Summary of Clinical Trial Results

A study of trastuzumab emtansine versus trastuzumab as adjuvant therapy in people with HER2-positive breast cancer who have residual tumour in the breast or axillary lymph nodes following pre-operative therapy (KATHERINE)

See the end of the summary for the full title of the study.

About this summary

This is a summary of the results of the KATHERINE 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 (January 2025).

The study started in April 2013. This summary includes the final results that were collected and analysed in October 2023.

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

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 early breast cancer and the medicines being studied.

1. General information about this study

Why was this study done?

Researchers were looking for a new way to improve the treatment of people with HER2-positive early breast cancer who are at risk of their cancer coming back after treatment. People with HER2-positive early breast cancer often receive treatment before surgery is performed ('pre-operative treatment') to remove breast cancer tumours or to reduce their size. Treatment can cause cancer to disappear in some people by the time of surgery, but in other people, some or all of the cancer still remains before surgery is carried out to remove it. People with tumours remaining at surgery are at a higher risk of their cancer returning, despite having more treatment after surgery to try to kill any remaining cancer cells in the body. Improved treatment options are needed for these people.

In this study, the researchers were studying a drug called trastuzumab emtansine. It is made of 'trastuzumab' (which blocks HER2 proteins on the cancer cells), attached to a chemotherapy drug called 'emtansine'. Researchers compared trastuzumab emtansine with trastuzumab (the standard medicine for these people at the time this study was designed).

What were the study medicines?

'Trastuzumab'

- You say this as 'trass – too – za – mab'
- Trastuzumab is an existing medicine that works by attaching to the HER2 protein on the surface of HER2-positive cancer cells. When trastuzumab attaches to HER2, it stops the protein from sending signals that make the cancer cells grow and make copies of themselves. It also makes cells in the immune system become active so that they can help attack the cancer.

'Trastuzumab emtansine'

- You say this as 'trass – too – za – mab – em – tan – zeen'
- Trastuzumab emtansine is the medicine being investigated in this study.
- This drug is made up of trastuzumab (as described above) attached to 'emtansine', which is a chemotherapy drug. Trastuzumab emtansine blocks HER2 in the same way as trastuzumab, but also contains the emtansine chemotherapy drug to help kill the cancer cells.

What did researchers want to find out?

- Researchers did this study to compare trastuzumab emtansine with trastuzumab – to see how well trastuzumab emtansine 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 and seeing how serious they were, 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:

1. Did more people who were given trastuzumab emtansine live longer without their cancer coming back than people given trastuzumab?

Other questions that researchers wanted to answer included:

2. Did people who were given trastuzumab emtansine live longer than people given trastuzumab?

What kind of study was this?

This study was a 'Phase 3' study. This means that trastuzumab emtansine had been tested in a smaller number of people with HER2-positive early breast cancer before this study.

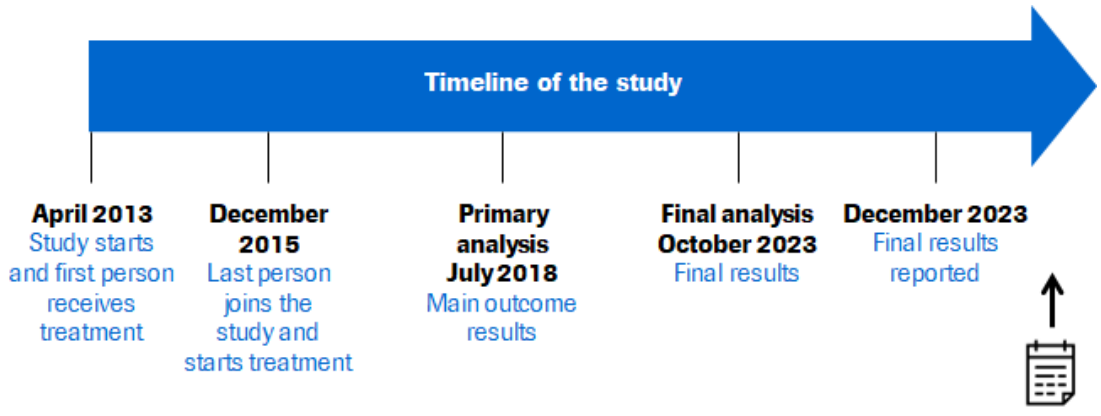
In this study, a larger number of people (1,486) with this cancer either took trastuzumab emtansine or trastuzumab. This was to find out whether trastuzumab emtansine is more effective than trastuzumab at helping people to live without their cancer coming back, and about the side effects of trastuzumab emtansine.

