Clinical Trial Results – Layperson Summary

A study of atezolizumab plus bevacizumab compared with active surveillance in people with liver cancer who are at high risk of their cancer coming back after surgery or ablation

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 research 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 (November 2023).

The study started in December 2019 and is still happening. This summary includes the results that were collected and analysed in October 2022, and will be updated when more results are available.

One study can't tell us everything about the possible side effects of a medicine and how well it works. It takes a lot of people in many studies to learn as much as we can about a medicine. This summary gives you information about the results from a study of a new treatment combination that may be an option for people with liver cancer who are at high risk of their cancer coming back after surgery or ablation. We have described the positive and negative results of this study in this summary, but all medical decisions regarding your individual case should be made by you and your doctor together, based on all of the available information. **You should not make decisions based on this one summary. Always talk to your doctor before making any decisions about your treatment.**

Contents of the summary

Glossary

- Active surveillance = being closely watched for cancer to come back with no treatment
- Ablation = method of removing cancer cells using heat

Thank you to the people who took part in this study

The people who took part in this study have helped researchers answer important questions about liver cancer and about treatment with a medicine called atezolizumab (the study medicine) taken with bevacizumab (another study medicine).

Key information about this study

- This study is being done to:
  - Compare treatment with atezolizumab plus bevacizumab versus active surveillance (defined as being closely watched for cancer to come back with no treatment) to see which type of care works better in people with liver cancer who have high risk of their cancer coming back after surgery (removing tumour) or ablation (removing cancer cells using heat).
  - Find out if atezolizumab plus bevacizumab could extend the length of time people were alive without their cancer coming back after surgery or ablation for liver cancer, compared with people under active surveillance.
  - Find out whether atezolizumab plus bevacizumab is safe in people who have high risk of their liver cancer coming back after surgery or ablation. How many people had side effects and how severe were the side effects?
- In this study, people are taking either the study medicine (a combination of atezolizumab plus bevacizumab – **Group A**) or getting existing standard of care (active surveillance – **Group B**).
- This study included 668 people in 26 countries/regions.
- The study has shown that:
  - People in **Group A** had a 28% lower risk of their cancer coming back or death than people in **Group B**.
  - There was not enough data to fully understand the impact of study medicines on how long people lived. About 8% of people (27 out of 334 people) in **Group A** died, compared with 6% of people (20 out of 334 people) in **Group B**.
  - Of the people who did not leave the study without receiving care, about 24% (80 out of 332 people) in **Group A** had a serious side effect, compared with about 10% (34 out of 330 people) in **Group B**.
- At the time of writing this summary, the study is still happening.

1. General information about this study

Why was this study done?

People with liver cancer that has not spread outside of the liver and is small enough may undergo surgery to remove the affected part of the liver or have their cancer removed using heat (also known as 'ablation') with the aim of curing their cancer. However, in most people, surgery or ablation only stops the cancer from coming back for a short time. Liver cancer that comes back early (within 1 to 2 years after surgery) usually grows and spreads faster, causing a person's health to worsen more in the long term compared with liver cancer that comes back later (after 4 to 5 years). People with a high risk of liver cancer coming back early usually had larger tumours, more tumours, tumours that had entered small blood vessels of the liver, or had uncontrolled tumor growth.

Adjuvant therapy is a type of medicine given after a tumour is removed by surgery or treated by ablation that may help to slow down or stop cancer from coming back. Currently, there is no approved adjuvant therapy for people with liver cancer. Instead, doctors closely watch them for signs of cancer coming back after their liver cancer surgery or ablation.

Immunotherapy is a type of medicine that helps a person's own immune system attack cancer cells. Immunotherapy medicines work better in some people than in others or work only for a short time. This may be because the cancer cells can 'hide' from the immune system and/or learn to 'escape' the immune system's attacks.

