

## Summary of Clinical Trial Results

### The KATE2 study: A study to see if atezolizumab added to trastuzumab emtansine (T-DM1) works and is safe in people with a type of breast cancer called ‘HER2-positive 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 of writing.

The study started in September 2016 and this summary includes the results that were analysed in December 2018. At the time of writing this summary, the study is over but further information on patient survival is being analysed. This summary will be updated when this is completed.

No single study can tell us everything about the risks and benefits of a medicine. 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.**

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#### Glossary

- HER2-positive = human epidermal growth factor receptor 2-positive; a type of breast cancer

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

The people who took part have helped researchers to answer important questions about HER2-positive breast cancer and the medicines studied – ‘atezolizumab’ and ‘T-DM1’.

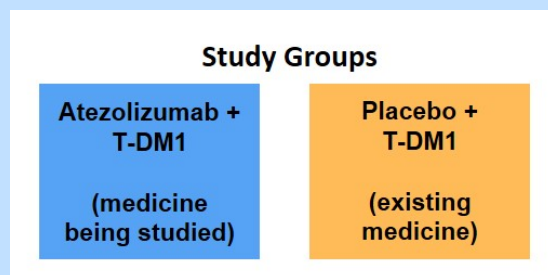
## Key information about this study

### Why is this study being done?

- This study was done to see if adding a medicine called 'atezolizumab' to a medicine called 'T-DM1' works better than T-DM1 by itself to treat a type of breast cancer called 'HER2-positive advanced breast cancer'.
- The study was also done to see what the side effects are of the combination of medicines.

### Which medicines were studied and who took part?

- In this study, people were given either the medicine being studied (atezolizumab) or a placebo. A 'placebo' looks the same as a medicine but does not contain any real medicine. This means that it does not have any medicine-related effect on the body.
  - A placebo is used so that the patient and the doctor do not know whether they are receiving the real medicine or not. This is because knowing can sometimes affect the results of the study.
- All people also received T-DM1.
- It was decided by chance which treatment each person was given.



- This study included 202 people in 9 countries.

### What were the results?

- The main finding was that people's cancer became worse after a similar amount of time in both groups (after 7-8 months).
- In the group of people that had a certain type of breast cancer called 'PD-L1-positive', it took twice as long for their cancer to get worse if they were taking atezolizumab plus T-DM1 compared to the people that were taking placebo plus T-DM1.

### What were the side effects?

- Around 33% of people (43 out of 132 people) taking atezolizumab plus T-DM1 had serious side effects, compared to around 19% of people (13 out of 68 people) taking placebo plus T-DM1.

# 1. General information about this study

## Why was this study done?

'HER2-positive' is a type of breast cancer where the cancer cells have a protein called human epidermal growth factor receptor 2 (HER2) on them. This HER2 protein encourages cancer cells to grow. HER2-positive breast cancers grow and spread faster than other types of breast cancer. About 1 out of every 5 breast cancers is HER2-positive.

If cancer has spread to other parts of the body, it is called advanced cancer. A medicine called T-DM1 (you say this as 'tee - dee - em - one') is used to treat advanced HER2-positive breast cancer. It slows the pace of the cancer getting worse and helps people live longer but it is not a cure. New medicines are needed to help people live even longer and to get closer to a cure.

## What were the study medicines?

This study looked at whether adding a new medicine to an existing medicine is better than the existing medicine on its own. The two medicines are:

- **T-DM1** – the existing medicine
- **Atezolizumab** – the medicine that was added

'T-DM1' is an existing medicine given to people with HER2-positive advanced breast cancer who were treated with other medicines for their breast cancer that didn't work or stopped working.

- T-DM1 is a targeted medicine – this means that the medicine targets the cancer cells and not the healthy cells.
  - This may mean that it is better at treating the cancer cells and causes fewer side effects than other medicines.
- T-DM1 works by killing the cancer cells.

'Atezolizumab' is the medicine that was studied here – it works in a different way than T-DM1.

- You say this as 'a - teh - zo - liz -oo - mab'.
- Cancer cells block certain cells in the immune system from attacking the cancer. Atezolizumab releases this blockage – meaning that the immune system is able to fight the cancer cells and make the tumour smaller (the cancer is reversed).
  - Atezolizumab releases the blockage by attaching to a protein on some cancer cells called 'PD-L1'.

In this study, T-DM1 plus atezolizumab together were compared to T-DM1 plus 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 it had no medicine-related effect on the body.
  - A placebo is used so that the patient and the doctor do not know whether they are receiving the real medicine or not. This is because knowing can sometimes affect the results of the study.
- Researchers compared T-DM1 plus atezolizumab with T-DM1 plus a placebo so they could show which benefits or side effects are caused by atezolizumab.

