A study looking at the use of atezolizumab in combination with standard of care in high-risk, HER2-positive, early breast cancer

See the end of the summary for the full title of the study.

About this summary

This is a summary of the results of the IMpassion050 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 IMpassion050 study started in January 2019 and this summary includes the results up until February 2021. At the time of writing this summary, this study is still happening – the doctors are still collecting safety information. Treatment with atezolizumab was stopped in February 2021 because it did not work as well as expected.

No single study can tell us everything about the risks and benefits of a treatment. 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 those of other studies with the same treatment.

- **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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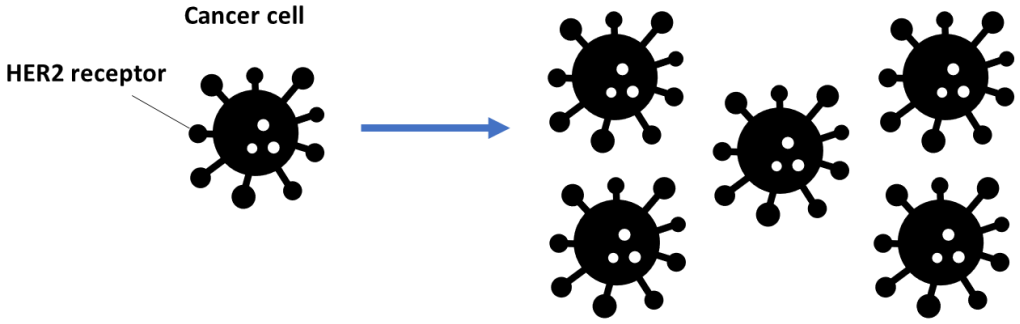
Thank you to the people who took part in this study

The people who took part in this study have helped researchers to answer important questions about high-risk, HER2-positive, early breast cancer and the treatments being studied.

1. General information about this study

Why was this study done?

Receptors are a type of protein found inside or on the surface of some cancer cells. Some breast cancer cells have higher than normal levels of a receptor called ‘HER2’ on their surface, which stimulates them to grow (see below). This type of breast cancer is called ‘HER2-positive breast cancer’. It is described as ‘early’ if the cancer cells have not spread to other parts of the body. If the tumour in the breast is at least 2 cm in size when it is diagnosed and/or cancer cells are found in the lymph nodes (small, oval-shaped organs that contain cells of the immune system) of the armpits, the breast cancer is also called ‘high-risk’.



People with high-risk, HER2-positive, early breast cancer often receive several types of treatment. First, anti-cancer treatments, like chemotherapy, are given to help shrink the tumour. Next, surgery is performed to remove any remaining tumour, which may be followed by radiation therapy to the breast and lymph nodes.

Additional anti-cancer treatments may be given to destroy any cancer cells that may not have been removed during surgery and radiation therapy. Other examples of an anti-cancer treatments are those targeting the HER2 receptor, including ‘trastuzumab’ and ‘pertuzumab’. These treatments are called HER2-targeted therapies and are given before and after surgery. People with high-risk, HER2-positive, early breast cancer are normally given a combination of pertuzumab, trastuzumab and chemotherapy treatment. This combination is called the ‘standard of care’ for this type of cancer.

Cancer immunotherapy is a treatment used to encourage the body’s immune system to attack tumours. For example, some cancer cells have high levels of a protein called ‘PD-L1’ on their surface, which can help cancer cells avoid being destroyed by the immune system. Atezolizumab is an example of a cancer immunotherapy treatment that 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. Cancer cells with high levels of the PD-L1 protein are called ‘PD-L1-positive’ cancers.

Researchers are interested to see if combining HER2-targeted therapies with cancer immunotherapy can help destroy cancer cells more effectively. This study was designed to look at whether adding atezolizumab (the study treatment) to the standard of care (pertuzumab, trastuzumab and chemotherapy) for people with high-risk, HER2-positive, early breast cancer was more effective at destroying these types of cancer cells than the standard of care alone.

What were the study treatments?

A treatment called ‘atezolizumab’ was the focus of this study.