Giving immunotherapy together with a different type of medicine acts like a 'double attack' on the cancer. This double attack may work better than either of the medicines given alone. One such combination is to give immunotherapy with a type of medicine called an 'anti-angiogenic' treatment. Anti-angiogenic treatments stop cancer cells from forming the new blood vessels that they need to grow and spread.

This combination of an immunotherapy medicine and an anti-angiogenic treatment is the standard of care for the first treatment of liver cancer that cannot be removed with surgery.

In this study, researchers wanted to see if the same combination of an immunotherapy medicine with an anti-angiogenic treatment as an adjuvant therapy would extend the length of time people were alive without their cancer coming back. Researchers also wanted to see whether the combination would be safe for people to take.

What medicines are being tested in the study?

This study looked at a study medicine called 'atezolizumab' (known by its brand name, Tecentriq®) taken together with another study medicine called bevacizumab (known by its brand name Avastin®) by the people in **Group A**.

- You say 'atezolizumab' 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 becomes able to fight the cancer cells.
    - This medicine is a type of immunotherapy.
- You say bevacizumab 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.
    - This is an anti-angiogenic medicine.

People with liver cancer who are at high risk of their cancer coming back after surgery or ablation in **Group A** were compared with people in **Group B** who received the existing standard of care—active surveillance (defined as being closely watched for cancer coming back with no treatment).

- People in **Group B** whose cancer came back during the study were given the choice to cross over and take atezolizumab plus bevacizumab.

What did researchers want to find out?

- Researchers wanted to see whether treating people who have a high risk of their cancer coming back after surgery or ablation with a combination of medicines (atezolizumab plus bevacizumab) would extend the length of time these people were alive without their cancer coming back, compared with being under active surveillance.
    - See section 4 “What were the results of the study?”.
- They also wanted to find out how safe this combination of medicines is, by counting how many people had side effects (and seeing how severe these side effects were) when taking both medicines together during this study.
    - See section 5 “What were the side effects?”.

The main questions that researchers wanted to answer were:

1. After surgery or ablation, how long did people live without their cancer coming back in **Group A** and **Group B**?
2. How safe is the combination of atezolizumab plus bevacizumab? How many people in **Group A** and **Group B** had side effects and how severe were the side effects?

Other questions that researchers wanted to answer included:

3. How long did people in **Group A** live in this study compared with people in **Group B**?

What kind of study is this?

This is a ‘Phase 3’ study. Phase 3 studies are carried out in a large number of people to see if a drug works better than the standard of care and is safe enough for it to be ‘approved’ by the authorities as a treatment that can be prescribed by a doctor. The combination of atezolizumab plus bevacizumab was proven effective in a large Phase 3 study called IMbrave150 in people with liver cancer that had spread to other parts of the body or was too large (or difficult) to remove with surgery. IMbrave050 was a similar study but was carried out with patients with an earlier stage of liver cancer that could be either removed surgically or with heat.

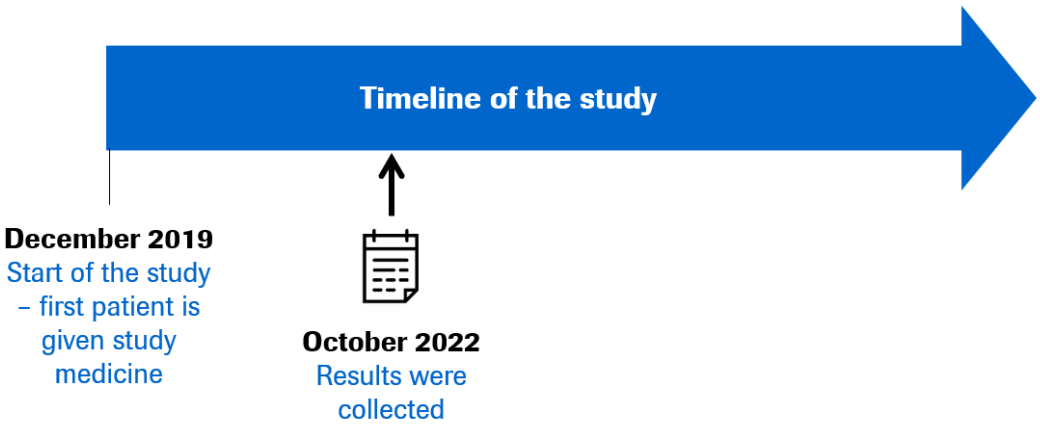
The study is ‘randomised’. This means that a computer randomly selected which of the two study groups, **A** or **B**, people were assigned to—like tossing a coin.

