Clinical Trial Results – Layperson Summary

Study of atezolizumab in people with untreated *BRAF*^{V600} wild-type melanoma: summary of the clinical trial cohort C

ClinicalTrials.gov study title: a phase Ib study evaluating cobimetinib plus atezolizumab in patients with advanced *BRAF*^{v600} wild-type melanoma who have progressed during or after treatment with anti-PD-1 therapy and atezolizumab monotherapy in patients with previously untreated advanced *BRAF*^{v600} wild-type melanoma

About this summary

This summary of the Phase 1b clinical trial (NCT03178851) was prepared to provide study participants and members of the public with information on why the study was done and the main results.

This summary is based on information known at the time of writing (March 2021). More information may now be known.

The people who took part in the study got different treatments in different groups; these different groups were called 'cohorts'. This summary is about people in cohort C of the trial. People in cohorts A and B received different study treatments, so a different summary has been written. The study started in June 2017 and finished in September 2020.

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.

Contents of the summary

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 skin cancer called 'melanoma' and to learn more about the study medicine.

F. Hoffmann-La Roche Ltd, the sponsor of this study, would like to thank the participants for their contribution. If you have any questions about treatment options in your country, please speak with your doctor.

Key information about this study

- This study assessed the effects and safety of atezolizumab in patients with untreated advanced *BRAF* wild–type melanoma.
- In this study, people were given a study medicine called 'atezolizumab', and the researchers measured what effects this had on peoples' cancer.
- This study cohort included 52 people in Bosnia and Herzegovina, Brazil, South Africa and Ukraine.
- The main finding was that atezolizumab was 'active' in patients with untreated advanced *BRAF* wild–type melanoma. This means that the drug had an effect on the patients' cancer.
- The majority of patients (83%) had side effects from the study drug
- This study is now finished and this document provides a summary of the final analysis.

1. General information about this study

Why was this study done?

Melanoma is a type of skin cancer. There are different types of melanoma but more than half of melanoma cases are linked to mutations in the *BRAF* gene. Some people with melanoma have *BRAF* genes that have no mutations, these people are said to have *BRAF* wild-type melanoma. Knowing the characteristics of the cancer can help doctors decide which treatments are likely to be successful.

Some people with *BRAF* wild-type melanoma are given medicines to encourage the body's immune system to attack the tumours. This is called immunotherapy. Developing new medicines for immunotherapy could help more people get a benefit from these treatments.

Cohort C included people with advanced *BRAF* wild-type melanoma, who had not previously received treatment for melanoma.

What were the study medicines?

In this study, a new cancer immunotherapy called atezolizumab was given to patients. Atezolizumab works by blocking a pathway called PD-1/PD-L1. This allows the body's own immune cells to become active and fight the cancer cells.

What did researchers want to find out?

Researchers wanted see how well atezolizumab would work to stop the cancer from getting worse (see section 4 "What were the results of the study?"). The study also looked at the safety (the side effects associated with a drug or treatment) of atezolizumab (see section 5 "What were the side effects?").

The objective of the study in cohort C was to see how well atezolizumab worked as a treatment for patients with previously untreated advanced *BRAF* wild-type melanoma. This will help to decide if atezolizumab could be offered as a treatment and whether it should be tested in bigger trials with more patients.

The main questions that researchers wanted to answer were:

1. **How well does atezolizumab work to stop cancer growth?**

The researchers measured how patients' cancer changed during treatment with atezolizumab.

They worked out how many patients' cancer got better during this time, including people whose cancer went away completely as well as people whose cancer got a bit better. This is known as the overall response rate.

They also monitored how many patients' cancer got better or stayed the same. This is called the disease control rate.

2. **How long did the drug last inside the body? Did the patients' immune systems respond to the drug?**

The researchers measured how much of the medicine was still in patients' blood at different times, and whether the patients' immune systems were reacting against the medicine. This will help researchers to figure out when and how much of the medicine to give in the future.

3. **How many people had side effects during the study, and how many were serious?**

Side effects are unwanted medical problems that happen during a study. The researchers looked at what side effects happened and how bad they were, to help learn more about the safety of the study medicines.

What kind of study was this?

This study was a 'Phase 1b' study. This means that atezolizumab has previously been tested in healthy people. In this study, atezolizumab was given to people with advanced melanoma.

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

2. Who took part in the study?

The study started in June 2017 and this summary includes the final results of the study, up to September 2020.

People could take part in the study if they met all of the following conditions:

- Aged older than 18 years
- Diagnosed with *BRAF*^{V600} wild-type melanoma
- Had not received any other anti-cancer therapy for their melanoma
- Fully physically active or restricted in physically strenuous activity only (ECOG PS 0–1)
- Had not been diagnosed with ocular melanoma, a type of cancer that develops in and around the eye
- Did not have any other active cancer that had spread from the original tumour within the last 3 years.

The people who took part in the study were an average of 61 years old, and 2 out of 3 people involved were male.

The study took place at 17 study centres across Bosnia and Herzegovina, Brazil, South Africa and Ukraine. This map shows the countries where the study took place.

