# Summary of Clinical Trial Results

## Two studies looking at how safe and effective different doses of cibisatamab were, with or without atezolizumab, in people with solid tumours who have a protein called 'human carcinoembryonic antigen' (CEA) on the outside of their cancer cells—and the best dose of cibisatamab to use

See the end of the summary for the full titles of these studies.

## About this summary

This is a summary of the results of 2 clinical trials (called 'studies' in this document) written for:

- members of the public and
- people who took part in the studies.

This summary is based on information known at the time of writing (March 2024).

**Study 1** (cibisatamab alone) started in December 2014 and finished in September 2019. **Study 2** (cibisatamab plus atezolizumab) started in January 2016 and finished in January 2020. This summary was written after both studies 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. The results from these two studies may be different than the results from other studies with the same medicines.

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

### Contents of the summary



- Solid tumour = an abnormal growth that can be in any organ of the body; it is different from cancer of the blood
- Human carcinoembryonic antigen (CEA) = a protein that can be found on the outside of cancer cells

### Thank you to the people who took part in these studies

The people who took part have helped researchers to answer important questions about solid tumours (cancers that are not blood cancers) that have a protein called 'human carcinoembryonic antigen' (CEA) on the outside of the cancer cells and the medicines studied, 'cibisatamab' and 'atezolizumab'.

## Key information about these studies

**Why were these studies done?**

- These studies were done to see how safe cibisatamab (with or without obinutuzumab before treatment) or cibisatamab plus atezolizumab were, and how much cibisatamab should be used to treat people with solid tumours that have a protein called 'human carcinoembryonic antigen' (CEA) on the outside of the cancer cells.

**Who took part in these studies?**

- The people in these studies had cancer that had gotten worse after taking 1 or more courses of existing treatment or were not able to take existing treatment.
- All of the people in these studies took cibisatamab with or without obinutuzumab before treatment (**Study 1**) or cibisatamab plus atezolizumab (**Study 2**). Different people received different amounts of cibisatamab.
- **Study 1** included 149 people in 6 countries, and **Study 2** included 228 people in 7 countries.

**What were the results?**

- The main findings of **Study 1** were that:
  - Around 93 out of every 100 people (93%) had a side effect related to cibisatamab.
  - Nearly 5 out of every 10 people (46%) had at least 1 serious side effect related to cibisatamab.
  - The highest dose of cibisatamab that could be given to people was 400 mg, either once a week or once every 3 weeks.
  - About 4 out of every 100 people (4%) had smaller tumours after taking cibisatamab.
  - On average, people's cancer got worse about 2 months after they started taking cibisatamab.
  - On average, people lived for about 7 months after starting the study.
- The main findings of **Study 2** were that:
  - Around 99 out of every 100 people (99%) had a side effect related to cibisatamab.
  - More than 5 out of every 10 people (53%) had at least 1 serious side effect related to cibisatamab.
  - About 7 out of every 100 people (7%) had smaller tumours after taking cibisatamab plus atezolizumab.
  - On average, people's cancer got worse about 2 months after they started taking cibisatamab plus atezolizumab.
  - On average, people lived for about 11 months after starting the study.
- Across both studies, around 50% to 70% of people developed anti-drug antibodies (ADAs) in response to cibisatamab treatment.
  - People with higher amounts of ADAs had lower levels of cibisatamab in the body.
  - There were more side effects relating to the immune response in people with ADAs than in people without ADAs.
  - In **Study 1**, people who were given obinutuzumab before treatment and had ADAs had a similar amount of cibisatamab in the body as people without ADAs.

# 1. General information about these studies

## Why were these studies done?

People with solid tumours (abnormal growths that can be in any organ of the body but are different from cancer of the blood) are treated with different types of medicine to kill the cancer cells or to stop the cancer cells from growing. These medicines do not work in everyone or they may work for only a short time before the cancer gets worse again. Sometimes people have to stop taking these medicines because the side effects are too bad.

New medicines are needed to help people live longer if their cancer has grown after taking standard treatments, if they have had to stop taking their medicine, or if they are not suitable for current standard treatments.

'Immunotherapy' is a type of medicine that helps a person's own immune system attack cancer cells. In both **Study 1** and **Study 2**, researchers wanted to test a new type of immunotherapy medicine to see whether it can be used to treat people with certain types of cancer. This new medicine, cibisatamab, recognises a protein called 'human carcinoembryonic antigen' (CEA) that can often be found on the outside of the cancer cells in different types of solid tumours. The people in this study had cancers with CEA on their cancer cells and had found that their cancer got worse after taking 1 or more courses of existing treatment or that they were not able to take existing treatment.

Researchers in these studies gave people different amounts of cibisatamab on different schedules to see what amount of medicine worked best without people having very bad side effects and how often the medicine should be given. This was done to help researchers choose the right dose to use in bigger studies that are needed to give more information about the disease and the medicine.

