

## Summary of Clinical Trial Results

**A study looking at whether adding cobimetinib to chemotherapy with or without atezolizumab is effective and safe in people with triple-negative breast cancer that has spread to other parts of the body.**

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

### About this summary

This is a summary of the results of a clinical trial (called a 'study' in this document) – written for:

- Members of the public and
- People who took part in the study.

This summary is based on information known at the time it was written (May 2021).

The study started in March 2015 and is expected to end in August 2021. This summary includes the results that were collected and analysed in March 2017 and August 2018 and was written before the study ended.

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

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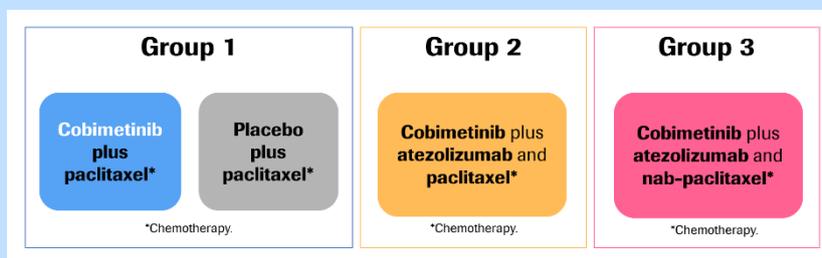
### Thank you to the people who took part in this study

The people who took part in this study helped researchers answer important questions about triple-negative breast cancer and the medicine studied – 'cobimetinib' – taken together with chemotherapy, with or without atezolizumab.

## Key information about this study

### Why was this study done?

- This study was done to compare how well 3 combinations of medicines worked in people with a type of breast cancer called 'triple-negative breast cancer' that had spread to other parts of the body.
- The combinations were:
  - The medicine being studied, called 'cobimetinib', taken together with existing chemotherapy called 'paclitaxel'. This combination was compared to a 'placebo' taken with paclitaxel
  - Cobimetinib taken with atezolizumab and paclitaxel
  - Cobimetinib taken with atezolizumab and a different type of chemotherapy called 'nab-paclitaxel'
- The people in the study were divided into 3 treatment groups as shown here:



- This study included **153 people in 13 countries or regions.**

### What were the results?

- The main findings for **Group 1** were:
  - For people who were given cobimetinib plus chemotherapy, their cancer did not get worse (in other words, it did not spread to another part of the body, spread further, or grow larger) for about **5.5 months** after starting treatment.
  - For people who were given placebo plus chemotherapy, their cancer did not get worse for about **3.9 months** after starting treatment.
  - 18 out of 47 people (38%) who were given cobimetinib plus chemotherapy responded to their treatment – their tumours shrunk or disappeared. 9 out of 43 people (21%) who were given placebo plus chemotherapy responded to their treatment.
- The main findings for **Group 2** and **Group 3** were:
  - In **Group 2**, 11 out of 32 people (34%) responded to their treatment (cobimetinib plus atezolizumab and paclitaxel).
  - In **Group 3**, 9 out of 31 people (29%) responded to their treatment (cobimetinib plus atezolizumab and nab-paclitaxel).

### How many people had serious side effects related to their treatment?

- **Group 1:** 19% of people who were given cobimetinib plus chemotherapy had a serious side effect related to treatment, compared with about 9% of people who were given placebo plus chemotherapy.

- **Group 2:** 9 out of 32 people (28%) had at least one serious side effect related to their treatment.
- **Group 3:** 9 out of 30 people (30%) had at least one serious side effect related to their treatment.

Overall, treatment with cobimetinib plus chemotherapy did not reduce the risk of the cancer getting worse or coming back compared with chemotherapy alone. People who were given the combination of cobimetinib plus atezolizumab and chemotherapy had more serious side effects than people who were given cobimetinib and chemotherapy without atezolizumab.

## 1. General information about this study

### Why was this study done?

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Breast cancer cells may have proteins ('receptors') on their surface that hormones (oestrogen or progesterone) or a protein called 'HER2' can attach to, which helps the cancer cells grow. Triple-negative breast cancers have low levels of oestrogen receptors, progesterone receptors, and HER2 protein, which means that treatment with hormonal therapy or drugs that target oestrogen, progesterone, or HER2 proteins will not work.

