

## Summary of Clinical Trial Results

### **KAMILLA: A study to look at the safety of trastuzumab emtansine in two groups of people (global group and Asia-only group) 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:

- 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 study started in November 2012 and was finished in July 2019 (with a small number of patients in China continuing treatment until July 2020). This summary includes the main results from the study that were collected in July 2019.

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

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## **Glossary**

HER2-positive breast cancer = a type of breast cancer that is positive for the 'HER2' protein

HER2 = human epidermal growth factor receptor 2

Thrombocytopenia = a condition in which there is a low level of the blood cell fragments that help blood to clot

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

The people who took part have helped researchers to answer important questions about the safety of trastuzumab emtansine in HER2-positive breast cancer.

## **Key information about this study**

### **Why was this study done?**

- This study was done to further understand the safety of trastuzumab emtansine in people with HER2-positive breast cancer that had advanced to nearby cells (locally advanced) or spread to other parts of the body (metastatic).

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

- This study included two groups of people. The global group included 2003 people globally (including people from Asia), and the Asia-only group included 182 people from China, Thailand, and Indonesia. Of these, one person in the global group and one person in the Asia-only group were not treated with trastuzumab emtansine because they did not qualify to receive the medicine. Therefore, a total of 2002 people in the global group and 181 people in the Asia-only group were treated with trastuzumab emtansine.

### **What were the results?**

- This study showed that the safety results in both the global group and the Asia-only group were consistent with what is already known about trastuzumab emtansine, and no new side effects were reported.
  - The percentage of people who had side effects that were of main interest in this study was higher in the Asia-only group (51%) than in the global group (23%). These side effects included those that were severe, life-threatening, or (rarely) fatal, including several specific events not necessarily related to the study medicine; and any lung inflammation (whether severe or not).
  - The higher percentage of these side effects in the Asia-only group was mainly due to a higher percentage of severe or life-threatening (but not fatal)

thrombocytopenia, a condition in which there is a low level of the blood cell fragments that help blood to clot. However, 63 out of 66 (95%) of these people made a full recovery.

- Around 6% of people (126 out of 2002 people) in the global group and 15% of people (28 out of 181 people) in the Asia-only group had serious side effects related to the medicine, such as thrombocytopenia.
- During this study, 1539 out of 2002 people (77%) in the global group and 164 out of 181 people (91%) in the Asia-only group had any side effect related to the medicine, such as thrombocytopenia.
- If people experienced side effects related to the medicine, in most cases (around 90%) this did not cause them to stop taking the medicine.
- In addition:
  - The length of time people lived, as well as the amount of time between the start of the study and people's cancer getting worse, was similar between the global group and the Asia-only group.
  - In both the global group and the Asia-only group, people who were given more treatments for their cancer before this study tended to live for a shorter time, and tended to experience a shorter time between the start of the study and their cancer getting worse, than people who were given fewer cancer treatments before this study.

## 1. General information about this study

### Why was this study done?

About 20% of people with breast cancer have 'HER2-positive breast cancer', which means that the tumour has too much of a protein called 'HER2'. Medicines that 'target' cancer cells with HER2 proteins can prevent tumour cells from growing.

Trastuzumab emtansine is a medicine that identifies cancer cells using the HER2 protein as a marker, ultimately causing cell death. Trastuzumab emtansine has been approved by the United States Food and Drug Administration and the European Medicines Agency for the treatment of HER2-positive breast cancer that has spread to other parts of the body, and has been shown to be well-tolerated and effective. This study was done to further understand the safety of trastuzumab emtansine in people with locally advanced or metastatic HER2-positive breast cancer. In an earlier analysis of the global group, the side effects were well-managed.

In previous studies, the safety profile of T-DM1 in people from Asia has been slightly different from that observed in other populations. For example, previous studies have shown that there is a higher rate of thrombocytopenia – a condition in which there is a low level of the blood cell fragments that help blood to clot – in people from Asia. Therefore, this study was set up to further understand the safety of trastuzumab emtansine in people from Asia, as well as in people globally.

## What were the study medicines?

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This study looked at a medicine called 'trastuzumab emtansine'.

- You say this as 'tras – too – zoo – mab em – tan– zeen'.
- Trastuzumab emtansine is a medicine that includes two drugs connected to each other to make a single drug:
  - Trastuzumab, a 'targeted' drug that blocks the growth and spread of cancer by using the HER2 protein to bind to cancer cells and eventually cause their death, and
  - Emtansine, which is a chemotherapy drug – a type of drug where chemicals are used to kill cancer cells.

