

## Summary of Clinical Trial Results

### A study that looked at whether adding atezolizumab to cobimetinib and vemurafenib works, and is safe, in people with a type of untreated skin cancer that cannot be removed by surgery

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 (January 2025).

The study started in January 2017 and finished in July 2024. This summary was written after the study had ended.

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. This study's results may differ from those of other studies that used 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

1. General information about this study
2. Who took part in this study?
3. What happened during the study?
4. What were the results of the study?
5. What were the unwanted effects?
6. How has this study helped research?
7. Are there plans for other studies?
8. Where can I find more information?

#### Thank you to the people who took part in this study

The people who took part have helped researchers answer important questions about treating a type of melanoma (skin cancer) that has spread to other organs in the body, and that cannot be removed by surgery. This study looked at treating this type of skin cancer with 'atezolizumab', 'cobimetinib' and 'vemurafenib'.

## Key information about this study

- This study was done to find out how well adding the study medicine (called atezolizumab) to existing cancer medicines (cobimetinib and vemurafenib) worked in people who have a specific type of skin cancer that has spread to other organs, and thus cannot be removed by surgery.
- In this study, people were given atezolizumab, cobimetinib and vemurafenib (**Group A**, atezolizumab combination) or placebo plus cobimetinib and vemurafenib (**Group B**, placebo combination). A placebo is something that looked the same as atezolizumab but did not contain any real medicine.
- The study was ‘randomised’, which means it was decided by chance which treatment each person was given.
- This study included 514 patients (256 in **Group A**, 258 in **Group B**) patients from 112 study centres in 20 countries
- The main findings were that:
  - Half of the people lived for 15 months (**Group A**) and half for 11 months (**Group B**) before their cancer got worse.
  - At the end of the study, the proportion of people whose cancer became worse was 58% (148 out of 256 people) in **Group A** and 69% (179 out of 258 people) in **Group B**.
  - Half of the people lived for more than 39.0 months (**Group A**) and half for more than 25.8 months (**Group B**)
  - At the end of the study, the proportion of people who died was 55% (140 out of 256) in **Group A**, and 63% of people (162 out of 258) in **Group B**.
  - Around 51% of people (118 out of 232) in **Group A** had serious unwanted effects related to their treatment compared with around 43% of people (120 out of 279) in **Group B**.
- This study is now finished, and this document provides a summary of the final analysis.
- This study showed that the addition of atezolizumab to combination treatment was safe, helped people to live longer and their cancer took longer to get worse compared to people who were given the placebo combination.

## 1. General information about this study

### Why was this study done?

Melanoma is a serious type of skin cancer that starts in pigment-producing cells called melanocytes. If it is found early enough, treatment usually works well. But if it

---

advances or spreads to other parts of the body, it becomes very dangerous. Only about 15–17% of people with this type of advanced skin cancer will live for five years after being diagnosed.

Nearly half of all skin cancers have a change in a gene (section of DNA) called *BRAF*, which helps the cancer grow. The most common change is called *V600E*. Medicines that treat advanced skin cancer with the *BRAF*<sup>V600E</sup> change have been developed. These medicines aim to block the pathways that help the cancer grow, and make the cancer cells more vulnerable to the immune system. Despite this, there is still a need for better treatments for advanced skin cancer.

Atezolizumab is a medicine that helps the immune system fight cancer. It works by binding to a protein on the surface of some cancer cells, which keeps cancer cells from suppressing the immune system. This allows the immune system to attack and kill the cancer cells. In the United States, it is approved to be used with two other cancer medicines, cobimetinib and vemurafenib, as part of triple therapy.

In this study, researchers wanted to see if adding atezolizumab to cobimetinib and vemurafenib could help people with a specific type of advanced skin cancer with the *BRAF*<sup>V600E</sup> change to live longer, or prevent the cancer from worsening.

---

### What was the medicine being studied?

---

This study looked at a medicine called ‘atezolizumab’ (known by its brand name Tecentriq®) in combination with other medicines.

- You say this as ‘at-ez-oh-liz-uh-mab’.
- Atezolizumab is a medicine that helps the immune system fight cancer.
- It works by blocking a protein which cancer cells use to hide from the immune system. By blocking this protein, atezolizumab helps the immune system find and attack the cancer cells. This makes it harder for the cancer to grow and spread.

