Clinical trial interim results

Research sponsor: F. Hoffmann-La Roche Ltd

Drug studied: Trastuzumab emtansine (T-DM1)

ClinicalTrials.gov Identifier: NCT01772472

Other identifiers: EudraCT number: 2012-002018-37;

NSABP B-50-I / GBG 77

Protocol number: BO27938

Trial dates: April 2013 to 2023 (Trial currently ongoing)

Trial title: A study of trastuzumab emtansine versus trastuzumab as adjuvant therapy in patients with HER2-positive breast cancer who have residual tumor in the breast or axillary lymph nodes following preoperative therapy (KATHERINE)

Date this summary was prepared: December 2018

Contents

1. About this summary

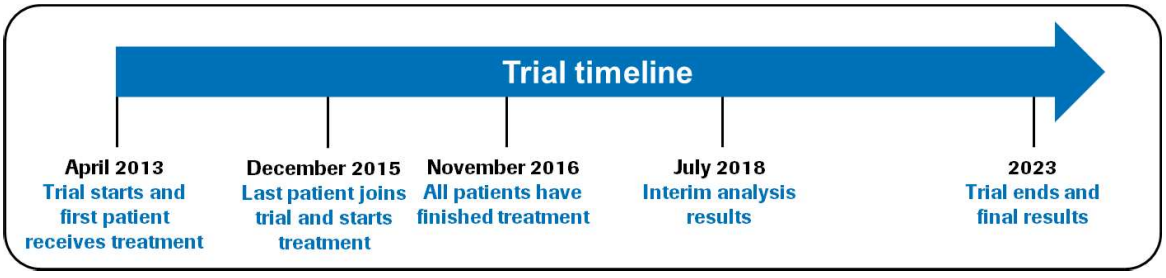
This summary is for participants in a global clinical trial for trastuzumab emtansine (also called ado-trastuzumab emtansine in the United States) and those who may be interested in this research.

Roche, the sponsor of this trial and manufacturer of trastuzumab emtansine, considers it of great importance to share the interim analysis results from trial with you.

If you are, or have been taking part in this trial, we would like to thank you for participating. You and all the trial patients are helping researchers to answer important medical questions and possibly discover new medical treatments for people with HER2-positive early breast cancer.

2. About the interim analysis trial results in this summary

This is a summary of a planned interim analysis from the trial in which you are participating (or participated). Interim analysis results are not final results but provide a summary of what has happened so far and help researchers to monitor treatments while a trial is still ongoing. The interim analysis was done after two-thirds of the predicted cases of cancer returning had occurred in the trial. The trial began in April 2013 and is still ongoing. The trial will end in 2023 when the final results are obtained. The final results are needed to help researchers to fully understand any potential benefits or risks from the treatments you have received on this trial.

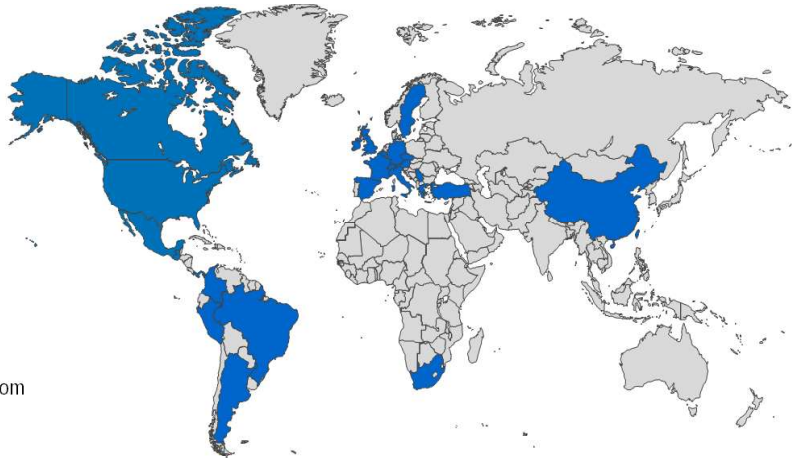


If you are, or have been, taking part in this trial and have any questions about these interim analysis results, please speak to your doctor or other medical staff at your trial site.

3. Introduction

1486 patients have taken part in this trial for about 60 months so far. The trial is taking place at 273 hospitals in 28 countries around the world.

