Summary of Clinical Trial Results

The KAITLIN study: A study to see if trastuzumab emtansine (T-DM1) works better than trastuzumab plus a taxane in people with a type of breast cancer called 'high-risk, 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 January 2014 and this summary includes the results up until November 2019.

No single study can tell us everything about the risks and benefits of a medicine. It takes many people in several studies to find out everything we need to know. The results from this study may be different from other studies even if they evaluate the same medicine.

- **This means that you should not make decisions based on the summary of this single study – 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 clinical researchers to answer important questions about HER2-positive breast cancer and the medicine studied – 'T-DM1'.

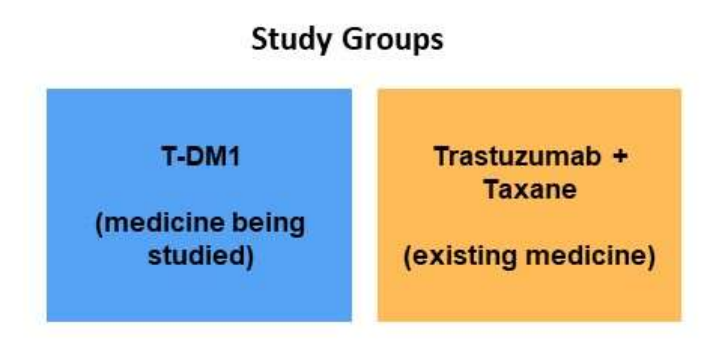
Key information about this study

Why is this study being done?

- This study was done to see if replacing the existing medicines called 'trastuzumab' and 'taxane' with a medicine called 'T-DM1' works better to treat a type of breast cancer called 'high-risk HER2-positive early breast cancer'.
- Since one of the existing medicines (taxane) has many side effects, another goal of the study was to see if T-DM1 would have fewer side effects than trastuzumab plus taxane treatment.

Which medicines were studied and who took part?

- People were given either the study medicine (called 'T-DM1') or an existing medicine (called 'trastuzumab plus a taxane').
- All people also received a medicine called 'pertuzumab' and a medicine called 'anthracycline'.
- It was decided by chance which treatment each person was given.



- 1846 people took part in this study.

What were the results?

- The main finding was that the new medicine did not work better than the existing medicine. It means that about the same number of people who took T-DM1 had their cancer return after 3 years as the people who took trastuzumab plus a taxane.

What were the side effects?

- Around 21% of people (21 out of 100 people) taking T-DM1 had serious side effects, compared to around 23% of people (23 out of 100 people) taking trastuzumab plus a taxane.

1. General information about this study

Why was this study done?

About 1 in 5 people with breast cancer have a type that makes an extra amount of protein called 'HER2 protein'. This type of breast cancer is called 'HER2-positive' breast cancer. People who are diagnosed with this type of breast cancer – and who do not have any spread of the cancer to other organs (metastasis) – have surgery to remove the cancer. After surgery, people are treated with medicine to kill the cancer that is still there after surgery. Some of the medicine (chemotherapy) kills any type of cancer, and some of it kills cancer that has HER2 protein on it (HER2-targeted therapies). In about 1 in 14 patients, the cancer has been found to return within 3 years of starting treatment.

Some people have breast cancer that has spread to parts of their immune system called 'lymph nodes'. Because this type of cancer is more likely to return after surgery, it is called "high-risk" cancer.

New medicines are needed to be able to kill the cancer more effectively.

The chemotherapy can cause side effects such as a low level of white blood cells, hair loss, nerve problems, and pain in the muscles or joints. New medicines with fewer side effects are needed to make it easier for patients to stay on their medicine without feeling unwell.

What are the study medicines?

This study looked at whether a new medicine would work better than an existing medicine. The medicines are:

- **Trastuzumab plus a taxane** – the existing medicine
- **T-DM1** – the new medicine being tested

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

- You say this as 'tras-too-zoo-mab'.
- Trastuzumab helps stop HER2-positive breast cancer from growing.
- Trastuzumab 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.
- Trastuzumab targets the cancer cells with HER2 protein on them.

A 'taxane' is an existing type of medicine given to people with breast cancer. There are different types of taxanes that all work in a similar way.

- You say this as 'tax-ane'.
- A taxane helps kill any kind of breast cancer (chemotherapy).
- It has more side effects than targeted therapies because it can also kill healthy cells.

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

- You say this as 'tee – dee – em – one'.