- In this study, the same number of people with liver cancer were in **Group A** (given atezolizumab plus bevacizumab) as in **Group B** (being under active surveillance, the standard care for liver cancer after surgery).
- Randomly assigning people to either of the study groups makes it more likely that the characteristics of the people in both groups (such as age, race, and how sick they are) will be similar at the start of the study.

This is an ‘open label’ study. This means that both the people taking part in the study and the study doctors know which types of care people are getting. Other than the different types of care being tested and how often people went to the clinic in **Group A** and **Group B**, all other aspects of care, including how often their cancer was monitored, were the same between the groups.

When and where did the study take place?

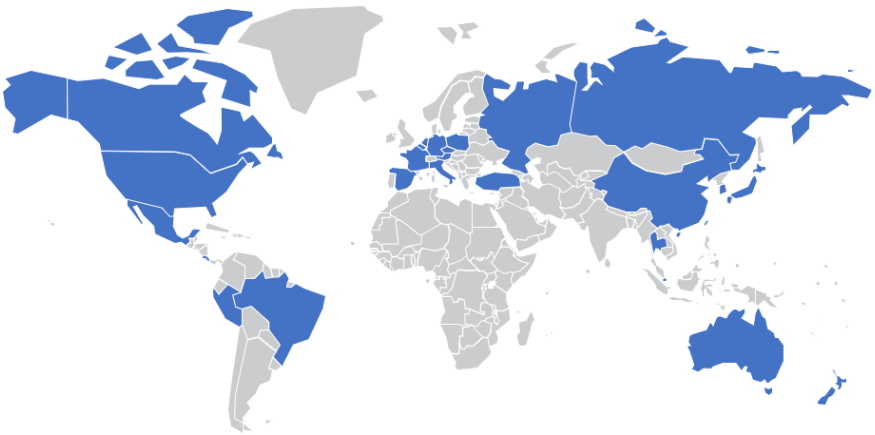
The study started in December 2019 and is still happening. This summary includes the results up until October 2022.



This study is still happening. The symbol on the timeline (📋) shows when the information shown in this summary was collected—about 34 months after the start of the study. There will be more results collected in the future.

The study is taking place at 134 study centres in 26 countries/regions around the world. The following map shows the countries/regions where this study is happening.

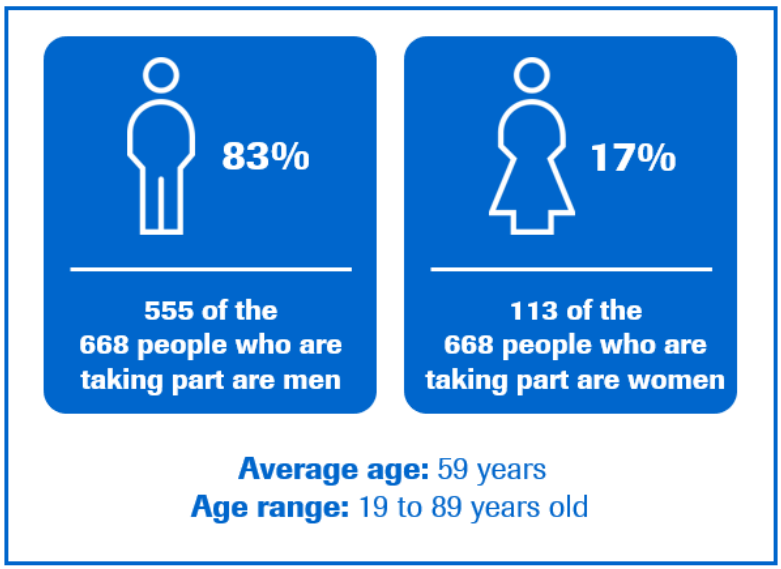
- Australia
- Austria
- Belgium
- Brazil
- Canada
- China
- Costa Rica
- Czech Republic
- France
- Germany
- Hong Kong
- Italy
- Japan
- Korea
- Mexico
- Netherlands
- New Zealand
- Peru
- Poland
- Russia
- Singapore
- Spain
- Taiwan
- Thailand
- Türkiye
- USA



