

Summary of Clinical Trial Results

A study of ipatasertib given with immunotherapy and chemotherapy in people with triple-negative breast cancer, which had spread to other parts of the body, and had not received treatment for it

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:

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

This summary is based on information known at the time of writing.

The study started in November 2019 and stopped in early February 2023. This summary includes the main results that were collected and analysed in August 2021 and results about the side effects that were collected and analysed in May 2023.

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 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.**

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Glossary

- TNBC = triple-negative breast cancer.

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) that had spread to other parts of the body and the medicine studied – 'ipatasertib' – taken together with chemotherapy and immunotherapy.

Key information about this study

Why was this study done?

- This study was done to research a combination of drugs in people with a type of breast cancer called TNBC.
- The medicine being studied was called '**ipatasertib**' – taken together with an immunotherapy called '**atezolizumab**' and chemotherapy called '**paclitaxel**'.
The treatment combinations were:
 - Atezolizumab + ipatasertib + paclitaxel
 - Atezolizumab + paclitaxel
 - Ipatasertib + paclitaxel
 - Paclitaxel
- People were put into one of two groups, depending on whether their cancer had or did not have a higher-than-normal amount of a protein called programmed death-ligand 1 (PD-L1).
- This study included 242 people in 34 countries.

What were the results?

- This study was stopped early and did not finish enrolling. Therefore, these results do not fully describe the treatment the way it was intended to when the study was started. No definitive conclusions can be drawn from these results.
- The main findings were:
 - People without PD-L1-positive cancer who were given atezolizumab + ipatasertib + paclitaxel had the longest amount of time between the start of treatment and their cancer getting worse compared with people given ipatasertib + paclitaxel or paclitaxel in the study.
 - However, people without PD-L1-positive cancer lived for a similar amount of time after starting study treatment, regardless of which treatment group they were in.
 - People with PD-L1-positive cancer had a similar amount of time between the start of treatment and their cancer getting worse in both treatment groups.

How many people had serious side effects?

- Around 22% of people (53 out of 242 people) in the study had serious side effects.

1. General information about this study

Why was this study done?

Doctors now use information about breast cancer cells to sort breast cancers into different types to help them decide which treatments will work best. People in this study had a type of breast cancer called TNBC, which means that their cancer cells did not have receptors for the hormone oestrogen or the hormone progesterone and did not have the human epidermal growth factor receptor 2 (HER2) protein. Although other types of breast cancers can be treated with therapies that target these receptors, these therapies do not work in TNBC.

On certain cancer cells, there is a protein called PD-L1. If cancer cells have a higher-than-normal amount of this protein, this is called PD-L1-positive cancer.

Chemotherapy is another type of treatment for breast cancer that kills cancer cells and/or stops the cancer from growing. However, chemotherapy may work for only a short time and then the cancer may get worse again. Also, in some people, the cancer still grows even with treatment.

This means that new medicines are needed to be able to treat the cancer more effectively – by stopping the growth of the tumour or shrinking the tumour – and to help people live longer. If the tumour stops growing or shrinks, people may also be able to manage their cancer better.

‘ipatasertib’ is a type of cancer drug called a ‘growth blocker’ that works by blocking a protein called ‘AKT’, which is part of a family of proteins that help cells grow. Everyone has AKT in their body. In some cancer cells, AKT acts differently from normal (for example, it becomes more active than usual, or there is a lot more AKT in the cell than usual), helping the cancer grow. However, a study that analysed a different type of breast cancer reported that these changes may help ipatasertib plus chemotherapy to work better.

This study also used an immunotherapy called ‘atezolizumab’. Atezolizumab works by attaching to the PD-L1 protein on cancer cells and blocking it. This stops the cancer cells from using the PD-L1 protein to avoid being destroyed by the immune system.

All the people who took part in this study had TNBC that had spread to other parts of the body (advanced) and had not received treatment once the cancer had spread to the other parts of the body. This study wanted to look at different combinations of chemotherapy, immunotherapy and ipatasertib in people whose cancer was PD-L1-positive and people whose cancer was not PD-L1-positive.

What were the study medicines?

The medicine being studied was ‘**ipatasertib**’:

- You say this as ‘eye – pat – a – sert – ib’.
- Ipatasertib is a cancer drug called a ‘growth blocker’. It works by blocking a protein called ‘AKT’ that helps cancer cells grow.