Argentina	Israel
Austria	Italy
Belgium	Mexico
Brazil	Panama
Canada	Peru
China	Serbia
Colombia	South Africa
Czech Republic	Spain
France	Sweden
Germany	Switzerland
Greece	Taiwan
Guatemala	Turkey
Hong Kong	United Kingdom
Ireland	United States



The trial reached the point for a planned interim analysis in July 2018, which was performed by an independent group in September 2018. This summary tells you the results up until July 2018.

4. What kind of trial is this?

This trial is a Phase III, randomised, open-label trial.

- Phase III trials are usually large trials that investigate new treatments.
- 'Open-label' means that the patients, doctors, and trial staff knew what drugs each patient was taking.
- A 'randomised' trial is one where researchers randomly assign patients into groups to receive a particular treatment.

5. Why was the trial needed and who took part?

Researchers were looking for a new way to improve the treatment of patients with HER2-positive early breast cancer who are at high risk of their cancer coming back after treatment.

Patients often receive treatment before surgery is performed to remove breast cancer tumours. Treatment can cause cancer to disappear in some patients by the time of surgery, but in other patients, some or all of the cancer still remains before surgery is carried out to remove it. These patients

are at a higher risk of their cancer returning despite usually having more treatment after surgery to try to kill any remaining cancer cells in the body and to try stopping the cancer from coming back. Improved treatment options are needed for these patients.

In this trial, the researchers are studying a drug called trastuzumab emtansine. It is made of trastuzumab, which blocks HER2, attached to a chemotherapy drug called emtansine.

The main question that researchers wanted to answer was:

1. Did more patients treated with trastuzumab emtansine live longer without cancer coming back than patients treated with trastuzumab?

Other key questions that researchers wanted to answer included:

2. Did trastuzumab emtansine reduce the risk of cancer spreading beyond the breast and surrounding lymph nodes to other parts of the body?
3. How many patients in the trial had adverse events? (An 'adverse event' is a medical problem that may or may not be caused by the treatments in the trial)
4. How many patients in this trial had adverse events related to the heart?

To answer the questions in this trial, researchers looked for men and women with HER2-positive early breast cancer who were at least 18 years old. Patients could participate in the trial if they:

- were diagnosed with early breast cancer that tested positive for the HER2 protein
- received treatment with trastuzumab and chemotherapy to shrink their breast cancer before surgery
- had evidence of some cancer cells remaining in the breast or lymph nodes at the time of surgery
- had surgery less than 12 weeks before starting the trial.

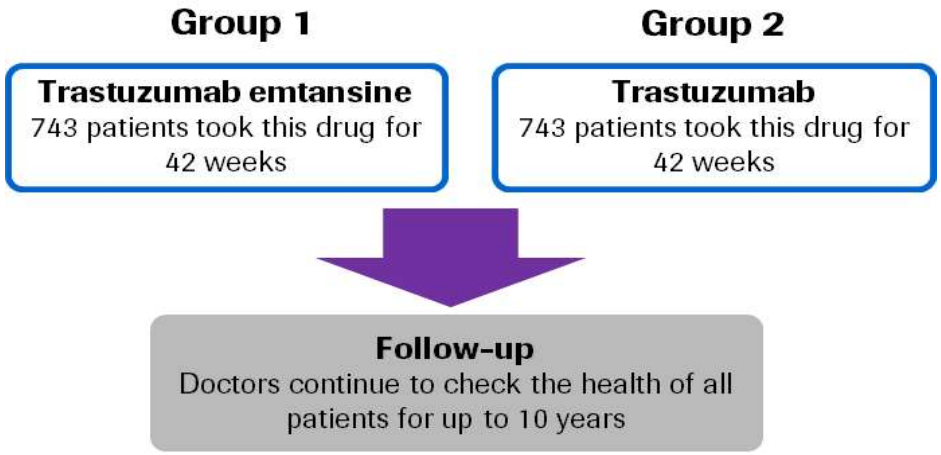
6. What happened during the trial?

During the trial, patients were randomly chosen to receive one of two treatments for 42 weeks:

- trastuzumab emtansine (the new treatment being tested)

OR

- trastuzumab (the standard-of-care treatment when this trial started).



In July 2018, the trial reached the point for a planned interim analysis of all of the data collected up until that time. This summary tells you the results of the trial so far.

