

Summary of Clinical Trial Results

A study to look at whether adding atezolizumab to chemotherapy works well in women with an aggressive type of breast cancer called ‘triple-negative breast cancer’ that has not spread to other parts of the body. The treatment was given before surgery to get rid of or shrink the tumour and help surgery be more successful.

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 it was written (September 2020).

The study started in July 2017 and is planned to end around October 2022. This summary includes the results up until April 2020. At the time of writing this summary, the study is still happening – this summary presents the complete results from one part of the study.

One study can’t tell us everything about how safe a medicine is and how well it works. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies of 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

1. General information about this study
2. Who took part in this study?
3. What happened during the study?
4. What were the results of the study?
5. What were the side effects?
6. How has this study helped research?
7. Are there plans for other studies?
8. Where can I find more information?

Glossary

- Triple-negative breast cancer = tumours that have low amounts of three proteins that interact with oestrogen, progesterone and human epidermal growth factor (HER2)
- Immunotherapy (for cancer) = medicine used in cancer to help the body’s immune system to attack tumours
- Neoadjuvant therapy = treatment given before surgery to get rid of or shrink the tumour and help surgery be more successful
- PD-L1 = ‘programmed death-ligand 1’, a protein that normally stops the immune system from attacking good cells. In cancer, tumour cells can use PD-L1 to hide from the immune system

Thank you to the people who took part in this study

The people who took part in this study helped researchers answer important questions about triple-negative breast cancer and the medicines studied – ‘atezolizumab’, ‘*nab*-paclitaxel’, ‘doxorubicin’ and ‘cyclophosphamide’.

Key information about this study

- This study was done to find out whether adding the study medicine (called ‘atezolizumab’) to chemotherapy (*nab*-paclitaxel, doxorubicin and cyclophosphamide) before surgery would get rid of the cancer (tumour) in women with a type of breast cancer called ‘triple-negative breast cancer’.
- In this study, women were given chemotherapy combined with either the study medicine or a placebo (something that looked the same as atezolizumab but did not contain any real medicine). It was decided by chance which treatment each person was given. The chemotherapy medicines were *nab*-paclitaxel first, and then doxorubicin plus cyclophosphamide.
- This study included 333 people in 13 countries or regions.
- So far, the study has shown that around 58% of women who got atezolizumab plus chemotherapy had their tumours go away completely by the time of surgery, compared with 41% of women who got placebo and chemotherapy (17% difference between groups).
- In women whose tumours had a protein called PD-L1, around 69% of women who got atezolizumab plus chemotherapy had their tumours go away completely by the time of surgery, compared with 49% of women who got placebo and chemotherapy (20% difference between groups). However, the results were not statistically significant.
- Around 23% of women (37 out of 164 women) who got atezolizumab plus chemotherapy had serious side effects related to treatment, compared with around 16% of people (26 out of 167 people) who got the placebo and chemotherapy.
- At the time of writing this summary, the study is still happening. It is planned to end around October 2022.

1. General information about this study

Why was this study done?

Triple-negative breast cancer is a type of breast cancer that is aggressive. Aggressive cancers grow or spread quickly. Triple-negative breast cancer has one of the highest death rates and there are fewer treatments than for other types of breast cancer.

- The 'triple-negative' means that three proteins (oestrogen, progesterone and HER2 receptors) appear on the breast cancer cells in low amounts. This type of cancer doesn't respond to some treatments as well as other breast cancers.
 - There are several different types of triple-negative breast cancer, which have different causes of tumour cell growth and different amounts of immune cells in the tumour.
- Breast cancer that has not spread to other parts of the body or has not spread far is called 'early-stage' cancer. Early-stage cancer is stage I, II or III.
 - Cancers that have spread to nearby lymph nodes are still called early-stage cancers.
 - About 10% to 20% of people (10 to 20 out of 100 people) with early-stage breast cancer have triple-negative breast cancer.
- People with early-stage triple-negative breast cancer are often treated with a combination of medicines that kill cancer cells – called 'chemotherapy'.
 - Chemotherapy may be given before surgery or after surgery. Chemotherapy before surgery can shrink the tumour to make the surgery easier. Also, how well the chemotherapy works on the tumour can help doctors to pick future treatments that might also work.
 - The chemotherapy combination used in this study has three different medicines – *nab*-paclitaxel is given first, then doxorubicin and cyclophosphamide.