The existing **immunotherapy** medicine used in this study was ‘**atezolizumab**’:

- You say this as ‘a – teh – zo – liz – oo – mab’.
- Atezolizumab works by stopping cancer cells from blocking cells in the immune system, meaning that the immune system is able to attack the cancer cells.

The **chemotherapy** medicine used in this study was '**paclitaxel**':

- You say this as 'pac – lee – tax – el'.
- This medicine works by stopping cancer cells from dividing into new cells, so it blocks the growth of the tumour.

This study used **placebos** for atezolizumab and ipatasertib:

- You say this as 'plah – see – bo'.
- The placebos looked the same as atezolizumab and ipatasertib but did not contain any real medicine. This means they had no medicine-related effect on the body.

What did researchers want to find out?

- Researchers did this study to see how well the different combinations of chemotherapy, immunotherapy and ipatasertib worked (see section 4 'What were the results of the study?').
- They also wanted to find out how safe the medicine was by checking how many people had side effects and seeing how serious they were, when taking each of the medicines during this study (see section 5 'What were the side effects?').

The main questions that researchers wanted to answer was:

1. In people with PD-L1-positive cancer, how much time was there between the start of treatment and the cancer getting worse or people dying?
2. On average, how long did people with PD-L1-positive cancer live after starting study treatment?
3. In people without PD-L1-positive cancer, how much time was there between the start of treatment and the cancer getting worse or people dying?
4. On average, how long did people without PD-L1-positive cancer live after starting study treatment?

What kind of study was this?

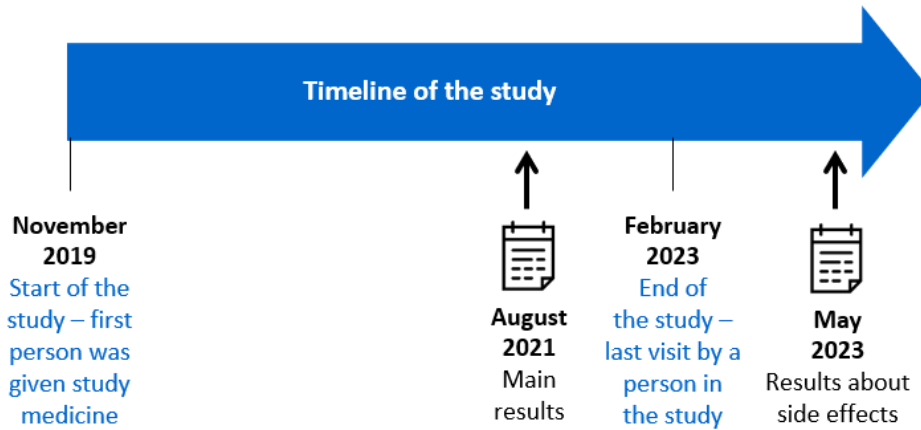
This study was a 'Phase 3' study. This means that ipatasertib had been tested in a smaller number of people with TNBC before this study. In this study, a larger number of people with TNBC either took ipatasertib or a placebo – this was to find out whether ipatasertib and atezolizumab worked to increase the time between the start of treatment and the cancer getting worse, as well as what side effects were reported with the drugs.

The study was 'randomised'. This means that it was decided by chance which of the medicines people in the study would take. Randomly choosing which medicine people take makes it more likely that the types of people in both groups (for example, based on age and race) will be a similar mix. Apart from the exact medicines being tested in each group, all other aspects of care were the same between the groups.

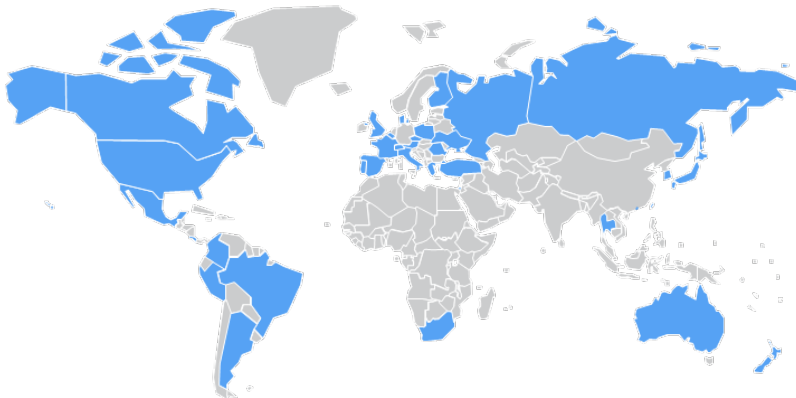
A placebo was used so that the patient and the doctor did not know whether they were receiving the real medicine or not. This is because knowing can sometimes affect the results of the study.