In **Study 1**, people were given cibisatamab to treat their cancer. Sometimes, the immune system can react strongly to medicines such as cibisatamab and produce substances called 'anti-drug antibodies' (ADAs). ADAs can affect how well the medicine works and may also cause side effects. 'Obinutuzumab' is a type of medicine that can stop the immune system from reacting too strongly. Researchers wanted to see if giving obinutuzumab before treatment could help prevent strong immune responses to cibisatamab. Therefore, a small group of people in this study were first given 1 or 2 doses of obinutuzumab (at 13 days or 12–13 days before the start of their cibisatamab treatment, respectively).

In **Study 2**, people were given cibisatamab with another immunotherapy medicine called 'atezolizumab'. Atezolizumab is a medicine that blocks cancer cells from escaping the body's immune system. Researchers in **Study 2** wanted to know if combining cibisatamab with atezolizumab was more effective than cibisatamab alone at helping the body's immune system kill cancer cells.

## What were the medicines being studied?

**'Cibisatamab'**

- Cibisatamab is a type of immunotherapy that works by helping the body's immune system to recognise and kill cancer cells.
- Cibisatamab was tested at different doses to find out which dose was the best.

**'Atezolizumab'**

- Atezolizumab is a type of immunotherapy that works by preventing cancer cells from avoiding the body's immune system.
- The body's immune system fights diseases like cancer, but 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 again.

## What did researchers want to find out?

- Researchers did these studies to find out how safe cibisatamab (with or without obinutuzumab before treatment) or cibisatamab plus atezolizumab were by checking how many people had side effects and seeing how serious the side effects were while taking the medicines (see Section 4 "What were the study results relating to side effects?").
- Researchers also wanted to find out how well cibisatamab worked alone or in combination with atezolizumab (see Section 5 "What were the other results of the studies?").

**The main questions that researchers wanted to answer were:**

1. How many people had side effects when taking cibisatamab or cibisatamab plus atezolizumab during these studies?
2. What was the highest dose of cibisatamab that could be given to people, and did any side effects limit the dose of cibisatamab that could be given?

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

3. How many people had smaller or no tumours after taking cibisatamab?
4. How much time was there between the start of the study and people's cancer getting worse?
5. How long did people live in these studies?
6. Did obinutuzumab given before treatment help prevent a strong immune response to cibisatamab?

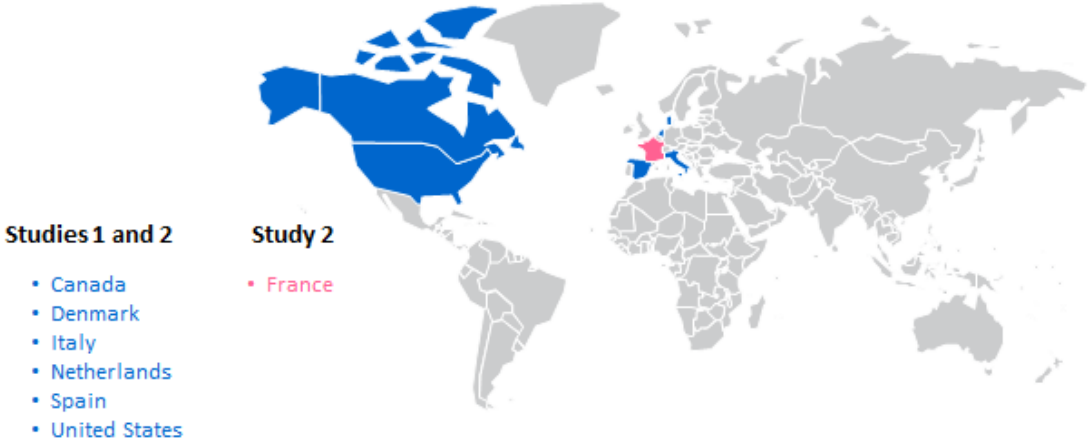
## What kinds of study were these?

These were both '**Phase 1**' studies, which means that these were the first studies where cibisatamab was given to people. A small number of people with solid tumours that have a protein called 'human carcinoembryonic antigen' (CEA) on the surface of their cancer cells took cibisatamab (**Study 1**) or cibisatamab plus atezolizumab (**Study 2**). The researchers did medical tests on the people who took part to find out more about these medicines.

## When and where did the studies take place?

**Study 1** started in December 2014 and finished in September 2019. **Study 2** started in January 2016 and finished in January 2020. This summary was written after both studies had ended.

