

Clinical Trial Results – Layperson Summary

A study to see whether combining two drugs – atezolizumab plus bevacizumab – works and is safe for people with liver cancer who have not had any chemotherapy, and to compare the combination with atezolizumab taken alone

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 (December 2019). More information may now be known.

The study started in July 2016 and is expected to end in August 2021. This summary includes the results up until June 2019. At the time of writing this summary, the study is still going on – study doctors are still collecting information. This summary will be updated when the study ends.

One study can’t tell us everything about the possible side effects of a medicine and how well the medicine works. It takes lots of people in many studies to learn as much as we can about a medicine. 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.**

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Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about liver cancer and about treatment with a drug called atezolizumab (the study medicine) taken either with another study medicine called bevacizumab or on its own.

Key information about this study

- This study is being done to:
 - See whether the combination of two study medicines, atezolizumab plus bevacizumab, works in people with liver cancer (Does it shrink their tumours and/or give them a longer time before their cancer gets worse?)
 - See whether the combination of atezolizumab plus bevacizumab is safe in people with liver cancer (how many people had side effects)
 - Compare the combination of atezolizumab plus bevacizumab with atezolizumab alone, to see which treatment works better in people with liver cancer
- The people in this study were in one of two groups: **Group 1** or **Group 2**.
 - All the people in **Group 1** are taking a combination of two study medicines (atezolizumab plus bevacizumab)
 - **Group 1** was started almost 2 years before **Group 2** so that the doctors could first learn if this combination worked and was safe
 - The people in **Group 2** are taking **either** both of the two study medicines (atezolizumab plus bevacizumab) **or** just atezolizumab. It was decided by chance using a computer which treatment each person in **Group 2** would take.
 - **Group 2** was designed to show whether or not the two drugs together worked better than atezolizumab alone
- This study included 223 people in 7 countries/regions.
- So far, the study has shown that:
 - Just over one-third of the people (36%) in **Group 1** had smaller or no tumours after taking both atezolizumab and bevacizumab for as long as almost 3 years (34 months).
 - In people in **Group 2** taking atezolizumab plus bevacizumab for as long as 11 months, their tumours stopped growing for longer (an average of 6 months) than in people taking atezolizumab alone (whose tumours stopped growing for an average of 3 months).
- In **Group 1**, 24% (25 out of 104 people) who took atezolizumab plus bevacizumab for as long as almost 3 years had serious side effects (side effects that were life-threatening, or for which they needed to go to hospital).
- In **Group 2**, 12% (7 out of 60 people) who took atezolizumab plus bevacizumab for almost 1 year had serious side effects compared to 3% (2 out of 58 people) taking atezolizumab alone.
- At the time of writing this summary, the study is still going on. It is expected to end in August 2021.

1. General information about this study

Why was this study done?

People with liver cancer that has spread to other parts of the body usually take ‘targeted’ medicines. They are called targeted medicines because they can tell the difference between cancer cells and normal healthy cells and they ‘target’ and kill only the cancer cells. However, targeted medicines do not work in everyone, or they only work for a short time and then the cancer gets worse again. Some people have to stop taking these medicines because the side effects are too bad.

Doctors can also choose to give a treatment called immunotherapy, which is medicine that helps a person’s own immune system to attack tumours. Immunotherapy medicines also work better in some people than in others, or work only for a short time. This may be because the cancer can ‘hide’ from the immune system and/or learn to ‘escape’ the immune system’s attacks.

Giving immunotherapy together with a different medicine acts like a ‘double attack’ on the cancer. This double attack may work better than either of the medicines on their own. Immunotherapy is sometimes combined with a type of medicine called an ‘anti-angiogenic’ medicine that stops the cancer cells from forming the new blood vessels that it needs to grow.

In this study, researchers wanted to see if combining an immunotherapy medicine with a medicine that stops blood vessels from forming would shrink tumours or stop them from growing in people with liver cancer. They also wanted to see if the combination of the two medicines is safe for people to take. Finally, they wanted to see if the combination would stop the cancer from growing for longer than the immunotherapy alone. The people in the study had liver cancer that had not been treated with chemotherapy before they started taking the study medicines.

What are the study medicines?

This study looked at a medicine called ‘atezolizumab’ (known by its brand name, Tecentriq®).