About 70% of people (7 out of 10 people) with early-stage triple-negative breast cancer who get standard chemotherapy treatment can live 5 years without the cancer spreading to other parts of the body. However, in about 30% to 40% of people (3 to 4 out of 10 people) the cancer does spread, and the people eventually die. People whose triple-negative breast cancer spreads to other parts of the body typically live about one and a half years or less. Therefore, better treatments are needed.

What are the study medicines?

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

- You say this as ‘a – teh – zo – liz – oo – mab’.
- The body’s immune system fights diseases like cancer. However, cancer cells can produce a protein called PD-L1 to stop the immune system from attacking the cancer. Atezolizumab stops PD-L1 from working – which means that the immune system can now fight the cancer cells.
- When people take atezolizumab, their tumour (cancer) may get smaller.
- This type of medicine is called immunotherapy.

Atezolizumab was compared with a ‘placebo’

- You say this as ‘plah – see – bo.’
- The placebo looked the same as atezolizumab but did not contain any real medicine. This means that it had no medicine-related effect on the body.

Both atezolizumab and placebo were given with chemotherapy. With larger tumours, chemotherapy can be given before surgery to shrink the size of the tumour and make the surgery easier. Researchers wanted to know if adding atezolizumab to chemotherapy given before surgery worked better than just chemotherapy.

- The chemotherapy was ‘*nab*-paclitaxel’ (known by its brand name Abraxane®) followed by ‘doxorubicin’ (known by its brand name Adriamycin®) plus ‘cyclophosphamide’.
- Chemotherapy works by killing cancer cells and stopping them from growing and dividing.

What did researchers want to find out?

- Researchers wanted to see if atezolizumab plus chemotherapy worked better than placebo plus chemotherapy (see section 4 ‘What were the results of the study?’).
- They also wanted to see how safe the medicine was – by looking at how many people had more side effects when taking atezolizumab plus chemotherapy during this study (see section 5 ‘What were the side effects?’).

The main questions that researchers wanted to answer were:

1. Could atezolizumab lead to more women having their tumours go away completely from the breast and nearby lymph nodes by the time of surgery?
2. In the women whose tumours had cells with the protein PD-L1 (called ‘PD-L1 positive’), could atezolizumab lead to more women having their tumours go away completely from the breast and nearby lymph nodes by the time of surgery?

Other questions that researchers wanted to answer included:

3. Could atezolizumab reduce the risk of the cancer getting worse?
4. Could atezolizumab reduce the risk of the cancer coming back after surgery?
5. Could atezolizumab reduce the risk of dying?
6. What kind of side effects were there? Which side effects were serious?

What kind of study was this?

This study was a 'Phase 3' study. In this study, a large number of people with triple-negative breast cancer took either atezolizumab plus chemotherapy or placebo plus chemotherapy. This study was done to find out about the side effects of combining atezolizumab with chemotherapy and if atezolizumab plus chemotherapy worked to get rid of the tumour.

The study was 'randomised'. This means that it was decided by chance which of the medicines people in the study would have – like tossing a coin.

This was a 'double-blind' study. This means that neither the people taking part in the study nor the study doctors knew which of the study medicines people were taking before surgery and finding out whether the treatment got rid of the tumour.

'Blinding' of a study is done so that any effect seen from the medicine is not due to something people would have expected to happen – if they had known which medicine they were taking.

When and where did the study take place?

The study started in July 2017 and is planned to end around October 2022. This summary includes the results up until April 2020. At the time of writing this summary, the study is still happening. This summary shows the complete results from one part of the study.

The study took place at 75 study centres – in 13 countries and regions in Asia, Europe, North America, Oceania and South America. The countries and regions are: Australia, Belgium, Brazil, Canada, Germany, Italy, Japan, Poland, South Korea, Spain, Taiwan, the United Kingdom and the United States.