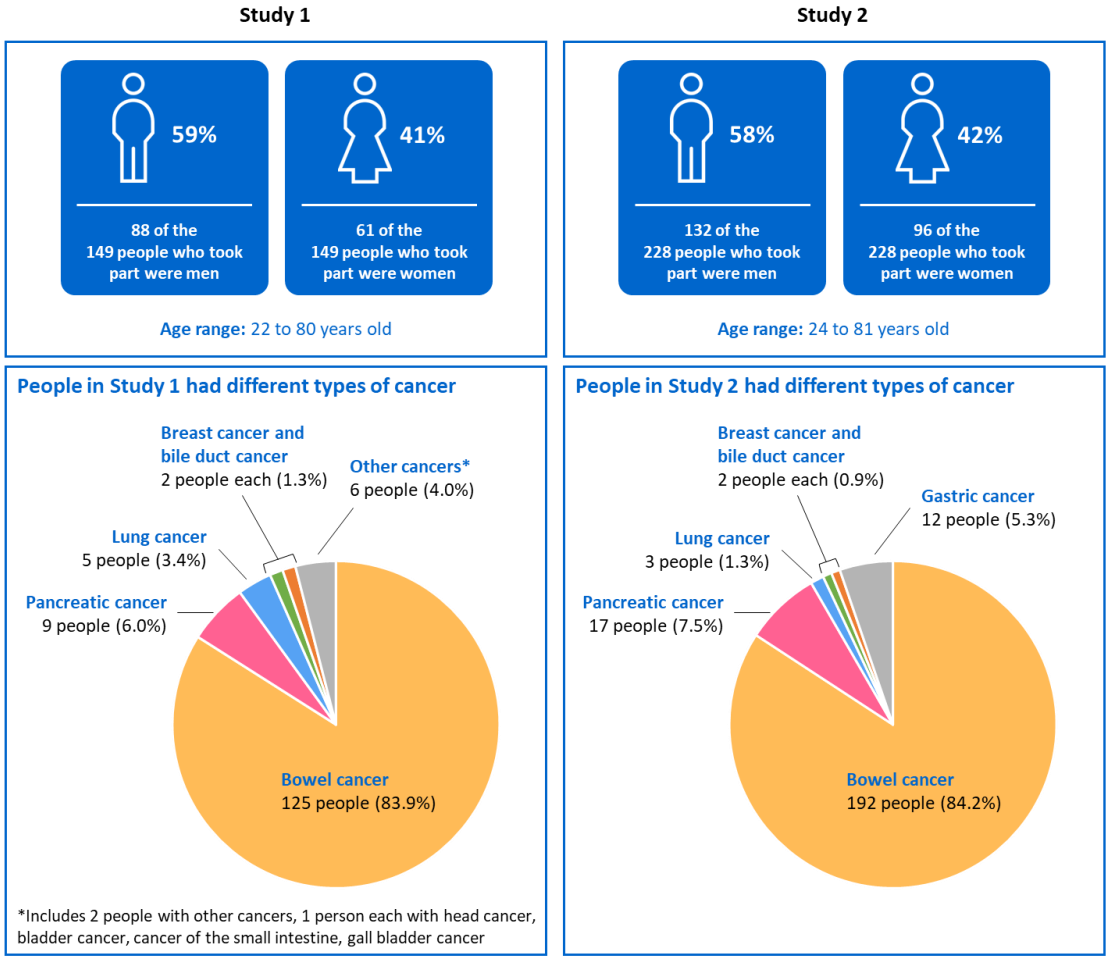
**Study 1** took place at 17 study centres across 6 countries in Europe and North America. **Study 2** took place at 23 study centres across 7 countries in Europe and North America. The following map shows the countries where these studies took place.




## 2. Who took part in these studies?

In total, 149 people (**Study 1**) and 228 people (**Study 2**) with solid tumours and CEA on the surface of their cancer cells took part in these studies. Most of these people had cancer of the bowel, but some had other types of cancer.

More information on the people who took part is given below.



People could take part in **Study 1** if:

- They had solid tumours that were advanced in nearby cells (locally advanced) or that had spread to other parts of their body (metastatic).
  - Metastatic cancers are generally considered not curable, and people with metastatic cancers are given treatments to help them live as long as possible.
- Their cancers had a protein called CEA on the outside of their cells.
- They found that their cancer got worse after taking 1 or more courses of existing treatment or they were not able to take existing treatment.

People could **not** take part in the **Study 1** if:

- They had cancer that had spread to the brain or spinal cord, unless it had been treated or did not cause any symptoms.
- They had a different type of cancer in the past 2 years.

People could take part in **Study 2** if:

- They had solid tumours that were locally advanced or metastatic.
- Their cancers had a protein called CEA on the outside of their cells.
- They found that their cancer got worse after taking 1 or more courses of existing treatment or they were not able to take existing treatment.