- T-DM1 is a combination of trastuzumab and a chemotherapy drug. The trastuzumab part of T-DM1 targets the HER2 on the breast cancer and delivers the chemotherapy to kill the breast cancer.
- This may mean that this drug is more effective and has fewer side effects than trastuzumab plus a taxane.

All people in this study were also given two other types of medicine:

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

- You say this as 'per-too-zoo-mab'.
- Pertuzumab helps stop HER2-positive breast cancer from growing, in a different way than trastuzumab does.

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

- You say this as 'an-thruh-sigh-kleen'.
- An anthracycline helps kill any kind of breast cancer (chemotherapy).

Pertuzumab and the anthracycline were given to people in both treatment groups of the study. The study was not comparing the efficacy or safety of these two medicines.

What did researchers want to find out?

- Researchers did this study to compare T-DM1 with trastuzumab plus a taxane – to see how well the study medicine worked (see section 4 "What were the results of the study?").
- They also wanted to find out how safe the medicine was – by checking how many people had side effects when taking each of the medicines during this study (see section 5 "What were the side effects?").

The main question that researchers wanted to answer was:

How many people who had cancer in their lymph nodes (also known as high-risk breast cancer) did not have their cancer return?

What kind of study was this?

This study was a 'Phase 3' study. This means that T-DM1 had already been tested in a smaller number of people with breast cancer before this study. In this study, a larger number of people with breast cancer either took T-DM1 or trastuzumab plus a taxane – this was to find out if T-DM1 worked to help stop their breast cancer from returning. Researchers also wanted to find out if T-DM1 had fewer side effects than trastuzumab plus a taxane.

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

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?

The study started in January 2014. This summary includes the results up until November 2019.

The study took place at 288 study centres – across 36 countries in Asia, Europe, Australia, North America, and South America.

2. Who took part in this study?

In this study, 1846 people with high-risk HER2-positive breast cancer took part. The average age of people who took part in the study was 52 years. 1839 of the 1846 people (over 99%) were female and 7 of the 1846 people (less than 1%) were male.

People could take part in the study if they had:

- HER2-positive breast cancer and
- surgery to remove the tumour.

People also had to have "high-risk" breast cancer which is one of the following:

- cancer that spread to the lymph nodes, or
- cancer that had not spread to the lymph nodes and:
  - was bigger than 2 cm, and
  - did not have a type of protein on the cancer that allows it to use the hormones oestrogen or progesterone to grow ('hormone receptor negative').

People could not take part in the study if they had:

- cancer that had spread to other parts of the body, besides the lymph nodes (metastasis)
- breast cancer before
- a type of cancer other than breast cancer in the past 5 years
- any treatment for their breast cancer, or
- certain problems with their lungs, heart, or liver.

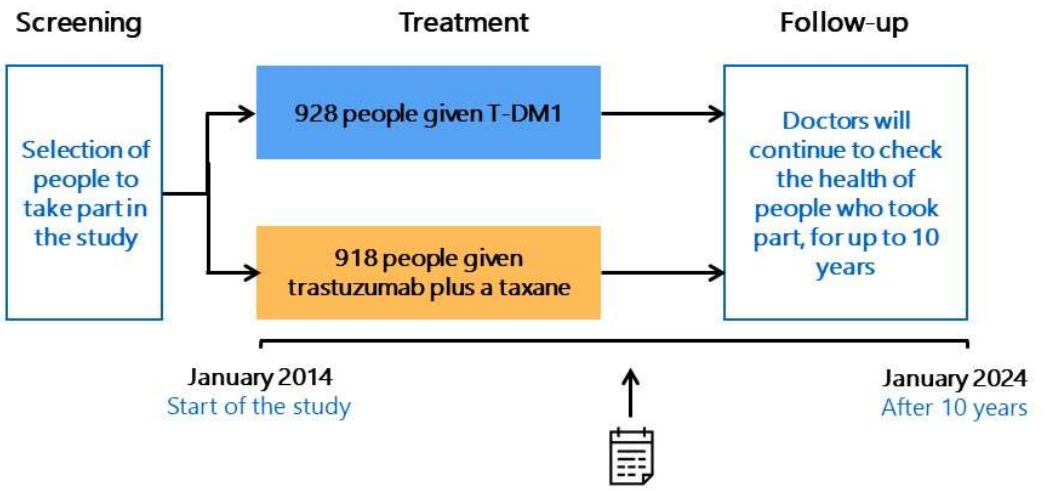
3. What happened during the study?