The study was 'randomised'. This means that it was decided by chance which of the medicines people in the study would have. Randomly choosing which medicine people take makes it more likely that the types of people in both groups (with regard, for example, to age or race) will be similar and comparable. Apart from the exact medicines being tested in each group, all aspects of care were the same between the groups.

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

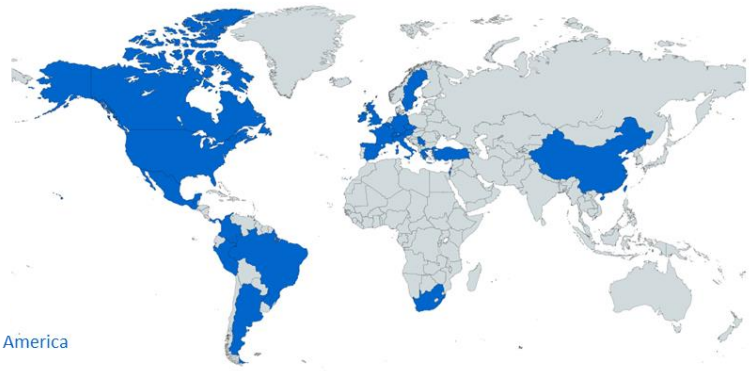
When and where did the study take place?

The study started in April 2013. The primary analysis results (main outcomes) have been reported previously and can be seen in the summary at this link (*click the dropdown arrow next to 'Show Clinical Trial Results' to find the PDF document*): https://forpatients.roche.com/en/trials/cancer/bc/a-study-of-trastuzumab-emtansine-versus-trastuzumab-as-adjuvant-.html.
The previous summary included the results collected up to July 2018. The final results were collected up until October 2023 and are reported in this summary (shown by the symbol on the timeline 📋).



The study took place at 273 study centres – across 28 countries in Africa, Asia, Europe, North America and South America. The following map shows the countries where this study took place.

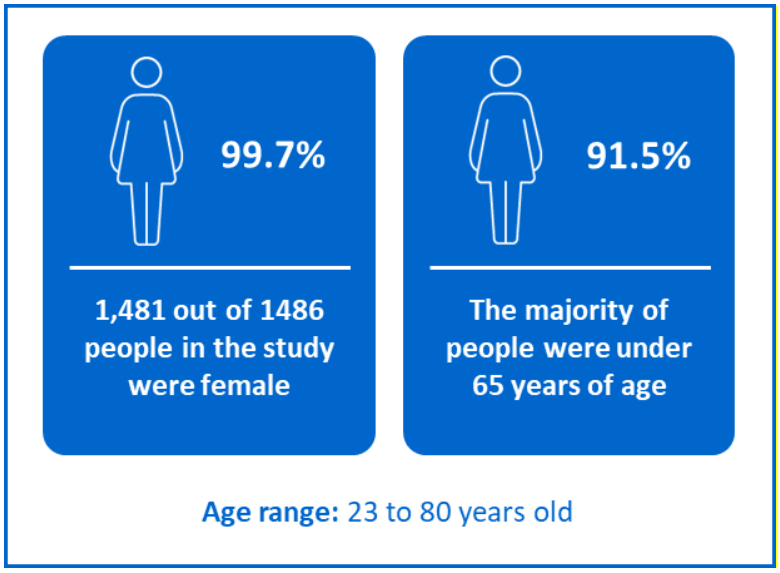
- Argentina
- Austria
- Belgium
- Brazil
- Canada
- China
- Colombia
- Czech Republic
- France
- Germany
- Greece
- Guatemala
- Hong Kong
- Ireland
- Israel
- Italy
- Mexico
- Panama
- Peru
- Serbia
- South Africa
- Spain
- Sweden
- Switzerland
- Taiwan
- Turkey
- United Kingdom
- United States of America



2. Who took part in this study?

In this study, 1,486 people with HER2-positive early breast cancer, with cancer cells remaining after pre-operative treatment, took part. They also had to have undergone surgery before entering the study.

People who took part in the study were between 23 and 80 years of age. More information on the people who took part is given below.



