Summary of Clinical Trial Results

A study to look at how safe atezolizumab and erlotinib or alectinib is and how well the medicines worked in 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 and
- people who took part in the study.

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

The study **started in April 2014 and ended in February 2020**. This summary was written after the study had ended.

One study cannot 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.**

Contents of the summary

Glossary

- NSCLC = non-small cell lung cancer
- EGFR = epidermal growth factor receptor
- ALK = anaplastic lymphoma kinase
- ICI = immune checkpoint inhibitor
- TKI = tyrosine kinase inhibitor

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 the medicines studied – '**atezolizumab**', '**erlotinib**' and '**alectinib**'.

Key information about this study

- **Atezolizumab**, **erlotinib** and **alectinib** are all medicines which are given to some people with a type of cancer called 'non-small cell lung cancer', or NSCLC, which has spread from where it started to nearby cells or to other parts of the body (this is called advanced NSCLC).
- **Atezolizumab** can be given to people with NSCLC to help their immune system to fight the cancer cells.
- **Erlotinib** is a type of drug called a 'tyrosine kinase inhibitor' (TKI) and can be given to people with NSCLC who have changes (alterations) in a gene called '*EGFR*'. **Alectinib** is also a TKI and can be given to people with NSCLC who have alterations in a gene called '*ALK*'.
- This study was done to see how safe these medicines are, and how well they work in people with NSCLC.
- The study had two parts:
    - In the first part, researchers looked at how safe **atezolizumab** and **erlotinib** were in people with NSCLC who had never taken a TKI. Some people had NSCLC with alterations in the '*EGFR*' gene, and some people did not. Researchers also looked at how safe **atezolizumab** and **alectinib** were in people with NSCLC with alterations in the '*ALK*' gene and who had never taken another medicine for their cancer. Findings from this part of the study helped researchers decide how much of each medicine was given to people in the second part of the study. In this part of the study, eight people were given **atezolizumab** and **erlotinib**, and seven people were given **atezolizumab** and **alectinib**.
    - The second part of the study looked at how safe the medicines were and how well they worked when given to more people. In this part of the study, 20 people who had an alteration in the '*EGFR*' gene and had never taken medicine for their cancer, or had taken only one medicine that was not an EGFR TKI were given **atezolizumab** with **erlotinib**. This part of the study also included fourteen people with NSCLC who were given **atezolizumab** with **alectinib**, who had an alteration in the '*ALK*' gene and who had never taken a medicine for their cancer.
- People in the **atezolizumab** and **erlotinib** group were first given **erlotinib** once a day for a week, and then **atezolizumab** was given every 3 weeks.
    - Overall, on average, people with NSCLC who had never taken a TKI took **atezolizumab** with **erlotinib** for 10 months.
- People in the **atezolizumab** and **alectinib** group were given **alectinib** twice a day in the first treatment cycle (which lasted for 28 days), and then twice a day for each 3-week treatment cycle after. People were given **atezolizumab** on day 8 of the first treatment cycle, and then every 3 weeks.

- Overall, on average, people took **atezolizumab** for 10 months and **alectinib** for 22 months.

- The study included a total of 49 people from 6 countries.
- The main findings in people who were given **atezolizumab** and **erlotinib** were:
  - On average, people were seen by researchers for 45 months after taking **atezolizumab** and **erlotinib**.
  - 50% of people (14 out of 28 people) had a serious unwanted effect of the study medicines also known as a serious side effect.
  - Serious side effects were thought to be related to the study medicines in 27% of people (8 out of 28 people). A side effect is 'serious' if it is life threatening, needs hospital care, or causes lasting problems.
  - In the second part of the study where people had NSCLC with alterations in the *EGFR* gene, 75% of people (15 out of 20 people) had their tumours get smaller and stay smaller for an average of 19 months. On average, people's lung cancer got worse about 15 months after they started taking the study medicines.
- The main findings in people who were given **atezolizumab** and **alectinib** were:
  - On average, people were seen by researchers for 29 months after taking **atezolizumab** and **alectinib**.
  - 38% of people (8 out of 21 people) had at least one serious side effect.
  - None of the side effects which were thought to be related to the study medicines were life threatening or led to death.
  - In the second part of the study where people had NSCLC with alterations in the *ALK* gene, 86% of people (18 out of 21 people) had their tumours get smaller after four months of taking **atezolizumab** and **alectinib**.
  - On average, 38% of people (8 out of 21 people) had their cancer get worse after taking the study medicines. This was less than the total number of people who took **atezolizumab** and **alectinib**, and so the average time that people's cancer got worse after starting the study medicines could not be calculated.
- In the entire population, 27% of people (13 out of 49 people) stopped taking **atezolizumab**, 11% of people (3 out of 28 people) stopped taking **erlotinib**, and 19% of people (4 out of 21 people) stopped taking **alectinib**, due to a side effect (see page 9 for more details).