2. Who is taking part in this study?

This study includes 668 adults with liver cancer that had not spread to other parts of the body and was small enough to be surgically removed or ablated. These people had surgery or ablation to treat their liver cancer before this study and had a high risk of their cancer coming back.

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



3. What happened during the study?

During the study, people were selected by chance to get one of two types of care. The types of care were selected at random by a computer.

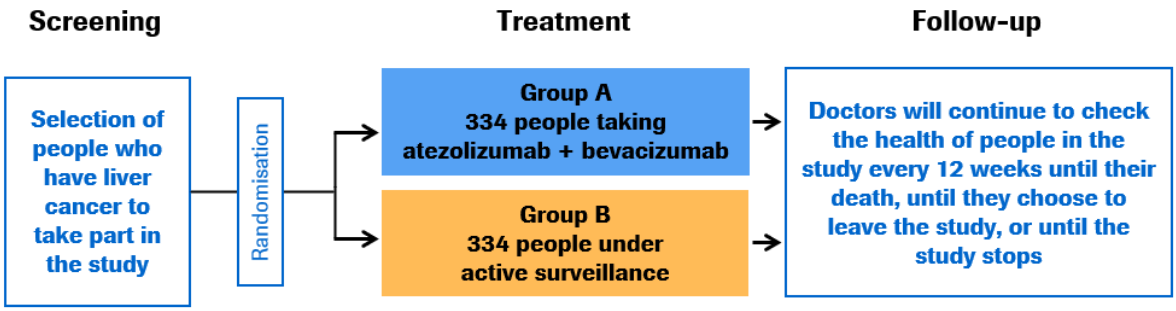
The types of care were:

- **Group A:** Atezolizumab plus bevacizumab (study medicine) for up to 1 year.
- **Group B:** Active surveillance (existing standard of care) for up to 1 year.

This table shows the number of people who got each type of care and how often the drugs were taken.

	Group A **Atezolizumab plus bevacizumab**	**Group B** **Active surveillance**
Number of people getting this type of care	334	334
When and how the drugs were taken	Injected into a vein once every 3 weeks	Not applicable

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



- When people in **Group A** finished getting the study medicines or when people in **Group B** finished 1 year of active surveillance, they were 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 it takes before their cancer comes back and how long people live on this study.
- At the time this information was collected, 593 of 668 people were still taking part in the study.

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

Question 1: After surgery or ablation, how long did people live without their cancer coming back in Group A and Group B?

- When this information was collected and analysed in October 2022, 34 months after the study started:
  - 110 out of 334 people in **Group A** (33%) had cancer that came back or had died.
  - 133 out of 334 people in **Group B** (40%) had cancer that came back or had died.
- At the time this information was collected in October 2022:
  - The average time that people in **Group A** and **Group B** survived without their cancer coming back after they started getting their study care could not be estimated because less than half of the people in each group had cancer that came back or had died and further data need to be collected.
  - People in **Group A** had a 28% lower risk of their cancer coming back or death, compared with people in **Group B.**

Question 2: How long did people in Group A live in this study compared with people in Group B?