People could take part in this study if they had:

- HER2-positive early breast cancer, confirmed by a specific test
- Completed treatment with trastuzumab and chemotherapy before surgery
- Evidence of cancer cells remaining in the tumour or axillary lymph nodes at the time of surgery
- Surgery less than 12 weeks before starting the study

People could NOT take part in this study if they had:

- Breast cancer that had spread to other parts of the body
- Breast cancer that grew while on treatment with trastuzumab and chemotherapy before their surgery
- Heart disease or heart problems
- Liver disease

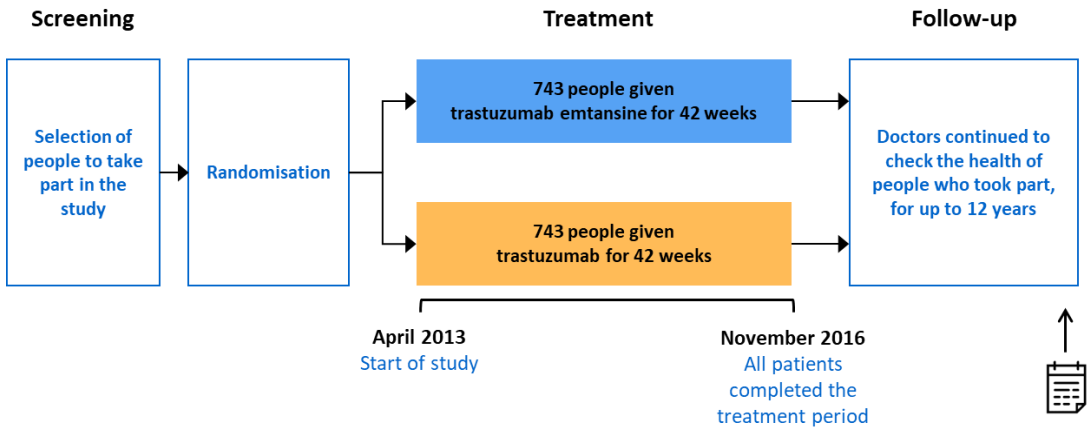
3. What happened during the study?

During the study, people were selected by chance to get one of two treatments for 42 weeks. The treatments were selected at random – by a computer.

The treatment groups were:

- **Group 1: trastuzumab emtansine** (study medicine) – given by infusion into a vein (intravenous) every 3 weeks for 42 weeks.
- **Group 2: trastuzumab** (existing medicine) – given by infusion into a vein every 3 weeks for 42 weeks.

When people had finished their treatment, they 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.

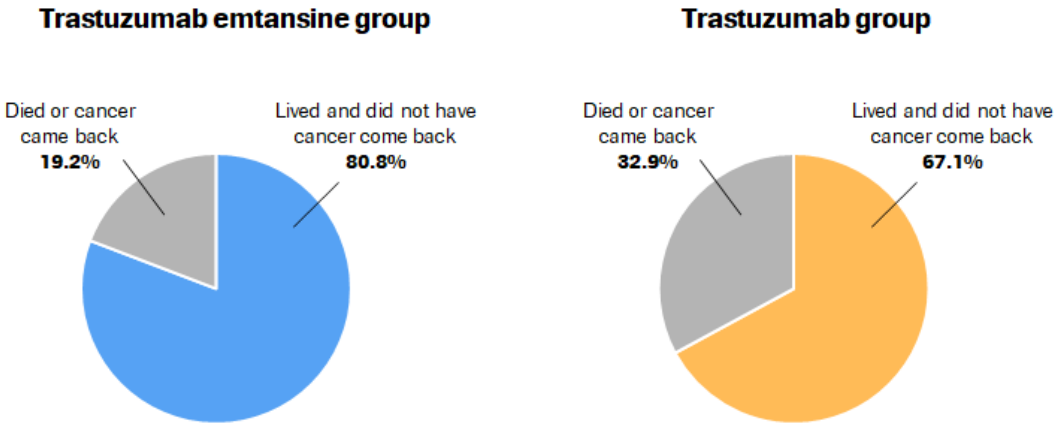


The symbol on the timeline (📋) shows when the information shown in this summary was collected – in October 2023.