- You say this as ‘a – teh – zo – liz – oo – mab’.
- The body’s immune system fights diseases like cancer. However, cancer cells can block (stop) the immune system from attacking the cancer. Atezolizumab releases this blockage – meaning that the immune system is able to fight the cancer cells.
- When people take atezolizumab, their tumour (cancer) may get smaller.
- This medicine is a type of immunotherapy.

In **Group 1**, atezolizumab was taken together with another medicine called bevacizumab (known by its brand name Avastin®).

- You say this as ‘beh – va – si – zoo – mab’.
- Cancers grow their own blood vessels so they can get food and oxygen from the blood. The cancer needs a protein called vascular endothelial growth factor (VEGF) to do this. Bevacizumab blocks VEGF and stops the cancer from growing blood vessels, so the cancer starves and can't grow.
- Researchers gave all the people in this group atezolizumab plus bevacizumab to see if this combination would shrink tumours or stop them from growing, and to see how many people had side effects when taking these medicines together.

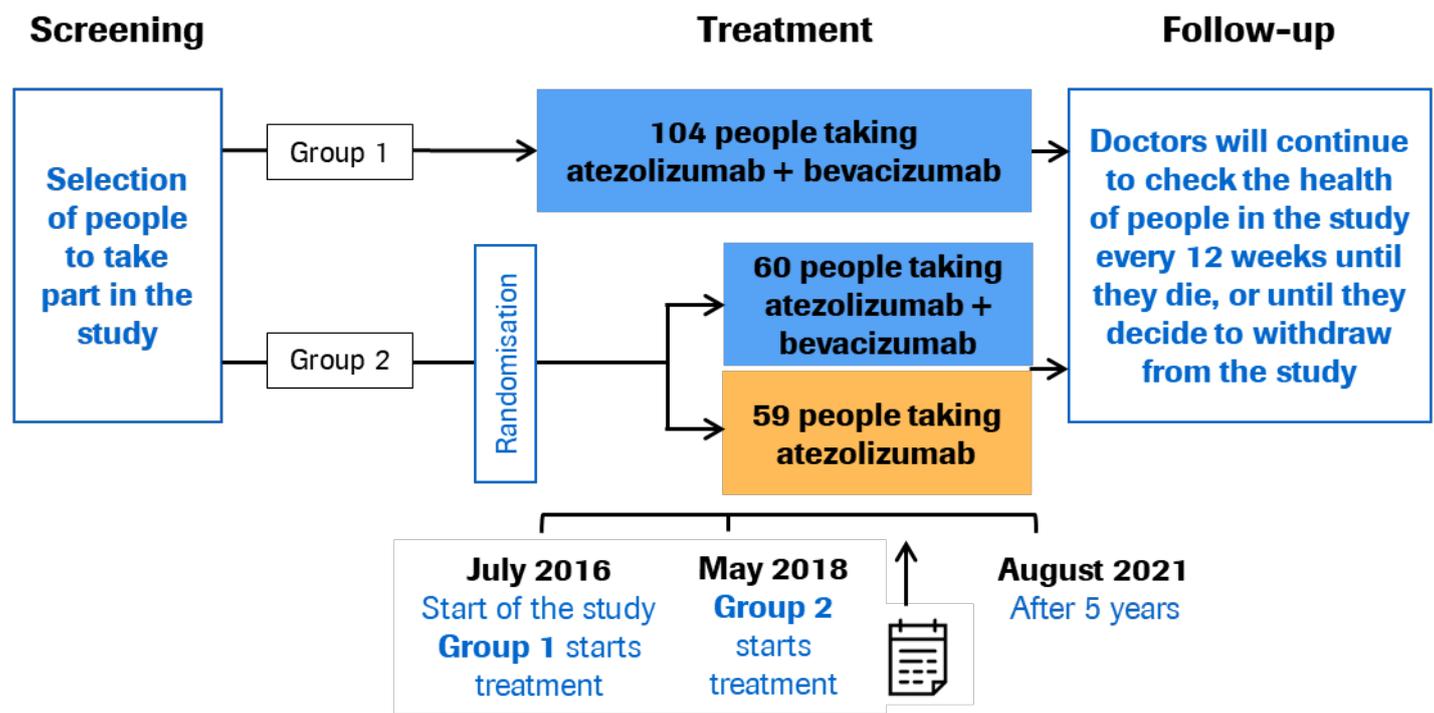
In **Group 2**, atezolizumab was taken either with bevacizumab or alone.

