

## Summary of Clinical Trial Results

### A study to look at whether adding atezolizumab to chemotherapy worked well in people with advanced breast cancer called ‘triple-negative 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 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 (July 2021).

The study started in June 2015, and this summary includes the complete results that were collected and analysed as of April 2020. At the time of writing this summary, further information is being collected until August 2021.

One study can’t tell us everything about how well a medicine works and how safe it is. 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

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

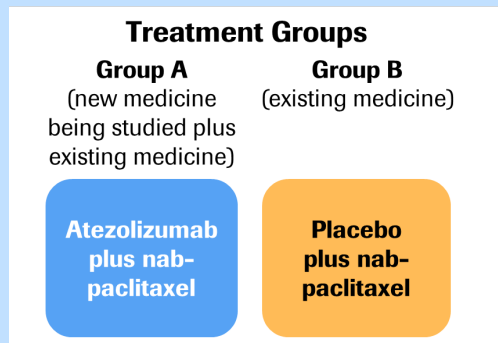
- **Triple-negative breast cancer (TNBC):** kind of breast cancer that does not have any of the receptors that are often found in breast cancer: oestrogen, progesterone, and human epidermal growth factor (HER2)
- **Immunotherapy:** medicine used in cancer treatment to help the body’s immune system attack 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 the immune system.

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

The people who took part in this study have helped researchers answer important questions about triple-negative breast cancer (TNBC) and the medicines studied – ‘atezolizumab’ combined with ‘nab-paclitaxel’.

## Key information about this study

- This study was done to see whether atezolizumab combined with nab-paclitaxel could lengthen the amount of time before the cancer got worse or help people live longer compared with placebo plus nab-paclitaxel alone in people with locally advanced or metastatic TNBC.
- People were given an existing medicine (called 'nab-paclitaxel') plus either the medicine being studied (called 'atezolizumab') or a placebo (no medicine). The study was 'randomised', which means it was decided by chance which treatment each person was given.

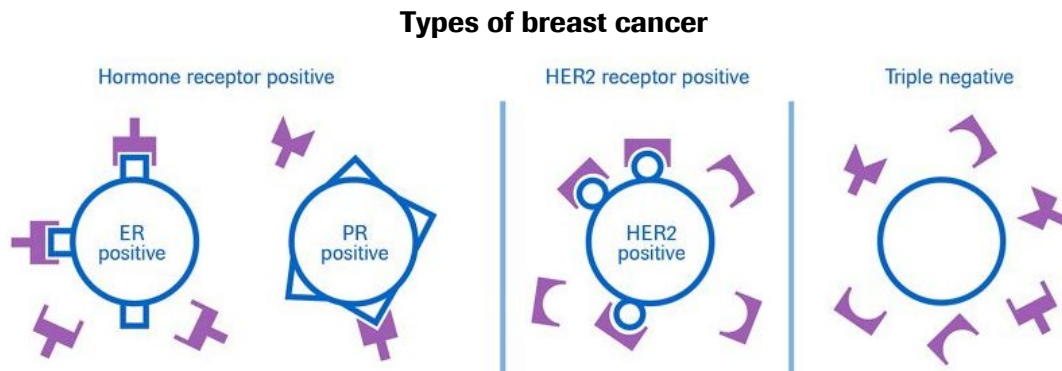


- This study included 902 people in 41 countries.
- The main findings were:
  - Adding atezolizumab to nab-paclitaxel lengthened the amount of time people had before their cancer got worse compared with placebo plus nab-paclitaxel alone. The differences between Group A and B were found to be real differences and not thought to be caused by chance.
    - Overall, for people in **Group A**, their cancer did not get worse until about 7.2 months from the start of the study on average, compared with about 5.5 months for those in **Group B**.
    - For people in **Group A** whose tumours had cells with the protein called programmed death-ligand 1 (PD-L1), their cancer did not get worse until about 7.5 months from the start of the study, compared with about 5.0 months for those in **Group B**.
  - Overall, people in **Group A** lived 21.0 months on average, and people in **Group B** lived 18.7 months on average. This difference in how long people lived was not big enough for the researchers to prove that being given atezolizumab helped people live longer. This difference could have been caused by chance.
  - Among people whose tumours had cells with the protein PD-L1, those in **Group A** lived 25.4 months on average, and those in **Group B** lived about 17.9 months on average. Statistical tests were not performed to compare how long these groups of people lived. So, it is not known if this difference is a real difference or caused by chance.
- About 24% of people (110 out of 460 people) given atezolizumab plus nab-paclitaxel had serious side effects, compared with about 19% of people (80 out of 430 people) given the placebo plus nab-paclitaxel.