## What did researchers want to find out?

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- Researchers did this study to further understand the safety of trastuzumab emtansine in people globally and in people specifically from Asia (see section 4 "What were the safety results of the study?").
- They also wanted to find out how well trastuzumab emtansine worked in both groups (see section 5 "How well did the medicine work?").

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

1. How safe was trastuzumab emtansine in people with locally advanced or metastatic HER2-positive breast cancer from around the world and in Asia, specifically?

### **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?

## What kind of study was this?

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This study was a 'Phase 3b' study. This means that trastuzumab emtansine was previously tested in studies of people with locally advanced or metastatic HER2-positive breast cancer; these studies led to approval of this drug by the health authorities. In this study, a larger number of people with locally advanced or metastatic HER2-positive breast cancer took trastuzumab emtansine so researchers could better understand the safety of this medicine in people globally and from Asia, specifically.

This was an 'open label' study. This means that both the people taking part in the study and their study doctors knew which study medicines people were taking.

This was also a 'single-arm' study. This means that all patients received the same study medicine.

## When and where did the study take place?

The study started in November 2012 and was finished in July 2019 (with a small number of patients in China continuing on treatment until July 2020). This summary includes the main results up until July 2019.

The study took place in 43 countries around the world.

## 2. Who took part in this study?

In this study, 2185 people with locally advanced or metastatic HER2-positive breast cancer took part. Of these, one person in the global group and one person in the Asia-only group were not treated with trastuzumab emtansine because they did not qualify to receive the medicine. Therefore, a total of 2183 people received trastuzumab emtansine and were studied to understand the safety of the medicine. These 2183 people consisted of two groups: the global group included 2002 people from around the world (Europe, South America, North America, Australia, and Asia), and the Asia-only group included 181 people from three Asian countries (154 people from China, 15 people from Thailand, and 12 people from Indonesia).

In the global group, people who took part in the study were between 26 and 88 years of age; almost all people (99%) were female. In the Asia-only group, people who took part in the study were between 25 and 67 years of age; all people (100%) were female.

People could take part in the study if:

- They had HER2-positive breast cancer that had come back after treatment, had spread to nearby cells and could not be removed using surgery (locally advanced), or had spread to other parts of the body (metastatic)
- They had been treated with a different medicine other than trastuzumab emtansine that targets the HER2 protein, in addition to chemotherapy
- Their cancer got worse while they were taking medicine or within 6 months of finishing a type of medicine that was given after surgery to help with the success of the surgery

People could not take part in the study if:

- They had been given trastuzumab emtansine before the study
- Their cancer had spread to the brain or spinal cord
- They had severe damage to the nerves outside of the brain or spinal cord

## 3. What happened during the study?

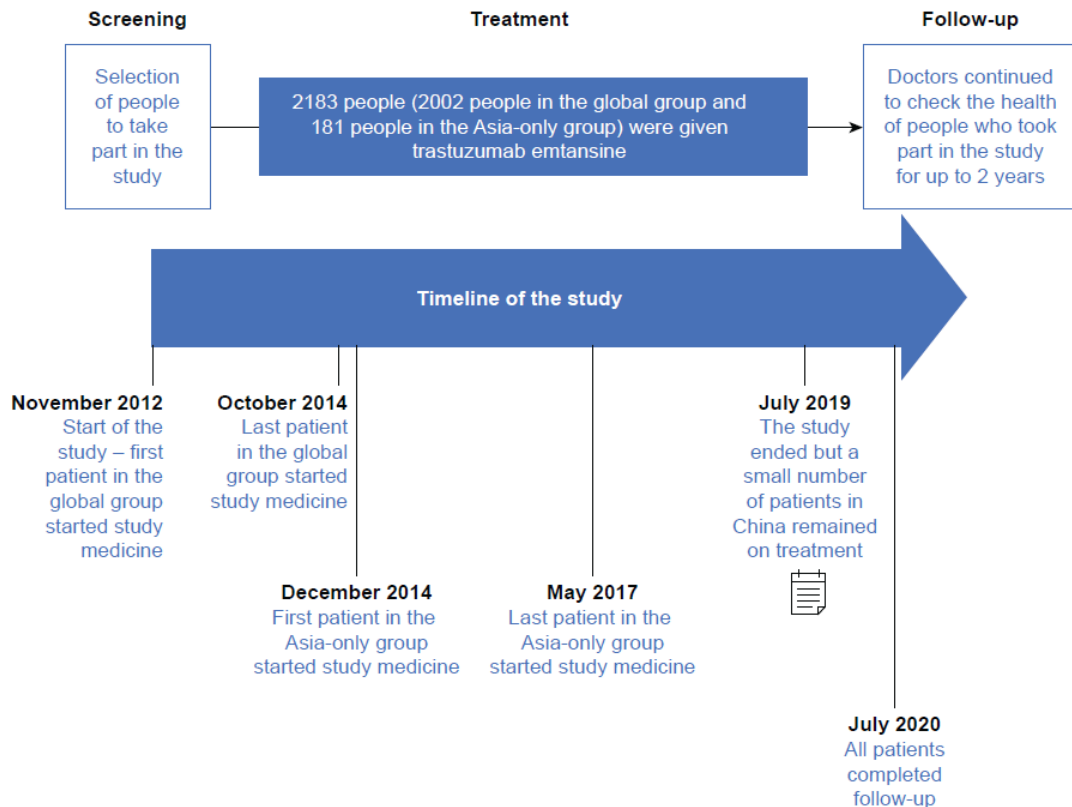
During the study, all people got the same treatment.