When and where did the study take place?

The study started in November 2019 and ended early in February 2023. This summary includes the main results up until August 2021 and results about side effects up until May 2023.



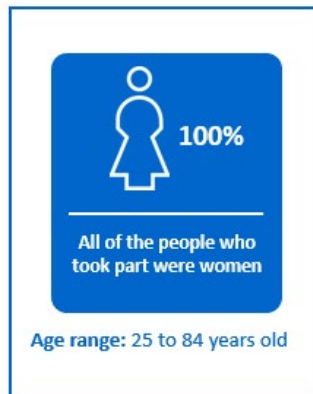
The study took place at 215 study centres across 34 countries. The countries are shown in the image below:



- Argentina
- Australia
- Austria
- Belgium
- Brazil
- Canada
- Colombia
- Costa Rica
- Czechia
- Denmark
- Finland
- France
- Greece
- Hong Kong
- Israel
- Italy
- Japan
- Republic of Korea
- Mexico
- New Zealand
- Peru
- Poland
- Portugal
- Romania
- Russian Federation
- South Africa
- Spain
- Switzerland
- Taiwan
- Thailand
- Turkey
- Ukraine
- United Kingdom
- United States

2. Who took part in this study?

In this study, 242 people with advanced TNBC took part.



People could take part in this study if they had:

- Triple-negative breast cancer
- Breast cancer that had spread from where it started to nearby cells or to other parts of the body
- A life expectancy of at least 6 months

People could NOT take part in this study if they had:

- Previously received treatment that spreads across the body for breast cancer that had spread to other parts of the body
- Taken a medicine that works in a similar way to ipatasertib
- Cancer that had spread to the brain or spinal cord
- Other types of cancer in the last 5 years before the start of the study
- Certain health problems, including a history of liver disease, inflammatory bowel disease or heart problems

3. What happened during the study?

Ipatasertib was given as a tablet on Days 1–21 of a 4-week cycle and atezolizumab and chemotherapy were given through a needle into a vein on certain days in the treatment cycle.

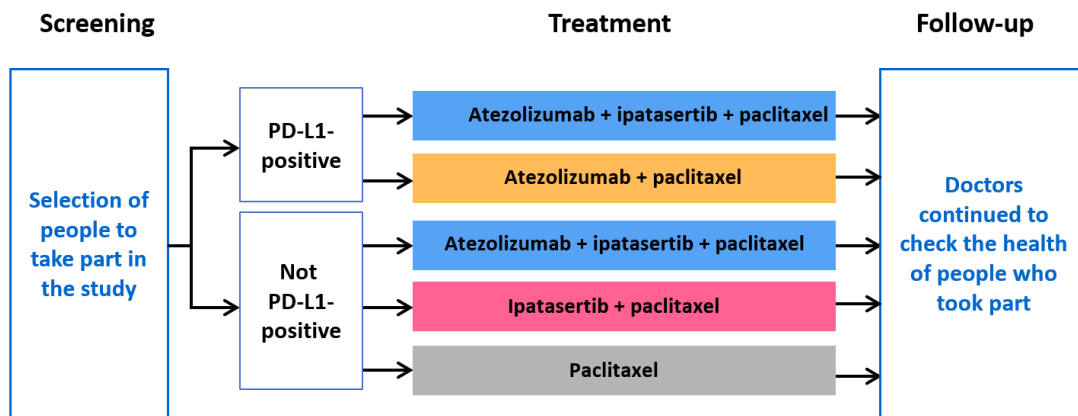
People with PD-L1-positive cancer were given one of two combinations of the study medicines:

- Atezolizumab + paclitaxel + placebo for ipatasertib
- Atezolizumab + ipatasertib + paclitaxel

People without PD-L1-positive cancer were given one of three combinations of the study medicines:

- Paclitaxel + placebo for ipatasertib + placebo for atezolizumab
- Ipatasertib + paclitaxel + placebo for atezolizumab
- Atezolizumab + ipatasertib + paclitaxel

When the study finished, the people who took part were asked to go back to their study centre for more visits to check their overall health. The following picture shows more information about what happened in the study.