## 1. General information about this study

### Why was this study done?

TNBC is a type of breast cancer. There are different types of breast cancer, based on the presence or absence of receptors on the cells of the tumour. Knowing the characteristics of the cancer can help decide which treatments are likely to work. People who took part in this study had TNBC, which means that their cancer cells do not have receptors for: 1) hormone oestrogen, 2) the hormone progesterone, or 3) the human epidermal growth factor receptor 2 (HER2) protein. Although therapies that target these receptors can be used to treat other types of breast cancer, they do not work in people with TNBC. People with TNBC have a high unmet need, and at the time this study was started, there were limited treatment options.



ER = oestrogen receptor; PR = progesterone receptor.

This study included people with TNBC that had spread from where it started to nearby tissue or lymph nodes (locally advanced cancer) and could not be removed by surgery. The study also included people with TNBC that had already spread to other parts of the body (metastatic TNBC). At the time the study started, chemotherapy was the main treatment option for this disease. In this study, the new cancer immunotherapy drug atezolizumab was investigated in combination with nab-paclitaxel (an existing chemotherapy), as an alternative to nab-paclitaxel alone. The medicines were given to people who had not received any other treatment for metastatic TNBC.

This Phase 3 study looked at whether atezolizumab combined with nab-paclitaxel could lengthen the amount of time before the cancer got worse or help people to live longer compared with nab-paclitaxel alone. The study also looked at how the medicines worked in people whose tumours had cells with the protein PD-L1. The study also looked at the safety (the adverse reactions associated with a drug or treatment) of the 2 drugs when given together. The goal of the study was to see if atezolizumab should be offered with chemotherapy as treatment, instead of chemotherapy alone, for people who have not received any other treatment for metastatic TNBC.

### What were the medicines being studied?

A new combination of medicines was used in this study. Based on earlier research and results from smaller clinical trials, researchers thought that this particular combination would work well in people with TNBC. The researchers compared atezolizumab plus nab-paclitaxel (the new combination of medicines) to placebo plus nab-paclitaxel to see which benefits or side effects are caused by the new medicine.

- **Group A: atezolizumab plus nab-paclitaxel** (new combination of medicines)
- **Group B: placebo** (no medicine) **plus nab-paclitaxel** (existing medicine)

One of the medicines in the new combination is called **'atezolizumab'**.

- You say this as 'a – the – zo – liz – oo – mab'.
- This medicine is a type of medicine called 'immunotherapy'.
- The body's immune system fights diseases like cancer. However, cancer cells can block the immune system from attacking the cancer. Atezolizumab releases this blockage – meaning that the immune system is able to fight the cancer cells.
- This may mean that when people are given atezolizumab, their tumour (cancer) may get smaller.

The other medicine in the new combination is called **'nab-paclitaxel'**, which is an existing medicine given to people with TNBC. In addition to atezolizumab or placebo, all the people in this study were given nab-paclitaxel.

- You say this as 'nab – pak – li – tak – sel'.
- This medicine combines paclitaxel with a protein called albumin, which helps paclitaxel reach the tumour.
- nab-paclitaxel works by stopping cancer cells from dividing into new cells, so it blocks the growth of the tumour.

**Atezolizumab plus nab-paclitaxel** (the new combination of medicines) was compared to the combination of a **'placebo'** (no medicine) **plus nab-paclitaxel** (the existing medicine).

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

In this study, people were given nab-paclitaxel (the existing medicine) plus either atezolizumab (the new medicine) or placebo (no medicine). A placebo is used so that the person who takes part in the study and the doctor do not know whether they are being given the real medicine (atezolizumab, the new medicine) or not. This is because knowing can sometimes affect the results of the study. The people given placebo with nab-paclitaxel were compared with the people given atezolizumab plus nab-paclitaxel to see if adding the new medicine (atezolizumab) helped people more than the existing medicine (nab-paclitaxel) alone.