- You say this as ‘ah-teh-zuh-li-za-mab’.
- The PD-L1 protein on the cancer cell attaches to the surface of immune cells, and tells the immune cells **not** to attack the cancer cell. Atezolizumab works by attaching to the PD-L1 protein on cancer cells and blocking it. This stops the cancer cells from using PD-L1 to avoid being destroyed by the immune system.
- This may mean that atezolizumab helps to keep the immune system active so that it can attack the tumour.

In this study, atezolizumab was used together with the standard of care for people with high-risk, HER2-positive, early breast cancer.

Standard of care

‘Trastuzumab’

- You say this as ‘trass-too-za-mab’.
- Trastuzumab works by attaching to the HER2 protein on the surface of HER2-positive cancer cells. When trastuzumab attaches to HER2, it stops the protein from sending signals that make the cancer cells grow and make copies of themselves.
- It also makes cells in the immune system become active so that they can help attack the tumour.

‘Pertuzumab’

- You say this as ‘per-too-za-mab’.
- Pertuzumab works in a similar way to trastuzumab but attaches to a different part of the HER2 protein and helps to complement the effects of trastuzumab.

What did researchers want to find out?

- Researchers did this study to find out how effective atezolizumab (the study treatment) was when combined with the standard of care, compared with the standard of care alone **(see section 4, “What are the results of this study so far?”)**.
- They also wanted to find out how safe this combination of treatments was – by checking how many people had side effects and seeing how serious they were, when taking either atezolizumab and standard of care, or standard of care alone **(see section 5, “What side effects have been seen in this study so far?”)**.

The main questions that researchers wanted to answer were:

1. Across everyone who took part in the study, did atezolizumab and standard of care destroy cancer cells in the breast and lymph nodes of the armpits more effectively than standard of care alone?
2. In people with PD-L1-positive cancers, did atezolizumab and standard of care destroy cancer cells in the breast and lymph nodes of the armpits more effectively than standard of care alone?

What kind of study is this?

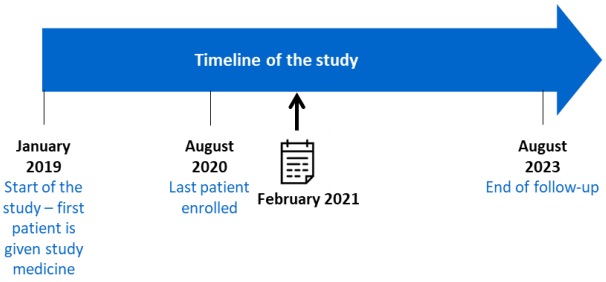
This study was a ‘Phase 3’ study. This means that a large number of people with high-risk, HER2-positive, early breast cancer received either atezolizumab or placebo (a placebo is not a treatment and has no active ingredients, but is made to look exactly like the treatment being tested), in addition to the standard of care. This was to find out whether adding atezolizumab to the standard of care is more effective at destroying cancer cells than the standard of care alone, and also to learn about the side effects of atezolizumab.

The study was ‘randomised’. This means that it was decided by chance whether people in the study would be given atezolizumab or placebo. Randomly choosing which treatment people take makes it more likely that the types of people in both groups (for example, according to age or race) will be similar. Apart from the exact treatments being tested in each group, all other aspects of care were the same between the groups.

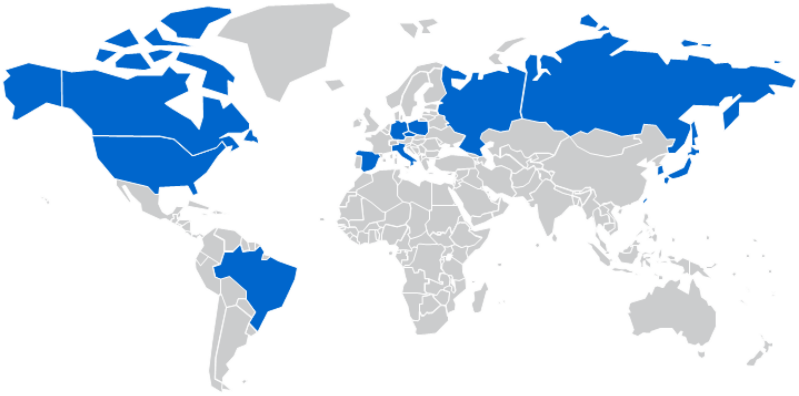
This was a ‘double-blind’ study. This means that neither the people taking part in the study nor the researchers knew which of the study treatments people were given. This helps to lower the chance of bias.