4. What were the results of the study?

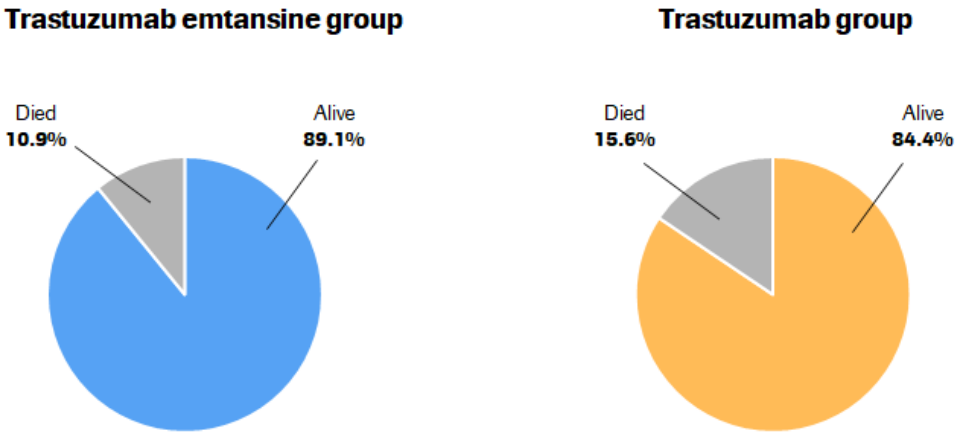
Question 1: Did more people who were given trastuzumab emtansine live longer without their cancer coming back than people given trastuzumab?

Yes – at 7 years after starting the study, more people (80.8%) who were given trastuzumab emtansine lived without their cancer coming back, compared with those who were given trastuzumab (67.1%), as shown in the figure below. The risk of the cancer coming back or of dying was 46% lower with trastuzumab emtansine treatment compared with trastuzumab.



Question 2: Did people who were given trastuzumab emtansine live longer than people given trastuzumab?

Yes – at 7 years after starting the study, more people (89.1%) who were given trastuzumab emtansine were alive, compared with those who were given trastuzumab (84.4%), as shown in the figure below. The risk of dying was 34% lower with trastuzumab emtansine treatment compared with trastuzumab.



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?

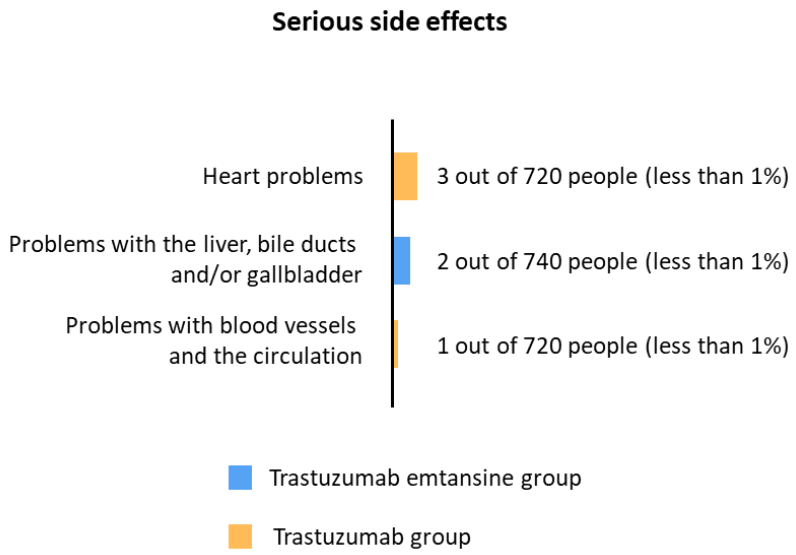
Side effects are medical problems that happen during the study.

- 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 mild to very serious and can be different from person to person.
- Side effects experienced by people during their treatment were reported in the previous summary (https://forpatients.roche.com/en/trials/cancer/bc/a-study-of-trastuzumab-emtansine-versus-trastuzumab-as-adjuvant-.html).
- In this summary, results of side effects collected after people had completed treatment (post-treatment period) are presented.