People could **not** take part in the **Study 2** if:

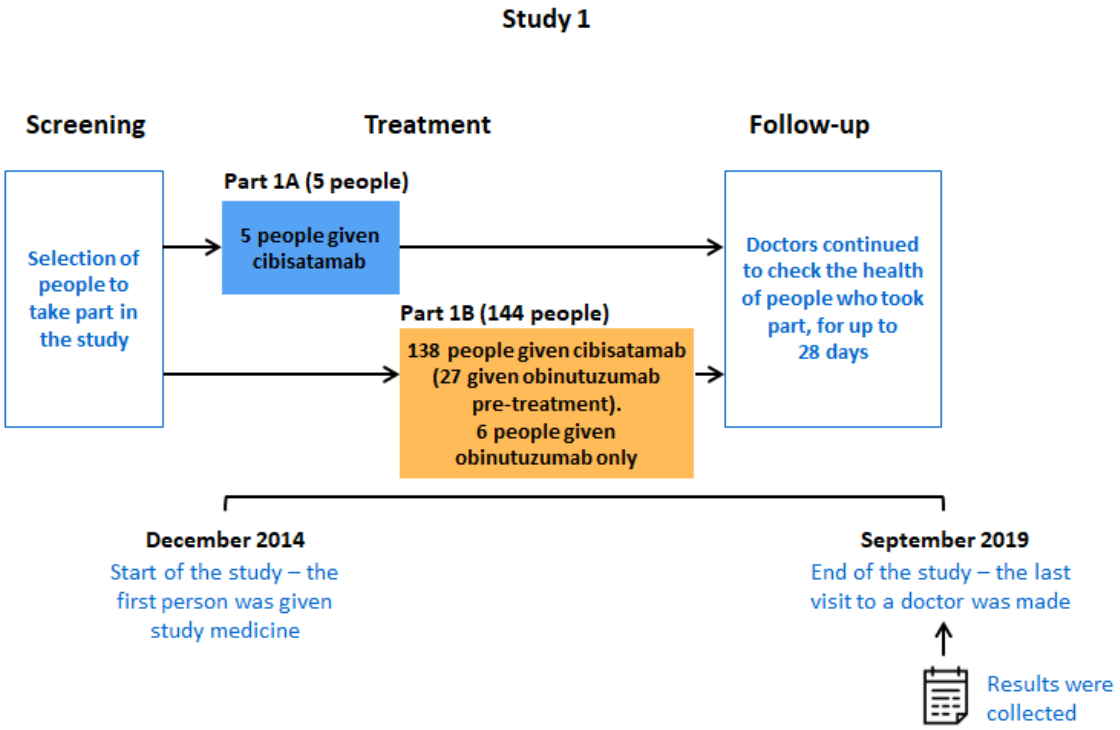
- They had cancer that had spread to the brain or spinal cord.
- They had a different type of cancer in the past 5 years.

## 3. What happened during the studies?

During **Study 1**, people were given different doses of cibisatamab. Some people were given obinutuzumab before starting their cibisatamab treatment. Cibisatamab was given by injection into a vein.

- **Part 1A** (5 people): Each person was given cibisatamab once (unless they and their doctor agreed that they could continue taking the medicine for longer), with each person getting a higher dose of medicine than the person before them.
  - Part 1A was done to see what starting dose of cibisatamab should be used in Part 1B of the study.
- **Part 1B** (144 people): 138 people were given cibisatamab (27 people were also given obinutuzumab before treatment). Six people were given obinutuzumab only, because they stopped their treatment before taking any cibisatamab.
  - People could receive the same dose of cibisatamab each time or receive increasing doses over time. The frequency of cibisatamab treatment could be once a week or once every 3 weeks.
  - People took the medicines until their cancer got worse, they died, or they had a side effect that was too bad to continue taking the medicines.
  - Part 1B was done to find the highest dose of cibisatamab that could be given to people, and to find the best dose to use and to figure out how often it should be given.

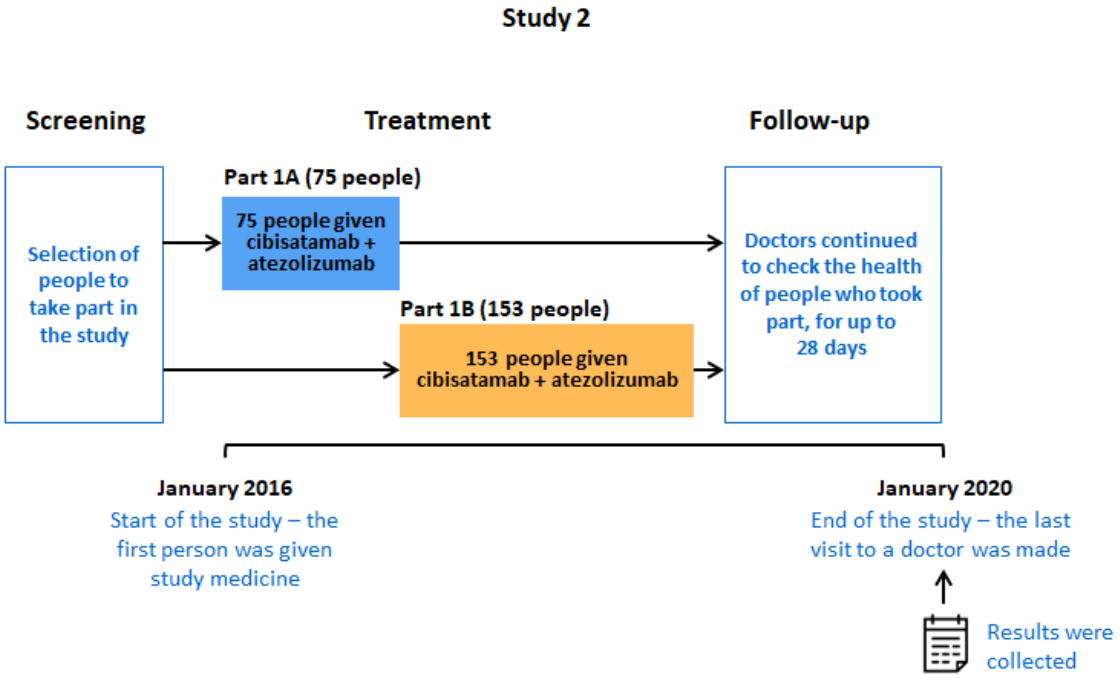
When their treatment finished, the people who took part were asked to go back to their study centre for 1 more visit to check their overall health. Look below to see more information about what happened in the study.