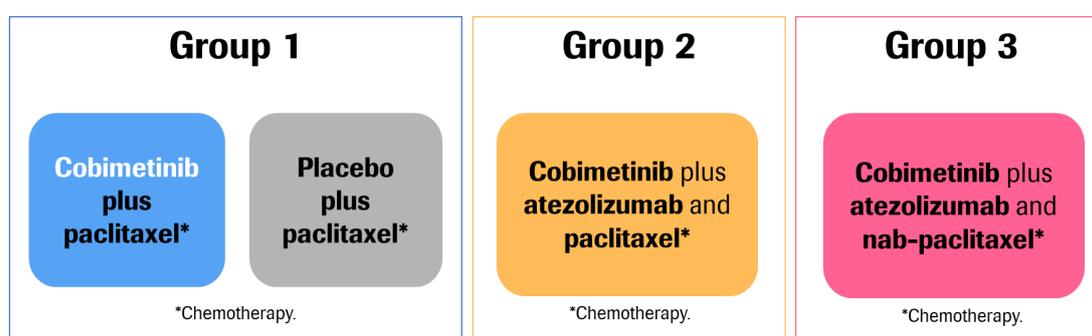
People with triple-negative breast cancer that has spread or 'advanced' to other parts of the body are often treated with medicines called 'chemotherapy' that kill cancer cells. However, there is always a need for new medicines that are better at shrinking tumours and help people better manage their cancer.

This study was designed to look at how effective and safe a new treatment option for people with triple-negative breast cancer is when combined with chemotherapy. The people in this study had not taken other medicine for triple-negative breast cancer before joining the study.

## What are the study medicines?

This study looked at different combinations of the study medicines (cobimetinib with or without atezolizumab) with existing chemotherapy treatment in people with triple-negative breast cancer. During the study, people with triple-negative breast cancer were put into 3 groups and were given different combinations of medicines:

- **Group 1:**
  - **Cobimetinib** (study medicine) plus **paclitaxel** (existing chemotherapy) *or*
  - **Placebo** plus **paclitaxel** (existing chemotherapy)
- **Group 2:** **cobimetinib** (study medicine) plus **atezolizumab** (immunotherapy) plus **paclitaxel** (existing chemotherapy)
- **Group 3:** **cobimetinib** (study medicine) plus **atezolizumab** (immunotherapy) plus **nab-paclitaxel** (existing chemotherapy).



### Cobimetinib

This study looked at a medicine called '**cobimetinib**'.

- You say this as 'co – bee – met – in – ib'.
- This is a type of medicine which blocks signals that cancer cells use to divide and grow.
- Cobimetinib may help other medicines such as chemotherapy and immunotherapy to work better.

### Atezolizumab

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

### Chemotherapy

Two types of chemotherapy were used in this study:

- 'Paclitaxel' (this is the generic name – brand names vary)
  - You say this as 'pac – li – tax – el'
- 'Nab-paclitaxel' (this is the generic name – brand names vary)
  - You say this as 'nab – pac – li – tax – el'
- Chemotherapy works by killing cancer cells and stopping them from growing and dividing.

## What did researchers want to find out?

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- Researchers wanted to see how well the different medicines worked in people with triple-negative breast cancer (see section 4 ‘What were the results of the study?’).
- They also wanted to see how safe these medicines were by seeing how many people had side effects (a side effect is an unwanted effect of a medicine or medical treatment) (see section 5 “What were the side effects?”).

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

1. How much time was there between the start of treatment and the cancer getting worse in people who were given cobimetinib plus chemotherapy compared with people who were given placebo plus chemotherapy?
2. How many people who were given cobimetinib plus chemotherapy responded to their treatment? In other words, how many people had their tumours shrink or disappear after treatment?
3. How many people who were given cobimetinib plus chemotherapy with atezolizumab responded to their treatment?

## What kind of study was this?

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This study was a ‘**Phase 2**’ study. This means that cobimetinib had been tested in people with triple-negative breast cancer in previous studies. In this study, people with triple-negative breast cancer either took cobimetinib or a placebo (a placebo is not a medicine and has no active ingredients but is made to look exactly like the medicine being tested) with chemotherapy, to find out if cobimetinib helped the chemotherapy to work better and stop the cancer from getting worse.