### **What did researchers want to find out?**

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- Researchers did this study to compare atezolizumab plus nab-paclitaxel with placebo plus nab-paclitaxel – to see how well atezolizumab plus nab-paclitaxel worked (see section 4 "What were the results of the study?").
- They also wanted to find out how safe the medicine was – by seeing how many people had side effects (a side effect is an unwanted effect of a medicine or medical treatment) and seeing how serious they were (see section 5 "What were the side effects?").

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

1. Did giving people the combination of atezolizumab plus nab-paclitaxel lengthen the amount of time it took for their cancer to get worse compared with giving people placebo plus nab-paclitaxel?

2. Did giving the combination of atezolizumab plus nab-paclitaxel to people whose tumours had cells with the protein PD-L1 lengthen the amount of time it took for their cancer to get worse compared with giving people placebo plus nab-paclitaxel?
3. Did giving people the combination of atezolizumab and nab-paclitaxel help them live longer compared with giving people placebo plus nab-paclitaxel?
4. Did giving the combination of atezolizumab and nab-paclitaxel to people whose tumours had cells with the protein PD-L1 help them live longer compared with giving people placebo plus nab-paclitaxel?

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

5. How safe are these medicines? How many people had side effects when taking each of the medicines during this study?

### **What kind of study was this?**

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This study was a 'Phase 3' study. This means that the combination of atezolizumab plus nab-paclitaxel had been tested in a smaller number of people with TNBC before this larger study. In this study, one group of people with locally advanced or metastatic TNBC was given atezolizumab (the new medicine) plus nab-paclitaxel (the existing medicine for TNBC). Another group of people was given a placebo plus nab-paclitaxel (the existing medicine alone). This study was done to find out if the new treatment lengthened the amount of time it took for peoples' cancers to get worse and how long they lived. The study was also done to look at the side effects of atezolizumab plus nab-paclitaxel. It can then be decided whether the treatment can be approved for doctors to prescribe.

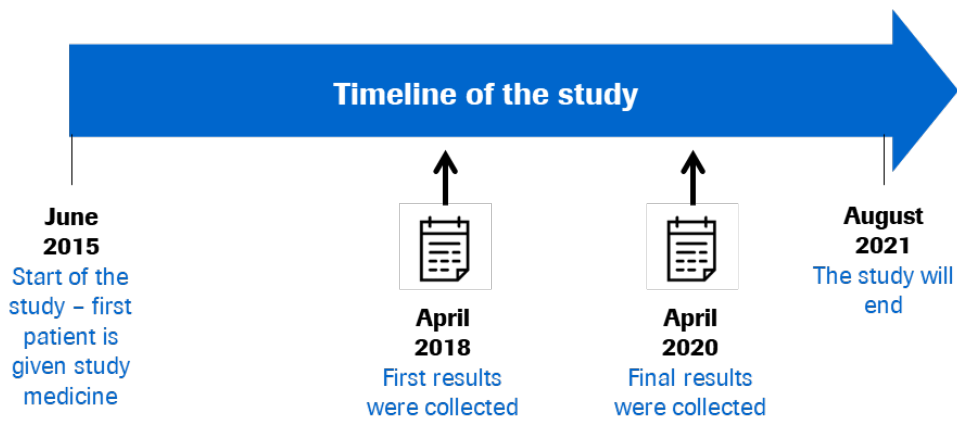
The study was 'randomised'. This means that it was decided by chance which of the medicines people in the study would have – like tossing a coin. Deciding by chance which medicine people take makes it more likely that the types of people in both groups will be a similar mix (for example, age, race). Other than the medicines 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 study doctors knew which of the study medicines people were taking. '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?**

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The study was started in June 2015, and this summary includes the complete results that were collected and analysed as of April 2020. At the time of writing this summary, further safety information on people that are still being given treatment is being collected until August 2021.



This study is still happening. The symbol on the timeline (📅) shows when the information in this summary was collected. The first results (collected in April 2018 – about 3 years after the study started) were used to look at how long it took for peoples’ cancers to get worse. The final results (collected in April 2020 – about 5 years after the study started) were used to look at how long people in the study lived.

