of-atezolizumab-plus-carboplatin-and-etoposide--78663.html>

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “SKYSCRAPER-02: Tiragolumab in Combination With Atezolizumab Plus Chemotherapy in Untreated Extensive-Stage Small-Cell Lung Cancer”. The authors of the scientific paper are: Charles M. Rudin, Stephen V. Liu, Ross A. Soo, Shun Lu, Min Hee Hong and others. The paper is published in the journal Journal of Clinical Oncology.

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

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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-plus-carboplatin-and-etoposide--78663.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?

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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

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The full title of this study is: “A Study of Atezolizumab Plus Carboplatin and Etoposide With or Without Tiragolumab in Patients With Untreated Extensive-Stage Small Cell Lung Cancer (SKYSCRAPER-02)”.

The study is known as ‘SKYSCRAPER-02’.

- The protocol number for this study is: GO41767
- The ClinicalTrials.gov identifier for this study is: NCT04256421.
- The EudraCT number for this study is: 2019-003301-97