- When this information was collected and analysed in October 2022, 34 months after the study started, the question could not be answered and more data are needed.
  - 27 out of 334 people in **Group A** (8%) had died.
  - 20 out of 334 people in **Group B** (6%) had died.
- At the time this information was collected in October 2022:
  - The average time that people in **Group A** and **Group B** survived after they started getting their study care could not be estimated because more than half of the people in each group were alive and further data need to be collected.

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

5. What were the side effects?

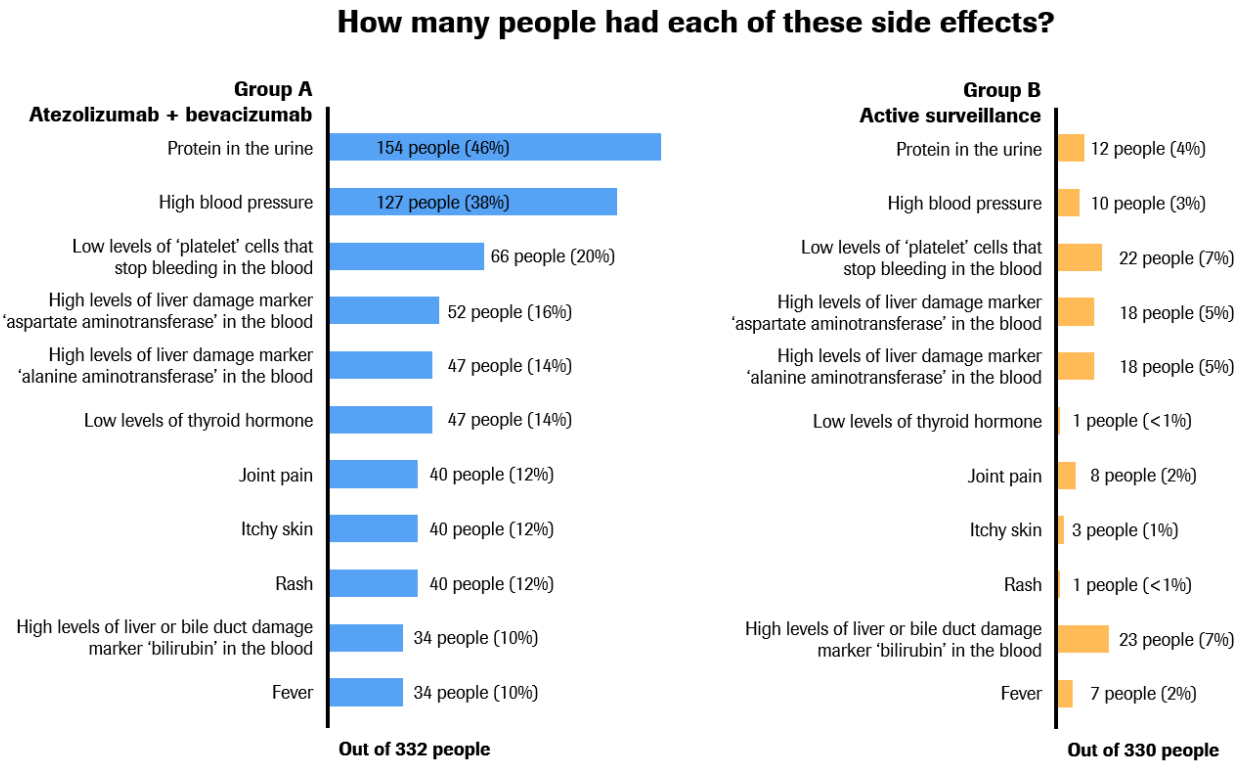
Side effects (also known as 'adverse reactions') are medical problems (such as vomiting) that happen during the study. Side effects can vary from mild to very serious and may be different from person to person.

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

Common and serious side effects are listed in the following sections. Some people left the study without getting any care and were not included in the total. This information was collected from December 2019 until October 2022.