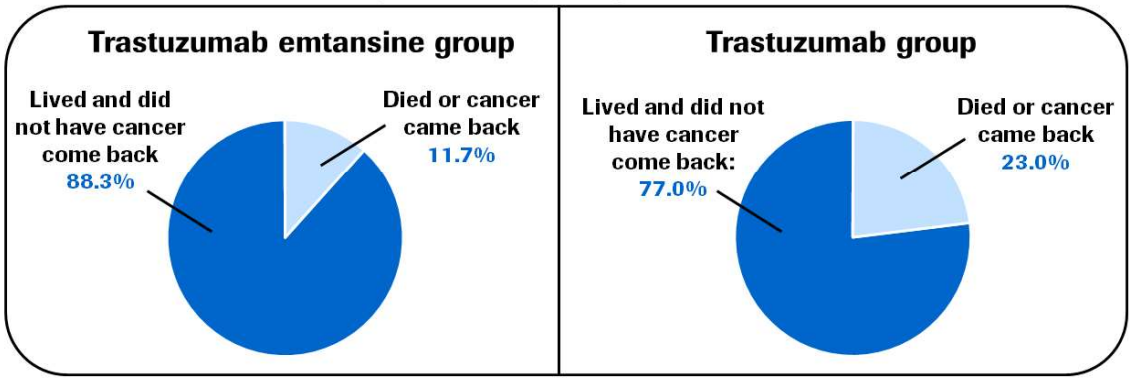
7. What are the interim results of the trial?

At this point in time in the trial, patients taking trastuzumab emtansine had a lower risk of their cancer returning than patients receiving trastuzumab.

1. Did more patients treated with trastuzumab emtansine live longer without cancer coming back than patients treated with trastuzumab?

At the time of the interim analysis, more patients receiving trastuzumab emtansine lived longer without their cancer coming back than patients receiving trastuzumab.

Patients who lived and did not have their cancer come back 3 years after joining the trial

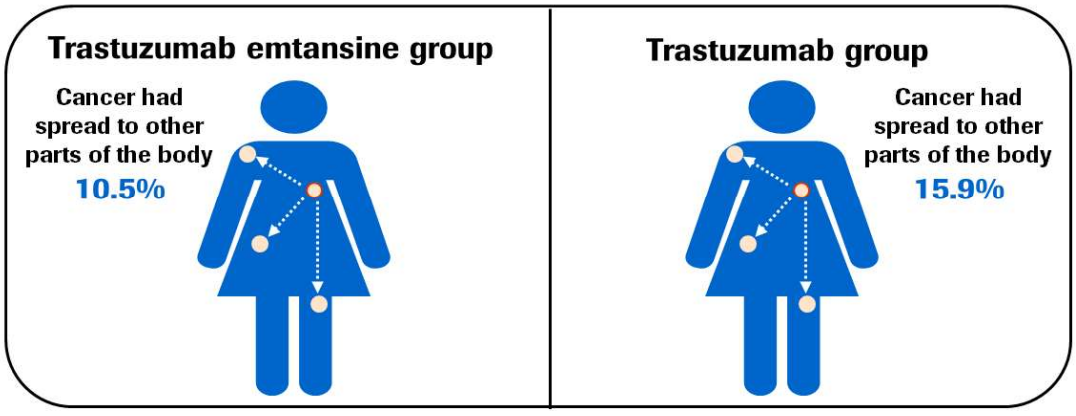


The interim results so far show that cancer has not returned in the majority of patients in both treatment groups but suggest that treatment with trastuzumab emtansine further reduces the risk of dying or cancer coming back by 50% as compared with treatment with trastuzumab.

2. Did trastuzumab emtansine reduce the risk of cancer spreading beyond the breast and surrounding lymph nodes to other parts of the body?

The interim analysis results showed that in patients whose cancer came back, the cancer spread beyond the breast and surrounding lymph nodes to other parts of the body in 10.5% of patients in the trastuzumab emtansine group and one in 15.9% of patients in the trastuzumab group.

Patients whose cancer came back and had spread to other parts of the body



3. How many patients in the trial had adverse events?

When new drugs are being studied, researchers keep track of all the medical problems that patients develop during a trial.