Atezolizumab was compared with a ‘placebo’.

- You say this as ‘plah – see – bo’
- The placebo looked the same as atezolizumab but contained no real medicine. This means it had no medicine-related effect on the body.

Both atezolizumab and placebo were given with existing cancer medicines. The cancer medicines used in this study were:

- Cobimetinib
  - Cobimetinib works by blocking a protein that is important for cell growth. This makes it harder for cancer cells to grow and spread.
- Vemurafenib
  - Vemurafenib works by blocking a protein that is often changed in skin cancer cells. This protein, called BRAF, helps the cancer cells grow and

divide. By blocking BRAF, vemurafenib slows down or stops the growth of the cancer cells.

### What did researchers want to find out?

---

- Researchers wanted to find out if the combination of atezolizumab, cobimetinib, and vemurafenib (**Group A, atezolizumab combination**) worked better than a placebo combined with cobimetinib and vemurafenib (**Group B, placebo combination**) in people with untreated skin cancer (see section 4, “What were the results of the study?”).
- They also wanted to find out how safe the medicine was. They did this by checking how many people had unwanted effects and seeing how serious they were when taking each of the medicines during this study (see section 5, “What were the unwanted effects?”).

#### The main question that researchers wanted to answer was:

1. How much time was there between the start of treatment and the cancer getting worse in **Group A** and **Group B**?

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

2. How long did people in **Group A** and **Group B** live (during the study)?
3. How many people had unwanted effects during the study, and how many of these unwanted effects were serious (meaning they were life-threatening, required hospital care, or caused lasting problems)?

### What kind of study was this?

---

This study was a ‘**Phase 3**’ study. This means that atezolizumab had been tested in a smaller number of people with skin cancer before this study. Phase 3 studies are done on a larger number of people to see if a drug works better than the standard existing treatment and is safe enough for it to be approved by the health authorities as a treatment that a doctor can prescribe.

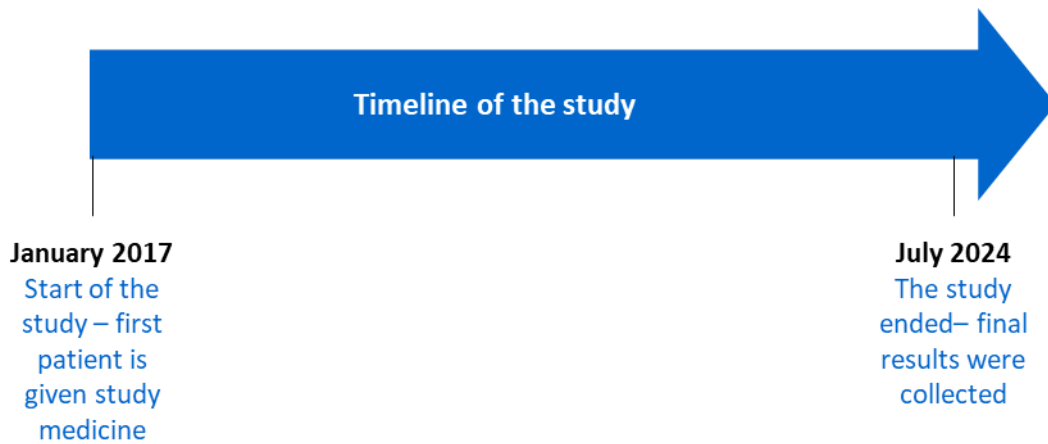
The study was ‘**randomised**’. This means it was decided by chance which medicine combinations people in the study would be given – like tossing a coin. Randomly choosing which medicine people take makes it more likely that the types of people in both groups (for example, age and race) will be similar. 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 nor 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?

The study started in January 2017 and finished in July 2024. This summary was written after the study had ended.

