Summary of Clinical Trial Results

The ELAINA study: A study to see if trastuzumab emtansine (T-DM1) works better than lapatinib with capecitabine in Chinese 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 April 2017. This summary includes the results up until July 2021.

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.**

Contents of the summary

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 – 'T-DM1' and 'lapatinib' and 'capecitabine'.

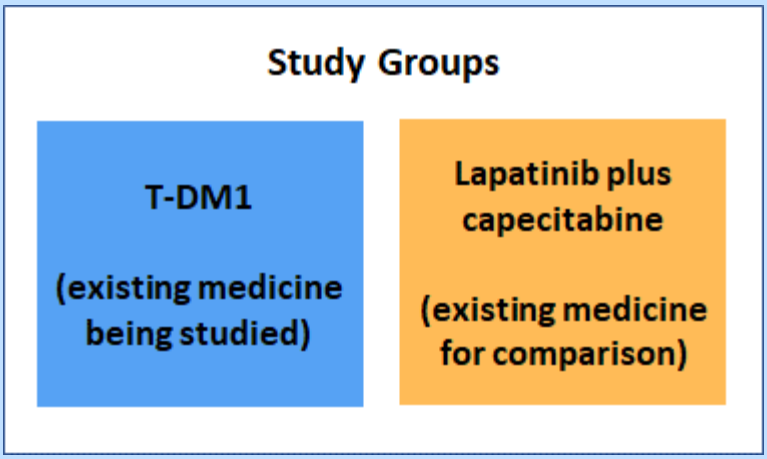
Key information about this study

Why is this study being done?

- This study was done to see if a medicine called 'T-DM1' works as well in Chinese people as it did in a worldwide population that didn't include people from China to treat a type of breast cancer called 'HER2-positive advanced breast cancer'.
- The study was also done to see what side effects T-DM1 had in Chinese people.

Which medicines were studied and who took part?

- In this study, people were given either the existing medicine being studied (called 'T-DM1') or a combination of two existing medicines (called 'lapatinib' and 'capecitabine').
- It was decided by chance which treatment each person was given, but the study was designed so that two times as many people got T-DM1 as got lapatinib plus capecitabine.



- 200 people took part in the study, all in China.

What were the results?

- The main finding was that the group of people taking T-DM1 had about a 15% lower risk of their cancer getting worse at any point in time compared to the group taking lapatinib plus capecitabine.

What were the side effects?

- Around 21% of people (31 out of 151 people) taking T-DM1 had serious side effects, compared to around 20% of people (10 out of 49 people) taking lapatinib plus capecitabine.

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 lot of 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. Sometimes the medicines given as the first treatment ('first-line') for HER2 positive advanced breast cancer don't work or stop working. In these people, a medicine called T-DM1 (you say this as 'tee – dee – em – one') increased the time between when people took T-DM1 and when their cancer got worse and increased the amount of time they lived compared to a combination of two other medicines 'lapatinib' and 'capecitabine'.

T-DM1 was previously studied in a large group of people (in the EMILIA study) that did not include people living in China. Before treating Chinese people with T-DM1, it is important to make sure it works in Chinese people and does not have new side effects.

What were the study medicines?

This study looked at whether an existing medicine would work better than a different existing medicine in Chinese patients, the medicines are:
Lapatinib and capecitabine – an existing medicine that was already tested in Chinese patients
T-DM1 – An existing medicine being tested in Chinese patients

'Lapatinib' is an existing medicine given to people with breast cancer that is HER2-positive.

- You say this as 'la-pa-tuh-nib'.
- Lapatinib helps stop HER2-positive breast cancer from growing.
- Lapatinib is a targeted medicine – this means that the medicine targets the cancer cells and not the healthy cells.
    - This may mean that it may be better at treating the cancer cells and cause fewer side effects than other medicines.
- Lapatinib targets the cancer cells with HER2 protein on them.

'Capecitabine' is an existing medicine given to people with breast cancer.

- You say this as 'cape-site-uh-bean'.
- Capecitabine (chemotherapy) helps kill any kind of fast-growing cells like breast cancer cells.
- It is not a targeted therapy meaning it can affect some healthy cells.