1. General information about this study

Why was this study done?

Most people who have lung cancer have a type of lung cancer called 'non-small cell lung cancer' (NSCLC). In some cases, people with NSCLC have changes (alterations) in their tumours (cancer) – in genes called '*epidermal growth factor receptor*' (*EGFR*) and '*anaplastic lymphoma kinase*' (*ALK*).

People who have NSCLC with alterations in the *EGFR* or *ALK* genes are given medicines called tyrosine kinase inhibitors (TKIs). TKIs work by blocking EGFR and ALK activity, which stops the cancer cells from growing. TKIs work well in people who have NSCLC with alterations in the *EGFR* or *ALK* genes, but usually only for a short time.

Immunotherapy is a medicine that helps a person's own immune system attack tumours. A type of immunotherapy called an 'immune checkpoint inhibitor' (ICI) works by blocking checkpoint proteins, such as PD-L1. Cancer cells can use PD-L1 and other checkpoint proteins to stop the immune system from killing the tumour. By blocking checkpoint proteins, ICIs 'release the brakes' and allow the immune system to attack the cancer cells.

In people who have NSCLC with alterations in the *EGFR* or *ALK* genes, ICI by itself does not work as well as it does in people who have NSCLC without these gene alterations. It is possible that giving people who have NSCLC with *EGFR* or *ALK* alterations an ICI and a TKI together will shrink their tumours and help them live longer.

In this study, researchers wanted to see if adding an ICI that blocks PD-L1 to an EGFR and ALK TKI would be safe for people who have NSCLC, and whether the medicines worked well when used together. People in the study had not been given an EGFR or ALK TKI before taking part in the study.

What were the study medicines?

This study looked at two combinations of an immunotherapy medicine with two different TKIs in people with NSCLC.

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

- You say '**atezolizumab**' as 'a – teh – zo – liz – oo – mab'.
- You say 'Tecentriq' as 'tee – sen – trik'.
- The body's immune system can fight diseases such as cancer. However, cancer cells containing PD-L1 can stop the immune system from attacking the cancer. **Atezolizumab** helps the immune system fight the cancer cells by stopping PD-L1 from working. This may mean that the cancer (tumour) gets smaller in some people.

The other medicine used in the study is called '**erlotinib**' (known by its brand name, Tarceva®).

- You say '**erlotinib**' as 'ur – law – tuh – nib'.
- You say 'Tarceva' as 'tar – see – va'.
- Lung cancers can have alterations in a gene called '*EGFR*' that help them grow. **Erlotinib** stops cancer growth caused by *EGFR* alterations. This means that taking **erlotinib** may make tumours smaller in some people with lung cancer.

The other medicine used in the study is called '**alectinib**' (known by its brand name, Alecensa®).

- You say '**alectinib**' as 'al – eck – tuh – nib'.
- You say 'Alecensa' as 'al – eh – sen – sa'.
- Lung cancers can also have alterations in a gene called '*ALK*' that help them grow. **Alectinib** stops or slows down the growth of cancers which are caused by *ALK* alterations. This means that taking **alectinib** may make tumours smaller in some people with lung cancer.

What did researchers want to find out?

- Researchers did this study to look at whether taking **atezolizumab** and **erlotinib** together or **atezolizumab** and **alectinib** together, led to any side effects (a side effect is an unwanted effect of a medicine or medical treatment).
- They also wanted to find out how well **atezolizumab** worked when used together with **erlotinib** or **alectinib**.