Most common side effects

The most common side effects are shown in the following picture. These are the side effects that happened in 10% or more of the people in either **Group A** or **Group B**.



The side effects in this study, shown in the graph above, were the same as side effects that have been experienced by other people who have taken atezolizumab and/or bevacizumab in other studies or as prescribed by their doctors in daily practice.

Treatment-related side effects

A side effect is considered 'treatment related' if the doctor thinks that it is caused by the study medicines that the person is taking.

During this study, 293 out of 332 people (88%) had a treatment-related side effect.

- In 175 out of 332 people (53%) in **Group A**, treatment-related side effects were mild or moderately severe (classified as 'grade 1 or 2' severity—they caused mild symptoms [grade 1] or some limitations of activities [Grade 2]).
- About 116 out of 332 people (35%) in **Group A** had a treatment-related side effect that was considered medically significant or required hospital care ('Grade 3' severity) or was life-threatening ('Grade 4' severity).

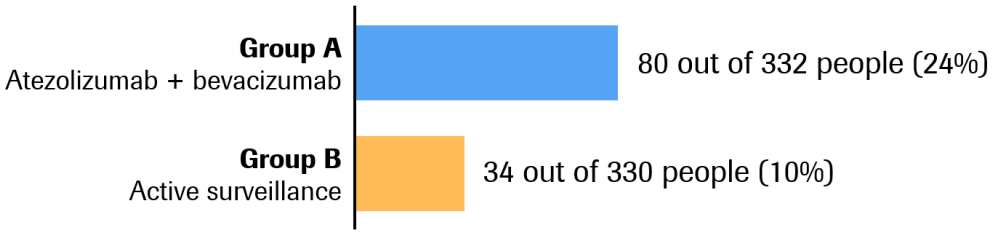
There were no treatment-related side effects in **Group B** since the people in this group did not take any study medicines.

Serious side effects

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

During this study, 114 out of 662 people (17%) had at least one serious side effect.

How many people had at least one serious side effect?

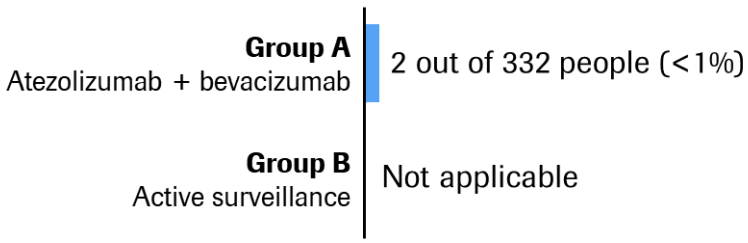


Treatment-related side effects leading to death

Some people in the study died because of treatment-related side effects.

- These side effects were seen in 2 out of 332 people (less than 1%) in **Group A**.
- There were no treatment-related side effects that led to death in **Group B** since the people in this group did not take any study medicines.

How many people died because of treatment-related side effects?



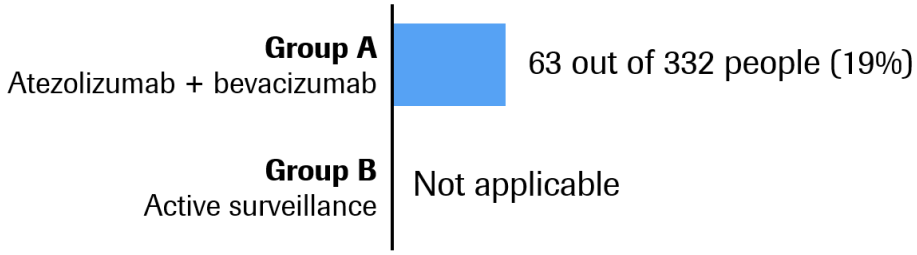
Stopping the medicine because of side effects

During the study, 63 out of 332 people (19%) in **Group A** decided to stop taking their medicine

because of side effects.