## What did researchers want to find out?

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- Researchers did this study to see how well the combination of atezolizumab and T-DM1 worked (see section 4 “What were the results of the study?”).
- They also wanted to find out how safe the combination was – by checking how many people had side effects and seeing how serious they were, when taking the medicines during this study (see section 5 “What were the side effects?”).

### **The main question that researchers wanted to answer was:**

1. How much time was there between the start of the study and people’s cancer getting worse?

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

2. How long did people live in this study?
3. How much time was there between the start of the study and people’s cancer getting worse in people who had a protein called ‘PD-L1’ on their cancer?
4. How long did people with PD-L1 on their cancer live in this study?

## What kind of study was this?

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This study was a ‘Phase 2’ study. This means that atezolizumab had been tested in a number of people with advanced breast cancer before this study. In this study, people with advanced HER2-positive breast cancer either took atezolizumab plus T-DM1 or a placebo plus T-DM1 – this was to find out if adding atezolizumab to T-DM1 could delay people’s cancer getting worse. Researchers also wanted to check the safety of atezolizumab plus T-DM1.

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. Randomly choosing which medicine people take, makes it more likely that the types of people in both groups (for example, age, race) will be a similar mix. Apart from the exact medicines being tested in each group, all other aspects of care were the same between the groups.

This was a ‘double-blind’ study. This means that neither the people taking part in the study nor the study doctors knew whether they were taking atezolizumab or placebo alongside T-DM1.

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

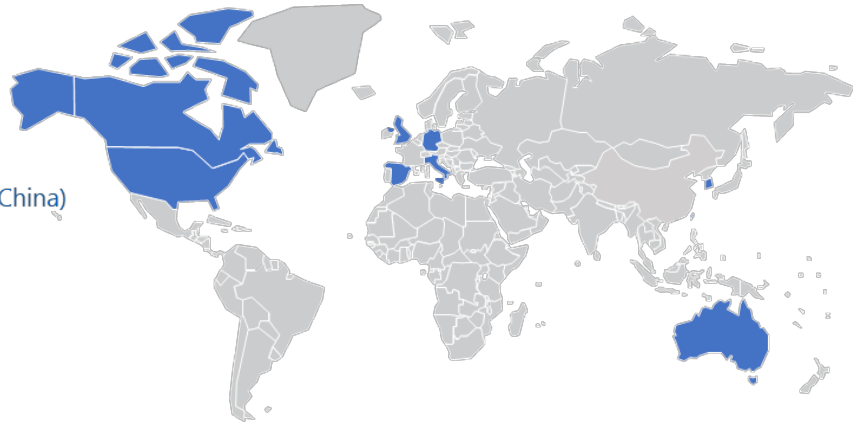
## When and where did the study take place?

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The study started in September 2016 and this summary includes the complete results up until December 2018. At the time of writing this summary, the study is over but further information on patient survival is being analysed. This summary will be updated when the additional information has been analysed.

The study took place at 68 research centres – across 9 countries. The following map shows the countries where this study took place.

- Australia
- Canada
- Germany
- Italy
- Republic of Korea
- Spain
- Taiwan (Republic of China)
- United Kingdom
- United States



## 2. Who took part in this study?

In this study, 202 people with advanced HER2-positive breast cancer took part.

People who took part in the study were between 28 and 78 years of age. 200 of the 202 people (99%) were female and 2 of the 202 people (1%) were male.

People could take part in the study if:

- they had HER2-positive breast cancer that had spread to nearby cells, or to other parts of the body
- they had previously received other medicines for their breast cancer that didn't work – these had to include a medicine called trastuzumab and also chemotherapy with a type of medicine called a taxane
- their cancer had become worse (progressed) during or within 6 months of receiving the most recent treatment for their breast cancer.

People could not take part in the study if:

- they had previously taken T-DM1 or any medicines that work in a similar way to atezolizumab
- they had certain heart or liver problems or viral infections
- they had cancer that had spread to the brain or spinal cord that wasn't being treated.

