# Summary of Clinical Trial Results

## A study of tiragolumab and atezolizumab given with chemotherapy in people with triple-negative breast cancer that was in its early stages or had already spread to other parts of the body

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.

The study started in September 2020 and finished in March 2023. This summary was written after the study had ended.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. 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



### Glossary

- Triple-negative breast cancer (TNBC) = a type of cancer where tumour cells: a) do not have receptors for the hormones oestrogen, and progesterone, and b) do not have too much of the protein HER2.
- Immunotherapy (for cancer) = medicine used in cancer to help the body's immune system attack tumours.
- Programmed death-ligand 1 (PD-L1) = a protein that normally stops the immune system from attacking healthy cells. In cancer, tumour cells can use PD-L1 to hide from, and avoid being destroyed by, the immune system.
- PD-L1 positive = describes tumours that have the PD-L1 protein present on the cells

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

The people who took part have helped researchers to answer important questions about triple-negative breast cancer (TNBC) in its early stages and after it has spread to other parts of the body and the medicines studied – 'tiragolumab' and 'atezolizumab'– taken together with chemotherapy.

## Key information about this study

**Why was this study done?**

- This study was done to research what combination of drugs would stop cancer (tumours) from growing in people with a type of breast cancer called TNBC.
    - 'Triple-negative' means the tumour cells a) do not have receptors for the hormones oestrogen and progesterone, and b) do not have too much of the protein HER2, compared with other breast cancer types. TNBC doesn't respond to some treatments as well as other breast cancers.
    - Breast cancer that has not spread from the breast and the armpit area to other parts of the body is called 'early-stage' cancer.
    - Breast cancer that has spread from the breast to other parts of the body is called 'late-stage' or 'advanced' cancer.
    - This study included people with both early- and late-stage TNBCs.
- In this study, people were given the medicine '**tiragolumab**' taken together with an immunotherapy called '**atezolizumab**' and one or more chemotherapies called '**nab-paclitaxel**', '**carboplatin**', '**doxorubicin**' and '**cyclophosphamide**'.
- Two factors determined which medicines people took. The first factor was if their tumours were positive for programmed death-ligand 1, also called PD-L1-positive tumours. The second factor was their cancer stage, either early-stage or late-stage. Based on these factors people were put into two groups:
    - Group 1 had had late-stage TNBC and PD-L1-positive tumours.
    - Group 2 had early-stage TNBC and PD-L1-positive or -negative tumours.
- The treatment combinations by group were:
    - Tiragolumab + atezolizumab + nab-paclitaxel (Group 1)
    - Tiragolumab + atezolizumab + nab-paclitaxel + carboplatin, then tiragolumab + atezolizumab + doxorubicin and cyclophosphamide (Group 2A)
    - Tiragolumab + atezolizumab + nab-paclitaxel, then tiragolumab + atezolizumab + doxorubicin and cyclophosphamide (Group 2B)
- This study included 83 people in eight countries.

**What were the results?**

The main findings for Group 1 were:

- 54% of people had their tumour shrink or stop growing.
- 100% of people had at least one side effect. The most common side effects that happened in 25% of people or more were low red blood cell count, rash, low neutrophil count, feeling sick (nausea), diarrhoea and headache.
- Generally, people who took tiragolumab with atezolizumab and nab-paclitaxel had relatively mild and manageable side effects that did not prevent them from continuing to take the medicines.

The main findings for Group 2 were:

- 100% of people had at least one side effect. The most common side effects that happened in at least 25% of people were low red blood cell count, feeling sick (nausea), rash, low neutrophil count, hair loss, feeling tired, and increased liver enzymes.

People who took carboplatin in addition to other study medicines had some additional side effects related to blood levels compared with people who did not take it. These side effects did not prevent people from taking the other study medicines.

# 1. General information about this study

## Why was this study done?

TNBC is a type of breast cancer that grows or spreads quickly. TNBC accounts for about 10–15% of all breast cancers.

There are fewer treatments for TNBC than other types of breast cancer. Surgery is a common option for people with early-stage breast cancer that has not spread to other parts of the body.

At the time of this study, people with early-stage TNBC were often treated with a combination of medicines that kill cancer cells – called 'chemotherapy'.