When and where is the study taking place?

The study started in January 2019 and this summary includes the results up until February 2021 – the symbol on the timeline ( ) shows when the information in this summary was collected.



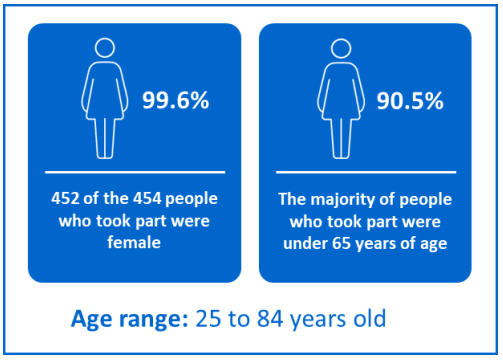
The study took place at 89 study centres. The following map shows the countries where this study took place.



- Brazil
- Canada
- Czech Republic
- Germany
- Italy
- Japan
- Republic of Korea
- Poland
- Russia
- Spain
- Taiwan
- United States of America

2. Who is taking part in this study?

In this study, 454 people (452 women and two men) with high-risk, HER2-positive, early breast cancer took part. More information on the people who took part is given below.



People could take part in this study if they had:

- Early breast cancer, with a breast tumour of at least 2 cm in size and cancer cells present in the lymph nodes of the armpits
- HER2-positive breast cancer (confirmed by testing)
- Normal heart function

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

- Breast cancer that had spread to other parts of the body
- Breast cancer before, or been treated before with anti-breast cancer drugs
- Been treated before with certain chemotherapy drugs, for any kind of disease

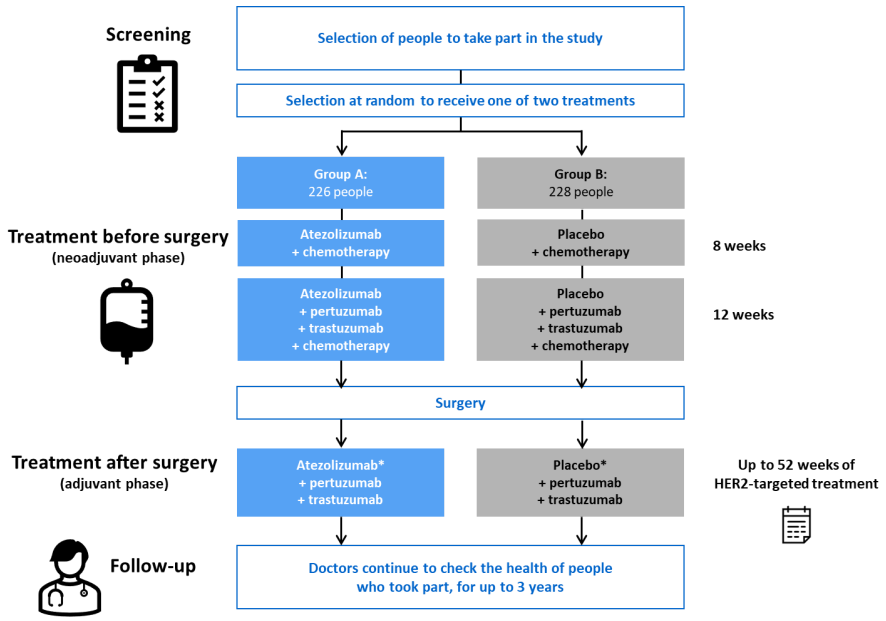
3. What has happened during this study?

During the study, people were randomly selected by chance to receive one of two treatments.