Treatment included 1 medicine:

- **Trastuzumab emtansine**– drip (infused) into a vein once every 3 weeks until the disease got worse, the medicine caused unacceptable toxic effects, people withdrew from the study, or people died.

At the start of the study, 2185 people were selected to get trastuzumab emtansine treatment. Of these, 2183 people were actually given the study medicine. People visited their doctors every 3 weeks during treatment, and every 3–6 months after the treatment was stopped. Serious side effects that were related to the medicine were checked up to 2 years after the last patient started taking part in the study. The symbol on the timeline (📄) shows when the information in this summary was collected (July 2019). A small number of patients from China continued on treatment until July 2020, after the formal end of the study in July 2019.

## Study timeline



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

Side effects are unwanted effects of a drug or medical treatment that happen during a study. Some of the side effects described below were related to the study medicine, while others were not necessarily related.

- 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 on the medicine leaflets. They may also overlap with side effects that have been observed in other studies.

### Question 1: How many people had side effects of main interest in this study?

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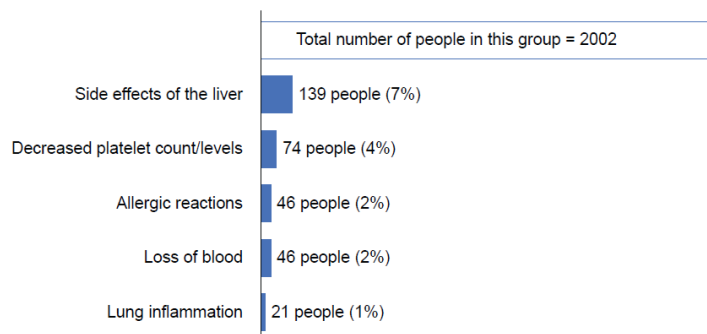
Researchers wanted to know how many people experienced the following side effects of main interest in this study: (1) severe, life-threatening, or (rarely) fatal side effects that were of main interest (but which were not necessarily related to the medicine); (2) any amount of lung inflammation that was not necessarily related to the medicine; and (3) any other severe, life-threatening, or fatal side effects of main interest that were related to the medicine. Overall, a greater percentage of people from the Asia-only group (51%) had a side effect of main interest than people from the global group (23%). This was mostly because a higher percentage of people in the Asia-only group had severe or life-threatening (but not fatal) thrombocytopenia, a condition in which there is a low level of the blood cell fragments that help blood to clot. However, most people in the Asia-only group fully recovered from this side effect within 15 days. Also, severe or life-threatening thrombocytopenia was not connected to severe, life-threatening, or fatal blood loss (note, fatal blood loss was rare). Results from each sub-category of the side effects of main interest are presented below.

### Question 2: How many people had severe, life-threatening, or fatal side effects that were of main interest, which were not necessarily related to the medicine?