The main questions that researchers wanted to answer were:

1. What amount (dose) of **atezolizumab** or **erlotinib** was safe for people to take?
2. What dose of **atezolizumab** or **alectinib** was safe for people to take?
3. How many people had side effects or serious side effects which were thought to be related to the study medicines?

Other questions that researchers wanted to answer included:

4. How many people had smaller tumours after taking the study medicines, and how long did their tumours stay smaller for?
5. How long did it take for people's cancer to get worse?
6. How long did people in the study live after taking the study medicines?

What kind of study was this?

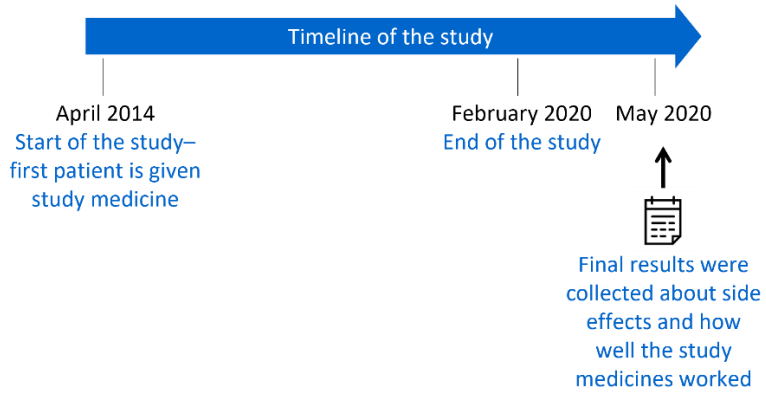
This study was a 'Phase 1' study, which means that this was done to look at how safe **atezolizumab** and **erlotinib** or **atezolizumab** and **alectinib** were, the best dose of the medicines to give to people, and how well the medicines worked together.

The study had two parts:

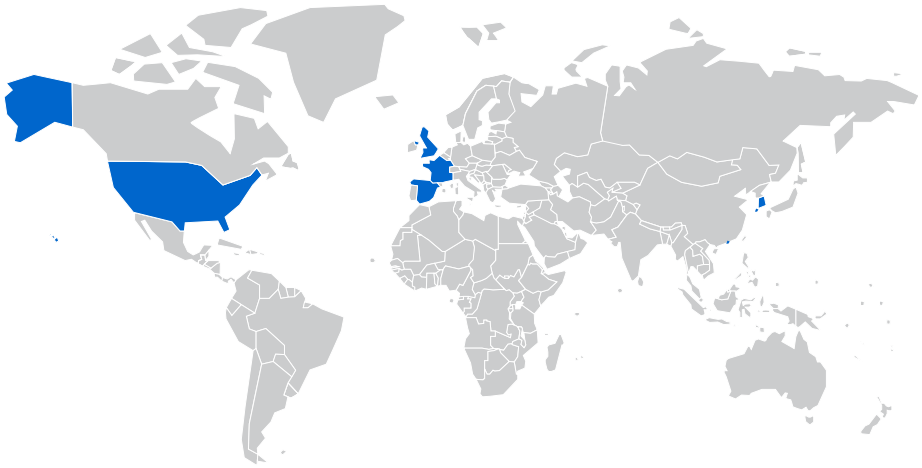
- The first part looked at how safe the medicines were when given together in a small group of people and what dose might work the best without a lot of side effects – the 'recommended dose'.
- The second part allowed researchers to learn more about how safe the medicines were and how well they worked together at the recommended dose from the first part of the study.

When and where did the study take place?

The study started in April 2014 and finished in February 2020. This summary was written after the study had ended.



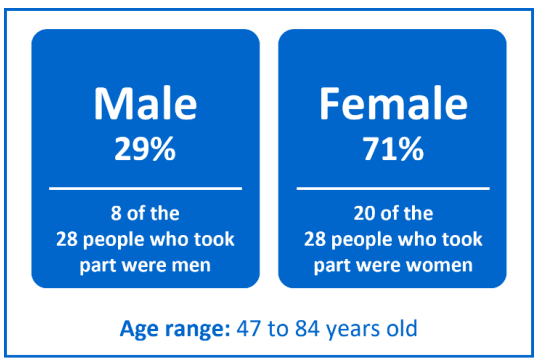
The study took place at 17 study centres – across 6 countries. The countries were: France, United Kingdom, Hong Kong, the Republic of Korea, Spain, and the United States.