The treatment groups were:

- **Group A** – Atezolizumab (study treatment) was infused into a vein (intravenous) every two weeks for the first eight weeks, and then every three weeks after that.
- **Group B** – The placebo (inactive substance) was infused into a vein (intravenous) every two weeks for the first eight weeks, and then every three weeks after that.
- Either atezolizumab or placebo was given together with standard of care (pertuzumab, trastuzumab and chemotherapy), before and after surgery, to finish up to 52 weeks of treatment.

On 5 February 2021, current treatment with atezolizumab or placebo was stopped because atezolizumab did not work as well as expected, but the study is still ongoing with standard of care alone. When the study finishes, the people who took part will be asked to go back to their study centre for more visits – to check their overall health. Look below to see more information about what has happened in the study so far – and what the next steps are. The symbol ( ) shows when the information in this summary was collected.

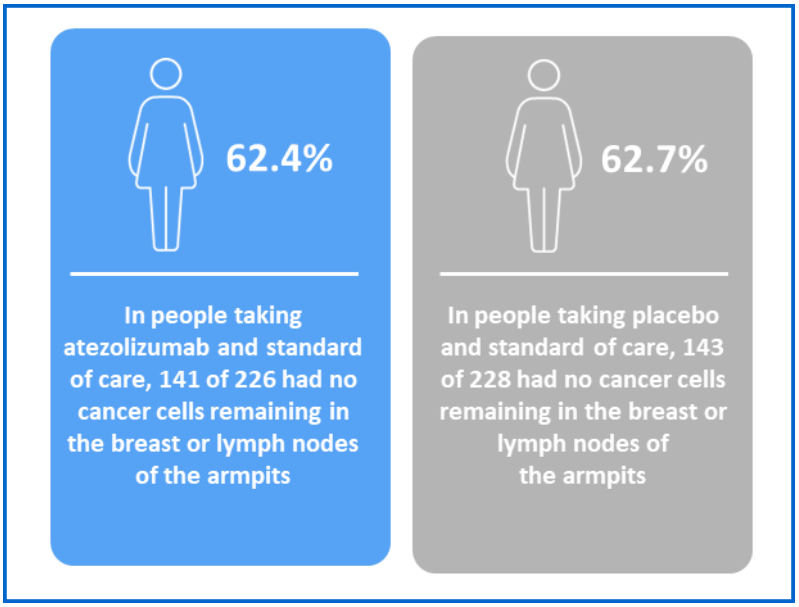


* People who still had cancer cells in the breast and/or lymph nodes of the armpits after neoadjuvant phase treatment had the option to switch to atezolizumab/placebo + 14 cycles of trastuzumab emtansine for their adjuvant phase treatment. Trastuzumab emtansine is the standard-of-care treatment for people with HER2-positive breast cancer who have cancer cells remaining in the breast and/or lymph nodes of the armpits after surgery.

4. What are the results of this study so far?

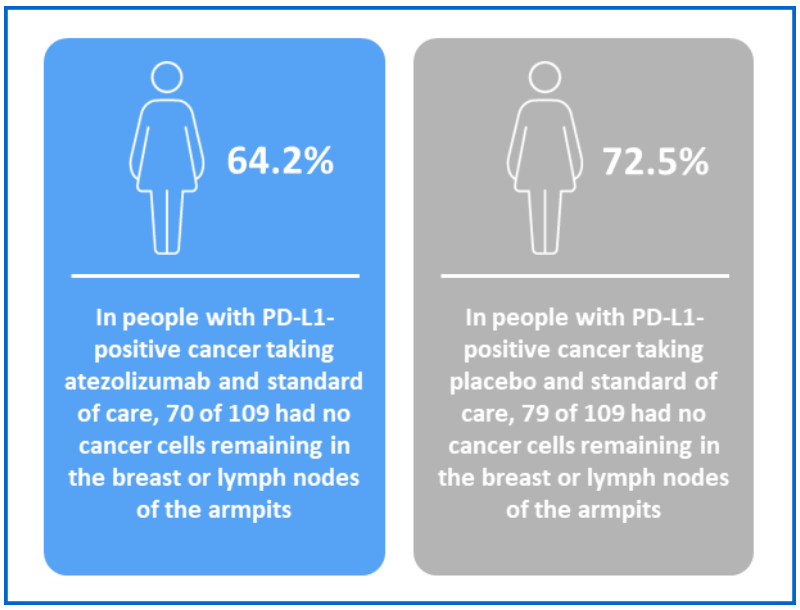
Question 1: Across everyone who took part in the study, did atezolizumab and standard of care destroy cancer cells in the breast and lymph nodes of the armpits more effectively than standard of care alone?