2. Who took part in this study?

In this study, 333 women with triple-negative breast cancer took part.

Women who took part in the study were between 22 and 78 years of age. In this study, 63% of the people were White, 26% were Asian, and 7% were Black or African American.

People could take part in the study if they:

- Had tumours with cells that have low amounts of three proteins – oestrogen, progesterone and HER2 receptor proteins
- Had tumours that were larger than 2 centimetres (about $\frac{3}{4}$ of an inch)
- Had tumours that had not spread or had spread only to the lymph nodes near the breast
- Were able to walk around and do light housework or office work

People could not take part in the study if they:

- Had tumours that spread to other parts of the body
- Were previously treated with chemotherapy for breast cancer
- Were previously treated with chemotherapy with taxanes (for example, docetaxel, paclitaxel or *nab*-paclitaxel) or anthracyclines (for example, doxorubicin or epirubicin) for any type of cancer
- Were treated with anticancer immunotherapy
- Previously had breast surgery to remove the tumour
- Had disorders called 'autoimmune diseases' that caused their immune system to attack healthy cells in the body

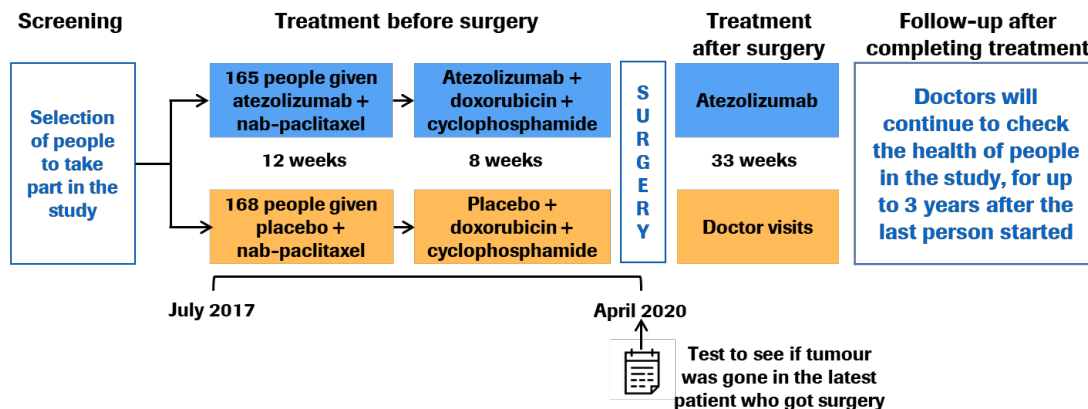
3. What happened during the study?

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

The two treatments were:

1. **Atezolizumab** 840 mg injected into a vein once every 2 weeks combined with **nab-paclitaxel** 125 mg for each square meter of body area (mg/m^2) injected into a vein once every week. These two drugs were given for 12 weeks. Then, **atezolizumab** 840 mg plus **doxorubicin** 60 mg/m^2 plus **cyclophosphamide** 600 mg/m^2 was injected into a vein every 2 weeks for 8 weeks. Filgrastim or pegfilgrastim was given to reduce the drugs' effects on white blood cells.
 - People then had breast surgery, and doctors did tests to see if the tumour was gone.
 - People were then treated with **atezolizumab** 1200 mg once every 3 weeks for 33 weeks.
 - If their tumours were not completely gone, then people could get treatments their doctor recommended in addition to atezolizumab.
 - People could also get radiotherapy after surgery if their doctor recommended it.
2. **Placebo** injected into a vein with the same timing as atezolizumab in the atezolizumab group. **Nab-paclitaxel** and **doxorubicin** plus **cyclophosphamide** were injected into a vein with the same timing as in the atezolizumab group.
 - People then had breast surgery, and doctors did tests to see if the tumour was gone.
 - Then people were monitored with regular doctor visits.
 - People no longer got placebo after surgery but could get radiotherapy or additional treatments if their doctor recommended it.

This study is still happening, so some people are still being treated with the study medicines. This picture shows what has happened in the study so far – and what the next steps are.