- Chemotherapy can be given before or after surgery. Chemotherapy given before surgery helps shrink the tumour to make the surgery easier and more successful.
- How well the chemotherapy works on the tumour can help doctors pick future treatments that also might work.

Chemotherapy is now commonly given to people with a type of medicine called 'immunotherapy'. Immunotherapy is intended to help a person's own immune system to fight the cancer. This study used two immunotherapies called 'atezolizumab' and 'tiragolumab'. Atezolizumab is an existing medicine that has been used to treat TNBC and other cancers, and helped some people live longer. Tiragolumab is a newer medicine that has been used with atezolizumab to treat lung cancer with good results.

This study looked at whether adding tiragolumab to a combination of atezolizumab and chemotherapy was safe for people to take and to determine if these medicines helped shrink tumours or stop them from growing.

## What were the study medicines?

This study focused on a new combination of medicines to treat TNBC. Based on positive results from previous studies, researchers believed these combinations could work well in people with TNBC and have manageable side effects.
The newer **immunotherapy** used in this study was '**tiragolumab**':

- Tiragolumab is an immunotherapy that works by stopping cancer cells from blocking cells in the immune system, meaning the immune system can go back to attacking the cancer cells.

The existing **immunotherapy** used in this study was '**atezolizumab**':

- Atezolizumab also works by stopping cancer cells from blocking cells in the immune system, meaning that the immune system can go back to attacking the cancer cells.

The **chemotherapy** medicines used in this study were:

- '**nab-paclitaxel**'
- '**carboplatin**'
- '**doxorubicin**'
- '**cyclophosphamide**'

- These medicines work by stopping cancer cells from dividing into new cells, blocking the growth of the tumour and killing the cancer cells.

In this study, people were put into two groups based on if their cancer was PD-L1 positive and if their cancer was in the early or late stage.

- In **Group 1**, people had late-stage cancer that was PD-L1 positive. These people were given tiragolumab plus atezolizumab and nab-paclitaxel. Their treatment was stopped if their cancer got worse or they couldn't handle the side effects of the medicines.
- In **Group 2**, people had early-stage cancer. These people were given either tiragolumab plus atezolizumab, nab-paclitaxel, carboplatin, doxorubicin and cyclophosphamide (Group 2A), or tiragolumab plus atezolizumab, nab-paclitaxel, doxorubicin and cyclophosphamide without carboplatin (Group 2B). People in Group 2 were given study medicines for 19 weeks and then underwent surgery to remove their tumours.

## What did researchers want to find out?

Researchers wanted to see if tiragolumab in combination with atezolizumab and chemotherapy was able to shrink or stop cancer from growing and if the study medicine combination was safe (see section 4 "What were the results of the study?").
They looked at how safe the medicine combinations were by checking how many people had side effects and seeing how serious these were (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 their tumours shrink or stop growing?
2. How many people in Groups 1 and 2 had side effects from the study medicines and what were the side effects?
3. In Group 2, did the people who took carboplatin have more side effects than those who did not take carboplatin?

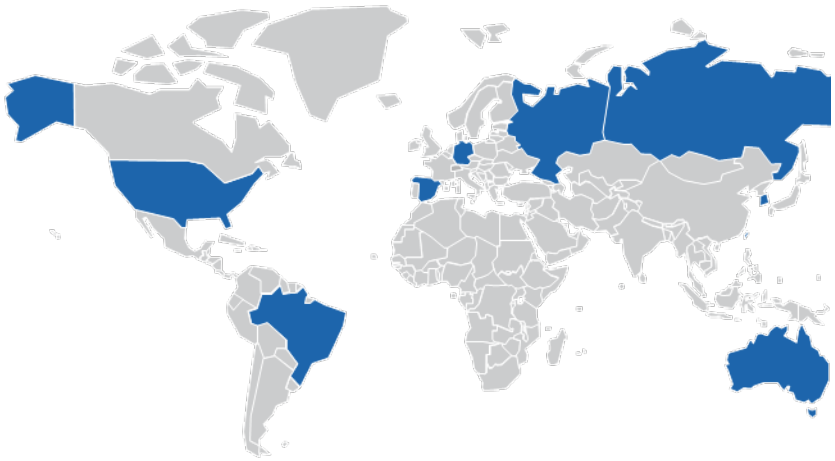
## What kind of study was this?