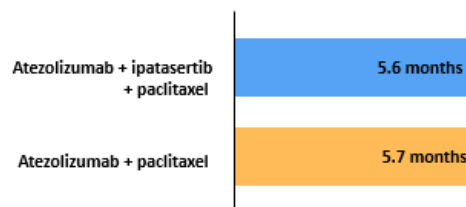
4. What were the results of the study?

Question 1. In people with PD-L1-positive cancer, how much time was there between the start of treatment and the cancer getting worse or people dying?

After starting the medicine, people in the study were monitored for about 11.6 months on average.

Researchers looked at how much time there was before the cancer became worse (in other words, spread, spread further or grew larger) or people died.

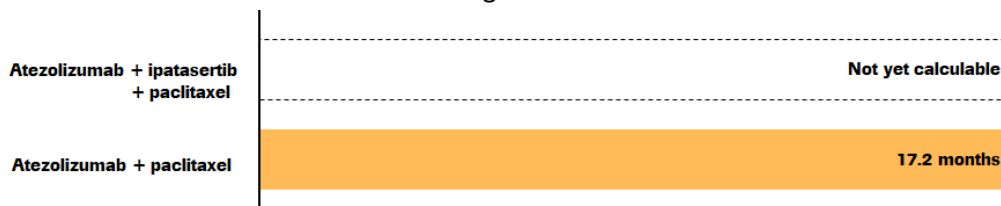
People with PD-L1-positive cancer had a similar amount of time between the start of treatment and their cancer getting worse or dying in both treatment groups.



Question 2. On average, how long did people with PD-L1-positive cancer live after starting study treatment?

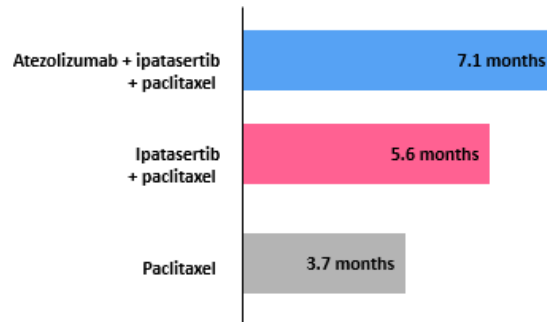
In the group with PD-L1-positive cancer who were given atezolizumab + paclitaxel, people lived on average for 17.2 months after starting treatment.

In the group of people with PD-L1-positive cancer who were given atezolizumab + ipatasertib + paclitaxel, not enough people had died by the time the study was stopped early to enable researchers to calculate this average.



Question 3. In people without PD-L1-positive cancer, how much time was there between the start of treatment and the cancer getting worse or people dying?

People without PD-L1-positive cancer who were given atezolizumab + ipatasertib + paclitaxel had the longest amount of time between the start of treatment and their cancer getting worse or dying in the study. People without PD-L1-positive cancer who were given paclitaxel had the shortest amount of time between the start of treatment and their cancer getting worse or dying in the study.



Question 4. On average, how long did people without PD-L1-positive cancer live after starting study treatment?

People without PD-L1-positive cancer lived for a similar amount of time before dying, regardless of which treatment group they were in.



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).

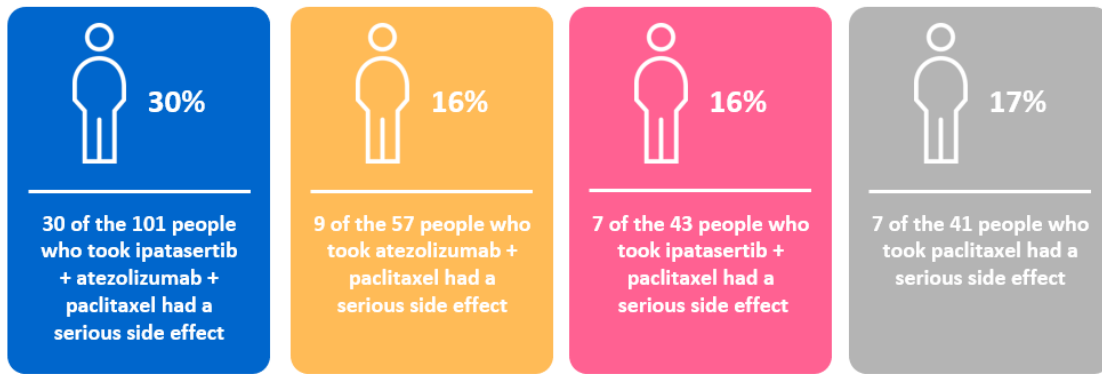
5. What were the side effects?