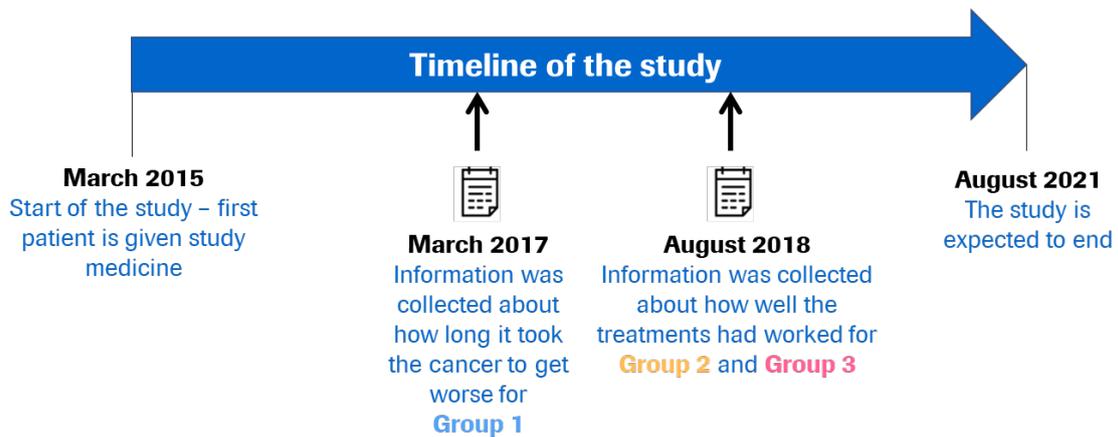
The study was ‘**randomised**’. This means that it was decided by chance which of the medicines people in the study would take – like tossing a coin.

The randomisation was ‘**double-blind**’ for people who were given cobimetinib or placebo plus chemotherapy. 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.

The randomisation was ‘**open label**’ for people who were given cobimetinib or placebo plus chemotherapy with atezolizumab. This means that both the people taking part in the study and the study doctors knew which of the study medicines people were taking.

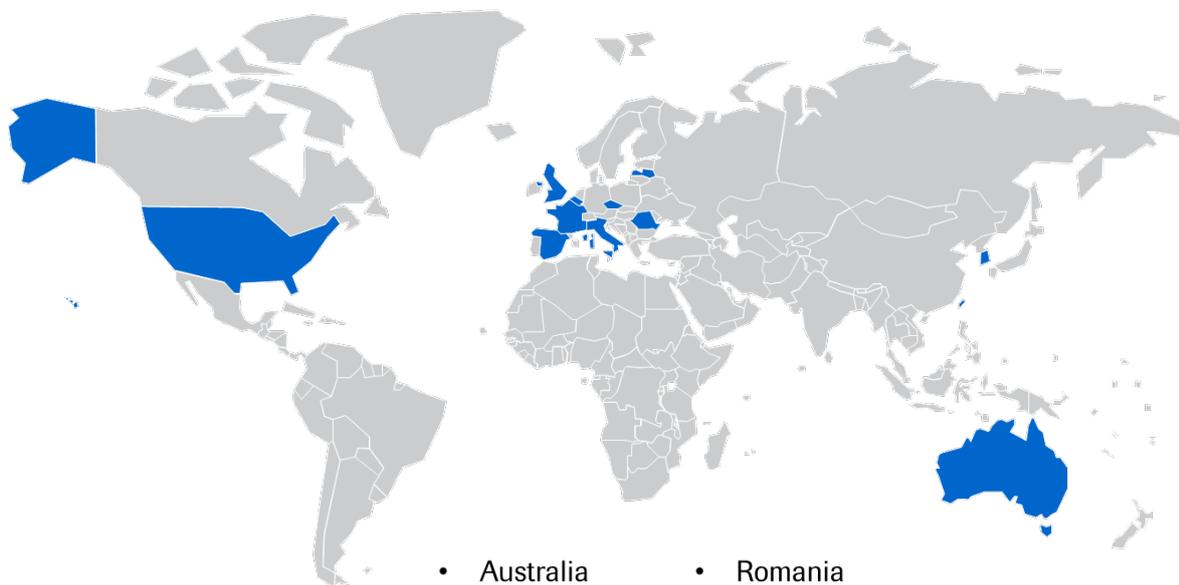
## When and where did the study take place?