During **Study 2**, people were given different doses of cibisatamab. Atezolizumab was always given once every 3 weeks at the same dose. Both cibisatamab and atezolizumab were given by injection into a vein.

- **Part 1A** (75 people): People were given cibisatamab once a week, with the dose of cibisatamab increasing over time.
  - Part 1A was done to find the highest dose of cibisatamab that could be given to people and to decide on the best dose to use.
- **Part 1B** (153 people): People could receive the same dose of cibisatamab each time or could receive increasing doses over time. The frequency of cibisatamab treatment could be once a week or once every 3 weeks.
  - People took the medicines until their cancer got worse, they died, or they had a side effect that was too bad to continue taking the medicines.
  - Part 1B was done to find the best dose of cibisatamab to use and to figure out how often it should be given.

When their treatment finished, the people who took part were asked to go back to their study centre for 1 more visit to check their overall health. Look below to see more information about what happened in the study.




This summary contains results for both **Study 1** and **Study 2**. It focusses on how safe and effective cibisatamab was overall, with or without atezolizumab. The results relating specifically to different doses and dose schedules, as well as the different cancers of people in the study, can be found in the scientific paper (see Section 8 "Where can I find more information?").

## 4. What were the study results relating to 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 doctors believe the side effects were related to the treatments in the studies.
- Not all of the people in these studies had all of the side effects.
- Side effects may be mild to very serious any can be different from person to person.
- It is important to be aware that the side effects reported here are from these 2 studies only. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflet.

Common side effects and serious side effects related to the study medicines are listed in the following sections.

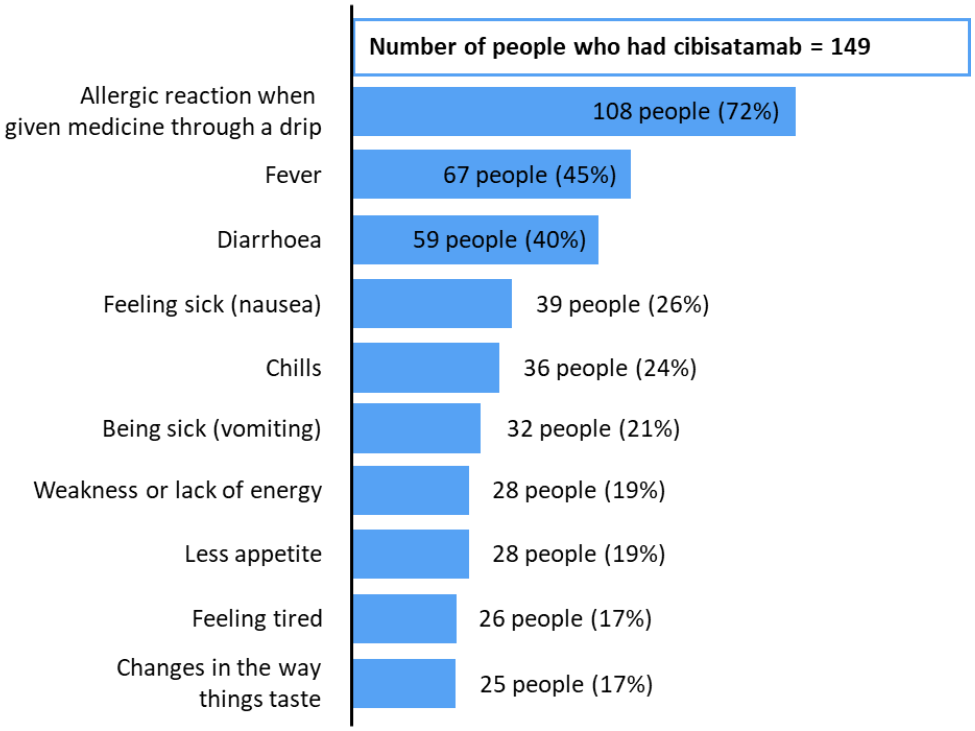
### Question 1: How many people had side effects when taking cibisatamab, with or without atezolizumab, during these studies?