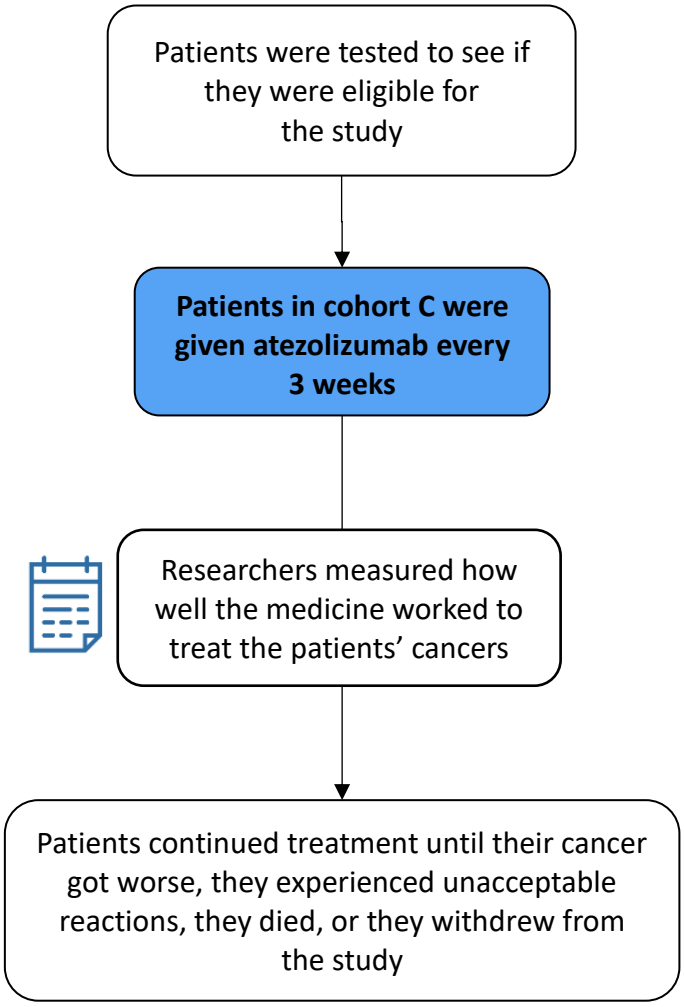
- Bosnia and Herzegovina
- Brazil
- South Africa
- Ukraine

3. What happened during the study?

All patients in cohort C received atezolizumab.

- **Atezolizumab:** Atezolizumab 1200 mg was given by drip (infusion) into a vein once every 3 weeks.

Patients continued treatment until: their cancer got worse, they experienced unacceptable side effects, they died, they became pregnant, or they withdrew from the study.



4. What were the results of the study?

How well did atezolizumab work to stop cancer growth?

Researchers monitored patients' cancers to see whether they got better or worse during treatment with atezolizumab. They worked out how many patients' cancers got better during this time. This is known as the overall response rate.

Out of 52 people in cohort C, 20 peoples' cancer got better during the study, so the overall response rate was 39%. In total, 24 peoples' cancers did not get worse during the study, so the disease control rate was 46%.

These results mean that atezolizumab was active in patients with previously untreated advanced *BRAF* wild-type melanoma. This means that atezolizumab could be investigated in other studies as a potential treatment for melanoma.

How long did the drug last inside the body? Did the patients' immune systems respond to the drug?

The amount of atezolizumab in the blood at different times was similar to that found in previous studies.

For around 10% of patients, their bodies had an immune response to atezolizumab. More research will be needed to work out if these immune responses affected how well atezolizumab worked as a treatment for melanoma.

5. What were the side effects?

Side effects (sometimes called 'adverse reactions') are unwanted medical problems that happen during a study, which may or may not be directly related to the medicines being tested in the study.

Moderate side effects are those that are not life threatening, but result in a patient needing additional treatment. Severe side effects are those that may result in death, or require or prolong time in hospital. It may be possible to reduce the number and severity of side effects by lowering the dose of medicine, or by giving the person new treatments.

The study looked at the safety of atezolizumab. Researchers did this by measuring the number and type of side effects in all the people in the study.

Around 8 out of every 10 people in study cohort C (83%) had a side effect related to atezolizumab.

A side effect is considered 'serious' if it is life threatening, needs hospital care, or causes lasting problems. In this cohort, about 3 in every 10 people (29%) had serious side effects.

Three patients in cohort C had a side effect that resulted in death. Three patients in cohort C decided to stop taking the study medicine because of side effects.

6. How has this study helped research?

The information presented here is a study cohort of 52 people with previously untreated advanced *BRAF* wild-type melanoma. These results helped researchers to learn more about melanoma cases and how they link to mutations in the *BRAF* gene. They also help researchers to understand more about the effects of treatment with atezolizumab.

The results in this summary are only relevant to people with untreated advanced *BRAF* wild-type melanoma.

In this study, atezolizumab was shown to be active in patients with previously untreated advanced *BRAF* wild-type melanoma. Around 39% of patients' cancer got better with the study medicine, and around 46% of patients' cancers did not get any worse.

Researchers monitored how long the medicines stayed in patients' blood. These results matched what was expected, and should help researchers to figure out when to give people the medicine. Some patients had an immune response to the study medicine. It was not possible to assess whether this affected how well the medicines worked in this study, so this is being investigated further.

The safety of atezolizumab was similar to previous studies. Most people had side effects from the study medicine, but were able to manage these side effects.

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 atezolizumab are taking place.

8. Where can I find more information?

You can find more information about this study on these websites:

- https://clinicaltrials.gov/ct2/show/NCT03178851
- https://forpatients.roche.com/en/trials/cancer/skin-cancer/cobimetinib--targeted-therapy--plus-atezolizumab--immunotherapy-.html

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/skin-cancer/cobimetinib--targeted-therapy--plus-atezolizumab--immunotherapy-.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 Ib study evaluating cobimetinib plus atezolizumab in patients with advanced *BRAF*^{V600} wild-type melanoma who have progressed during or after treatment with anti-PD-1 therapy and atezolizumab monotherapy in patients with previously untreated advanced *BRAF*^{V600} wild-type melanoma

- The protocol number for this study is: CO39721
- The ClinicalTrials.gov identifier for this study is: NCT03178851
- The EudraCT number for this study is: 2016-004402-34