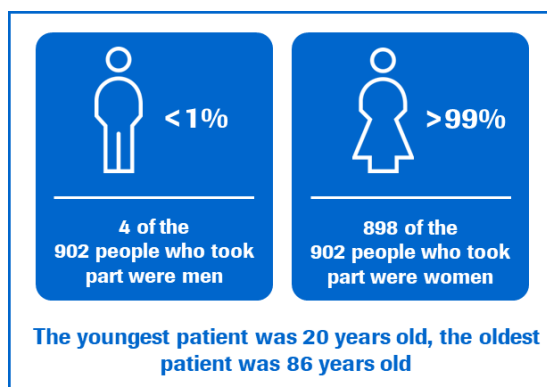
The study took place at 246 study centres across 41 countries or regions. This map shows the countries where this study took place.



## 2. Who took part in this study?

In this study, 902 people with locally advanced or metastatic TNBC took part.

People who took part in the study were between 20 and 86 years of age. Four of the 902 people (<1%) were male and 898 of the 902 people (>99%) were female. Here is more information about the people who took part in the study.



People could take part in the study if they:

- Were at least 18 years old.
- Had advanced TNBC in nearby cells that could not be removed completely through surgery, or TNBC that had spread to other parts of the body.
- Had a tumour that could be accurately measured in size.
- Had a tumour sample that could be tested for the protein PD-L1.
- Were able to perform activities as well or almost as well as they could before they had the illness.

People could not take part in the study if they:

- Had received any other treatment for advanced TNBC or TNBC that had spread to other parts of the body.
- Had cancer that had spread to the brain, except for people who had been treated for cancer that had spread to the brain and did not have symptoms.
- Had an illness that affected the spinal cord.
- Were pregnant or breastfeeding.
- Had an illness where their immune system attacks their own body.

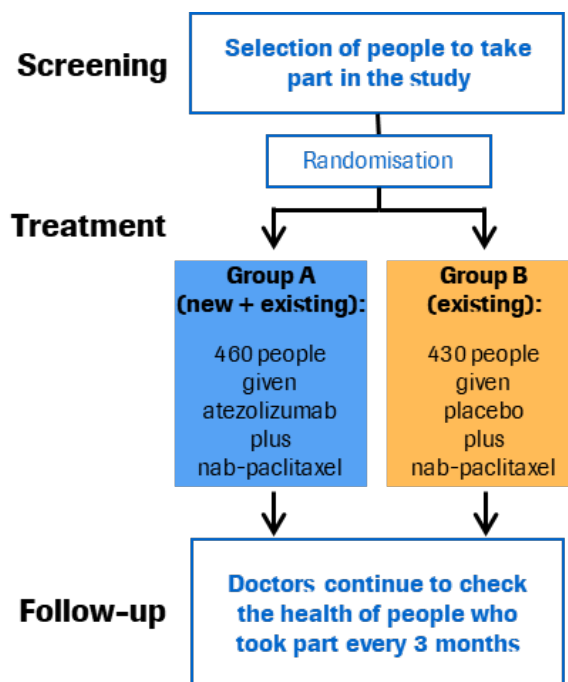
### 3. What happened during the study?

During the study, people were selected by chance to get 1 of 2 treatments. The treatments were selected at random – by a computer.

The treatment groups were:

- **Group A:** Atezolizumab (the medicine being studied) plus nab-paclitaxel (the existing medicine) – people in this group had atezolizumab injected into a vein once every 2 weeks. These people also had nab-paclitaxel injected into a vein once a week for 3 out of every 4 weeks.
- **Group B:** Placebo (no medicine) plus nab-paclitaxel (the existing medicine) – people in this group were treated the same way as group A, except instead of atezolizumab they were given a placebo (which looks the same as a medicine but does not contain any real medicine).

This picture shows what happened in the study for each of the 2 groups.



This table shows the number of people who were given each study treatment. Sometimes people who enrol in a study do not end up taking part. For example, some people may decide not to be involved or may have other reasons for not taking part after enrolling. In this study, several people also received the wrong treatment or changed treatments in some cases.

	<b>Group A Atezolizumab plus nab-paclitaxel</b>	<b>Group B Placebo plus nab-paclitaxel</b>
<b>Number of enrolled people randomly chosen to be included in each group</b>	451	451
<b>Number of people given this medicine or being observed for safety</b>	460	430

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

In this study, researchers looked at how long it took for people's cancer to get worse and how long people in the study lived.

The effects of the different treatments in Groups A and B were assessed in all people enrolled in the study and in a smaller group of people whose tumours had cells with the protein PD-L1 (41% of all people in the study).