- There were no people in **Group B** who decided to stop taking their medicine because of side effects since the people in this group did not take any study medicines.

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



Other side effects

You can find information about other side effects (not shown in the sections above) in the medical journal article 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 668 people with liver cancer who are at high risk of their cancer coming back after surgery or ablation. The study is still happening. These results have helped researchers learn more about liver cancer and treatment with atezolizumab plus bevacizumab.

- The study showed that:
  - People in **Group A** had a 28% lower risk of their cancer coming back or death than people in **Group B**.
  - There was not enough data to fully understand the impact of study medicines on how long people lived. About 8% of people (27 out of 334 people) in **Group A** died, compared with 6% of people (20 out of 334 people) in **Group B**.
  - Of people who did not leave the study without getting any care, the most common side effects in **Group A** were protein in the urine (154 out of 332 people [46%]), high blood pressure (127 out of 332 people [38%]), and low levels of 'platelet' cells that stop bleeding in the blood (66 out of 332 people [20%]).
  - The most common side effects in **Group B** were high levels of liver or bile duct damage marker 'bilirubin' in the blood (23 out of 330 people [7%]), low levels of 'platelet' cells that stop bleeding in the blood (22 out of 330 people [7%]), high levels of liver damage marker 'aspartate aminotransferase' in the blood (18 out of 330 people [5%]), and high levels of liver damage marker 'alanine aminotransferase' in the blood (18 out of 330 people [5%]).
  - About 24% of people (80 out of 332 people) in **Group A** had a serious side effect, compared with 10% of people (34 out of 330 people) in **Group B**.
  - In **Group A**, 2 out of 332 people (less than 1%) died because of treatment-related side effects; people in **Group B** did not take any study medicines.

This summary includes information about the results from a large phase 3 study of a new treatment combination. However, one study can't tell us everything about how safe a medicine is and how well it works. We have described all of the positive and negative results of this study in this summary, but all medical decisions regarding your individual case should be made by you and your doctor together, based on all available information.

- 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 trial (MORPHEUS Neoadjuvant HCC; NCT05908786) is happening now in people who have liver cancer that can be removed with surgery and who have not received any treatment. In MORPHEUS Neoadjuvant HCC, these people will receive either atezolizumab plus bevacizumab, atezolizumab plus bevacizumab plus tiragolumab, or tobemstomig plus bevacizumab.

8. Where can I find more information?

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

- https://www.clinicaltrials.gov/study/NCT04102098?tab=results
- https://www.clinicaltrialsregister.eu/ctr-search/search?query=2019-002491-14
- https://forpatients.roche.com/en/trials/cancer/rcc/a-study-of-atezolizumab-plus-bevacizumab-versus-active--52983.html

If you would like to find out more about the results of this study, the full title of the scientific paper that describes this study is:

- "Atezolizumab plus bevacizumab versus active surveillance in patients with resected or ablated high-risk hepatocellular carcinoma (IMbrave050): a randomised, open-label, multicentre, phase 3 trial". The authors of the scientific paper are: Shukui Qin, Minshan Chen, Ann-Lii Cheng, and others. The paper is published online ahead of print in the journal *The Lancet*, volume number 402, on pages 1835-1847.

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/rcc/a-study-of-atezolizumab-plus-bevacizumab-versus-active--52983.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, whose headquarters are in Basel, Switzerland, and Genentech, Inc, a member of the Roche group, whose headquarters are in South San Francisco, California, USA.

Full title of the study and other identifying information

The full title of this study is: “A Study of Atezolizumab Plus Bevacizumab Versus Active Surveillance as Adjuvant Therapy in Patients With Hepatocellular Carcinoma at High Risk of Recurrence After Surgical Resection or Ablation (IMbrave050)”.

- The protocol number for this study is: WO41535.
- The ClinicalTrials.gov identifier for this study is: NCT04102098.
- The EudraCT number for this study is: 2019-002491-14.