The symbol on the timeline (📅) shows when the information in this summary was collected. The first person who took part in the study started in July 2017, and people continued to be recruited until September 2019. April 2020 was the latest time a person in the study was checked to see if their tumour was gone.

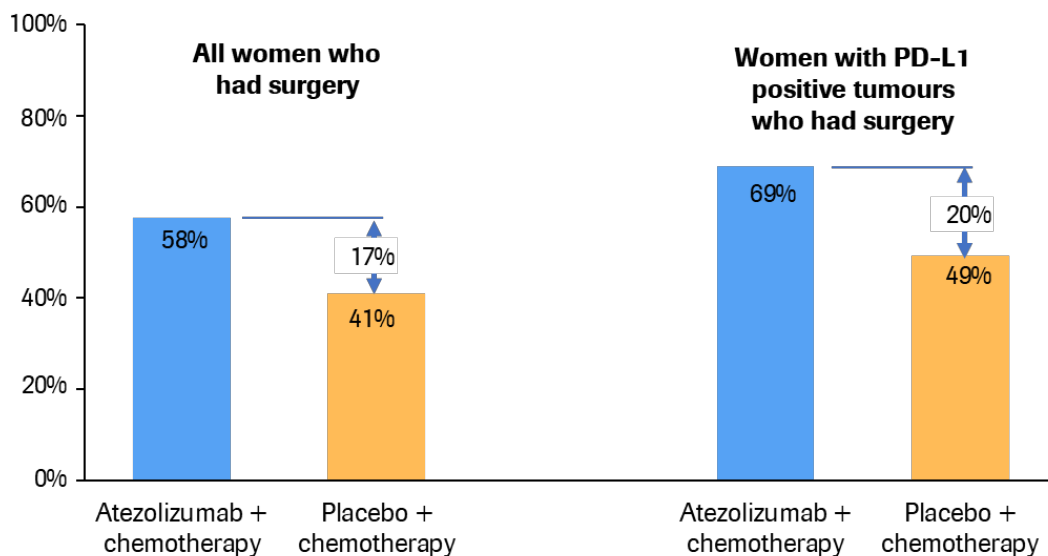
4. What were the results of the study?

Question 1: Could atezolizumab lead to more women having their tumours go away completely?

Researchers looked at the tissue taken out during surgery to see if the tumour was completely gone from the breast and nearby lymph nodes.

- When treated before surgery, 58% of women who got atezolizumab plus chemotherapy had their tumours go away completely, compared with 41% of women who got placebo plus chemotherapy.
- That means women had their tumours go away completely with a 17% difference between women who got atezolizumab plus chemotherapy compared with women who got placebo plus chemotherapy.

Percentage of women whose tumours went away completely after surgery



Question 2: In the women who had PD-L1 positive tumours, could atezolizumab lead to more women having their tumours go away completely?

Researchers looked at what percentage of women with PD-L1 positive tumours had their tumours go away completely from the breast and nearby lymph nodes. However, the results were not statistically significant

- When treated before surgery, 69% of women who got atezolizumab plus chemotherapy had their tumours go away completely, compared with 49% who got placebo plus chemotherapy.
- This means women had their tumours go away completely with a 20% difference between women who got atezolizumab plus chemotherapy compared with women who got placebo plus chemotherapy.

Question 3: Could atezolizumab reduce the risk of the cancer getting worse?

Researchers also looked at whether atezolizumab could reduce the risk of the cancer getting worse. They looked at whether the tumour grew before surgery or came back after it was removed during surgery. They also looked at how many of the participating women died.

- These results are very early and not yet clear. Also, the study was not designed to make any definite conclusions about the long-term risk of the cancer getting worse.
- Women who got atezolizumab plus chemotherapy seemed to have a 24% lower risk of the cancer getting worse than women who got placebo plus chemotherapy.

Question 4: Could atezolizumab reduce the risk of the cancer coming back after surgery?

Researchers also looked at whether atezolizumab could reduce the risk of the cancer coming back after surgery. They looked at whether participating women's cancer came back and also whether women died.