Researchers looked for any cancer cells remaining in the breast and/or lymph nodes of the armpits after surgery. Across everyone who took part in the study, around six in every 10 people had no cancer cells in the breast or lymph nodes of the armpits after surgery, whether they were given atezolizumab and standard of care (Group A), or placebo and standard of care (Group B).



Question 2: In people with PD-L1-positive cancers, did atezolizumab and standard of care destroy cancer cells in the breast and lymph nodes of the armpits more effectively than standard of care alone?

Researchers also wanted to know if atezolizumab was more effective than placebo at destroying cancer cells in people with PD-L1-positive cancers **(see section 1**, **"General information about this study")**. Around six in every 10 people given atezolizumab and standard of care had no cancer cells in the breast or lymph nodes of the armpits after surgery, compared with around 7 in every 10 people who were given placebo and standard of care.



5. What side effects have been seen in this study so far?

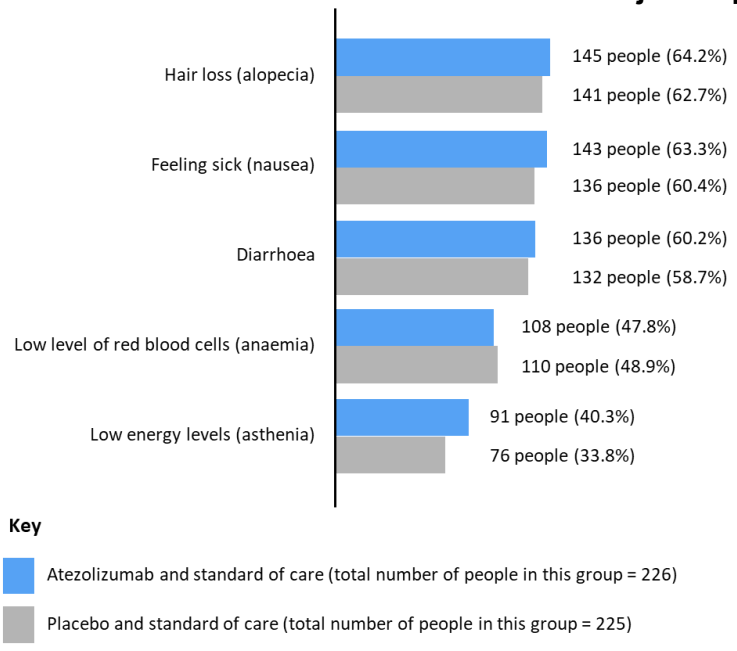
Side effects (also known as 'adverse reactions') are unwanted medical problems (such as feeling dizzy) that can happen during the study.

- Not all of the people in this study experienced all of the side effects.
- Common and serious side effects are listed in the following sections.