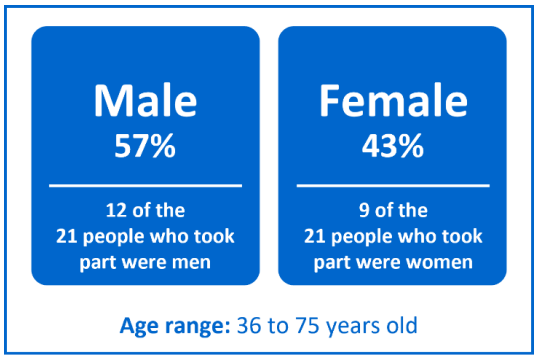
2. Who took part in this study?

In this study, 49 people with NSCLC took part. Here is more information about the people in this study.

In the group that were given **atezolizumab** and **erlotinib**:



In the group that were given **atezolizumab** and **alectinib**:



People could take part in the study if they:

- Were at least 18 years old.
- Had advanced NSCLC – called 'advanced' because the cancer had spread from where it started to nearby cells or to other parts of the body.
- Had not taken more than one medicine for their advanced disease before participating in the second part of the study (in the group that were given **atezolizumab** and **erlotinib**).
- Had not taken any medicine for their advanced disease before participating in the study (in the group that were given **atezolizumab** and **alectinib**).
- Had *EGFR* alterations (in the group that were given **atezolizumab** and **erlotinib**).
    - People in the first part of the study could have *EGFR* alterations in their tumours but having tumours with *EGFR* alterations was not required.
    - People in the second part of the study had to have *EGFR* alterations in their tumours.
- Had *ALK* alterations (in the group that were given **atezolizumab** and **alectinib**).

3. What happened during the study?

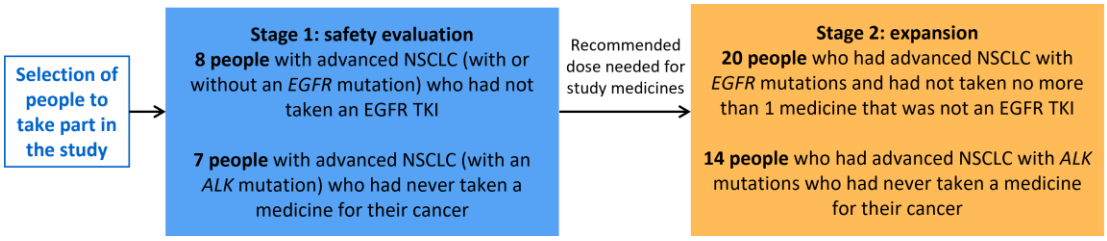
During the study, 28 people with NSCLC and *EGFR* alterations were given **atezolizumab** and **erlotinib**, and 21 people with NSCLC and *ALK* alterations were given **atezolizumab** and **alectinib**.

In the first part of the study, the medicines were first tested in one person to see how safe the medicines were when taken together. In the person who was given a starting dose of **erlotinib** once a day for a week, **atezolizumab** was then given every 3 weeks. In the person who was given a starting dose of **alectinib** twice a day for the first treatment cycle (which lasted for 28 days) and then twice a day for each 3-week treatment cycle which followed, **atezolizumab** was given on day 8 of the first treatment cycle, and then every 3 weeks. If the first person did not have side effects that would stop them from taking the medicines, the other people in the first part of the study could be treated with the study medicines.

After researchers looked at the side effects in all of the people in the first part – called the 'safety evaluation stage' (stage 1), they selected the dose given to the people in the second part of the study – called the 'expansion stage' (stage 2). A total of 15 people were given the study medicines in stage 1.

In the second part, researchers wanted to know more about how safe the study medicines were and how well they worked in people with NSCLC, so they were given to more people with NSCLC. A total of 34 people were given the study medicines in stage 2.