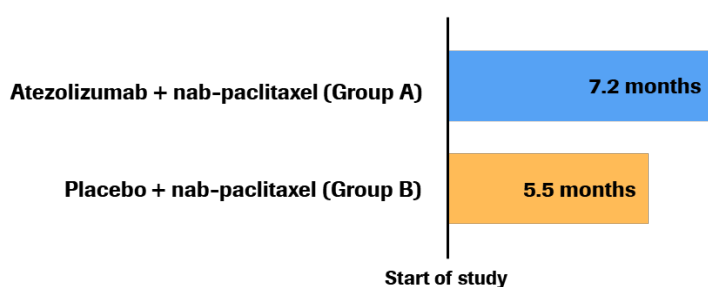


**Question 1:** Did giving people the combination of atezolizumab plus nab-paclitaxel lengthen the amount of time it took for their cancer to get worse compared with giving people placebo plus nab-paclitaxel?

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- The first results were collected in April 2018.
- At that time, researchers found that adding atezolizumab to nab-paclitaxel lengthened the amount of time people had before their cancer got worse compared with placebo plus nab-paclitaxel alone. The differences between Groups A and B were found to be real differences and not thought to be caused by chance.
- In Group A, people's cancer got worse after 7.2 months on average. Some people's cancer got worse more quickly than this, and some people's cancer took longer to get worse. In Group B, people's cancer got worse after an average of 5.5 months.

**On average, how long did it take for the cancer to get worse?**

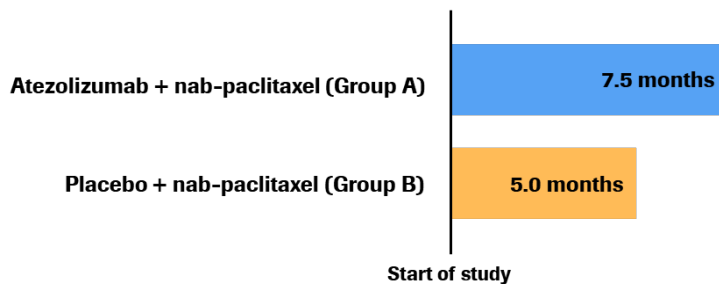


**Question 2:** Did giving the combination of atezolizumab plus nab-paclitaxel to people whose tumours had cells with the protein PD-L1 lengthen the amount of time it took for their cancer to get worse compared with giving people placebo plus nab-paclitaxel?

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- The first were results collected in April 2018.
- At that time, researchers found that adding atezolizumab to nab-paclitaxel lengthened the amount of time people whose tumours had cells with the protein PD-L1 had before their cancer got worse compared with placebo plus nab-paclitaxel alone.
- In Group A, people's cancer got worse after an average of 7.5 months. Some people's cancer got worse more quickly than this, and some people's cancer took longer to get worse. In Group B, people's cancer got worse after an average of 5.0 months.

**On average, how long did it take for the cancer to get worse in people whose tumours had cells with protein PD-L1?**



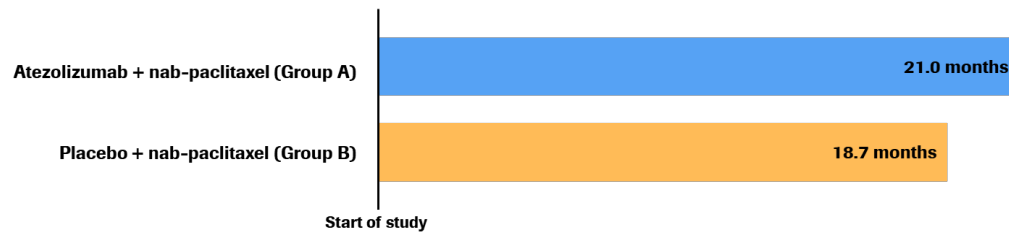
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**Question 3:** Did giving people the combination of atezolizumab and nab-paclitaxel help them live longer compared with giving people placebo plus nab-paclitaxel?

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- The final results were collected in April 2020 and told researchers how long people in the study lived.
- Overall, people in **Group A** lived 21.0 months on average. Some people lived longer than this, and some did not live as long. People in **Group B** lived 18.7 months on average.
- This difference in how long people lived was not big enough to show researchers that being given atezolizumab helped people live longer. This difference could have been caused by chance.