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 study medicine) – dripped (infused) into a vein every 3 weeks.
- **Trastuzumab plus a taxane** (existing medicines)
  - Trastuzumab – dripped into a vein every 3 weeks.
  - A taxane – dripped into a vein either every week or every 3 weeks.

All patients have stopped getting treatment in this study. 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 has happened in the study so far – and what the next steps are.



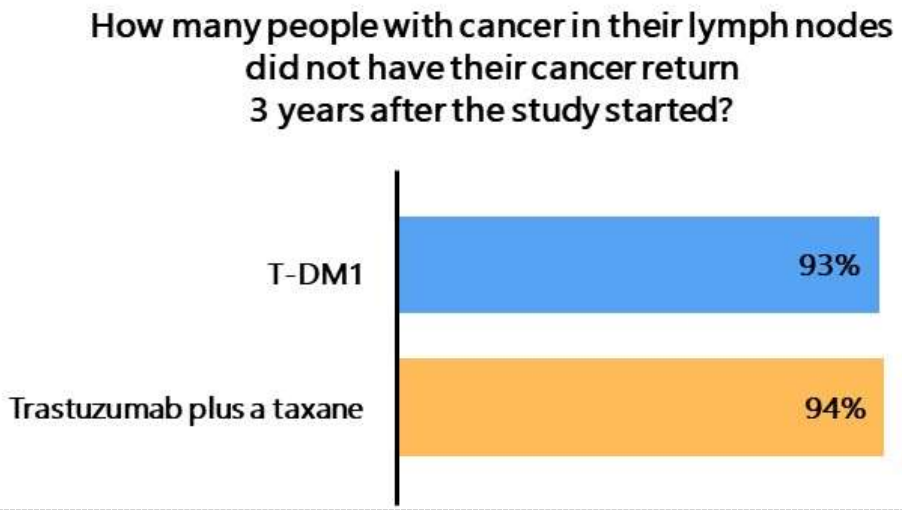
This study is still happening, so the symbol on the timeline (📋) shows when the information shown in this summary was collected – after 5 years and 11 months (November 2019).

4. What were the results of the study at this point?

Question 1: How many people – who had cancer in their lymph nodes – did not have their cancer return?

90% (9 of every 10 people) in this study had cancer in their lymph nodes. Researchers looked at how many of these people did not have their cancer return by 3 years after they started the study.

- 93% of people – with cancer in their lymph nodes – who were given T-DM1 did not have their cancer return 3 years after they started the study.
- 94% of people – with cancer in their lymph nodes – who were given trastuzumab plus a taxane did not have their cancer return 3 years after they started the study.



This section only shows the key result from the study at this point. 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 study only. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear in the medicine leaflets.
- For this information, the researchers only included the people who had actually been given study medicines (912 received T-DM1 and 926 received trastuzumab plus a taxane).
- Serious and common side effects are listed in the following sections.

Serious side effects

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

During this study, about 1 in every 5 people (22%) had at least one serious side effect. Around 21% of people taking T-DM1 had a serious side effect, compared with around 23% of people taking trastuzumab plus a taxane.

The most common serious side effect was low levels of white blood cells accompanied by a fever. The serious side effects that occurred in at least 20 people taking a study medication are listed in the table below. Some people had more than one side effect – this means that they are included in more than one row in the table.

Serious side effects reported in this study	**People taking T-DM1** (912 people total)	**People taking trastuzumab plus a taxane** (926 people total)
Low levels of white blood cells accompanied by a fever	3% (31 out of the 912 people in this treatment group)	6% (51 out of the 926 people in this treatment group)
Fever	2% (19 out of 912)	1% (13 out of 926)
Pneumonia	1% (12 out of 912)	1% (12 out of 926)
Low levels of white blood cells	1% (10 out of 912)	2% (16 out of 926)
Diarrhoea	1% (8 out of 912)	2% (20 out of 926)

There were some people in the study who died because of side effects. The study doctors did not think any of these side effects were related to the study treatments. This happened in:

- 5 out of 912 people (less than 1%) in the T-DM1 group.
- 2 out of 926 people (less than 1%) in the trastuzumab plus a taxane group.
- Of the 7 people who died, 3 died of pneumonia, 2 died of other cancers, 1 died of severe depression leading to suicide and 1 died of metabolic acidosis, a condition where too much acid builds up in your body.