'Trastuzumab emtansine' which is also called 'T-DM1' is the medicine that was studied here – it works in a different way than lapatinib and capecitabine.

- T-DM1 is a combination of trastuzumab (you say this as 'tras-too-zoo-mab') and a chemotherapy in the same medicine.
  - Trastuzumab helps stop HER2-positive breast cancer from growing.
- The trastuzumab part of T-DM1 targets the HER2 on the breast cancer and delivers the chemotherapy to kill the breast cancer cells.
  - This may mean that it may be better at treating the cancer cells and cause fewer side effects than other medicines.

What did researchers want to find out?

- Researchers did this study to compare T-DM1 with lapatinib plus capecitabine – to see if T-DM1 worked as well in Chinese people with HER2-positive advanced breast cancer as in the worldwide population (see section 4 "What were the results of the study?").
- They also wanted to find out if there were any new side effects in Chinese people 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. What were the chances of people's cancer getting worse?

Other questions that researchers wanted to answer were:
2. What were the chances of people dying?

What kind of study was this?

This study was a 'Phase 3' bridging study. This means that T-DM1 had already been tested in a large number of non-Chinese people with the same type of breast cancer (HER2-positive advanced breast cancer) before this study. In this study, a large number of Chinese people with HER2-positive advanced breast cancer either took T-DM1 or lapatinib plus capecitabine (a standard treatment for HER2-positive advanced breast cancer) – this was to find out if T-DM1 could delay people's cancer getting worse like it did in the large group of non-Chinese people it was tested in before this study. Researchers also wanted to find out about the side effects of 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, except that this study was designed so that people had twice the chance of receiving T-DM1 as receiving lapatinib plus capecitabine.
  - 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.

This study was 'open label'. 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?

This study started in April 2017. This summary includes the results up to July 2021.

The study took place at 19 study centres in China.

2. Who took part in this study?

In this study, 200 people with HER2-positive advanced breast cancer took part.

People who took part in the study were between 28 and 78 years of age. All of the people were female.

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 a type of chemotherapy called a taxane
- their cancer had become worse (progressed) during or after the most recent treatment for their advanced breast cancer.

People could not take part in the study if:

- they had previously taken T-DM1, lapatinib, or capecitabine
- they had severe nerve problems that cause pain, numbness, and tingling in different parts of the body (peripheral neuropathy)
- they had certain heart problems.

Since advanced breast cancer cannot currently be cured, unfortunately it is to be expected that many people will experience progression of their disease and some will die during a study like this.

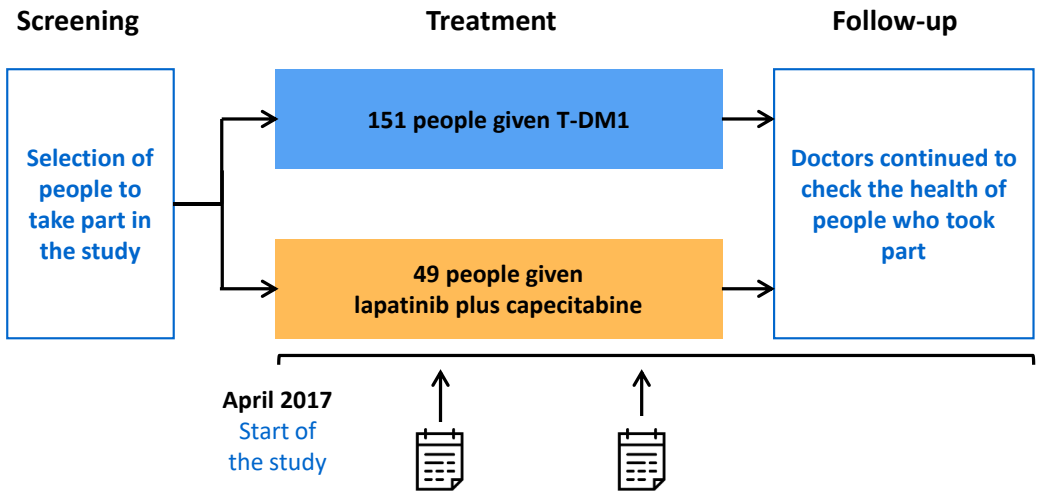
3. What happened during the study?