On average, how long did people in each group live?



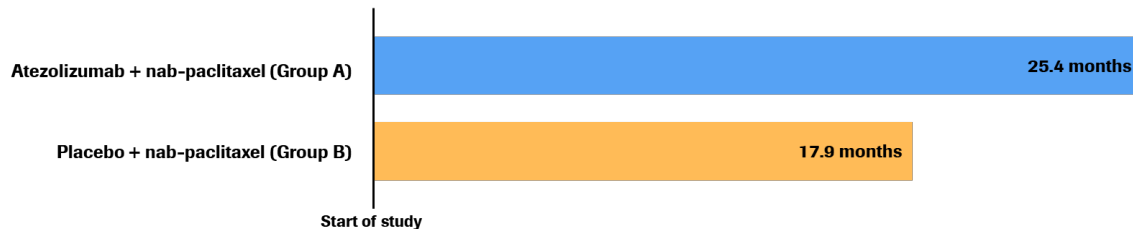
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**Question 4:** Did giving the combination of atezolizumab and nab-paclitaxel to people whose tumours had cells with the protein PD-L1 help them live longer compared with giving people placebo plus nab-paclitaxel?

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- The final results were collected in April 2020 and told researchers how long people in the study lived.
- People in **Group A** whose tumours had cells with the protein PD-L1 lived about 25.4 months on average. People in Group B whose tumours had cells with the protein PD-L1 lived about 17.9 months on average. Some people lived longer than this, and some did not live as long.
  - Statistical tests were not performed to see if the differences were because of the medicines. So, it is not known if this difference is a real difference or caused by chance.

On average, how long did people in each group whose tumours had cells with the protein PD-L1 live?



This section only shows the key results from this study. You can learn 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 could possibly be related to one or more of 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 one study. Therefore, the side effects shown here may be different from those seen 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

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

- During this study, about 2 in every 10 people (21%) had at least one serious side effect. About 24% of people taking atezolizumab plus nab-paclitaxel had a serious side effect, compared with about 19% of people taking placebo plus nab-paclitaxel. These serious side effects could have happened for reasons other than the treatments.
- When considering only side effects that the doctors said were related to the treatments, about 13% of people taking atezolizumab plus nab-paclitaxel had a serious side effect, compared with about 7% of people taking placebo plus nab-paclitaxel.

Some people in the study died because of side effects that may have been related to one of the study medicines. These were:

- 2 out of 460 people (less than 1%) in group A (atezolizumab plus nab-paclitaxel). One of those people had autoimmune hepatitis (inflammation of liver due to attack by immune system) that may have been related to atezolizumab. The other person had septic shock (dangerously low blood pressure after an infection) that may have been related to the combination of atezolizumab plus nab-paclitaxel.
- 1 out of 430 people (less than 1%) in group B (placebo plus nab-paclitaxel). This person had liver failure that may have been related to the combination of placebo plus nab-paclitaxel.

During the study, some people stopped taking their medicine because of side effects:

- In group A (atezolizumab plus nab-paclitaxel), 88 out of 460 people (19%) stopped taking their medicine.
- In group B (placebo plus nab-paclitaxel), 36 out of 430 people (8%) stopped taking their medicine.

### Most common side effects

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During this study, more than 9 out of every 10 people (99%) had a side effect.

- About 99% of people taking atezolizumab plus nab-paclitaxel had a side effect, and the majority of these (about 75%) were not considered serious.
- About 98% of people taking placebo plus nab-paclitaxel had a side effect, and the majority of these (about 79%) were not considered serious.

These are all side effects – including those that could have happened for reasons other than the treatments.

**How many people overall (both groups A and B) had side effects?**



**Most people** had at least one side effect

The most common side effects are shown in this table – these are the 20 most common side effects in both treatment groups and could have happened for reasons other than the treatments. These side effects happened in at least 15 out of 100 people (15%) in either treatment group. Some people had more than one side effect – this means that they are included in more than one row in the table.