During **Study 1**, around 93 out of every 100 people (**93%**, or 139 out of 149 people in the study) had a side effect related to cibisatamab.
During **Study 2**, around 99 out of every 100 people (**99%**, or 225 out of 228 people in the study) had a side effect related to cibisatamab or atezolizumab.

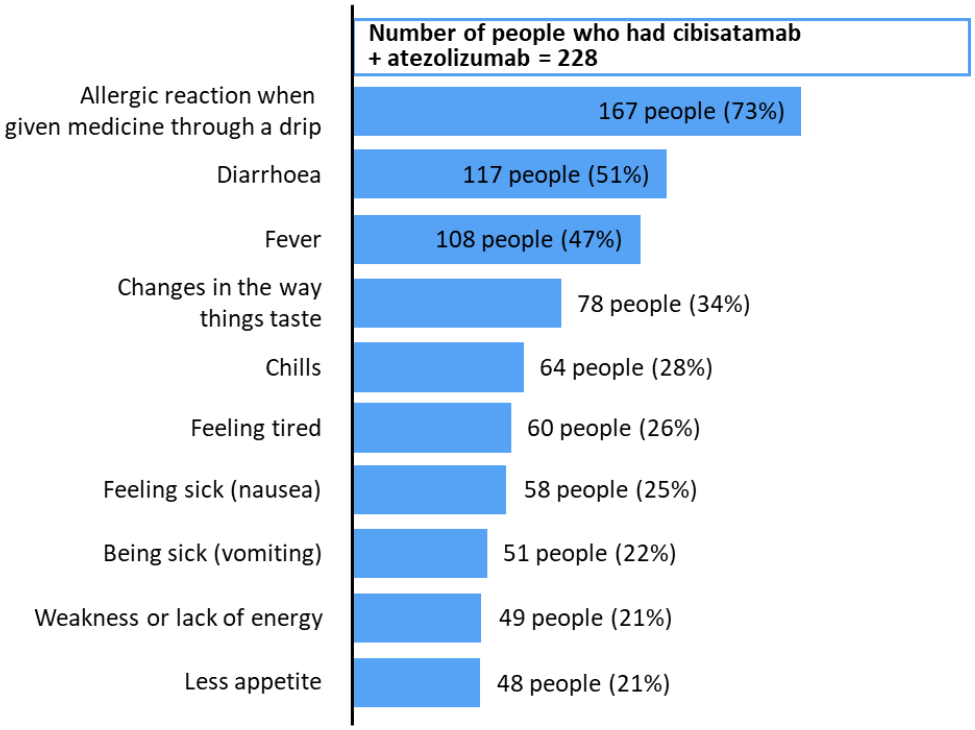
The most common side effects related to cibisatamab or atezolizumab are shown in the following charts. These are the 10 most common side effects seen in people who took cibisatamab or cibisatamab plus atezolizumab.

Some people had more than 1 side effect. This means that they are included in more than 1 row in the chart.

**How many people had each of these side effects in Study 1?**




**How many people had each of these side effects in Study 2?**




## Question 2: What was the highest dose of cibisatamab that could be given to people, and did any side effects limit the dose of cibisatamab that could be given?

In **Study 1**, the highest dose of cibisatamab that could be given to people was 400 mg once a week or once every 3 weeks. There were 7 side effects related to cibisatamab treatment that limited the dose of cibisatamab that could be given; 2 of these were fatal (respiratory failure and shortness of breath).

In **Study 2**, researchers did not find out the highest dose of cibisatamab that could be given to people in combination with atezolizumab. This was because people had serious side effects when given the 300-mg dose, and researchers decided not to test higher doses. There were 17 side effects related to cibisatamab (with or without atezolizumab) treatment that limited the dose of cibisatamab that could be given; 1 of these was fatal (severe blood or fluid loss resulting in the heart being unable to pump enough blood around the body).