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

The treatment groups were:

- **T-DM1** (the existing medicine being studied in Chinese patients) – dripped (infused) into a vein every 3 weeks.
- **Lapatinib plus capecitabine** (the existing medicine that was already studied in Chinese patients)
  - Lapatinib – tablet swallowed one time per day, every day
  - Capecitabine – tablet swallowed two times per day, on days 1 to 14 of a repeating 21-day (3-week) cycle

People continued to receive their medicines until they stopped working or if they had unmanageable side effects. Some people in the study took the treatments for up to 17 months. When the study finished, the people who took part were asked to go back to their study centre for more visits – to check their overall health. Look below to see more information about what happened in the study.



The symbol on the timeline (📋) shows when the information shown in this summary was collected. Some information was collected after 1 year and 6 months (October 2018) and some was collected after 4 years and 3 months (July 2021).

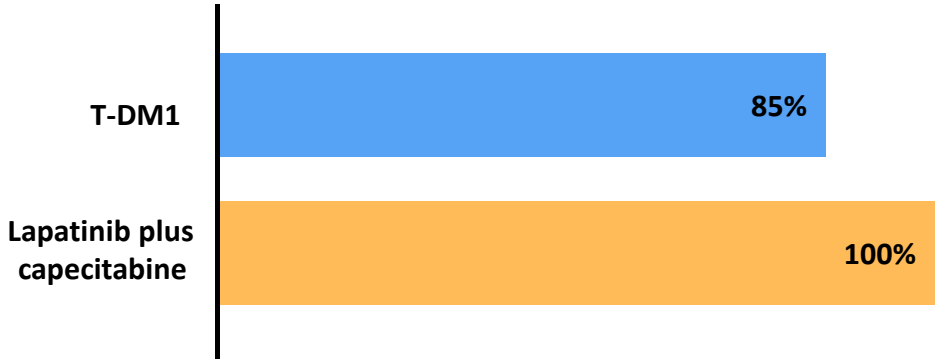
4. What were the results of the study?

Question 1: What were the chances of people's cancer getting worse while on the study?

Researchers looked at what the chances were of people's cancer getting worse. This information was collected from the start of the study until October 2018.

- The group taking T-DM1 had about a 15% lower risk of their cancer getting worse during the study compared to the group taking lapatinib plus capecitabine.

What were the chances of people's cancer getting worse?



Question 2: What were the chances of people dying while on the study?

Researchers looked at what the chances were of people dying. This information was collected from the start of the study until July 2021.

- The group taking T-DM1 had about the same chance of dying during the study compared to the group taking lapatinib plus capecitabine.

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 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 of various intensity from mild to very severe 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.
- Serious and common side effects are listed in the following sections.

Overall side effects

During this study, around 99 out of every 100 people (99%) had a side effect that was not considered serious. Around 97% of people taking T-DM1 had a side effect that was not considered serious, compared with 100% of people taking lapatinib plus capecitabine.

Serious side effects

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 5 people (21%) had at least one serious side effect. Around 21% of people taking T-DM1 had a serious side effect, compared with around 20% of people taking lapatinib plus capecitabine.

Other side effects

Because T-DM1 has been shown to cause certain side effects in other people, researchers looked at how often those side effects happened in people taking T-DM1 compared with people taking lapatinib plus capecitabine in this study. These 'selected' side effects are shown in the following table. Some people had more than one side effect – this means that they are included in more than one row in the table.