The study started in March 2015 and is expected to end in August 2021. This summary shows the complete results from all parts of the study.



The study took place at 52 hospitals and clinics in 13 countries and regions in Asia, Europe, North America, and Oceania.

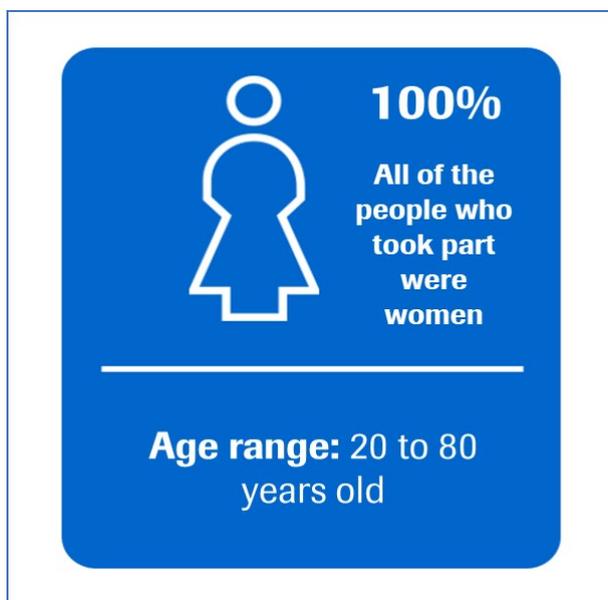
This map shows the countries where this study took place.



- Australia
- Belgium
- Czechia
- France
- Israel
- Italy
- Latvia
- Romania
- South Korea
- Spain
- Taiwan
- United Kingdom
- United States

## 2. Who took part in this study?

In this study, 153 people with triple-negative breast cancer took part.



People could take part in the study if they:

- Had tumours with cells that had low levels of 3 proteins: oestrogen, progesterone, and HER2 receptor proteins
- Had tumours that could not be fully removed with surgery
- Had tumours that had spread to the lymph nodes near the breast or other parts of the body

People could not take part in the study if they:

- Had tumours that had spread to the brain
- Were previously treated with chemotherapy, hormone therapies, or targeted therapies for triple-negative breast cancer
- Had disorders called 'autoimmune diseases' that caused their immune system to attack healthy cells in the body
- Had taken other medicines that work in the same way as cobimetinib or atezolizumab