- These results are very early and not yet clear. Also, the study was not designed to make any definite conclusions about the long-term risk of the cancer coming back after surgery.
- Women who got atezolizumab plus chemotherapy appeared to have a 26% lower risk of the cancer coming back than women who got placebo plus chemotherapy.

Question 5: Could atezolizumab reduce the risk of dying?

Researchers also looked at whether atezolizumab could reduce the risk of the women who took part in the study dying from any cause.

- These results are very early and not yet clear. Also, the study was not designed to make any definite conclusions about the long-term risk of dying.
- Women who got atezolizumab plus chemotherapy seemed to have a 31% lower risk of dying from any cause than women who got placebo plus chemotherapy.

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 'Where can I find more information?').

5. What were the side effects?

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

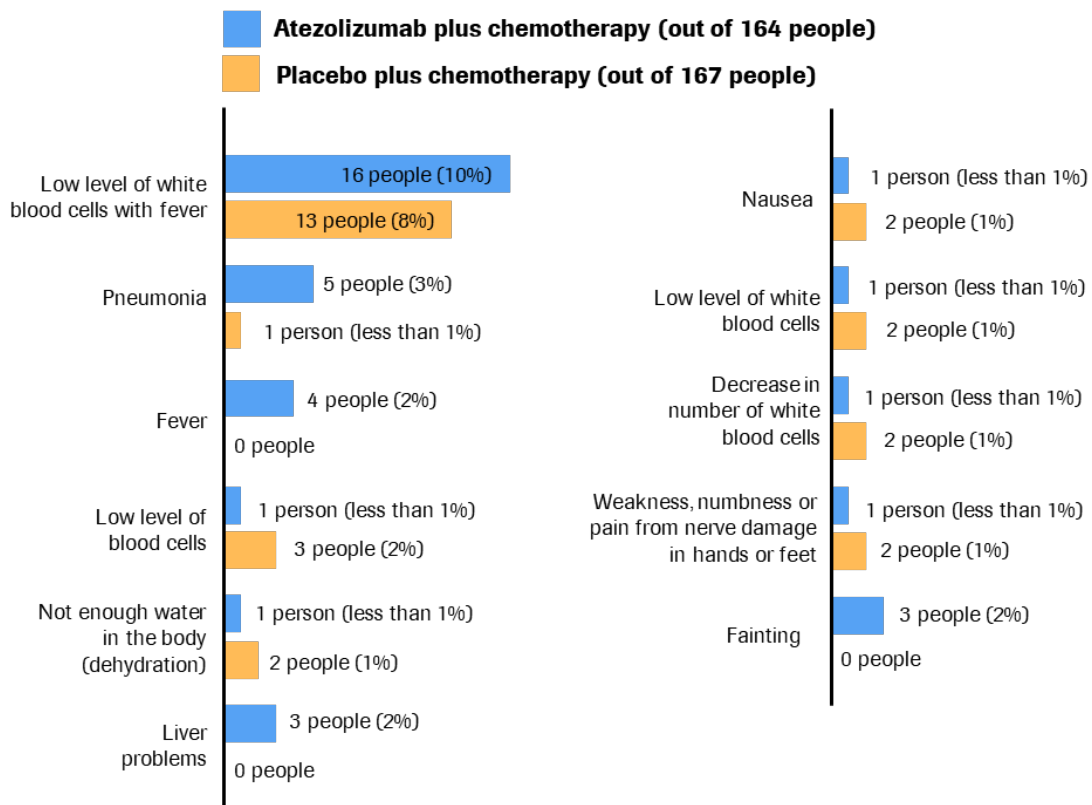
- Not all of the people in this study had all of the side effects.
- Side effects may be mild to very severe and can be different from person to person.
- It is important to know that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies or those listed on the medicine leaflets.

Serious side effects

A side effect is considered ‘serious’ if it is life-threatening, needs hospital care or causes lasting problems or death. They are described in this summary because the study doctor believes that the side effects were related to the treatments in the study.