This study was a 'Phase 1b' study. In this study, a relatively small number of people with TNBC took tiragolumab and atezolizumab plus different combinations of chemotherapy.
This study was done to find out what medicine combination made people's tumours shrink or stop growing and how safe the study medicines were when taken together.
This study was 'open label' meaning everyone involved, including people in the study and their doctors, know which study medicines were given.
This study was a 'multicohort study' meaning it had groups of people who took different study medicines. This study had two groups.
People were divided into **Group 1** or **Group 2** based on their cancer characteristics. Further, **Group 2** was 'randomised' 1:1 into two smaller groups, 2A and 2B. This means that it was decided by chance (like flipping a coin) if people in Group 2 took study medicines in combination with carboplatin (**Group 2A**) or not (**Group 2B**).

## When and where did the study take place?

The study started in September 2020 and finished in March 2023. This summary was written after the study had ended.
The study took place at 24 study centres – across eight countries or regions. The following map shows the countries or regions where this study took place.

- United States
- Brazil
- Russia
- Spain
- Republic of Korea
- Germany
- Australia
- Taiwan



## 2. Who took part in this study?

In this study, 83 people with TNBC took part.

All people who took part in this study were women and aged between 26 to 79 years old. In this study, most people were White (64%) or Asian (22%).

People could take part in the study if they:

- Were men or women and aged 18 years or older.
- Had TNBC (tumours without receptors for the hormones oestrogen and progesterone, or too much of the protein HER2 compared with other breast cancer types).
- Group 1 only: late-stage TNBC, and tumours that were PD-L1-positive.
- Group 2 only: early-stage TNBC and agreed to undergo curative surgery after study treatment.

People could not take part in the study if:

- They had already received treatment for their late-stage TNBC before the start of this study (people in Group 1 only).

## 3. What happened during the study?

During the study, people were selected by their cancer characteristics to get one of the following treatments.

In **Group 1,** people with late-stage TNBC and PD-L1-positive tumours were given:

- **Tiragolumab** 840 mg combined with **atezolizumab** 1680 mg both injected into a vein once every 4 weeks plus **nab-paclitaxel** 100 mg for each square metre of body area (mg/m$^2$) injected into a vein once a week for 3 out of every 4 weeks.

In Group 2, people with early-stage TNBC were given one of the two combinations:

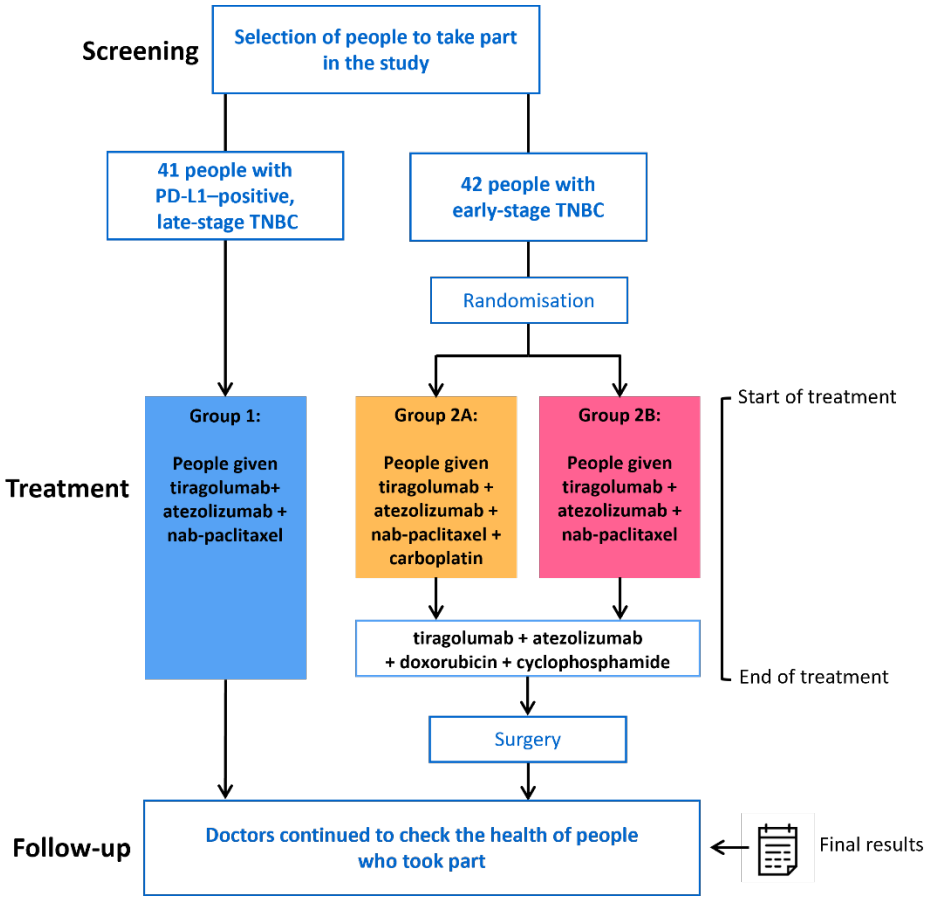
**Group 2A:**

- **Tiragolumab** 420 mg combined with **atezolizumab** 840 mg both injected into a vein every 2 weeks plus **nab-paclitaxel** 125 mg/m$^2$ injected into a vein once a week. **Carboplatin** 5 mg/mL/min was injected into a vein every 3 weeks a total of four times. Then, **tiragolumab** 420 mg and **atezolizumab** 840 mg combined with **doxorubicin** 60 mg/m$^2$ and **cyclophosphamide** 600 mg/m$^2$ were injected into a vein every 2 weeks a total of four times. People kept taking the study medicines for a total of 19 weeks followed by surgery or until their cancer got worse or they couldn't handle the side effects of the medicines.

**Group 2B:**

- **Tiragolumab** 420 mg combined with **atezolizumab** 840 mg injected into a vein every 2 weeks plus **nab-paclitaxel** 125 mg/m$^2$ injected into a vein once a week for 12 weeks. Then, **tiragolumab** 420 mg and **atezolizumab** 840 mg combined with **doxorubicin** 60 mg/m$^2$ and **cyclophosphamide** 600 mg/m$^2$ were injected into a vein every 2 weeks a total of four times. People kept taking the study medicines for a total of 19 weeks followed by surgery or until their cancer got worse or they couldn't handle the side effects of the medicines.

This study has ended, and this picture shows what happened in the study.

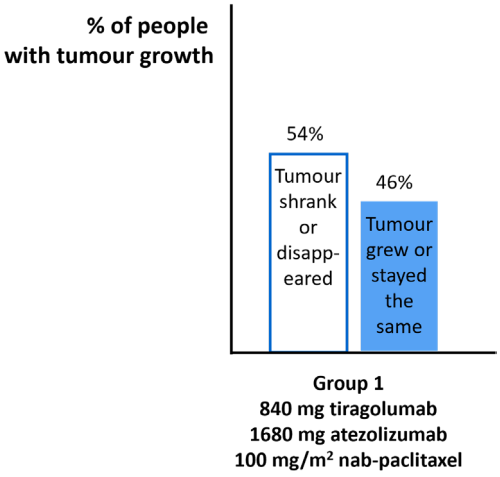



In **Group 1,** people's treatments were stopped if their cancer got worse or they couldn't handle the side effects of the medicines. People in **Group 2** kept taking the study medicines for a total of 19 weeks followed by surgery. When the study treatment finished, the people who took part were asked to go back to their study centre for more visits – to check their overall health. Look below to see more information about what happened in the study.

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

### **Question 1:** How many people in Group 1 had their tumours shrink or disappear?

At study completion, researchers found 54% of people (22 of 41 people) in this group who took tiragolumab plus atezolizumab and nab-paclitaxel had their tumours shrink or disappear. 46% of people (19 of 41 people) had their tumours grow or stay the same size.




### **Question 2:** How many people in Group 1 and Group 2 had side effects from the study medicines and what were the side effects?

Another piece of information that researchers collected was how many people had side effects, including what kind of side effects and how serious they were.
Overall, in **Group 1**,

- 100% of people (41of 41 people) experienced at least one side effect from the study medicines.
- 22% of people (9 of 41 people) experienced side effects that made them stop taking any of the study medicines.