Most common side effects

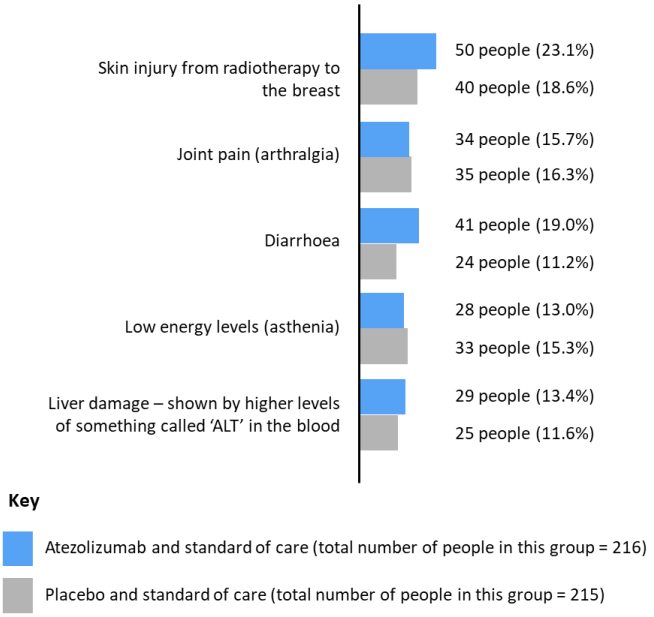
During the neoadjuvant phase, everyone had a side effect. The five most common side effects across both groups are shown below. People could report multiple side effects at a time.

The five most common side effects in the neoadjuvant phase



During the adjuvant phase, around 91% of people (196 out of 216) given atezolizumab and standard of care had a side effect, compared with around 85% of people (183 out of 215) who were given placebo and standard of care. The five most common side effects across both groups are shown below.

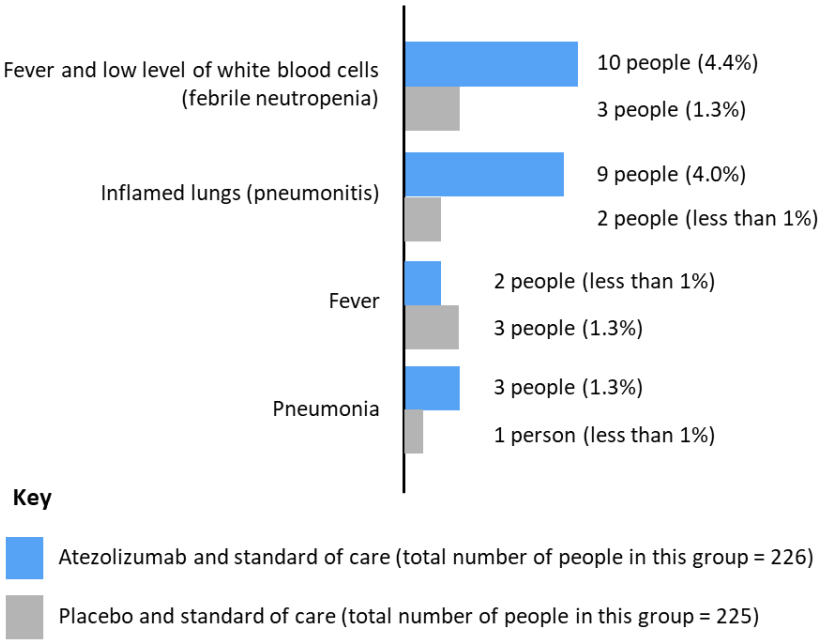
The five most common side effects in the adjuvant phase



Serious side effects

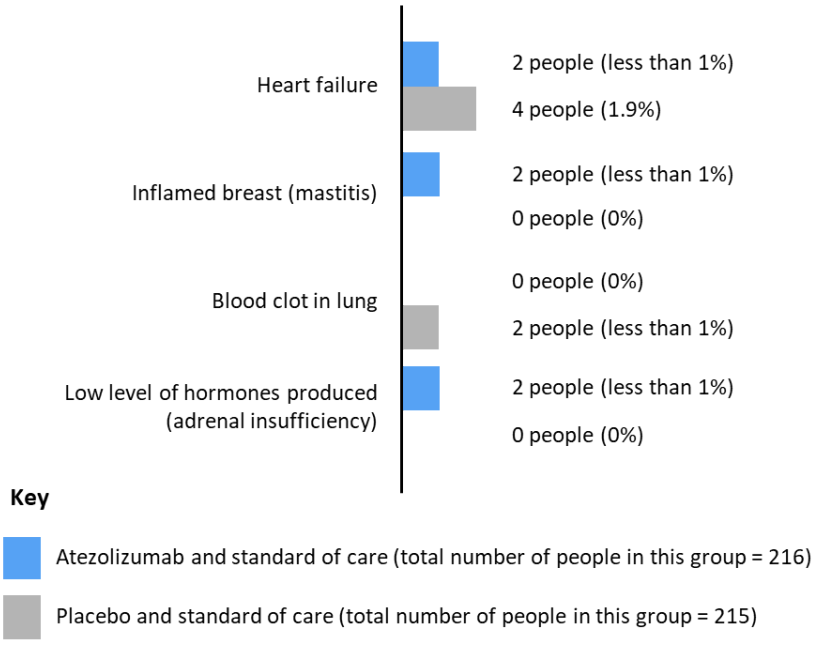
A side effect is considered ‘serious’ if it is life-threatening, needs hospital care or causes long-lasting problems or death. During the neoadjuvant phase, around 20% of people (44 out of 226) given atezolizumab and standard of care had a serious side effect, compared with around 13% of people (30 out of 225) who were given placebo and standard of care.