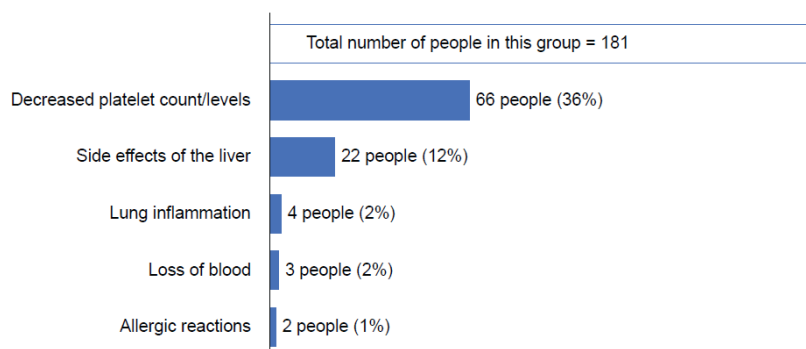
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Researchers studied how many people in the global group and the Asia-only group had severe, life-threatening, or (rarely) fatal side effects that were of main interest but were not necessarily related to the medicine. These side effects were: decreased platelet count/levels (thrombocytopenia; platelets are cell components that help blood to clot), side effects of the liver, allergic reactions, loss of blood, and lung inflammation. These side effects happened after people had taken the medicine, but were not necessarily caused by the medicine. The numbers of people in each group who had these side effects are shown in the below figure.

**Global group:  
Severe, life-threatening, or (rarely) fatal side effects that were of main interest**



**Asia-only group:  
Severe, life-threatening, or (rarely) fatal side effects that were of main interest**



**Question 3: How many people had any amount of lung inflammation that was not necessarily related to the medicine?**

Researchers were also interested in how many people had any amount of lung inflammation that was not necessarily related to the medicine. One percent of people in the global group and 2% of people in the Asia-only group had any amount of lung inflammation.

**Question 4: How many people had any other severe, life-threatening, or fatal side effects of main interest that were related to the medicine?**

Researchers also wanted to know how many people had any other severe, life-threatening, or fatal side effects of main interest that were related to the medicine. This percentage was 18% (severe, 17%; life-threatening, 2%; fatal, 1%) in the global group and 49% (severe, 43%; life-threatening, 15%; fatal, 1%) in the Asia-only group.



## Serious side effects related to the medicine

A side effect is considered ‘serious’ if it is fatal, life-threatening, if hospital care is needed, or if it is considered a significant medical event according to the researcher.

During this study, 126 out of 2002 (6%) of people in the global group and 28 out of 181 (15%) of people in the Asia-only group had a serious side effect (eg. thrombocytopenia) that was related to the medicine.

## Side effects that caused people to stop taking their medicine

Additionally, during this study, some people decided to stop taking their medicine because of side effects that were not necessarily related to the medicine:

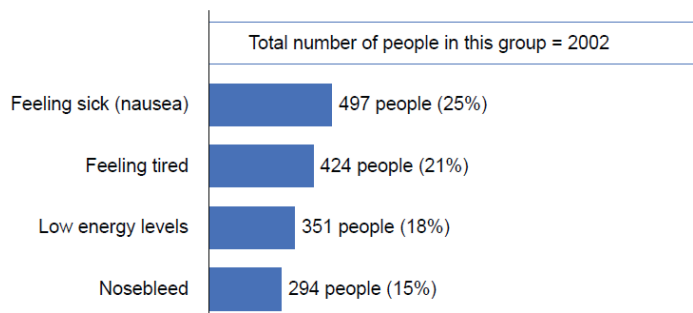
- In the global group, 237 out of 2002 people (12%) stopped taking their medicine.
- In the Asia-only group, 20 out of 181 people (11%) stopped taking their medicine.

## Most common side effects related to the medicine

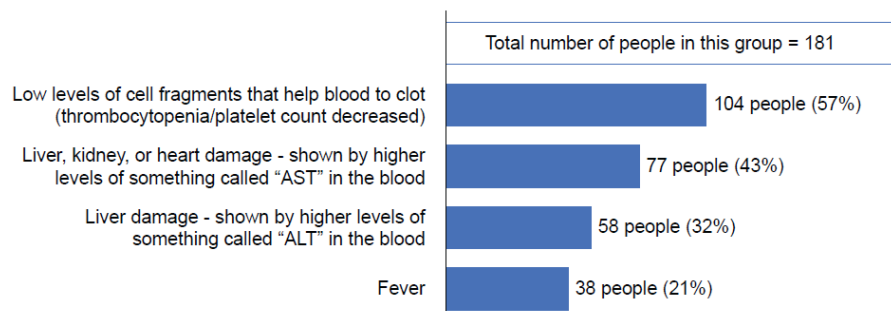
During this study, 1539 out of 2002 people (77%) in the global group and 164 out of 181 people (91%) in the Asia-only group had any type of side effect that was related to the medicine.

The four most common side effects in each group are shown in the following picture. Some people had more than one side effect – this means that they are included in more than one row in the picture.