## 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.

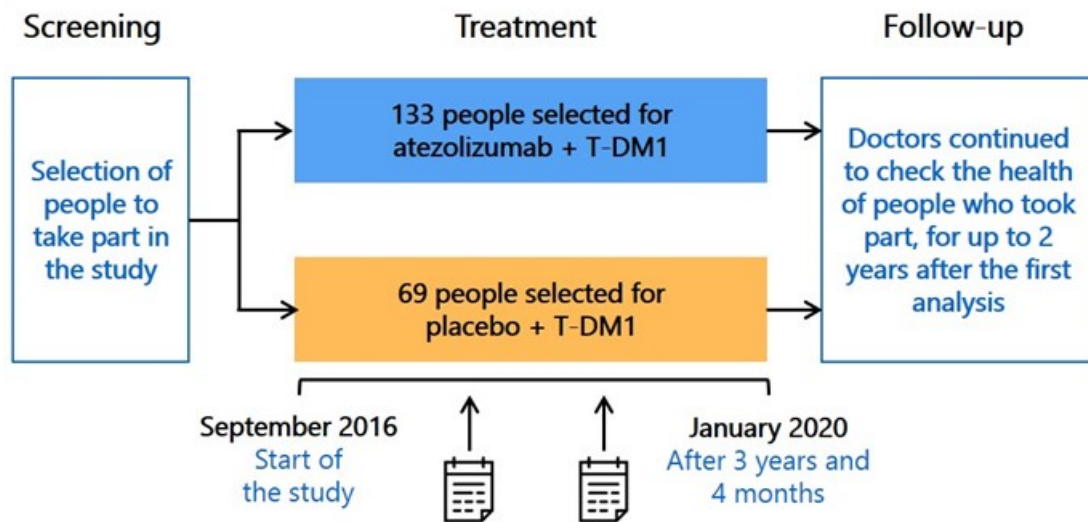
The treatment groups were:

- **Atezolizumab + T-DM1** (the medicine being studied) – atezolizumab was dripped into a vein once every 3 weeks.
- **Placebo + T-DM1** (the existing medicine) – placebo was dripped into a vein once every 3 weeks.

In both groups, **T-DM1** was dripped into a vein after each atezolizumab or placebo injection.

At the start of the study, 133 people were selected to get atezolizumab plus T-DM1 and 69 people were selected to get placebo plus T-DM1. One person in each group did not end up receiving any medicine but they were still included in the study results.

Although this study has finished, information for some people is still being analysed. Below, is more information about what happened in the study so far.



The symbols on the timeline (📅) show when the information shown in this summary was collected. Some information was collected after 1 year and 3 months (December 2017) and some was collected after 2 years and 3 months (December 2018).

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

### Question 1: How much time was there between the start of the study and people's cancer getting worse?

Researchers looked at how much time there was before people's cancer got worse – this information was collected from the start of the study until December 2017.

People's cancer became worse after a similar amount of time in both groups:

- In the atezolizumab plus T-DM1 group, people's cancer got worse after around 8 months.
- In the placebo plus T-DM1 group, people's cancer got worse after around 7 months.

These numbers for each treatment group are averages, which means that some people's cancer got worse more quickly than this, and some people's cancer took longer to get worse.

### On average, how long before people's cancer got worse?



### Question 2: How long did people live in this study?

Another piece of information that researchers collected was how long people lived for during the study. This information was collected from the start of the study until December 2018. At the time the information was collected, there was not enough information to work out the average length of time people in the study lived because most patients were still alive when the information was collected.

89% of people in each group were alive at 1 year after the start of study treatment.

### **Question 3: How much time was there between the start of the study and people's cancer getting worse in people who had a protein called 'PD-L1' on their cancer?**

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Researchers also collected information from a group of people within the study who had a protein called PD-L1 on their cancer (called 'PD-L1-positive cancer'). PD-L1 is a protein that helps cancer cells avoid being attacked by the immune system. Atezolizumab allows the immune system to attack cancer cells that have PD-L1 on them.

In this study, 84 people had PD-L1-positive cancer. 57 of these people were treated with atezolizumab plus T-DM1 and 27 were treated with placebo plus T-DM1.

- People with PD-L1-positive cancer in the atezolizumab plus T-DM1 group got worse after around 8.5 months.
- People with PD-L1-positive cancer in the placebo plus T-DM1 group got worse after around 4 months.

We do not know if this is a real difference – it could have been caused by chance.

### **Question 4: How long did people with PD-L1 on their cancer live in this study?**

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Researchers also collected information about how long people with PD-L1-positive cancer lived. This information was collected from the start of the study until December 2018. At the time the information was collected, there was not enough information to work out the average length of time people in the study lived because most patients were still alive when the information was collected.

This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see section 8).

## **5. What were the side effects?**

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

- They are described in this summary whether or not the study doctor believes they 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 and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear in the medicine leaflets.
- Serious and common side effects are listed in the following sections.
- This information was collected up to December 2017. For this information, the researchers only included the people who had actually been given study medicines (132 received T-DM1 plus atezolizumab and 68 received T-DM1 plus placebo).

### **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 1 in every 3 people (28%) had at least one serious side effect. Around 33% of people taking atezolizumab plus T-DM1 had a serious side effect, compared with around 19% of people taking placebo plus T-DM1.

The most common serious side effect was fever that led to hospitalisation. This side effect only happened to people taking atezolizumab plus T-DM1. The serious side effects that occurred in at least 2% of people in either group and in more people in one group than in the other are listed in the table below. In the atezolizumab plus T-DM1 group, the threshold to be included is 3 people; in the placebo plus T-DM1 group, it is 2 people. Some people had more than one side effect – this means that they are included in more than one row in the table.