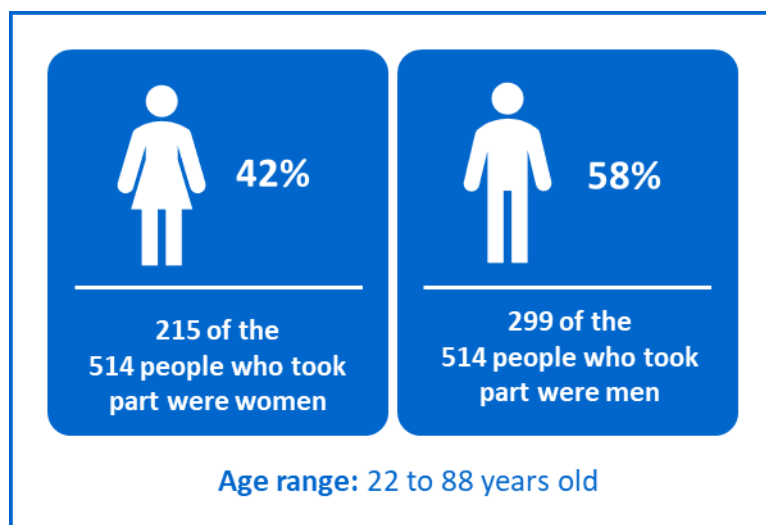


The study took place at 112 study centres in 20 countries.

## 2. Who took part in this study?

In this study, 514 people with untreated skin cancer that had spread and that could not be removed by surgery took part.

People who took part in the study were between 22 and 88 years of age. More information on the people who took part is given below:



People could take part in the study if:

- They were at least 18 years old.
- They had untreated *BRAF*<sup>V600E</sup> skin cancer that had spread and that could not be treated with surgery.
- They could perform activities as well or almost as well as they could before they got cancer.

People could not take part in the study if:

- They had previously received any treatment for their cancer.

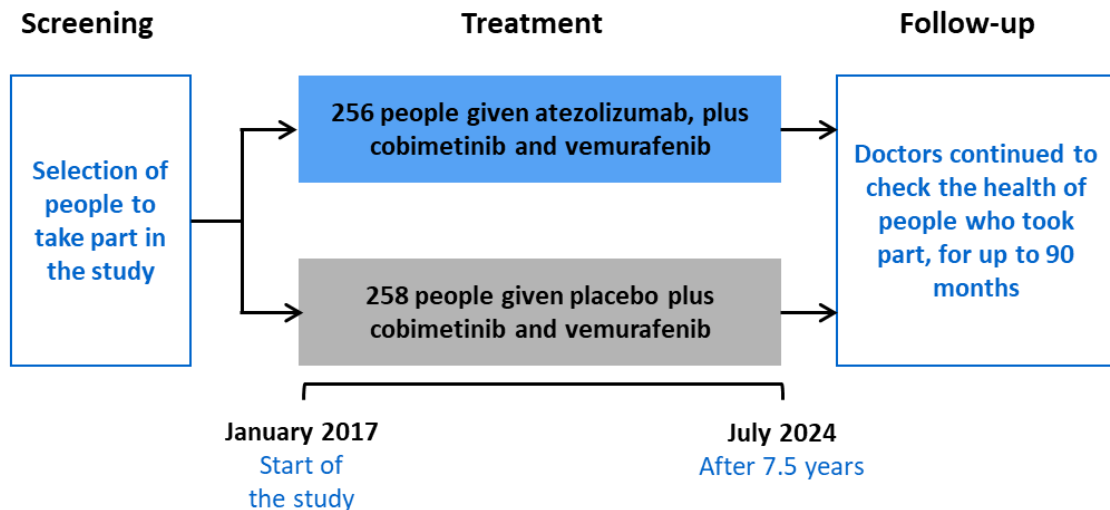
### 3. What happened during the study?

During the study, people with *BRAF*<sup>V600E</sup> skin cancer were selected by chance to get one of two treatments. The treatments were chosen at random – by a computer.