### Global group: Most common side effects related to the medicine



### Asia-only group: Most common side effects related to the medicine



## 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.

## 5. How well did the medicine work?

### Question 1: How long did people live in this study?

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Researchers looked at how long people in the global group and the Asia-only group lived on average in this study. People who were given trastuzumab emtansine in the global group lived for around 27 months on average after starting the medicine. In the Asia-only group, people who were given trastuzumab emtansine lived for around 30 months on average. These numbers for each treatment group are averages, which means that some people lived for a longer time and some people lived for a shorter time.

In both the global group and the Asia-only group, people who were given more treatments for their cancer before this study tended to live for a shorter time than people who were given fewer cancer treatments before this study. This is often the case with cancer treatments.

### Question 2: How long from the start of the study did it take for people's cancer to get worse?

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Researchers also looked at how much time there was before people's cancer got worse – this information was collected from the start of the study until July 2019. In the global group, people's cancer got worse after around 7 months on average of starting the medicine. This compares with around 6 months on average for people who were given trastuzumab emtansine in the Asia-only group. 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.

In both the global group and the Asia-only group, people who were given more treatments for their cancer before this study tended to experience a shorter time between the start of the study and their cancer getting worse than people who were given fewer cancer treatments before this study.

This section only shows the key results from this study. You can find information about all other results 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 2183 people with locally advanced or metastatic HER2-positive breast cancer who were treated with trastuzumab emtansine. These results helped researchers learn more about treating HER2-positive breast cancer with trastuzumab emtansine, adding to data from previous studies. This study fulfilled a commitment to the regulators for safety assessment.

All patients took the same medicine in this study. This means that researchers cannot compare the effects of the study medicine with the effects of different medicines in different studies – they cannot say that the study medicines were ‘better’ than other medicines that were not part of this study.

The main results of the study have shown that:

- Safety results for both the global group and the Asia-only group showed a safety profile of trastuzumab emtansine that is consistent with what is already known about the medicine, and no new side effects were reported.
- People from the Asia-only group had a higher percentage (51%) of side effects that were of main interest than people from the global group (23%), mainly because people from the Asia-only group had a higher percentage of severe or life-threatening (but not fatal) thrombocytopenia. This is in line with prior observations.
- Most patients from the Asia-only group with severe/life-threatening thrombocytopenia made a full recovery.
- The length of time people lived, as well as the amount of time between the start of the study and people’s cancer getting worse, was similar between the global group and the Asia-only group.
- The data did not show anything unexpected with regard to safety, and further confirmed the safety of trastuzumab emtansine, a medicine that was already being prescribed to people in daily clinical practice during this trial.

This study provides more comprehensive information for doctors to help them make treatment decisions about trastuzumab emtansine. Improved understanding of the safety profile of trastuzumab emtansine can also help doctors determine how to best manage side effects of the medicine and improve quality of life of patients with metastatic breast cancer.

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?

Studies with trastuzumab emtansine in patients with HER2-positive breast cancer patients are still happening, including patients from around the world and from Asian countries. Some of these are single-arm studies that only look at trastuzumab emtansine, while others look at trastuzumab emtansine compared with, or combined with other treatments for HER2-positive breast cancer.

Trastuzumab emtansine is a proven medicine approved by authorities all over the world for patients with 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/>
- <https://clinicaltrials.gov/ct2/show/results/NCT01702571>

If you would like to find out more about the results of this study, the full title of the relevant scientific meeting poster is: “Safety of trastuzumab emtansine (T-DM1) in patients (pts) with HER2-positive locally advanced or metastatic breast cancer (mBC): final results from KAMILLA Cohorts 1 (global) and 2 (Asia).” The authors of the scientific meeting poster are: R. Wuerstlein, P. Ellis, F. Montemurro, A. A. Torres, S. Delalogue, and others. At the time of this summary, the paper had been accepted for poster presentation at the American Society for Clinical Oncology meeting, held in June 2021.

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

If you have any further questions after reading this summary:

- Visit the ForPatients platform (<https://forpatients.roche.com/>) and fill out the contact form.
- 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 two-cohort, open-label, multicenter study of trastuzumab emtansine (T-DM1) in HER2-positive locally advanced or metastatic breast cancer patients who have received prior anti-HER2 and chemotherapy-based treatment.”

The study is known as ‘KAMILLA’.

- The protocol number for this study is: MO28231.
- The ClinicalTrials.gov identifier for this study is: NCT01702571.