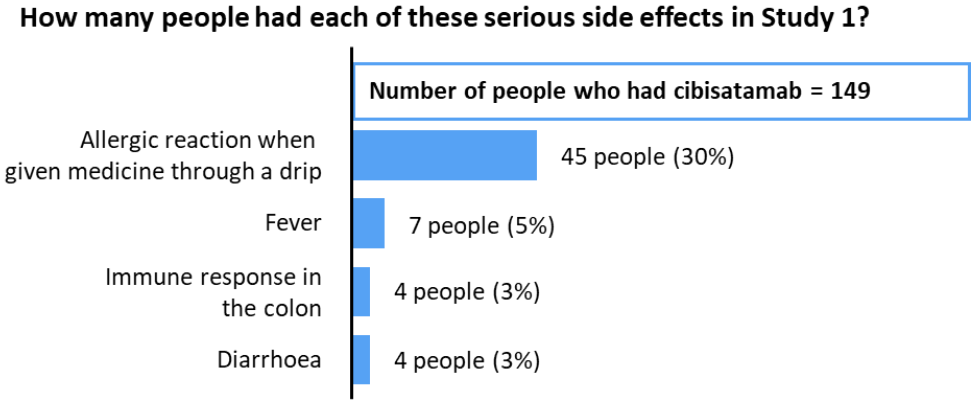
## Serious side effects

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

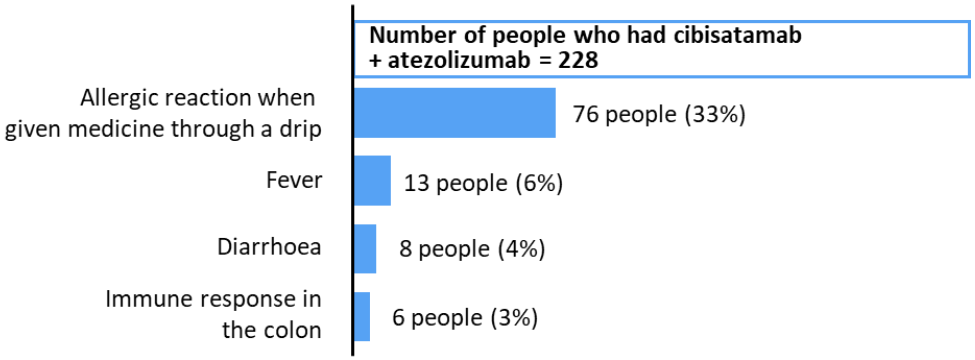
During **Study 1**, around 46 out of every 100 people (**46%**, or 69 out of 149 people in the study) had at least 1 serious side effect.
During **Study 2**, around 53 out of every 100 people (**53%**, or 120 out of 228 people in the study) had at least 1 serious side effect.

The most common serious side effects are shown in the following chart. These are the 4 most common serious side effects in people treated with cibisatamab or cibisatamab plus atezolizumab.

- Some people had more than 1 serious side effect. This means that they are included in more than 1 row in the chart.



**How many people had each of these serious side effects in Study 2?**




### Deaths related to side effects

During **Study 1**, 2 out of every 100 people (**2%**, or 3 out of 149 people in the study) died due to side effects that may have been related to cibisatamab.

During **Study 2**, fewer than 1 in every 100 people (**less than 1%**, or 1 out of 228 people in the study) died due to side effects that may have been related to cibisatamab.

### Stopping the medicine because of side effects

During **Study 1**, 4 out of every 100 people (**4%**, or 6 out of 149 people in the study) stopped taking cibisatamab because of side effects.

During **Study 2**, 7 out of every 100 people (**7%**, or 15 out of 228 people in the study) stopped taking cibisatamab because of side effects. Six out of every 100 people (**6%**, or 13 out of 228 people in the study) stopped taking atezolizumab because of side effects.

### 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).

## 5. What were the other results of the studies?

### Question 3: How many people had smaller or no tumours after taking cibisatamab?

Researchers also looked at how many people had their tumours get smaller or become so small that they could not be seen in tests anymore. This information was collected from all of the people in the studies.

- In **Study 1**, around 4 in every 100 people (**4%**, or 6 out of 149 people in the study) had smaller tumours after taking this medicine.
- In **Study 2**, around 7 in every 100 people (**7%**, or 15 out of 228 people in the study) had smaller tumours after taking this medicine.

### Question 4: How much time was there between the start of treatment and people's cancer getting worse?

Researchers looked at how much time passed from the start of the study until people's cancers got worse.

- In **Study 1**, the average amount of time from the start of the study until people's cancers got worse (or they died) was **2.3 months**.
- In **Study 2**, the average amount of time from the start of the study until people's cancers got worse (or they died) was **2.2 months**.

### Question 5: How long did people live in these studies?

Cancers that have spread to other parts of the body (metastatic cancer) are generally considered not curable. People with metastatic cancers are given treatments to help them live as long as possible. Researchers therefore wanted to know how long people lived in this study when given cibisatamab or cibisatamab plus atezolizumab.

- In **Study 1**, people given cibisatamab lived for an average of **7.1 months**.
- In **Study 2**, people given cibisatamab plus atezolizumab lived for an average of **11.0 months**.

### Question 6: Did obinutuzumab given before treatment help prevent a strong immune response to cibisatamab?

Researchers looked at how many people developed anti-drug antibodies (ADAs), which are substances produced by the immune system in response to certain types of medicine. ADAs can affect how well the medicine works and may cause side effects.