### 3. What happened during the study?

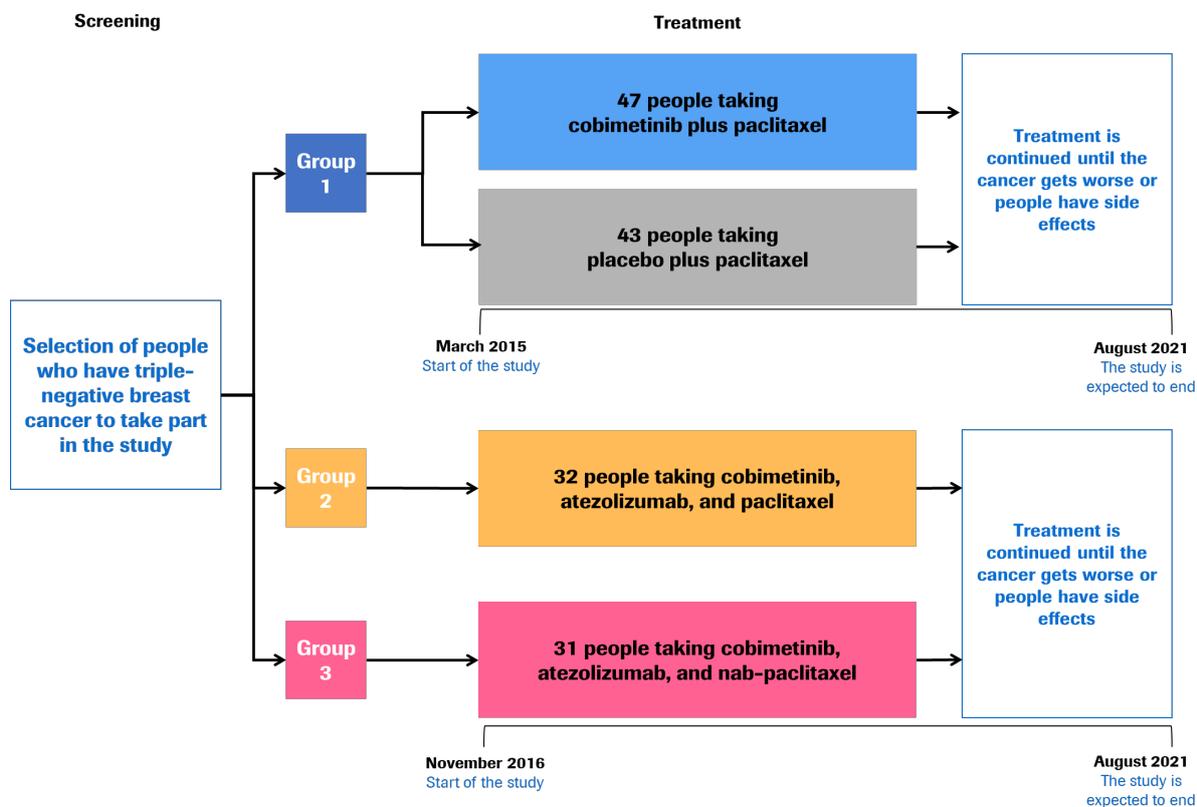
During the study, people were put into 3 groups and given different combinations of medicines:

- The first 90 people were included in **Group 1** and were chosen at random to be given cobimetinib plus paclitaxel or placebo plus paclitaxel.
- All other people who joined this study were randomly chosen to be in Group 2 or Group 3:
  - In **Group 2**, people were given cobimetinib plus atezolizumab and chemotherapy (paclitaxel).
  - In **Group 3**, people were given cobimetinib plus atezolizumab and chemotherapy (nab-paclitaxel).

This table shows the number of people who took each study treatment, and how often the medicines were taken.

	Group 1		Group 2	Group 3
	Cobimetinib plus paclitaxel	Placebo plus paclitaxel	Cobimetinib plus atezolizumab and paclitaxel	Cobimetinib plus atezolizumab and nab-paclitaxel
<b>Number of people in group (randomly chosen)</b>	47	43	32	31
<b>Number of people who actually took the medicine</b>	47	43	32	30
<b>How the drugs were taken</b>	Cobimetinib: tablet, taken by mouth Paclitaxel: injected into a vein	Placebo: tablet, taken by mouth Paclitaxel: injected into a vein	Cobimetinib: tablet, taken by mouth Atezolizumab and paclitaxel: injected into a vein	Cobimetinib: tablet, taken by mouth Atezolizumab and nab-paclitaxel: injected into a vein
<b>When the drugs were taken in each 3-week treatment cycle</b>	Cobimetinib: every day between days 3 and 23 Paclitaxel: days 1, 8, and 15	Placebo: every day between days 3 and 23 Paclitaxel: days 1, 8, and 15	Cobimetinib: every day between days 3 and 23 Atezolizumab: days 1 and 15 Paclitaxel: days 1, 8, and 15	Cobimetinib: every day between days 3 and 23 Atezolizumab: days 1 and 15 Nab-paclitaxel: days 1, 8, and 15

This picture shows what happened in the study for each of the 3 groups.



The first person who took part in the study started in March 2015, and people continued to join the study until November 2016. The information in this summary was collected in March 2017 for Group 1 (about 2 years after the study started) and August 2018 for Group 2 and Group 3 (about 3.5 years after the study started).