- Researchers gave some people the combination of atezolizumab plus bevacizumab and some people atezolizumab alone. They did this so they could see which treatment would stop the cancer from growing for longer, and which benefits or side effects would be caused by the combination.

How the study was done

During the study:

- All the people in **Group 1** took atezolizumab plus bevacizumab
- In **Group 2**, which started almost 2 years after **Group 1**, people were selected by chance to take either atezolizumab plus bevacizumab, or just atezolizumab
 - The treatments were selected at random for the people in **Group 2** by a computer.
- This picture shows what has happened in the study so far – and what the next steps are.



- This study is still going on. The  symbol on the timeline shows when the information in this summary was collected – almost 3 years after the study started (June 2019). Some people are still being treated with the study medicines.
- The people in **Group 2** started taking the study medicine later than the people in **Group 1**, so doctors have been studying the people in **Group 2** for a shorter time – just over 1 year.
- When the study ends, the people who took part will be asked to go back to their study centre for more visits – to check their overall health. These people will continue to be checked until the study ends. These visits are important to determine how long people live on this study.

What did researchers want to find out?

- Researchers wanted to see (1) whether treating people who have liver cancer with a combination of study medicines (atezolizumab plus bevacizumab) would make their tumours shrink and/or give them a longer time before their cancer got worse (by looking at the results of **Group 1** and **Group 2**), and (2) whether the combination would work better than atezolizumab alone (by looking at the results of **Group 2**)
 - See section 4 'What were the results of the study?'
- They also wanted to find out how safe the combination of study medicines is – by checking how many people had side effects when taking both medicines together during this study (by looking at the results of **Group 1** and **Group 2**)
 - See section 5 'What were the side effects?'

The main questions that researchers wanted to answer were:

1. How many people in **Group 1** had smaller or no tumours after taking their study medicines (atezolizumab plus bevacizumab)?
2. In **Group 1**, how much time was there between the start of the study treatment and people’s cancer getting worse?
3. How long did people in **Group 1** live?
4. In **Group 2**, how much time was there between the start of the study treatment (atezolizumab plus bevacizumab or atezolizumab alone) and people’s cancer getting worse?
5. How many people in **Group 2** had smaller or no tumours after taking their medicine?
6. For people whose tumours got smaller during the study in **Group 1** and **Group 2** – how much time was there until their cancer then got worse again?
7. How safe is the combination of these medicines? How many people had side effects when taking both medicines together during this study?

What kind of study was this?

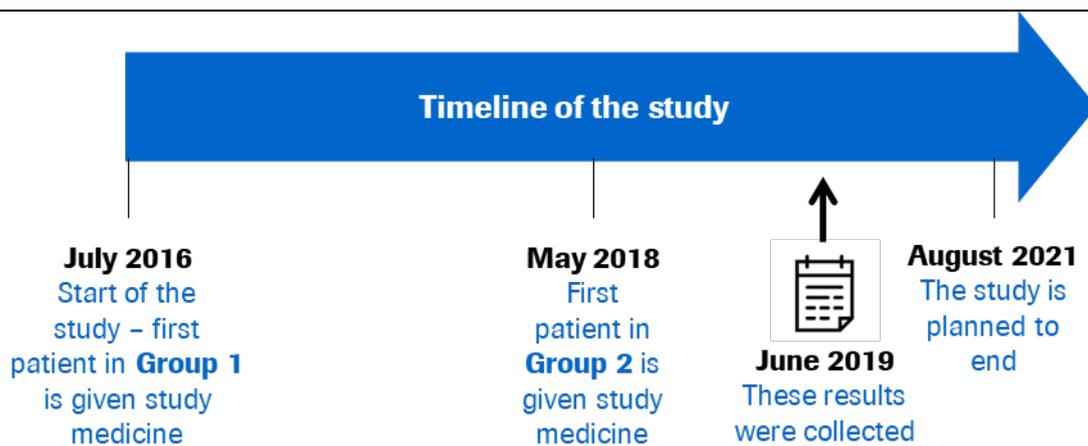
This study was a ‘Phase 1’ study, which means that this was one of the first studies of atezolizumab taken together with bevacizumab. A small number of people with liver cancer took atezolizumab plus bevacizumab, and the researchers did medical tests on the people who took part to find out more about the combination.