This picture shows more information about what happened in the study:



Overall, on average, people with NSCLC who had never taken a TKI in the **atezolizumab** and **erlotinib** group took **atezolizumab** with **erlotinib** for 10 months.

Overall, on average, people in the **atezolizumab** and **alectinib** group took **atezolizumab** for 10 months and **alectinib** for 22 months.

4. What were the side effects?

Side effects are medical problems (such as feeling dizzy) 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.
- 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 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.
- Serious and common side effects are listed in the following sections.

Serious side effects

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

In the group of people who were given **atezolizumab** and **erlotinib**:

- 14 out of 28 people (50% of people) had at least one serious side effect.
- Serious side effects were thought to be related to **atezolizumab** and **erlotinib** in 8 out of the 28 people (27% of people).

In the group of people who were given **atezolizumab** and **alectinib**:

- 8 out of 21 people (38% of people) had at least one serious side effect.
- No side effects which were thought to be related to **atezolizumab** and **alectinib** were life threatening or led to death.

No people died due to a side effect during the study.

During the study, some people stopped taking one of the study medicines because of the side effects – this is called 'treatment withdrawal'.

- 13 out of 49 people (27% of people) stopped taking **atezolizumab** due to a side effect.
- 3 out of 28 people (11% of people) stopped taking **erlotinib** due to a side effect.

- 4 out of 21 people (19% of people) stopped taking **alectinib** due to a side effect.

Side effects leading to treatment withdrawal	All people in the study (49 people in total)		
	People who stopped taking **atezolizumab** (out of 49 people)	People who stopped taking **erlotinib** (out of 28 people)	People who stopped taking **alectinib** (out of 21 people)
Skin rash	4% (2 out of 49)	0	0
Joint pain	2% (1 out of 49)	0	0
Chest pain	2% (1 out of 49)	0	0
Bleeding from swollen veins in the anus or lower rectum	2% (1 out of 49)	0	0
Muscle weakness	2% (1 out of 49)	0	0
Fever	4% (2 out of 49)	0	5% (1 out of 21)
Shortness of breath	0	4% (1 out of 28)	0
Blood clot in a deep vein	0	4% (1 out of 28)	0
High level of liver enzymes	4% (2 out of 49)	4% (1 out of 28)	0
High liver function test	0	0	10% (2 out of 21)
Pain	2% (1 out of 49)	0	5% (1 out of 21)
Low white blood cell (neutrophil) count	2% (1 out of 49)	0	5% (1 out of 21)
Nausea	2% (1 out of 49)	0	0
Pneumonitis	2% (1 out of 49)	0	0

Side effects related to people's immune systems being made more active (stimulated) by the study medicines are of special interest

Sometimes activating the immune system using immunotherapy causes it to attack healthy parts of the body in addition to the cancer. Doctors call this type of side effect an 'immune-related side effect'. This is an example of a type of side effect which doctors have a special interest in because they can sometimes become serious or life threatening and can lead to death.

In the group who were given **atezolizumab** and **erlotinib**:

- 27 out of 28 people (96% of people) had an immune-related side effect.

- In 9 out of 28 people (32% of people), these immune-related side effects were medically significant.

In the group who were given **atezolizumab** and **alectinib**:

- 18 out of 21 people (86% of people) had an immune-related side effect related to taking **atezolizumab**.
- In 9 out of 21 people (43% of people), these immune-related side effects related to taking **atezolizumab** were medically significant.

Other side effects

You can find more information about other side effects (not shown in the sections above) in the resources listed at the end of this summary – see section 8.

5. How well did the study medicines work together?

Researchers collected information about how well the study medicine worked in the 20 people from stage 2 who had *EGFR* alterations in their tumours and the 21 people who had *ALK* alterations in their tumours – this information was collected from the start of the study until May 2020. Information about how well the study medicines worked in the people with NSCLC with or without *EGFR* alterations from stage 1 have not been reported.

Question 1: How many people had smaller tumours after taking the study medicines, and how long did their tumours stay smaller for?

Researchers looked at how many people had their tumours get smaller after taking **atezolizumab** and **erlotinib** or **alectinib**. They also looked at how long people's tumours stayed smaller for.