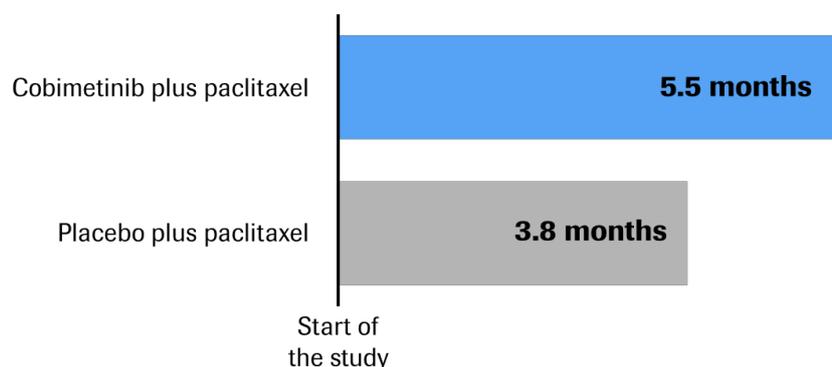
## 4. What were the results of the study?

**Question 1:** How much time was there between the start of treatment and the cancer getting worse in people in Group 1 who were given cobimetinib plus chemotherapy compared with people who were given placebo plus chemotherapy?

Researchers compared how much time there was between the start of the study and people's cancer getting worse between the 2 groups in **Group 1**.

- For people who were given cobimetinib plus chemotherapy, the cancer became worse after about **5.5 months**, on average (in some people it took longer to become worse and in others it became worse sooner than 5.5 months).
- For people who were given placebo plus chemotherapy, the cancer became worse after about **3.8 months**, on average (in some people it took longer to become worse and in others it became worse sooner than 3.8 months).
- This difference was not big enough to show researchers that being given cobimetinib with chemotherapy helped to slow down the cancer getting worse. This difference could have been caused by chance.

**In Group 1, on average, how much time was there between the start of treatment and the cancer getting worse?**



This information was collected from March 2015 until March 2017.

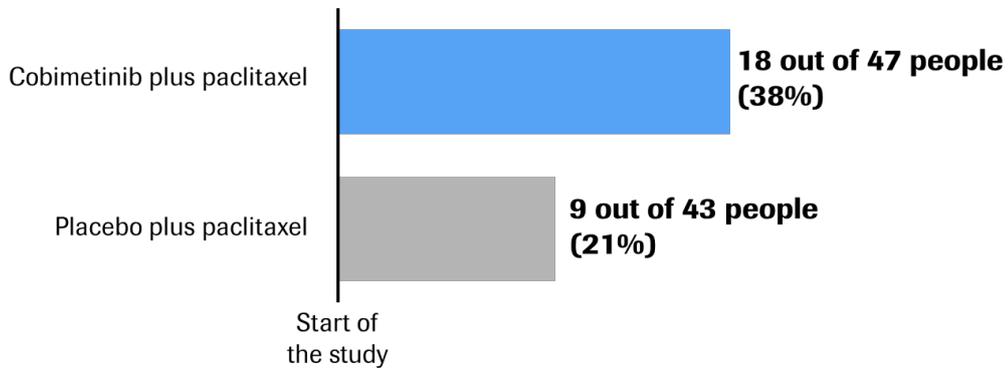
**Question 2:** How many people in Group 1 responded to their treatment? In other words, many people had their tumours shrink or disappear after treatment?

Researchers looked at what percentage of people in **Group 1** had their tumours shrink or disappear after treatment.

- **18 out of 47 people (38%)** who were given cobimetinib plus chemotherapy responded to their treatment and saw their tumours shrink or disappear.
- **9 out of 43 people (21%)** who were given placebo plus chemotherapy responded to their treatment and saw their tumours shrink or disappear.
- This difference was not big enough to show researchers that significantly more people responded to treatment with cobimetinib and chemotherapy compared with chemotherapy alone. This difference could have been caused by chance.

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### In Group 1, how many people responded to their treatment?



This information was collected from March 2015 until March 2017.