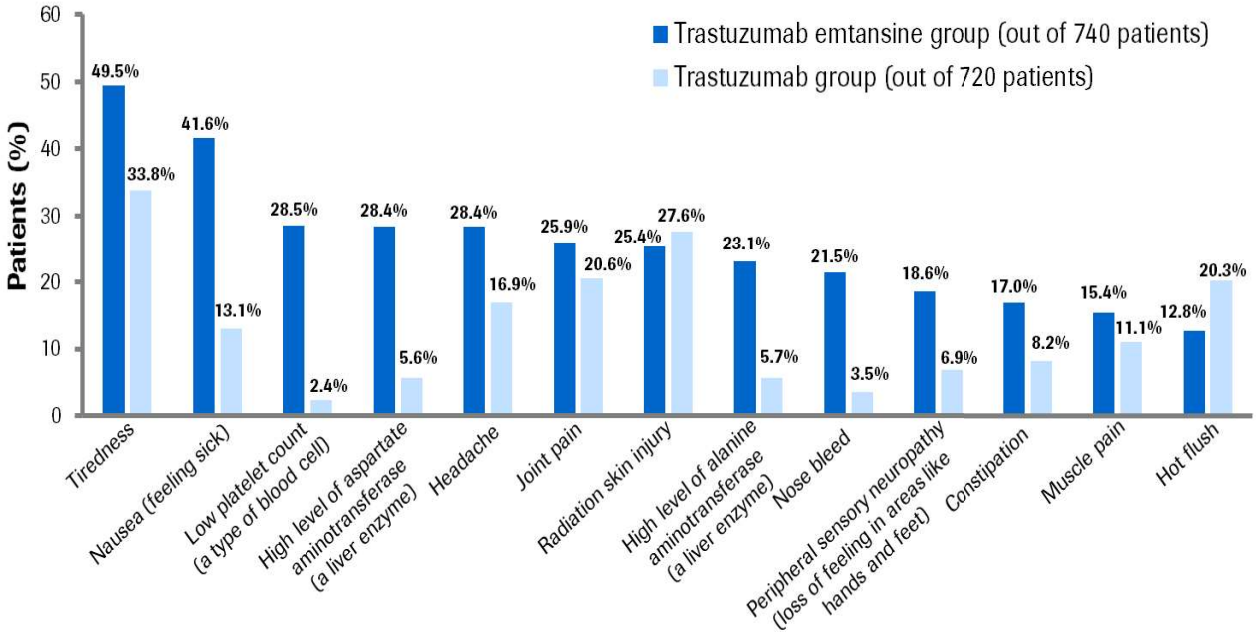
- These medical problems (such as a headache) are called 'adverse events'.
- Adverse events are reported by the trial doctor (investigator) and may or may not be caused by the treatments in the trial.

Not all the patients in this trial had adverse events. Serious and common adverse events are described below.

What were the most common adverse events that patients experienced in this trial?

At the time of interim analysis in this trial, adverse events were more common in patients treated with trastuzumab emtansine. Most patients had at least one adverse event. The chart below shows the most common types of adverse events that happened. There were other adverse events, but fewer patients had them.

The most common adverse events that patients experienced in this trial

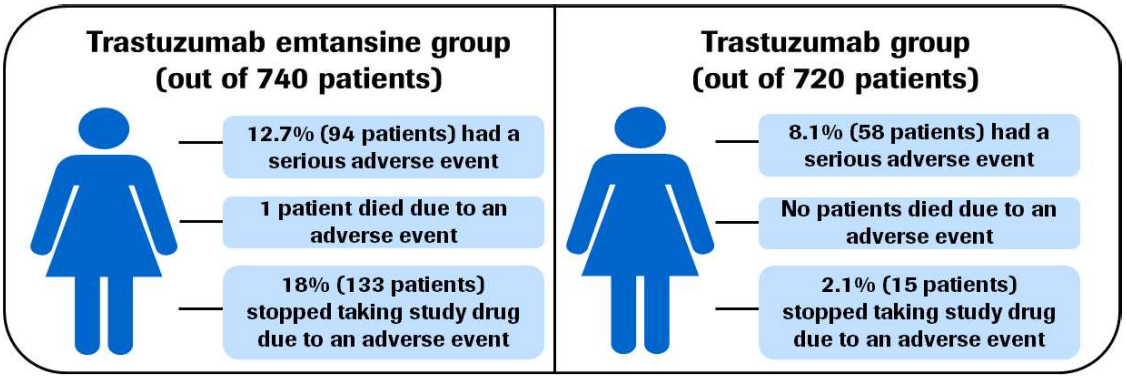


Did any patients have serious adverse events?