'Selected' side effects reported in this study	**People taking T-DM1** (151 people total)	**People taking lapatinib plus capecitabine** (49 people total)
Liver damage	79% (119 out of 151 people in this treatment group)	84% (41 out of 49 people in this treatment group)
Low level of the blood cell fragments that help blood to clot – called 'platelets'	76% (115 out of 151)	20% (10 out of 49)
Reactions to a medicine given by drip into a vein (infusion reaction) – including itching, rash, swollen tongue and lips, redness on face and neck (flushing), fever or chills, coughing, nausea, joint pain, feeling short of breath	8% (12 out of 151)	0
Lung inflammation	1% (1 out of 151)	0
Heart problems	2% (3 out of 151)	0
Nerve problems that cause pain, numbness, tingling in different parts of the body (peripheral neuropathy).	8% (12 out of 151)	6% (3 out of 49)
Bleeding	33% (49 out of 151)	4% (2 out of 49)

There was more bleeding in the T-DM1 group than in the lapatinib plus capecitabine group. None of this bleeding was severe in either group and was mostly nose bleeds and gum bleeding.

During the study, some people stopped taking their medicine because of side effects:
- In the T-DM1 group, 18 out of 151 people (12%) stopped taking their medicine.
- In the lapatinib plus capecitabine group, 2 out of 49 people (4%) stopped taking their medicine.

During the study, some people needed to lower the dose of their medicine because of side effects:
- In the T-DM1 group, 17 out of 151 people (11%) lowered the dose of their medicine
- In the lapatinib plus capecitabine group, 24 out of 49 people (49%) lowered the dose of their medicine

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 200 people with a type of breast cancer called 'HER2-positive advanced breast cancer'. These results helped researchers learn more about breast cancer and T-DM1, especially how T-DM1 works in Chinese people with breast cancer.

The group taking T-DM1 had about a 15% lower risk of their cancer getting worse during the study compared to the group taking lapatinib plus capecitabine.

More people who took T-DM1 than who took lapatinib plus capecitabine had these side effects:

- Low level of the blood cell fragments that help blood to clot – called 'platelets'
- Bleeding (mostly nose bleeds and bleeding from the gums)
- Reactions to a medicine given by drip into a vein (infusion reaction)
- Heart problems (3 people). This was severe in 1 person
- Lung inflammation (1 person)

More people who took lapatinib plus capecitabine than who took T-DM1 had these side effects:

- Liver damage

The main goal of this study in Chinese people was to see if the results were similar to those from a larger global study (EMILIA) of the same medicines (T-DM1 and lapatinib plus capecitabine) used to treat HER2-positive advanced breast cancer in mostly (74%) White people.

In that study (EMILIA) the group taking T-DM1 also had a lower risk (about 35% lower) of their cancer getting worse at any particular point in time compared to the group taking lapatinib plus capecitabine.

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?

A study of T-DM1 in combination with a medicine called atezolizumab that helps the immune system fight cancer is being studied as a treatment for advanced HER2-positive breast cancer.

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/results/NCT03084939
- https://forpatients.roche.com/en/trials/cancer/bc/efficacy-and-safety-of-trastuzumab-emtansine-in-chinese-particip.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “Primary results of ELAINA: A randomized, multicenter, phase III open-label study of the efficacy and safety of trastuzumab emtansine versus lapatinib plus capecitabine in Chinese patients with HER2-positive locally advanced or metastatic breast cancer who have received prior trastuzumab-based therapy”. The authors of the scientific paper are: X. Wang, W. Li , Y. Yin, Z. Tong, Q. Zhang and others. The paper is published in the journal ‘Translational Breast Cancer Research’, volume number 4:3. https://dx.doi.org/10.21037/tbcr-23-2

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

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – https://forpatients.roche.com/en/trials/cancer/bc/efficacy-and-safety-of-trastuzumab-emtansine-in-chinese-particip.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/Roche (China) Holding Co. Ltd, Shanghai, China

Full title of the study and other identifying information

The full title of this study is: “A Randomized, Multicenter, Phase III Open-Label Study of the Efficacy and Safety of Trastuzumab Emtansine Versus Lapatinib Plus Capecitabine in Chinese Patients With HER2-Positive Locally Advanced or Metastatic Breast Cancer Who Have Received Prior Trastuzumab-Based Therapy”.

The study is known as ‘ELAINA’.

- The protocol number for this study is: BO29919.
- The ClinicalTrials.gov identifier for this study is: NCT03084939.
- There is no EudraCT number for this study.