The study was ‘randomised’ for **Group 2** only. This means that it was decided by chance which of the medicines people in **Group 2** would be treated with – like tossing a coin.

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

When and where did the study take place?

The study started in July 2016 and is expected to end in August 2021. This summary includes the results up until June 2019. The study is still going on – study doctors are still collecting information.

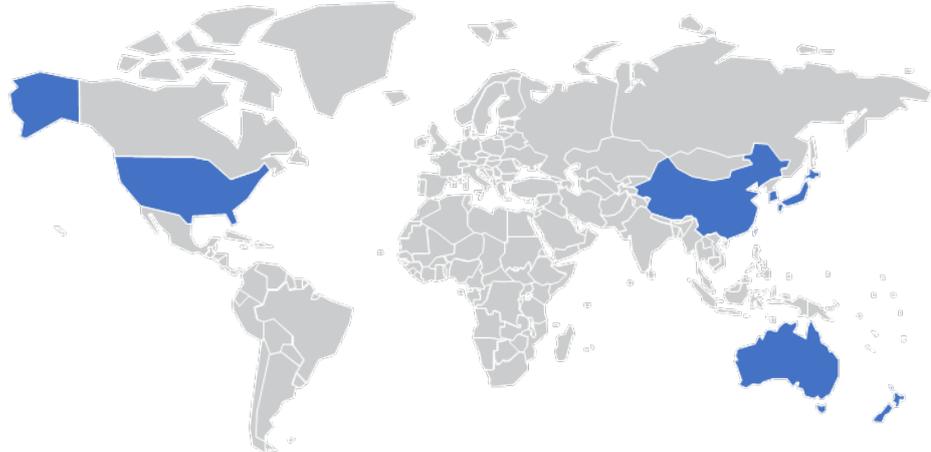


This study is still going on. The  on the timeline shows when the information in this summary was collected – after almost 3 years (June 2019).

- The people in **Group 2** started taking their study medicine later than people in **Group 1**, so doctors have been studying the people in **Group 2** for a shorter time.

The study was done at 30 study centres across seven countries/regions in Asia Pacific and the United States. This map shows the countries and regions where this study was done.

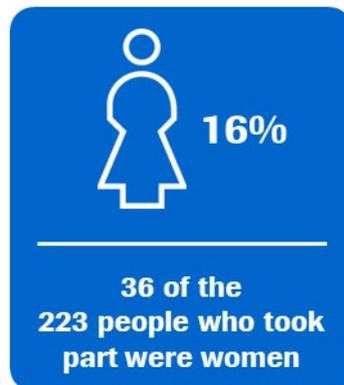
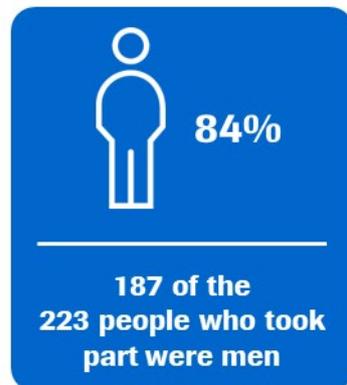
- Australia
- China
- Japan
- Korea
- New Zealand
- Taiwan
- USA



2. Who took part in this study?

In this study, 223 adults with liver cancer that had spread to other parts of their body and could not be cured with surgery took part. They had not taken chemotherapy or other medicine to treat their liver cancer before this study.

Here is more information on the people who took part in the study.



Age range: 22 to 85 years old

3. What happened during the study?

This table shows the groups in the study, what drugs they were taking, and how often the drugs were taken.

	Atezolizumab plus bevacizumab	Atezolizumab
Number of people taking this medicine in Group 1	104	-
Number of people taking this medicine in Group 2	60	59
When and how the drugs were taken	Injected into a vein once every 3 weeks	Injected into a vein once every 3 weeks

4. What were the results of the study at this point?

Question 1: How many people in Group 1 had smaller or no tumours after taking their study medicine?

Researchers looked at how many people in **Group 1** had smaller or no tumours for as long as almost 3 years (34 months) after they started their medicine

- More than one-third of the people's tumours got smaller (36%)
- In just over 1 out of 10 people (12%), their tumours had gone away or were so small they could no longer be measured

Question 2: In Group 1, how much time was there between the start of the study treatment and people's cancer getting worse?