An adverse event is considered 'serious' if it is life-threatening, requires hospital care or causes lasting problems. The interim results of this trial as of July 2018 show:

- Serious adverse events happened in more patients receiving trastuzumab emtansine than patients receiving trastuzumab.
- One patient receiving trastuzumab emtansine died from a brain haemorrhage following a fall at home.
- More patients stopped taking their study drug because of an adverse event in the trastuzumab emtansine group than the trastuzumab group.
- The most common adverse events leading to patients stopping taking trastuzumab emtansine were abnormal blood and liver enzyme tests, peripheral sensory neuropathy (loss of feeling in areas like hands and feet) and a lower amount of blood being pumped by the heart.

The figure below shows how many patients had serious adverse events, how many patients died due to adverse events, and how many patients stopped taking study drugs because of adverse events.

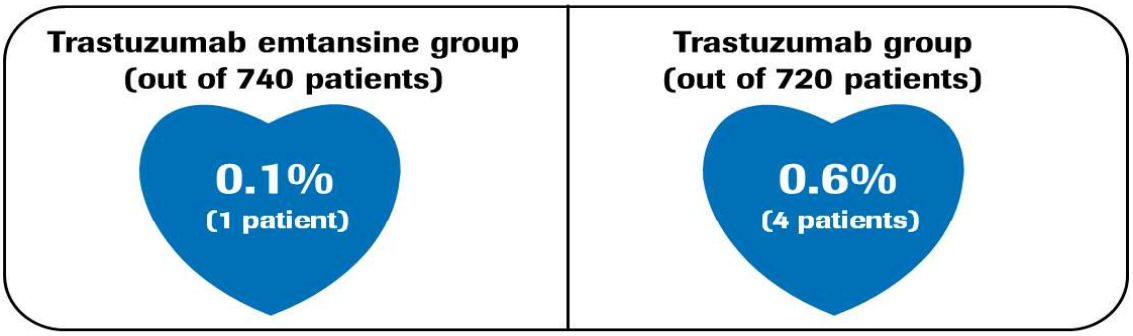


4. How many patients in this trial had adverse events related to the heart?

It is known that treatment containing trastuzumab may affect the heart. Researchers wanted to learn whether patients who received trastuzumab emtansine or trastuzumab experienced any heart problems.

In the interim results of this trial, very few adverse events related to the heart occurred.

Patients who had adverse events related to the heart



8. How has this trial helped patients and researchers and what does this mean for me?

The interim results up until July 2018 suggest that for the majority of patients with HER2-positive early breast cancer who had some remaining cancer cells in the breast or lymph nodes at the time of surgery, cancer has not returned in both treatment groups. At this point in time in the trial, the interim results suggest that patients taking trastuzumab emtansine had a lower risk of their cancer returning than patients receiving trastuzumab (the standard-of-care treatment when this trial started).

No single clinical trial can give a complete understanding of the risks and benefits of a drug. The results from this trial may differ from other studies with the same drug.

If you are taking part, or have been taking part, in this trial and have any questions about the interim results, please speak to your doctor or other medical staff at your trial site.

9. Why is the trial still ongoing?

The researchers will be collecting information from all the trial patients until the trial ends in 2023 so that the final results can be obtained. These are needed to help researchers to fully understand any potential benefits or risks from the treatments that patients received on this trial.

10. Are there plans for other studies?

There are no further clinical trials planned with trastuzumab emtansine in the same type of patients.

Other clinical studies involving trastuzumab emtansine may be ongoing and may be listed on a number of public websites such as those listed at the end of this summary.

11. Where can I learn more about this trial?

The full title of this trial is “A study of trastuzumab emtansine versus trastuzumab as adjuvant therapy in patients with HER2-positive breast cancer who have residual tumor in the breast or axillary lymph nodes following preoperative therapy (KATHERINE)”.

You can find more information about this trial on the websites listed below:

- https://clinicaltrials.gov/ct2/show/NCT01772472
- https://www.clinicaltrialsregister.eu/ctr-search/search?query=2012-002018-37

The final results of this trial will be shared when the study ends in 2023.

This trial was sponsored by F. Hoffmann-La Roche Ltd which has its headquarters at Grenzacherstrasse 124, CH-4070 Basel, Switzerland.

If you are taking part, or have been taking part, in this trial and have any questions about the interim results, please speak to your doctor or other medical staff at your trial site.

F. Hoffmann-La Roche Ltd

4070 Basel, Switzerland

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