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

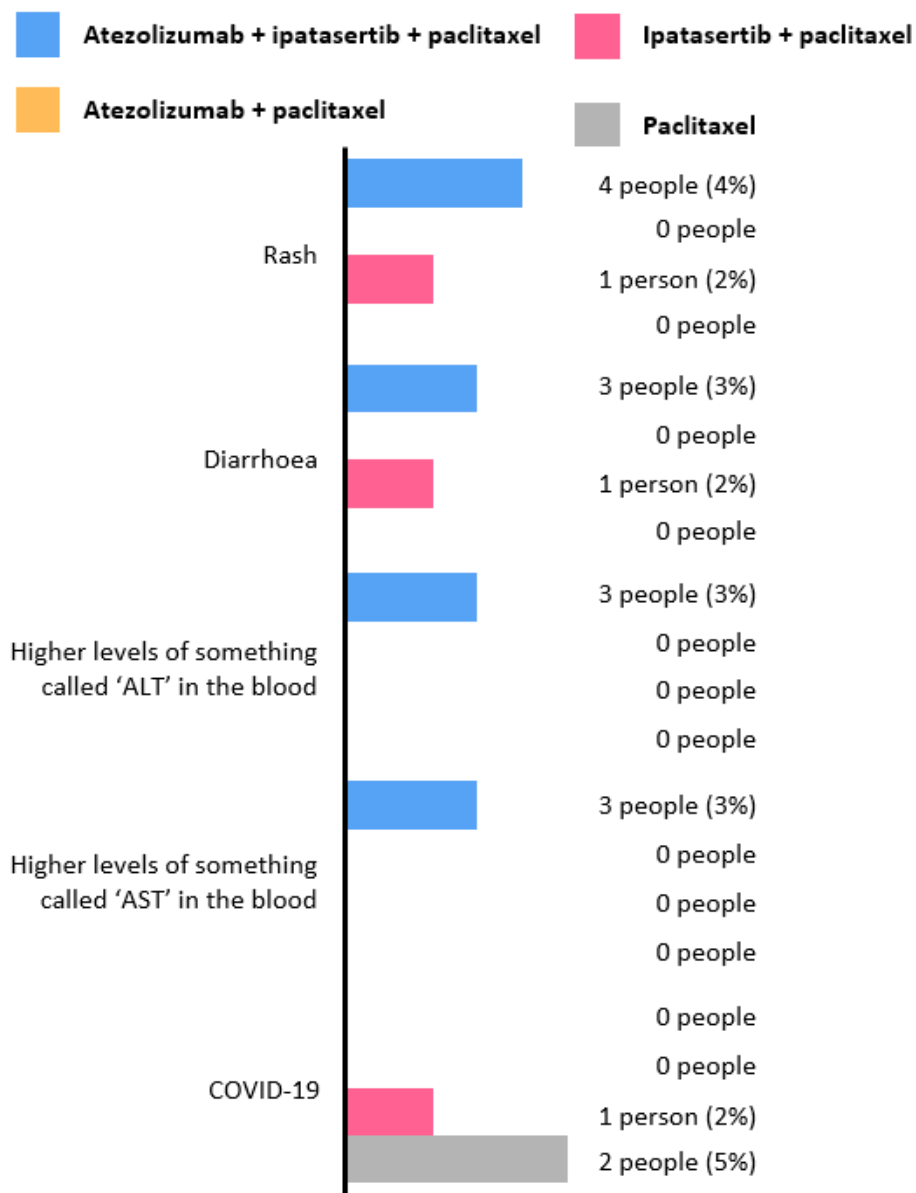
- Not all the people in this study had all the side effects.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects may be different from those reported in other studies or those that appear on the medicine leaflets.
- Serious and common side effects are listed in the following sections.

Serious side effects

A side effect is considered 'serious' if it is life-threatening, needs hospital care or causes lasting problems. The number of people who had serious side effects is shown below.