In **Group 1**, researchers looked at how much time there was before people's cancer got worse – this information was collected over 34 months, from July 2016 until June 2019.

So far, the study showed that for the people in **Group 1** (who all took atezolizumab + bevacizumab), their cancer got worse after an average of 7 months (some people's cancer took longer to get worse and some people's cancer got worse sooner than 7 months)

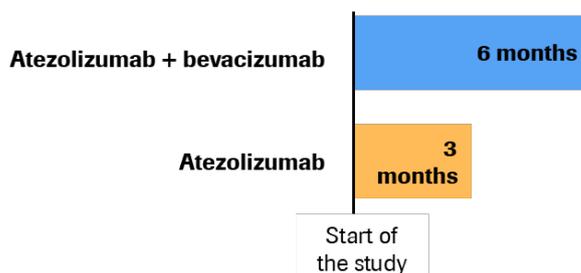
Question 3: How long did people in Group 1 live in this study?

- So far, the study showed that the people in **Group 1** (who all took atezolizumab + bevacizumab), lived for an average of 17 months after they started taking their study treatment (some people lived longer and some people died sooner than 17 months).
- This information was collected from July 2016 until June 2019
- This average of 17 months may change as the study continues and people are checked for longer

Question 4: In Group 2, how much time was there between the start of the study treatment and people's cancer getting worse?

In **Group 2**, researchers looked at how much time there was before people's cancer got worse – this information was collected from May 2018 until June 2019.

On average, how much time was there between the start of the study treatment in Group 2 and people's cancer getting worse?



- The study showed so far that for people in **Group 2** who took atezolizumab + bevacizumab, their cancer got worse after an average of 6 months (some people's cancer took longer to get worse and some people's cancer got worse sooner than 6 months).
- For people in **Group 2** who took just atezolizumab, their cancer got worse after an average of 3 months (some people's cancer took longer to get worse and some people's cancer got worse sooner than 3 months).

- These average times may change as the study continues and people are checked for longer

Question 5: How many people in Group 2 had smaller or no tumours after taking their medicine?

Researchers looked at how many people in **Group 2** had smaller or no tumours for as long as 13 months after they started taking their study medicine

How many people in Group 2 had smaller or no tumours after taking their study medicine?



- **For people taking atezolizumab plus bevacizumab:** One-fifth (20%) of these people’s tumours got smaller, and in 2 out of 10 people (20%), their tumours were gone or were too small to be measured.
- **For people taking atezolizumab:** Just under one-fifth (17%) of these people’s tumours got smaller, and in 5 out of 10 people (50%), their tumours were gone or were too small to be measured.
- These figures show us that, so far in **Group 2:**
 - slightly more of the people taking both drugs than the people taking atezolizumab alone had tumours that got smaller
 - more of the people taking atezolizumab alone than the people taking both drugs had tumours that were gone or could no longer be measured
- The study is still going on, so these differences between the treatments may change as people are checked for longer

Question 6: For people in Group 1 and Group 2 whose tumours become smaller during the study– how much time was there until their cancer then got worse again?

Researchers looked at people whose tumours had become smaller during the study, and recorded how long it took for people’s cancer to then get worse again. This information was collected from the start of the study until June 2019.

- For people in **Group 1** and **Group 2**, we still cannot determine the average number of months until their cancer got worse again. These patients will need to be checked for longer.

This section only shows the key results from the study at this point. You can find information about all other results at the end of this summary (see section 8).

5. What were the side effects?

Side effects (also known as ‘adverse reactions’) are medical problems (such as a headache) that that happen while people are taking a medicine. Side effects can vary from mild to very serious and may vary from person to person.

- Some side effects may be caused by the treatments in the study.
- Not all of the people in this study had all of the side effects.

Common and serious side effects are listed in the following sections.

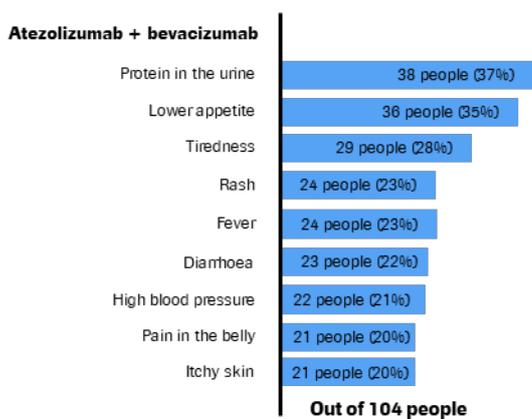
Most common side effects

The most common side effects are shown in the following picture.