- On average, people were seen by researchers for 45 months after taking **atezolizumab** and **erlotinib**.
- 15 out of 20 people (75% of people) had their tumours get smaller after taking **atezolizumab** and **erlotinib**.
- People taking **atezolizumab** and **erlotinib** had their tumours stay smaller for about 19 months. This number is an average – that means that some people's tumours stayed smaller for less time than this, and some people's tumours stayed smaller for more time than this.
- On average, people were seen by researchers for 29 months after taking **atezolizumab** and **alectinib**.
- 18 out of 21 people (86% of people) had their tumours get smaller after taking **atezolizumab** and **alectinib**. Most people had their tumours get smaller around 4 months after taking **atezolizumab** and **alectinib**.
- The average time that people taking **atezolizumab** and **alectinib** had their tumours stay smaller for could not be calculated because less than half of the people who were given **atezolizumab** and **alectinib** had tumours that grew bigger.

Question 2: How long did it take for people's cancer to get worse?

Another piece of information that researchers collected was how much time it took for people's cancer to get worse after starting **atezolizumab** and **erlotinib**, or **atezolizumab** and **alectinib**.

This number is an average – that means that some people's cancer got worse sooner than this, and some people's cancer got worse after a longer time than this.

- People's cancer worsened about 15 months after starting **atezolizumab** and **erlotinib**.
- Eight people who received **atezolizumab** and **alectinib** had their cancer get worse. Since this is less than half of the total number of people who were given these two drugs, the average time that people's cancer got worse after starting **atezolizumab** and **alectinib** could not be calculated.

Question 3: How long did people in the study live after starting the study medicines?

Researchers also looked at how long people in the study lived.

- The average time people lived after starting **atezolizumab** and **erlotinib** or **alectinib** could not be calculated because less than half of people had died.

6. How has this study helped research?

The information presented here is from a single study of 49 people with NSCLC. These results helped researchers learn more about **atezolizumab** and **erlotinib** when given to people with NSCLC (with or without *EGFR* alterations) not treated with an EGFR TKI before. These results also helped researchers learn more about **atezolizumab** and **alectinib** when given to people with NSCLC with *ALK* alterations who had never taken a medicine for their cancer.

No single study can tell us everything about how safe a medicine is and how well it works. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- **This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.**

7. Are there plans for other studies?

At the time of writing this summary, no more studies looking at **atezolizumab** and **erlotinib** or **alectinib** are planned.

Other studies looking at **atezolizumab** alone or taken with other medicines for people with NSCLC are taking place.

8. Where can I find more information?

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

- https://www.clinicaltrials.gov/ct2/show/record/NCT02013219
- https://forpatients.roche.com/en/trials/cancer/lung-cancer/a-phase-1b-study-of-atezolizumab-in-combination-with-er-86113.html

If you would like to find out more about the results of this study, the titles of the relevant scientific papers are:

- "Safety and Clinical Activity of Atezolizumab Plus Erlotinib in Non-Small Cell Lung Cancer". The authors of this scientific paper are Charles M. Rudin, Andres Cervantes, Afshin Dowlati, Scott N. Gettinger, and others. The paper is published in the journal 'ESMO Open', volume number 8, on page 101160. The paper was published online on March 03, 2023.
- "Brief Report: Safety and Antitumor Activity of Alectinib Plus Atezolizumab From a Phase 1b Study in Advanced ALK-Positive NSCLC". The authors of this scientific paper are Dong-Wan Kim, Shirish Gadgeel, Scott N. Gettinger, Sai-Hong Ignatius Ou, and others. The paper is published in the journal 'JTO Clinical and Research Reports', volume number 3, on page 100367. The paper was published online on June 25, 2022.

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-phase-1b-study-of-atezolizumab-in-combination-with-er-86113.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 phase 1b study of the safety and pharmacology of atezolizumab (anti-PD-L1 antibody) administered with erlotinib or alectinib in patients with advanced non-small cell lung cancer".

- The protocol number for this study is: WP29158.
- The ClinicalTrials.gov identifier for this study is: NCT02013219.
- The EudraCT number for this study is: 2013-004382-13.