- In **Group A**, 256 people were given **atezolizumab**, plus **cobimetinib** and **vemurafenib**
  - **Atezolizumab** 840 mg given by drip (infusion) into a vein over 1 hour, followed by over 30 minutes to 1 hour depending on tolerance and repeated every 2 weeks for 16.7 monthly rounds
  - **Cobimetinib** 60 mg taken by mouth once daily for 3 weeks (followed by a week break from treatment) and repeated for each monthly round
  - **Vemurafenib** 720 mg taken by mouth twice daily
- In **Group B**, 258 people were given a **placebo** plus **cobimetinib** and **vemurafenib**
  - **Placebo** given by drip (infusion) into a vein with the same timing as atezolizumab in Group A
  - **Cobimetinib** 60 mg taken by mouth once daily for 3 weeks (followed by a week break from treatment) and repeated for each monthly round
  - **Vemurafenib** 960 mg taken by mouth twice daily

**Group A** and **group B** continued treatment until their cancer got worse or they experienced unacceptable unwanted effects. Treatment would stop after a maximum of 80 rounds or if people decided to stop participating in the study.

When the study finished, the people who took part were asked to go back to their study centre for more visits – to check their overall health. More information about what happened in the study is shown below.



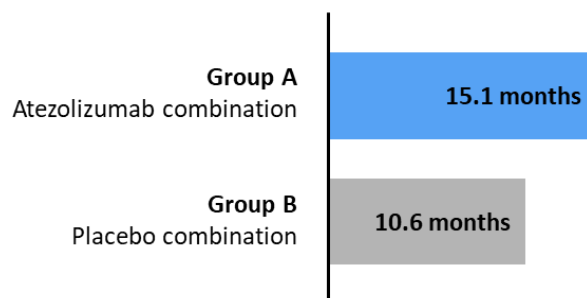
#### 4. What were the key results of the study?

##### Question 1: How much time was there between the start of treatment and the cancer getting worse in **Group A** and **Group B**?

Researchers looked at how much time there was before the cancer became worse (in other words, spread to another part of the body, spread further, or grew larger) in **Group A** and **Group B**.

- In **Group A**, half of the people in this group lived for 15.1 months before their cancer got worse.
- In **Group B**, half of the people in this group lived for 10.6 months before their cancer got worse.

How long did half of the people in each group live without their cancer getting worse?



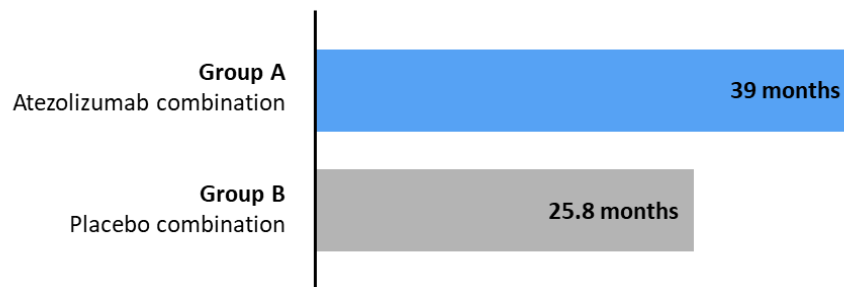
At the end of the study, the proportion of people whose cancer became worse was 58% (148 out of 256 people) in **Group A** and 69% (179 out of 258 people) in **Group B**.

## Question 2: How long did people in **Group A** and **Group B** live (during the study)?

Researchers looked at how long people lived on average during the study. This was compared between **Group A** and **Group B**. This information was collected from both groups from **January 2017** until **July 2024**.

- **Group A** (atezolizumab combination) tended to live longer compared to Group B (placebo combination).
- In **Group A**, half of the people in this group lived longer than 39.0 months.
- In **Group B**, half of the people in this group lived longer than 25.8 months.

On average, how long did people in each group live for after receiving treatment?



At the end of the study, 55% of people (140 out of 256 people) in **Group A** and 63% of people (162 out of 258 people) in **Group B** had died.

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 unwanted effects?

Unwanted 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 unwanted effects were related to the treatments in the study.
- Not all of the people in this study had all of the unwanted effects.
- Unwanted effects may be mild to very serious, and can be different from person to person.
- It is important to be aware that the unwanted effects reported here are from this single study. Therefore, the unwanted effects shown here may differ from those seen in other studies or on the medicine leaflet.
- Unwanted effects can vary from mild to serious and vary from person to person.
- Serious and common unwanted effects are listed in the following sections.



Sometimes, people who join a study do not receive the treatment they were assigned. The safety results shown in this section are for all the people who took the medicines during the study. Results were collected and analysed for 232 people in **Group A** and 279 people in **Group B**.