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

- In the T-DM1 group, about 1 out of 4 people (27%) stopped taking their T-DM1.
- In the trastuzumab plus a taxane group, about 1 in 20 people (4%) stopped taking their trastuzumab.
- In the trastuzumab plus a taxane group, about 1 in 14 people (7%) stopped taking their taxane.

Most common side effects

During this study, around 99 out of every 100 people (99%) in each treatment group had a side effect that was not considered serious.

The most common side effects are shown in the following table. These are side effects that occurred in at least 1 in 10 people in either treatment group. To be included in this list, the side effect also had to occur more often in one treatment group than in the other: there had to be at least a difference of 50 or more people between the groups. Some people had more than one side effect – this means that they are included in more than one row in the table.

Most common side effects reported in this study	**People taking T-DM1** (912 people total)	**People taking trastuzumab plus a taxane** (926 people total)
Diarrhoea	44% (405 out of the 912 people in this treatment group)	65% (605 out of the 926 people in this treatment group)
Nose bleed	37% (333 out of 912)	20% (182 out of 926)
Liver, heart or kidney damage – shown by higher levels of something called 'AST' in the blood	35% (317 out of 912)	11% (98 out of 926)
Liver damage – shown by higher levels of something called 'ALT' in the blood	33% (300 out of 912)	12% (108 out of 926)
Fever	25% (227 out of 912)	19% (175 out of 926)
Low level of the blood cell fragments that help blood to clot – called 'platelets'*	18% (162 out of 912)	3% (25 out of 926)
Muscle pain	17% (153 out of 912)	23% (215 out of 926)
Low level of the blood cell fragments that help blood to clot – called 'platelets'*	16% (143 out of 912)	2% (15 out of 926)
Hot flush/flash	11% (100 out of 912)	18% (167 out of 926)
Swelling	8% (74 out of 912)	17% (156 of 926)

*This side effect is listed twice because there are two different names for this side effect in the recording system and doctors can indicate one or both of them.

Other side effects

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 1846 people with a type of breast cancer called 'high-risk, HER2-positive breast cancer'. These results helped researchers learn more about breast cancer and T-DM1.

About the same number of people taking T-DM1 had their cancer return in 3 years as people taking trastuzumab plus a taxane.

More people who took T-DM1 than who took trastuzumab plus a taxane had these side effects:

- Nose bleeds
- Liver, heart or kidney damage – shown by higher levels of something called 'AST' in the blood
- Liver damage – shown by higher levels of something called 'ALT' in the blood
- A low level of the blood cell fragments that help blood to clot – called 'platelets'
- Fever

More people who took trastuzumab plus a taxane than who took T-DM1 had these side effects:

- Diarrhoea
- Muscle pain
- Hot flush/flash
- Swelling

No single study can tell us everything about the risks and benefits of a medicine. It takes many people in several 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?

Since T-DM1 + pertuzumab did not work better than trastuzumab + taxane + pertuzumab, there are no future studies of T-DM1 + pertuzumab 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/results/NCT01966471
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2012-004902-82/results
- https://forpatients.roche.com/en/trials/cancer/bc/a-study-of-trastuzumab-emtansine--kadcyla--plus-pertuzu-91245.html

The main results of this study were presented at the American Society of Clinical Oncology scientific conference in May 2020. The title of the presentation is: "Primary Analysis of KAITLIN: A Phase 3 Study of Trastuzumab Emtansine (T-DM1) + Pertuzumab Versus Trastuzumab + Pertuzumab + Taxane, after Anthracyclines as Adjuvant Therapy for High-Risk HER2-Positive Early Breast Cancer." The authors of the presentation are: N. Harbeck, S-A. Im, C. Barrios, H. Bonnefoi, J. Gralow and others.

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/a-study-of-trastuzumab-emtansine--kadcyla--plus-pertuzu-91245.html
- Contact a representative at your local Roche office.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

Who organised and paid for this study?

This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: "Trastuzumab emtansine plus pertuzumab versus trastuzumab plus taxane plus pertuzumab after anthracycline as adjuvant therapy for high-risk HER2-positive early breast cancer: a randomised phase 3 study (KAITLIN)".

The study is known as 'KAITLIN'.

- The protocol number for this study is: BO28407.
- The ClinicalTrials.gov identifier for this study is: NCT01966471.
- The EudraCT number for this study is: 2012-004902-82.