The four most common serious side effects during the neoadjuvant phase



During the adjuvant phase, this was around 11% (24 out of 216) for people given atezolizumab and standard of care, and around 8% (18 out of 215) for people who were given placebo and standard of care.

The four most common serious side effects during the adjuvant phase



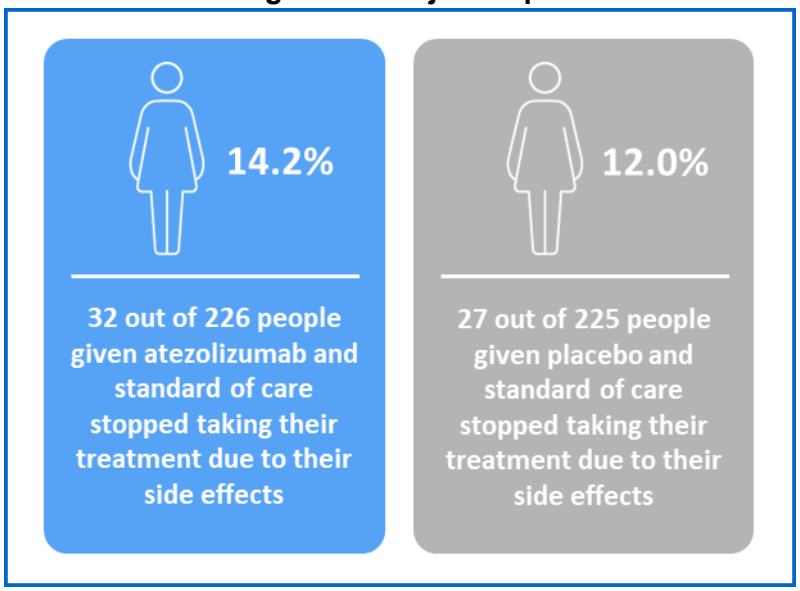
There were some people in the study who died due to their side effects. Four out of 226 people taking atezolizumab and standard of care died due to their side effects in

the neoadjuvant phase, and one person out of 216 died due to their side effects in the adjuvant phase. Two deaths (from inflammation of the lungs and low blood pressure) were considered by the study doctors to be related to the study treatment. There were no deaths from side effects in people taking placebo and standard of care.