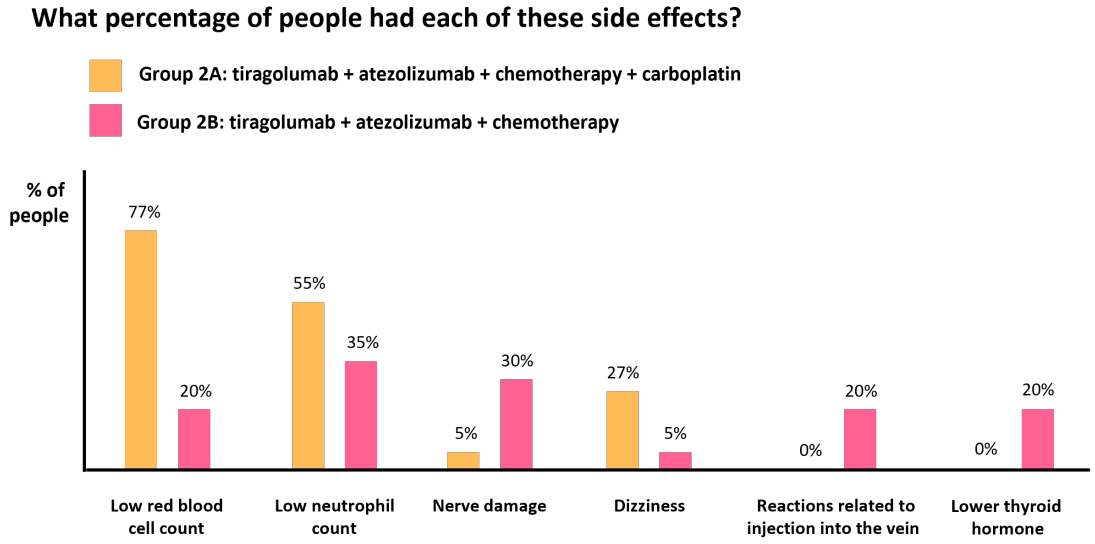
In **Group 2**,

- 100% of people (42 of 42 people) experienced at least one side effect from the study medicines.
- 21% of people (9 of 42 people) experienced side effects that made them stop taking any of the study medicines.

### **Question 3:** In Group 2, did people who took carboplatin have more side effects than those who did not take carboplatin?

Researchers also wanted to know if people taking carboplatin (**Group 2A**) made people have more side effects compared with people who did not take carboplatin (**Group 2B**).

In the graph below are the side effects between **Groups 2A** and **2B** that have a difference of greater than 20%.




Chemotherapy includes the other study medicines nab-paclitaxel, doxorubicin, and cyclophosphamide.
People who took carboplatin had more side effects related to their blood levels than people who did not take carboplatin. However, taking carboplatin did not affect the person's ability to take the other study medicines.
This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see section 8).

## 5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happen during the study.

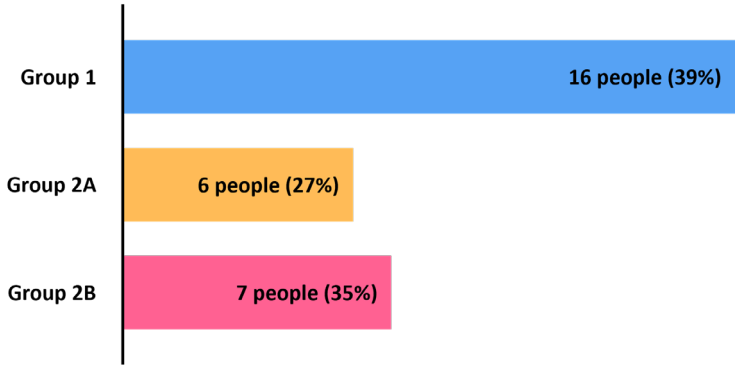
- They are described in this summary because the study doctor believes the side effects were related to the treatments in the study.
- Not all of the people in this study had all of the side effects.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to know that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies or those listed on the medicine pamphlets.
- Side effects can vary from mild to very serious and may vary from person to person.