<b>Serious side effects reported in this study</b>	<b>People taking atezolizumab plus T-DM1</b> (132 people total)	<b>People taking placebo plus T-DM1</b> (68 people total)
Fever	8% (10 out of 132 people in this group)	0
Liver damage – shown by higher levels of something called ‘ALT’ in the blood	2% (3 out of 132)	0
Liver, heart or kidney damage – shown by higher levels of something called ‘AST’ in the blood	2% (3 out of 132)	0
Being sick (vomiting)	2% (3 out of 132)	0
Stomach pain	0	3% (2 out of 68 people in this group)
Fit (seizure)	0	3% (2 out of 68)

One person in the study died due to a side effect that may have been related to one of the study medicines. The person developed a very unusual condition called haemophagocytic syndrome - you say this as hee – moe – fag – o – sit – ick syndrome. This is caused by an overactive immune system and causes symptoms such as fever, blood problems, and liver problems. The patient was taking atezolizumab plus T-DM1.

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

- In the atezolizumab plus T-DM1 group, around 1 out of 4 people (26%) stopped taking their medicine.
- In the placebo plus T-DM1 group, around 1 out of 7 people (15%) stopped taking their medicine.

## Most common side effects

During this study, around 98 out of every 100 people (98%) had any kind of side effect. Around 99% of people taking atezolizumab plus T-DM1 had a side effect, compared with around 96% of people taking placebo plus T-DM1.

The most common side effects are shown in the following table – these are the ten most common side effects across both treatment groups. 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 T-DM1</b> (132 people total)	<b>People taking placebo plus T-DM1</b> (68 people total)
Feeling tired	38% (50 out of 132 people in this treatment group)	43% (29 out of 68 people in this treatment group)
Feeling sick (nausea)	36% (48 out of 132)	41% (28 out of 68)
Fever	35% (46 out of 132)	16% (11 out of 68)
Headache	27% (35 out of 132)	25% (17 out of 68)
Low level of the blood cell fragments that help blood to clot – called 'platelets'	28% (37 out of 132)	13% (9 out of 68)
Diarrhoea	23% (31 out of 132)	18% (12 out of 68)
Liver, heart or kidney damage – shown by higher levels of something called 'AST' in the blood	23% (30 out of 132)	16% (11 out of 68)
Decreased appetite	22% (29 out of 132)	16% (11 out of 68)
Being sick (vomiting)	20% (27 out of 132)	18% (12 out of 68)
Constipation	20% (26 out of 132)	15% (10 out of 68)

## Other side effects

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You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see section 8.

## 6. How has this study helped research?

The information presented here is from a single study of 202 people with advanced HER2-positive breast cancer. These results helped researchers learn more about treating HER2-positive breast cancer with atezolizumab plus T-DM1.

The main limitation of the study is that it was a small study. More research is needed with more people to understand more about how atezolizumab plus T-DM1 might help people with HER2-positive breast cancer.

So far the study has shown that:

- people taking atezolizumab plus T-DM1 or placebo plus T-DM1 had a similar time before their cancer got worse.
- atezolizumab seems to work best in patients with HER2-positive breast cancer that has PD-L1 on it.
- more people in the atezolizumab plus T-DM1 group had serious side effects and more people withdrew from the study because of side effects than people in the placebo plus T-DM1 group.

No single study can tell us everything about the risks and benefits of a medicine. 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?

Further studies with atezolizumab plus T-DM1 are planned.

## 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/NCT02924883>
- <https://www.clinicaltrialsregister.eu/ctr-search/search?query=2015-004189-27>
- <https://forpatients.roche.com/en/trials/cancer/bc/a-study-to-evaluate-the-efficacy-and-safety-of-trastuzu-87572.htm>

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “Trastuzumab emtansine plus atezolizumab versus trastuzumab emtansine plus placebo in previously treated, HER2-positive advanced breast cancer (KATE2): a phase 2, multicentre, randomised double-blind trial”. The authors of the scientific paper are: Leisha A. Emens, Francisco J. Esteva, Mark Beresford, and others. The paper is published in the journal “*Lancet Oncology*”, volume number 21, on pages 1283-1295.

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

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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-trastuzu-87572.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 Randomized, Multicenter, Double-Blind, Placebo-Controlled Phase II Study of the Efficacy and Safety of Trastuzumab Emtansine in Combination with Atezolizumab or Atezolizumab-Placebo in Patients with HER2-Positive Locally Advanced or Metastatic Breast Cancer Who Have Received Prior Trastuzumab- and Taxane-Based Therapy”.

The study is known as ‘KATE2’.

- The protocol number for this study is: WO30085.
- The ClinicalTrials.gov identifier for this study is: NCT02924883.
- The EudraCT number for this study is: 2015-004189-27.