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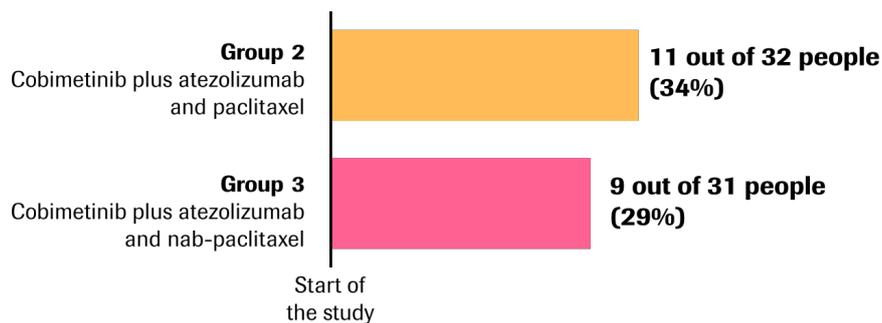
### Question 3: In Group 2 and Group 3, how many people responded to their treatment? In other words, how many people had their tumours shrink or disappear after treatment?

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Researchers looked at what percentage of people had their tumours shrink or disappear after treatment.

- In **Group 2**, 11 out of 32 people (34%) responded to their treatment – their tumours shrank or disappeared.
- In **Group 3**, 9 out of 31 people (29%) responded to their treatment – their tumours shrank or disappeared.

### In Group 2 and Group 3, how many people responded to their treatment?



This information was collected from November 2016 until August 2018.

## 5. What were the side effects?

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

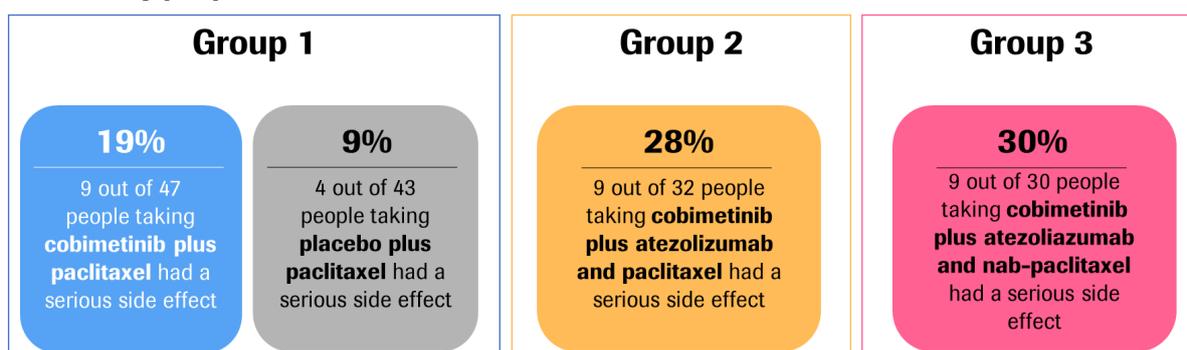
- They are described in this summary because the study doctor believes the side effects were related to the treatments in the study.
- Not all of the people in this study had all of the side effects.
- Side effects may be mild to very serious.
- Side effects can be different from person to person.
- It is important to be aware 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 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.

- In **Group 1**, 14 out of 100 people (14%) had at least one serious side effect related to their treatment. About 19% of people who got cobimetinib plus chemotherapy had a serious side effect related to treatment, compared with about 9% of people who got placebo plus chemotherapy.
- In **Group 2**, 9 out of 32 people (28%) had at least one serious side effect related to their treatment.
- In **Group 3**, 9 out of 30 people (30%) had at least one serious side effect related to their treatment.

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



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

- In **Group 1**, no people died.
- In **Group 2**, 2 out of 32 people (6%) died.
- In **Group 3**, no people died.

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

- In **Group 1**, 14 out of the 47 people (30%) taking cobimetinib plus paclitaxel stopped taking at least one of the drugs in their treatment. Nobody in the group that was given placebo plus paclitaxel stopped their treatment.
- In **Group 2**, 10 out of 32 people (31%) stopped taking at least one of the drugs in their treatment.
- In **Group 3**, 10 out of 30 people (33%) stopped taking at least one of the drugs in their treatment.

### Most common side effects

During treatment, about 99 out of 100 people (99%) across all groups had a side effect that was not considered serious. These side effects were due to any cause.

The diagram below shows the most common side effects. These are the 10 most common side effects that happened in at least 20 out of 100 people (20%) in any treatment group.