Serious and common side effects thought to be related to the study medicines are listed in the following sections.

## Serious side effects

A side effect is considered 'serious' if it is life-threatening, leads the patient to need hospital care, or causes lasting problems.
During this study, 29 of the 83 people (35%) had at least one serious side effect.

**How many people had at least one serious side effect?**




- In **Group 1**, 39% of people (16 of 41 people) taking tiragolumab plus atezolizumab and nab-paclitaxel had a serious side effect.
- In **Group 2A**, 27% of people (6 of 21 people) taking tiragolumab plus atezolizumab, nab-paclitaxel, carboplatin, doxorubicin, and cyclophosphamide had a serious side effect.
- In **Group 2B**, 35% of people (7 of 21 people) taking tiragolumab plus atezolizumab, nab-paclitaxel, doxorubicin, and cyclophosphamide had a serious side effect.

People in **Group 1** did not have any serious side effects that affected more than two people.
The most common serious side effect in **Groups 2A** and **2B** was low neutrophil count.
There were some people in the study who died due to side effects. These were:

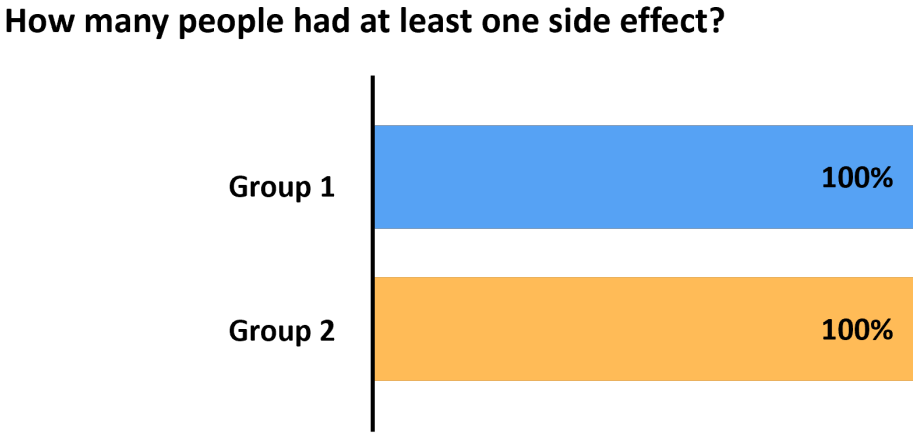
- 2 out of 41 people (5%) in **Group 1**.
- 0 out of 21 people (0%) in **Group 2A**.
- 0 out of 21 people (0%) in **Group 2B**.

The two people who died in **Group 1** died from severe lung inflammation (related to nab-paclitaxel treatment) and COVID-19 (unrelated to any study treatment).
During the study, some people stopped taking their medicine because of side effects:

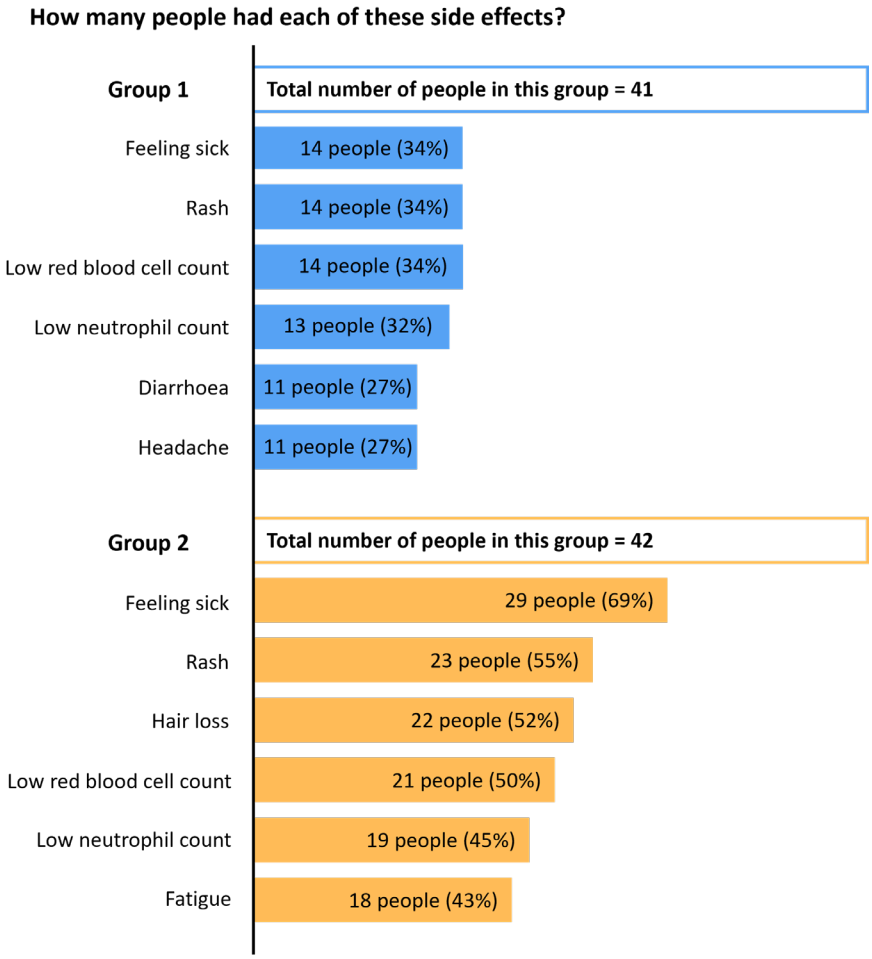
- In **Group 1**, 9 out of 41 people (22%) stopped taking their medicine.
- In **Group 2A**, 5 out of 21 people (23%) stopped taking their medicine.
- In **Group 2B**, 4 out of 21 people (20%) stopped taking their medicine.

## Most common side effects

Around 100% of people in Group 1 taking tiragolumab in combination with atezolizumab and nab-paclitaxel had a side effect. 100% of people in Group 2 taking tiragolumab, atezolizumab, nab-paclitaxel, doxorubicin, and cyclophosphamide with or without carboplatin had a side effect.




The most common side effects are shown in the following picture – these are the six most common side effects across both treatment groups. Some people had more than one side effect – this means that they are included in more than one row in the figure.



### 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, Phase 1b study of 83 people with TNBC from eight countries or regions. These results helped researchers learn more about TNBC treatment.

In this study, people with TNBC were treated with tiragolumab in combination with another immunotherapy and different types of chemotherapy. Researchers wanted to know if the study medicines could shrink or stop cancer (tumours) from growing and if the medicines were safe to take together.

People in the study were divided into two groups based on characteristics of their cancer.

- Group 1 had late-stage TNBC and PD-L1-positive tumours.
- Group 2 had early-stage TNBC and PD-L1-positive or -negative tumours. Group 2 was divided into two groups, 2A and 2B.

Group 1 had 41 people who took tiragolumab in combination with atezolizumab and nab-paclitaxel until their cancer got worse.

Group 2 had 42 people in it. Group 2A had 21 people in it who took tiragolumab, atezolizumab, nab-paclitaxel, doxorubicin, cyclophosphamide and carboplatin. Group 2B had 21 people in it who took tiragolumab, atezolizumab, nab-paclitaxel, doxorubicin, and cyclophosphamide. People in Group 2 took their study medicines for 19 weeks and then underwent surgery to remove their tumour.

54% of people in Group 1 had their tumours shrink or disappear. Generally, people treated with any of the study medicines had relatively mild and manageable side effects. People treated with carboplatin had some additional 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?

At the time of writing this summary, no more studies looking at tiragolumab in breast cancer are planned.

## 8. Where can I find more information?

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

- https://clinicaltrials.gov/study/NCT04584112
- https://forpatients.roche.com/en/trials/cancer/bc/a-study-of-the-safety--efficacy--and-pharmacokinetics-o-75095.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/bc/a-study-of-the-safety--efficacy--and-pharmacokinetics-o-75095.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, Efficacy, and Pharmacokinetics of Tiragolumab in Combination With Atezolizumab and Chemotherapy in Participants With Triple-Negative Breast Cancer".
The study is known as 'CO42177'.

- The protocol number for this study is: CO42177.
- The ClinicalTrials.gov identifier for this study is: NCT04584112.