During treatment given before surgery, 19 out of 100 people (19%) had at least one serious side effect. Around 23% of people who got atezolizumab plus chemotherapy had a serious side effect related to treatment, compared with around 16% of people who got placebo plus chemotherapy.

The picture below shows the most common serious side effects related to treatment – these are the 11 most common serious side effects that happened in at least 1 out of 100 people (1%) in either treatment group. The blue bars show the number of side effects that happened in women who got atezolizumab plus chemotherapy. The orange bars show side effects in women who got placebo plus chemotherapy. The most common side effect in people who got atezolizumab plus chemotherapy was low levels of white blood cells accompanied by fever. The other most common side effects in this group were pneumonia and fever. Adding atezolizumab did not keep people from getting chemotherapy. The ability to get chemotherapy is important for getting long-term benefits in early-stage triple-negative breast cancer, which is a disease that can potentially be cured.



No women in the study died because of side effects that may have been related to one of the study medicines.

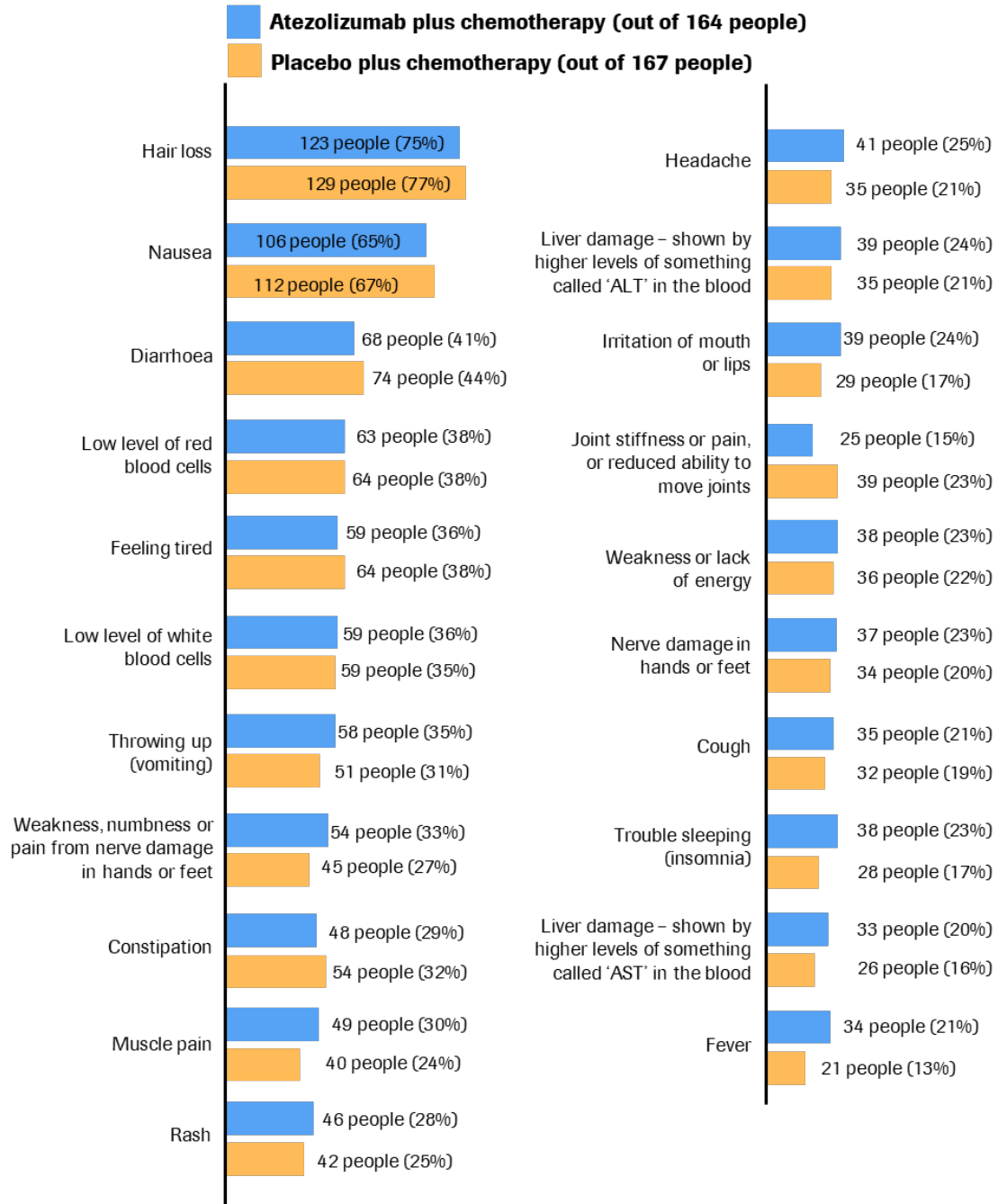
During treatment given before surgery, some people stopped taking their medicine because of the side effects:

- In the atezolizumab plus chemotherapy group, 37 out of 164 people (23%) stopped taking any of the drugs in their treatment.
- In the placebo plus chemotherapy group, 33 out of 167 people (20%) stopped taking any of the drugs in their treatment.

Most common side effects

During treatment given before surgery, around 99 out of 100 people (99%) in both groups had a side effect that was not considered serious. These side effects were due to any cause.

This picture shows the most common side effects – these are the 21 most common side effects that happened in at least 20 out of 100 people (20%) across both treatment groups. The blue bars show the number of side effects that happened in women who got atezolizumab plus chemotherapy. The orange bars show side effects in women who got placebo plus chemotherapy.



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 'Where can I find more information?').

6. How has this study helped research?

The information presented here is from one study of 333 people with triple-negative breast cancer. These results helped researchers learn more about triple-negative breast cancer and treatment with atezolizumab plus chemotherapy (*nab*-paclitaxel followed by doxorubicin and cyclophosphamide).

Treatment with atezolizumab plus chemotherapy before surgery increased the number of women whose tumours had completely gone away by the time of surgery. The results are not yet clear, but treatment appeared to reduce the risk of the cancer getting worse or coming back. Women who got atezolizumab plus chemotherapy had more serious side effects than women who got placebo plus chemotherapy. The most common serious side effects related to treatment were pneumonia and a low level of white blood cells. The most common side effects were hair loss, nausea, diarrhoea and feeling tired. Side effects were mostly related to the chemotherapy.

One study can't tell us everything about the side effects of a medicine and how well it works. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

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

7. Are there plans for other studies?

This study is still going on, and doctors are collecting more information about treatment with atezolizumab plus chemotherapy. Other studies with atezolizumab using different chemotherapy medicines for the treatment of early-stage triple-negative breast cancer are ongoing.

8. Where can I find more information?

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

- <https://clinicaltrials.gov/ct2/show/results/NCT03197935>
- <https://www.clinicaltrialsregister.eu/ctr-search/trial/2016-004734-22/DE>
- <https://forpatients.roche.com/en/trials/cancer/bc/a-study-to-investigate-atezolizumab-and-chemotherapy-compared-wi.html>

If you want to find out more about the results of this study, the full title of the relevant scientific paper is: “Neoadjuvant atezolizumab in combination with sequential *nab*-paclitaxel and anthracycline-based chemotherapy vs placebo and chemotherapy in patients with early-stage triple-negative breast cancer (Impassion031): a randomised, double-blind, phase 3 trial”. The authors of the scientific paper are: Elizabeth A. Mittendorf, Hong Zhang, Carlos H. Barrios, Shigehira Saji, Kyung Hae Jung and others. The paper is published in the journal *The Lancet*, published online 20 September 2020.

Who can I contact if I have questions about this study?

If you have any more 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-to-investigate-atezolizumab-and-chemotherapy-compared-wi.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 to Investigate Atezolizumab and Chemotherapy Compared With Placebo and Chemotherapy in the Neoadjuvant Setting in Participants With Early Stage Triple Negative Breast Cancer (IMpassion031)”.

The study is known as ‘IMpassion031’.

- The protocol number for this study is: WO39392.
- The ClinicalTrials.gov identifier for this study is: NCT03197935.
- The EudraCT number for this study is: CT2016-004734-22.