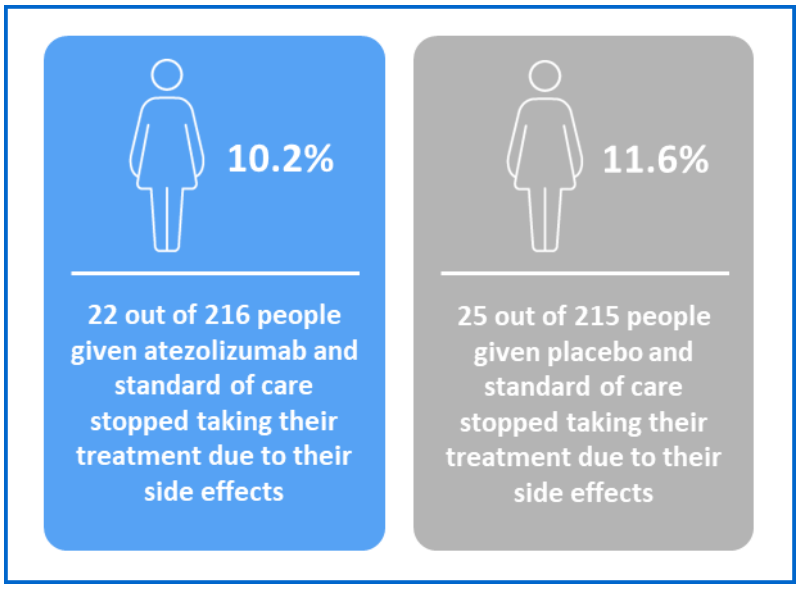
Side effects leading to people stopping their treatment

During the study, 59 people stopped taking their treatment because of side effects in the neoadjuvant phase, and 47 people stopped taking their treatment because of side effects in the adjuvant phase.

Number of people who stopped taking their treatment because of side effects during the neoadjuvant phase



Number of people who stopped taking their treatment because of side effects during the adjuvant phase



Other side effects

You can find out more information about other side effects 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 a single study of 454 people with high-risk, HER2-positive, early breast cancer. These results helped researchers understand whether adding atezolizumab to the standard of care for high-risk, HER2-positive, early breast cancer (pertuzumab, trastuzumab and chemotherapy) was more effective at destroying cancer cells than standard of care alone.

The number of people with no cancer cells remaining in the breast or lymph nodes of the armpits after treatment was similar between those who were given atezolizumab and standard of care, and those who were given placebo and standard of care.

In people with PD-L1-positive cancers, around six out of every 10 people who were given atezolizumab and standard of care had no cancer cells remaining in the breast or lymph nodes of the armpits, compared with around seven out of every 10 people who were given placebo and standard of care. We do not know if the higher number of people with no cancer cells remaining in the breast or lymph nodes of the armpits for placebo and standard of care is a real difference – it could have been caused by chance. Overall, this study has helped researchers understand that the current standard of care, without adding atezolizumab, remains suitable for people with high-risk, HER2-positive, early breast cancer.

7. Are there plans for other studies?

At the time of writing this summary, other studies looking at combining atezolizumab with HER2-targeted therapies are still happening. These studies are using different types of chemotherapy in people at other stages of their breast cancer.

8. Where can I find more information?

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

- https://forpatients.roche.com/en/trials/cancer/bc/a-study-to-evaluate-the-efficacy-and-safety-of-atezoliz-39916
- https://clinicaltrials.gov/ct2/show/results/NCT03726879
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2018-001881-40/results

If you would like to find out more about the results of this study, the title of the relevant scientific paper is: "Atezolizumab With Neoadjuvant Anti–Human Epidermal Growth Factor Receptor 2 Therapy and Chemotherapy in Human Epidermal Growth Factor Receptor 2–Positive Early Breast Cancer: Primary Results of the Randomized Phase III IMpassion050 Trial". The authors of the scientific paper are: Jens Huober, Carlos H. Barrios, Naoki Niikura, Michał Jarząb, Yuan-Ching Chang, and others. The paper is published in the 'Journal of Clinical Oncology', volume number 40, on pages 2946–2956.

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-to-evaluate-the-efficacy-and-safety-of-atezoliz-39916
- 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 Phase III, Randomized, Double-Blind, Placebo-Controlled Clinical Trial To Evaluate the Efficacy and Safety Of Atezolizumab or Placebo in Combination With Neoadjuvant Doxorubicin + Cyclophosphamide Followed By Paclitaxel + Trastuzumab + Pertuzumab In Early Her2-Positive Breast Cancer”.

The study is known as ‘IMpassion050’.

- The protocol number for this study is: BO40747.
- The ClinicalTrials.gov identifier for this study is: NCT03726879.
- The EudraCT number for this study is: 2018-001881-40.