### Serious unwanted effects

---

An unwanted effect is considered ‘serious’ if it is life-threatening, needs hospital care, or causes lasting problems.

Around 51% of people taking the atezolizumab combination (118 out of 232 people) had at least one serious unwanted effect, compared with around 43% of people taking the placebo plus combination (120 out of 279 people).

The most common serious unwanted effects that were related to the treatments in the study are shown in the following table. These are unwanted effects that happened in at least 2% of people in either group. Some people had more than one unwanted effect – this means that they are included in more than one row in the table.

<b>Most common serious unwanted effects reported in this study in at least 2% of people</b>	<b>Group A</b> Atezolizumab combination (232 people)	<b>Group B</b> Placebo combination (279 people)
Fever	6% (14 out of 232)	4% (11 out of 279)
Increased levels of a muscle protein	0.9% (2 out of 232)	2.5% (7 out of 279)
Increased levels of a liver protein	2% (5 out of 232)	0.7% (2 out of 279)
Pneumonia	3.9% (9 out of 232)	1.8% (5 out of 279)
Sudden kidney injury	3.0% (7 out of 232)	0.4% (1 out of 279)
Inflammation of lung tissue	2.2% (5 out of 232)	1.1% (3 out of 279)

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

- In **Group A**, 97 out of 232 people (42%) stopped taking their medicine.
- In **Group B**, 92 out of 279 people (33%) stopped taking their medicine.

### Other unwanted effects

---

You can find information about other unwanted 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 514 people with a specific type of skin cancer which has spread, and that cannot be removed by surgery. These results helped researchers learn more about the effects of adding atezolizumab to the existing cancer medicines cobimetinib plus vemurafenib.

Overall, this study showed that in people who were given the atezolizumab combination, their cancer took longer to get worse than in people who were given the placebo combination. Also, the results suggest that people who were given the atezolizumab combination lived longer than people who were given the placebo combination. The unwanted effects observed in this study were similar to what doctors already know about atezolizumab, cobimetinib, and vemurafenib.

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. This study's results may differ from those of other studies that used 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 safety and effects of atezolizumab are still happening.

## 8. Where can I find more information?

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

- <https://clinicaltrials.gov/study/NCT02908672>
- <https://forpatients.roche.com/en/trials/cancer/skin-cancer/a-study-of-atezolizumab-plus-cobimetinib-and-vemurafenib-versus-.html>

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

- [Ascierto PA et al. Overall survival with first-line atezolizumab in combination with vemurafenib and cobimetinib in \*BRAF\*<sup>V600</sup> mutation-positive advanced melanoma \(IMspire150\): second interim analysis of a multicentre, randomised, phase 3 study. \*Lancet Oncol.\* 2023;24\(1\):33–44.](#)
- [Dummer R, Welti M, Ramelyte E. The role of triple therapy and therapy sequence in treatment of BRAF-mutant metastatic melanoma. Response to overall survival with first-line atezolizumab in combination with vemurafenib and cobimetinib in BRAFV600 mutation-positive advanced melanoma \(IMspire150\): second interim](#)

[analysis of a multicentre, randomised, phase 3 study. \*Journal of Translational Medicine\* 2023;21\(1\):529.](#)

- [Gutzmer R et al. Atezolizumab, vemurafenib, and cobimetinib as first-line treatment for unresectable advanced BRAF<sup>V600E</sup> mutation-positive melanoma \(IMspire150\): primary analysis of the randomised, double-blind, placebo-controlled, phase 3 trial. \*Lancet\*. 2020;395\(10240\):1835–1844.](#)

### 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 here](#)
- Contact a representative at your local Roche office.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

### Who organised and paid for this study?

---

This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland.

### Full title of the study and other identifying information

---

The full title of this study is: “A Study of Atezolizumab Plus Cobimetinib and Vemurafenib Versus Placebo Plus Cobimetinib and Vemurafenib in Previously Untreated BRAF<sup>V600</sup> Mutation-Positive Patients With Metastatic or Unresectable Locally Advanced Melanoma”.

The study is known as ‘CO39262’.

- The protocol number for this study is: CO39262.
- The ClinicalTrials.gov identifier for this study is: NCT02908672.
- Study Report CO39262, Roche data on file.