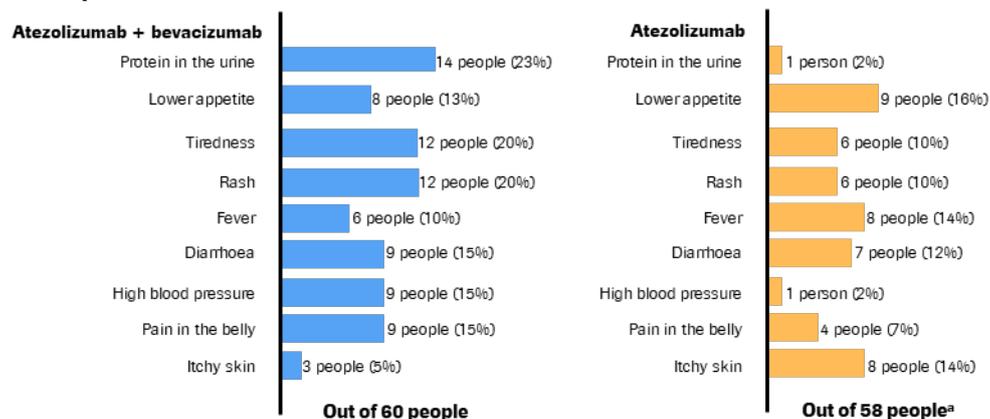
- The people in **Group 2** started taking their study medicine later than those in **Group 1**.
- The people in **Group 2** have been taking their study medicines for a shorter time than the people in **Group 1**. That might explain why fewer people taking atezolizumab plus bevacizumab in **Group 2** had side effects than people in **Group 1** who are also taking atezolizumab plus bevacizumab.
- The side effects in this study were the same as side effects that have been experienced by other people who have taken either atezolizumab or bevacizumab in other studies, or as prescribed by their doctors.
- The people taking these two study medications together in this study did not experience any new or unexpected side effects, compared to people in other studies of each individual medicine.

How many people had each of these side effects?

Group 1



Group 2



This information was collected from **Group 1** over 34 months, and from **Group 2** over 14 months

^a One person left the study without taking any study medicine, so was not included in the total number in this group.

Side effects thought to be caused by study medicines

During this study, about 7 out of every 10 people (70%) had a side effect that their doctors thought were caused by the study medicines they were taking (called a 'treatment-related' side effect).

- In **Group 1**, nearly half of people taking atezolizumab plus bevacizumab (45 out of 100 people or 45%) had a treatment-related side effect that was not considered serious (life-threatening, needed hospital care, or caused lasting problems).

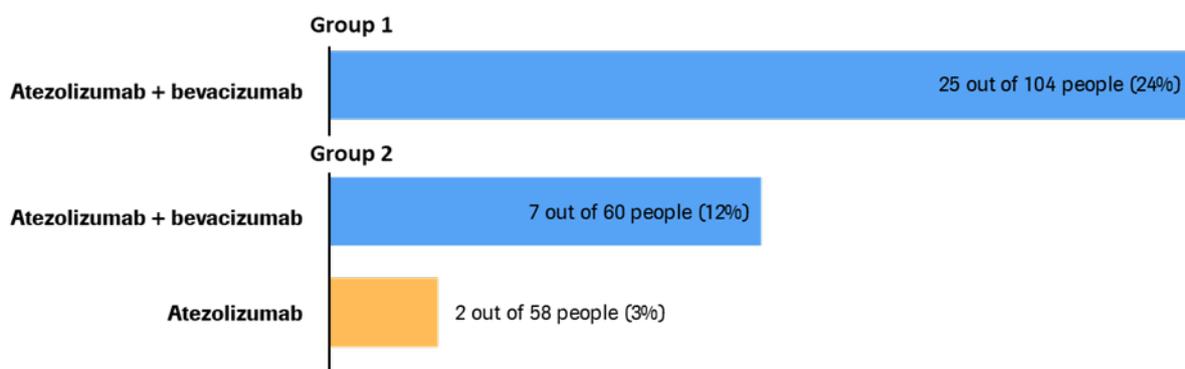
- In **Group 2**, nearly half of people taking atezolizumab plus bevacizumab (48 out of 100 people or 48%) had a treatment-related side effect that was not considered serious, compared with just over one-third (36%) of people taking atezolizumab alone.