The five most common serious side effects are shown in the following image. Some people had more than one side effect – this means that they are included in more than one row in the image.



There were some people in the study who died due to side effects. These were:

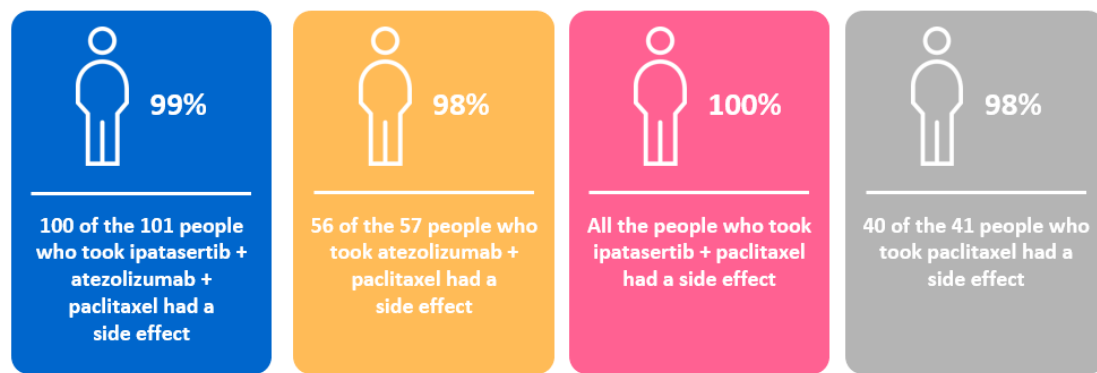
- 6 out of 101 people (6%) who were given atezolizumab + ipatasertib + paclitaxel.
- 1 out of 43 people (2%) who were given ipatasertib + paclitaxel.
- 1 out of 41 people (2%) who were given paclitaxel.

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

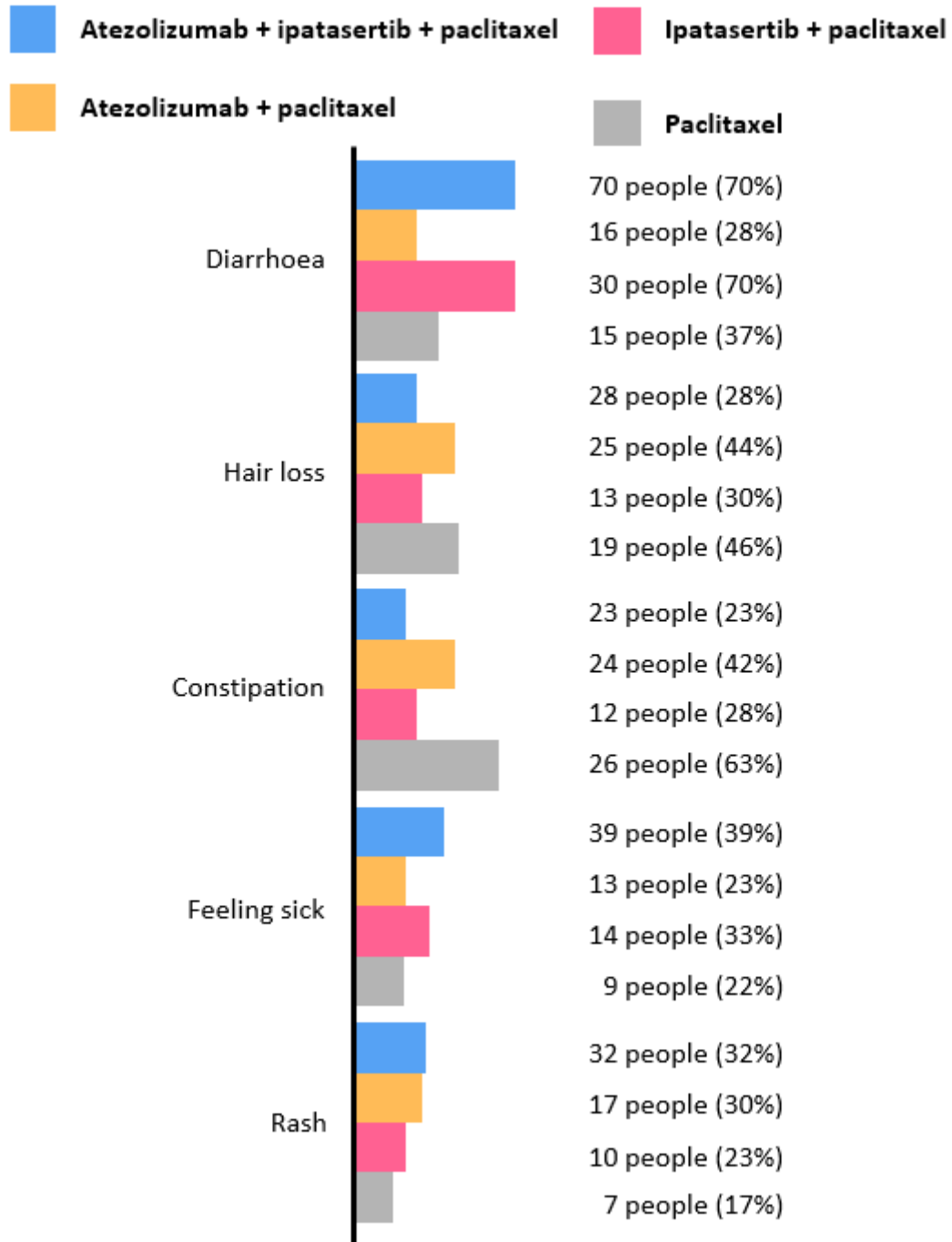
- 12 of the 242 people in the study stopped taking atezolizumab or the placebo.
- 18 of the 242 people in the study stopped taking ipatasertib or the placebo.
- 33 of the 242 people in the study stopped taking paclitaxel.