<b>Most common side effects reported in this study</b>	<b>People taking atezolizumab plus nab-paclitaxel (460 people total)</b>	<b>People taking placebo plus nab-paclitaxel (430 people total)</b>
Hair loss	57% (263 out of 460)	57% (247 out of 430)
Feeling tired	47% (216 out of 460)	45% (194 out of 430)
Feeling sick to stomach (nausea)	47% (215 out of 460)	38% (165 out of 430)
Frequent, loose watery stools (diarrhoea)	33% (151 out of 460)	35% (149 out of 430)
Low level of red blood cells	28% (130 out of 460)	27% (116 out of 430)
Cough	27% (126 out of 460)	19% (80 out of 430)
Constipation	25% (117 out of 460)	25% (108 out of 430)
Headache	25% (116 out of 460)	22% (93 out of 430)
Low level of white blood cells	22% (102 out of 460)	15% (65 out of 430)
Nerve damage in hands or feet	22% (100 out of 460)	23% (97 out of 430)
Fever	20% (93 out of 460)	11% (46 out of 430)
Throwing up (vomiting)	20% (92 out of 460)	17% (75 out of 430)
Decreased appetite	20% (92 out of 460)	19% (80 out of 430)
Joint pain	19% (89 out of 460)	16% (70 out of 430)
Rash	18% (84 out of 460)	17% (71 out of 430)
Numbness or pain from nerve damage in hands or feet	16% (75 out of 460)	12% (52 out of 430)
Being short of breath	16% (75 out of 460)	14% (62 out of 430)

Back pain	16% (74 out of 460)	13% (58 out of 430)
Swelling of the lower legs or hands	16% (73 out of 460)	16% (68 out of 430)
Itchy skin	16% (73 out of 460)	10% (45 out of 430)
Muscle pain	15% (71 out of 460)	16% (67 out of 430)
Dizziness	15% (69 out of 460)	10% (43 out of 430)

When only considering effects that the doctors said were related to the treatments, about 97% of people taking atezolizumab plus nab-paclitaxel had side effects, compared with about 94% of people taking placebo plus nab-paclitaxel.

### Other side effects

You can learn 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 one study of 902 people with TNBC that had spread to other parts of the body. These results helped researchers learn more about this type of breast cancer and treatment with atezolizumab.

People who were given atezolizumab plus nab-paclitaxel for TNBC that had spread to nearby cells or other parts of the body were less likely to have their cancer get worse than people given placebo plus nab-paclitaxel. In particular, people whose tumours had cells with the protein PD-L1 were more likely to benefit from the combination of atezolizumab plus nab-paclitaxel. Researchers were not able to show that people given atezolizumab plus nab-paclitaxel lived longer than people given placebo plus nab-paclitaxel, but the results in people whose tumours had cells with the protein PD-L1 indicate that those people could benefit from atezolizumab plus nab-paclitaxel.

No one study can tell us everything about how well a medicine works and how safe it is. 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?

Studies with combinations of atezolizumab and other medicines in TNBC are still happening. Information on these studies can be found at <https://www.clinicaltrials.gov>.

## 8. Where can I find more information?

You can learn more about this study on these websites:

- <https://www.clinicaltrials.gov/ct2/show/NCT02425891>
- <https://www.clinicaltrialsregister.eu/ctr-search/trial/2014-005490-37/results>

- <https://forpatients.roche.com/en/trials/cancer/bc/a-phase-iii--multicenter--randomized--placebo-controlled-study-o.html>

If you want to learn more about the results of this study, the full title of the relevant scientific paper is: "First-line atezolizumab plus nab-paclitaxel for unresectable locally advanced or metastatic triple-negative breast cancer: IMpassion130 final overall survival analysis". The authors of the scientific paper are: Leisha A. Emens, Sylvia Adams, Carlos H. Barrios, Véronique Diéras, Hiroji Iwata, and others. The paper is published in the journal 'Annals of Oncology', volume number 32, on pages 983-993.

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

If you have any questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – <https://forpatients.roche.com/en/trials/cancer/bc/a-phase-iii--multicenter--randomized--placebo-controlled-study-o.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 Atezolizumab in Combination With Nab-Paclitaxel Compared With Placebo With Nab-Paclitaxel for Participants With Previously Untreated Metastatic Triple-Negative Breast Cancer (IMpassion130)".

The study is known as 'IMpassion130'.

- The protocol number for this study is: WO29522.
- The ClinicalTrials.gov identifier for this study is: NCT02425891.
- The EudraCT number for this study is: 2014-005490-37.