Serious side effects

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

- During this study, overall, 15 in every 100 people (15%) had at least one serious side effect.

How many people had at least one serious side effect?



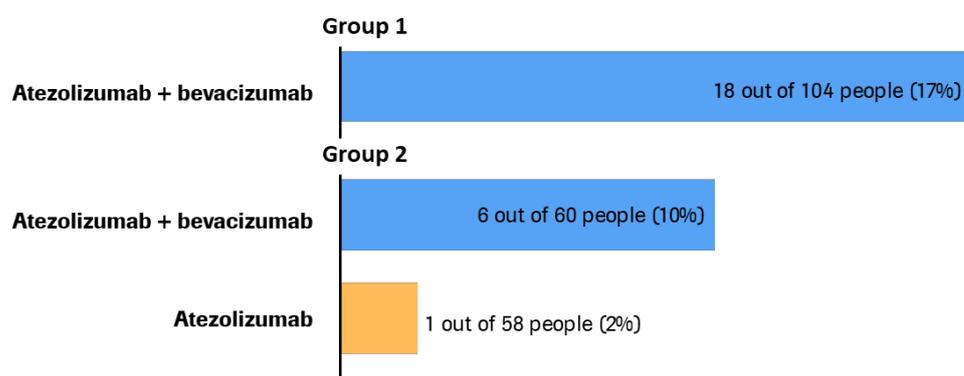
This information was collected from **Group 1** over 34 months, and from **Group 2** over 14 months.

Some people in the study died due to side effects that may have been related to one of the study medicines. These were:

- 3 out of 104 people (3%) in **Group 1** who took atezolizumab plus bevacizumab.
- 0 out of 60 in **Group 2** who took atezolizumab plus bevacizumab
- 0 out of 58 in **Group 2** who took atezolizumab
 - This information was collected from **Group 1** over 34 months, and from **Group 2** over 14 months

During the study, some people decided to stop taking their medicine because of side effects.

How many people decided to stop taking their medicine because of side effects?



This information was collected from **Group 1** over 34 months, and from **Group 2** over 14 months

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 223 people with liver cancer. The study is still going on, but researchers have been able to review the results to date. These results are helping researchers learn more about liver cancer and treatment with atezolizumab plus bevacizumab.

The people in **Group 2** started taking their study medicine later than the people in **Group 1**, so doctors have been studying people in **Group 2** for a shorter time.

- So far, the results in **Group 1** have shown that for people taking atezolizumab plus bevacizumab for as long as nearly 3 years, just over one-third (36%) had smaller or no tumours.
- So far, the results in **Group 2** have shown that for people taking atezolizumab plus bevacizumab for as long as 11 months, their cancer took an average of 6 months to get worse, compared to an average of 3 months for people taking atezolizumab alone.

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. 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?

Another study looking at the effects of atezolizumab plus bevacizumab in people with liver cancer is taking place: IMbrave150 (NCT03434379).

This study started in July 2016 and is expected to end in August 2021. This summary includes the results up until June 2019. This study is still going on – study doctors are still collecting information.

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/results/NCT02715531>
- <https://www.clinicaltrialsregister.eu/ctr-search/trial/2018-002009-67/results>
- <https://forpatients.roche.com/en/trials/cancer/a-study-of-the-safety-and-efficacy-of-atezolizumab-administered-.html>

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: "Efficacy and safety of atezolizumab with or without bevacizumab in unresectable hepatocellular carcinoma: A phase 1b study". The authors of the scientific paper are: Michael S. Lee, Baek-Yeol Ryoo, Chih-Hung Hsu, Kazushi Numata, Stacey Stein and others. The paper is published in the journal *'The Lancet Oncology'*, volume number 21, on pages 808-820.

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/a-study-of-the-safety-and-efficacy-of-atezolizumab-administered-.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 Study of the Safety and Efficacy of Atezolizumab Administered in Combination with Bevacizumab and/or Other Treatments in Participants With Solid Tumors”.

- The protocol number for this study is: GO30140.
- The ClinicalTrials.gov identifier for this study is: NCT02715531.
- The EudraCT number for this study is: 2018-002009-67.