Most common side effects

The number of people who had side effects due to the medicines taken is shown below.



The five most common side effects are shown in the following image. Some people had more than one side effect – this means that they are included in more than one row in the image.



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 242 people with advanced TNBC. These results helped researchers learn more about this type of breast cancer and treatment with ipatasertib. In addition, these results helped researchers learn more about how well ipatasertib plus chemotherapy and immunotherapy works to treat this type of breast cancer as well as how safe it is.

People without PD-L1-positive cancer who were given atezolizumab + ipatasertib + paclitaxel had the longest amount of time between the start of treatment and their cancer getting worse compared with people given ipatasertib + paclitaxel or paclitaxel in the study. However, there was no real difference between the treatment groups in how long people lived after starting study treatment. People with PD-L1-positive cancer had a similar amount of time between the start of treatment and their cancer getting worse in both treatment groups. The study was stopped early, so no definitive conclusions can be drawn from these results. The numbers and types of side effects were comparable between treatment groups.

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 this study may be different from other studies with the same medicine.

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

7. Are there plans for other studies?

Other studies looking at the safety and effects of ipatasertib are happening. These studies are looking at the use of ipatasertib in different situations, for example:

- Together with other treatments
- In other types of breast cancer, including hormone receptor-positive and HER2-negative
- In other types of cancer

8. Where can I find more information?

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

- <https://clinicaltrials.gov/study/NCT04177108>
- <https://www.clinicaltrialsregister.eu/ctr-search/search?query=2019-000810-12>
- <https://forpatients.roche.com/en/trials/cancer/bc/a-study-of-ipatasertib-in-combination-with-atezolizumab-93464.html>

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: 'First-Line Ipatasertib, Atezolizumab, and Taxane Triplet for Metastatic Triple-Negative Breast Cancer: Clinical and Biomarker Results'. The authors of the scientific paper are: Peter Schmid, Nicholas C. Turner, Carlos H. Barrios, Steven Jay Isakoff, Sung-Bae Kim and others. The paper is published in the journal 'Clinical Cancer Research', volume number 30, on pages 767–778. <https://doi.org/10.1158/1078-0432.CCR-23-2084>

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 under 'Contact Us' – <https://forpatients.roche.com/en/trials/cancer/bc/a-study-of-ipatasertib-in-combination-with-atezolizumab-93464.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 Ipatasertib in Combination with Atezolizumab and Paclitaxel as a Treatment for Participants with Locally Advanced or Metastatic Triple-Negative Breast Cancer'.

The study is known as 'IPATunity170'.

- The protocol number for this study is: CO41101.
- The ClinicalTrials.gov identifier for this study is: NCT04177108.
- The EudraCT number for this study is: 2019-000810-12.