- Across **Studies 1 and 2**, around 50%–70% of people developed ADAs in response to cibisatamab treatment. People with higher amounts of ADAs had lower levels of cibisatamab in the body, meaning that their immune system was affecting the amount of medicine staying in the body. There were also more side effects relating to the immune response in people with ADAs than in people without ADAs.
- In people who were given obinutuzumab before treatment (**Study 1**) and who had ADAs, the amount of cibisatamab in the body was similar to the amount in the body of people who did not have ADAs. This means that obinutuzumab was able to help prevent the immune system from having a strong response to cibisatamab.

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).

## 6. How have these studies helped research?

The information presented here is from 2 studies of people with solid tumours that have a protein called 'human carcinoembryonic antigen' (CEA) on the outside of their cells. These results helped researchers learn more about this type of cancer and about treatment with cibisatamab or cibisatamab plus atezolizumab.

These studies showed that between 93 and 99 out of every 100 people (93%–99%) had a side effect with cibisatamab and between 46 and 53 out of every 100 people (46%–53%) had a serious side effect. The number of people having side effects in these studies was high because researchers were testing different amounts of medicine to find out which was the best to use.

Researchers wanted to find out the highest dose of cibisatamab that could be given to people.
In **Study 1**, the highest dose that could be used is 400 mg of cibisatamab, given either every week or every 3 weeks.
In **Study 2**, researchers did not find out the highest dose of cibisatamab that could be given to people in combination with atezolizumab. This was because people had serious side effects when given the 300-mg dose, and researchers decided not to test higher doses.

Researchers also wanted to find out how well cibisatamab or cibisatamab plus atezolizumab work. In **Study 1**, about 4 out of every 100 people (4%) had smaller tumours after taking cibisatamab, and in **Study 2**, about 7 out of every 100 people (7%) had smaller tumours after taking cibisatamab plus atezolizumab.

No single study can tell us everything about the risks and benefits of a medicine. It takes a lot of people in many studies to find out everything we need to know. The results from these studies may be different from the results of other studies with the same medicine.

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

## 7. Are there plans for other studies?

There are no plans for other studies of cibisatamab.

Other studies of atezolizumab are happening. These studies are looking at atezolizumab alone or in combination with other medicines for the treatment of people with various types of cancer (such as breast cancer or lung cancer).

## 8. Where can I find more information?

You can find more information about these studies on the websites listed below:

**Study 1**:

- https://clinicaltrials.gov/study/NCT02324257
- https://forpatients.roche.com/en/trials/cancer/solid-tumors/a-study-of-ro6958688-in-participants-with-locally-advan-08287.html

**Study 2**:

- https://clinicaltrials.gov/study/NCT02650713
- https://forpatients.roche.com/en/trials/cancer/a-study-of-the-safety--pharmacokinetics--and-therapeuti-98047.html

If you would like to find out more about the results of these studies, the full title of the relevant scientific paper is: “CEA-CD3 Bispecific Antibody Cibisatamab With or Without Atezolizumab in Patients with CEA-Positive Solid Tumors”. The authors of the scientific paper are: Neil H. Segal, Ignacio Melero, Victor Moreno, Neeltje Steeghs, Aurelien Marabelle, and others. The paper is published in the journal ‘*XXXX*’, volume number XX, on pages XX–XX.

## Who can I contact if I have questions about these studies?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form:
  **Study 1**: https://forpatients.roche.com/en/trials/cancer/solid-tumors/a-study-of-ro6958688-in-participants-with-locally-advan-08287.html.
  **Study 2**: https://forpatients.roche.com/en/trials/cancer/a-study-of-the-safety--pharmacokinetics--and-therapeuti-98047.html.
- Contact a representative at your local Roche office.

If you took part in one of these studies 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 these studies?

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

## Full titles of the studies and other identifying information

The full title of **Study 1** is: "An Open-Label, Multicenter, Dose-Escalation Phase I Study to Evaluate the Safety, Pharmacokinetics, and Therapeutic Activity of RO6958688, A Novel T-cell Bispecific Antibody That Targets the Human Carcinoembryonic Antigen (CEA) on Tumor Cells and CD3 on T Cells, Administered Intravenously in Patients With Locally Advanced and/or Metastatic CEA(+) Solid Tumors".

The full title of **Study 2** is: "An Open-Label, Multicenter, Dose Escalation and Expansion Phase Ib Study to Evaluate the Safety, Pharmacokinetics, and Therapeutic Activity of RO6958688 in Combination With Atezolizumab in Patients With Locally Advanced and/or Metastatic CEA-Positive Solid Tumors".

- The protocol numbers are: BP29541 (**Study 1**) and WP29945 (**Study 2**).
- The ClinicalTrials.gov identifiers are: NCT02324257 (**Study 1**) and NCT02650713 (**Study 2**).
- The EudraCT numbers are: 2014-003075-30 (**Study 1**) and 2015-003771-30 (**Study 2**).