	Group 1		Group 2	Group 3
Most common side effects reported in this study	Cobimetinib plus paclitaxel (47 people total)	Placebo plus paclitaxel (43 people total)	Cobimetinib plus atezolizumab and paclitaxel (32 people total)	Cobimetinib plus atezolizumab and nab-paclitaxel (30 people total)
Diarrhoea	77% (36 out of 47)	28% (12 out of 43)	66% (21 out of 32)	90% (27 out of 30)
Feeling sick (nausea)	45% (21 out of 47)	37% (16 out of 43)	41% (13 out of 32)	50% (15 out of 30)
Hair loss	45% (21 out of 47)	44% (19 out of 43)	25% (8 out of 32)	33% (10 out of 30)
Rash	43% (20 out of 47)	12% (5 out of 43)	38% (12 out of 32)	53% (16 out of 30)
Feeling tired	28% (13 out of 47)	30% (13 out of 43)	34% (11 out of 32)	33% (10 out of 30)
Fever	28% (13 out of 47)	16% (7 out of 43)	16% (5 out of 32)	37% (11 out of 30)
Weakness or lack of energy	26% (12 out of 47)	26% (11 out of 43)	19% (6 out of 32)	17% (5 out of 30)
Swelling and/or	26%	7% (3 out of 43)	16% (5 out of 32)	17% (5 out of 30)

irritation of the lips and mouth	(12 out of 47)			
Low level of red blood cells (anaemia)	23% (11 out of 47)	14% (6 out of 43)	44% (14 out of 32)	33% (10 out of 30)
Itching	21% (10 out of 47)	2% (1 out of 43)	13% (4 out of 32)	7% (2 out of 30)

## 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 'Where can I find more information?').

## 6. How has this study helped research?

The information presented here is from one study of 153 people with triple-negative breast cancer that had spread to other parts of the body. These results helped researchers learn more about triple-negative breast cancer and treatment with cobimetinib plus chemotherapy (paclitaxel or nab-paclitaxel) with and without atezolizumab.

Treatment with cobimetinib plus chemotherapy did not reduce the risk of the cancer getting worse or coming back compared with chemotherapy alone. A similar number of people responded to their treatment when atezolizumab was added to the combination of cobimetinib and chemotherapy (paclitaxel or nab-paclitaxel). People who were given the combination of cobimetinib plus atezolizumab and chemotherapy had more serious side effects than people who were given cobimetinib and chemotherapy without atezolizumab. The most common serious side effect related to treatment was diarrhoea.

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?

Other studies with cobimetinib and atezolizumab using different chemotherapy medicines for the treatment of other types of breast cancer are ongoing.

## 8. Where can I find more information?

You can learn more about this study on these websites:

- <https://clinicaltrials.gov/ct2/show/NCT02322814>
- <https://www.clinicaltrialsregister.eu/ctr-search/search?query=2014-002230-32>
- <https://forpatients.roche.com/en/trials/cancer/bc/a-study-of-cobimetinib-plus-paclitaxel--cobimetinib-plus-atezoli.html>

If you want to find out more about the results of this study, the full title of the relevant scientific paper is: “A phase II randomized trial of cobimetinib plus chemotherapy, with or without atezolizumab, as first-line treatment for patients with locally advanced or metastatic triple-negative breast cancer (COLET): primary analysis”. The authors of the scientific paper are: Adam Brufsky, Soo-Bong Kim, Zanete Zvirbule, Alexandru Eniu, Jeroen Mebis, and others. The paper is published in the journal *Annals of Oncology*, volume number 32, pages 652-660.

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

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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-study-of-cobimetinib-plus-paclitaxel--cobimetinib-plus-atezoli.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?

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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

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The full title of this study is: “A Study of Cobimetinib Plus Paclitaxel, Cobimetinib Plus Atezolizumab Plus Paclitaxel, or Cobimetinib Plus Atezolizumab Plus Nab-Paclitaxel as Initial Treatment for Participants With Triple-Negative Breast Cancer That Has Spread (COLET)”.

The study is known as ‘COLET’.

- The protocol number for this study is: WO29479.
- The ClinicalTrials.gov identifier for this study is: NCT02322814.

- The EudraCT number for this study is: 2014-002230-32.