Serious side effects

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

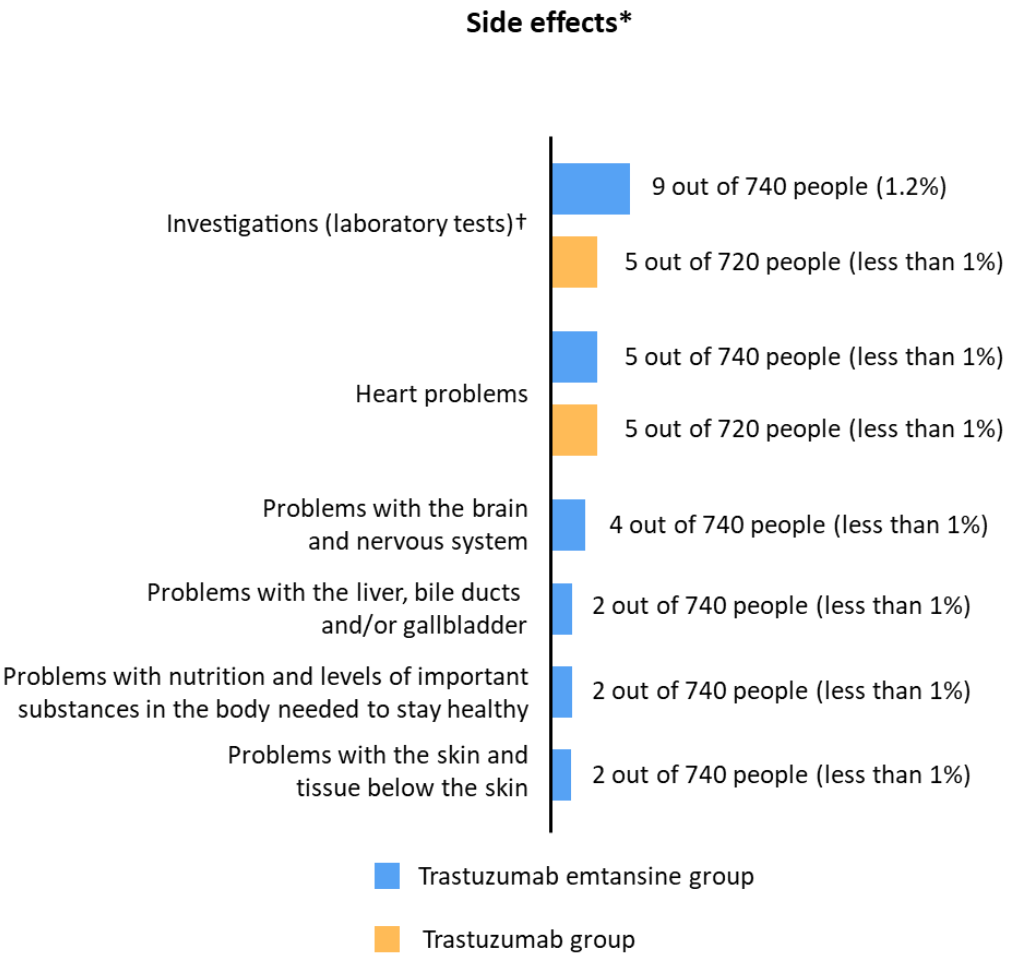
During the post-treatment period of the study reported in this summary, less than one in every 200 people (0.4%) had at least one serious side effect. In the trastuzumab emtansine group, less than one in every 200 people (0.3%) had a serious side effect, compared with around one in every 200 people (0.6%) in the trastuzumab group. Serious side effects are shown in the figure below.



Most common side effects

During the post-treatment period of the study, around two to three out of every 100 people (2.5%) had a side effect.

In the trastuzumab emtansine group, around three out of every 100 people (3.2%) had a side effect, compared with around two out of every 100 people (1.7%) in the trastuzumab group. The most common side effects are shown in the figure below.



* This graph shows side effects that were experienced by at least one person in each treatment group.
† 'Investigations' included a number of different tests that looked at heart, liver, bile duct, bone, blood and kidney functions or disorders.

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 results of this study show that for people with HER2-positive early breast cancer who had some remaining cancer cells in the breast or lymph nodes at the time of surgery, trastuzumab emtansine treatment helped more people to live longer without their cancer coming back, compared with trastuzumab (the standard medicine for these people at the time this study was designed). The number of people alive in the study after around 8.4 years of follow-up was high in both treatment groups, with more people alive in the trastuzumab emtansine group compared with the trastuzumab group.

Following the primary results (reported previously at https://forpatients.roche.com/en/trials/cancer/bc/a-study-of-trastuzumab-emtansine-versus-trastuzumab-as-adjuvant-.html; *click the dropdown arrow next to 'Show Clinical Trial Results' to find the PDF document*), trastuzumab emtansine was approved by drug regulatory authorities for the treatment of people with HER2-positive early breast cancer who have cancer cells remaining in the breast or lymph nodes at surgery, and is the current standard treatment for these people.

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.

7. Are there plans for other studies?

Studies with trastuzumab emtansine are still happening and may be listed on a number of public websites such as those listed at the end of this summary.

8. Where can I find more information?

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

- https://clinicaltrials.gov/study/NCT01772472
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2012-002018-37/results
- https://forpatients.roche.com/en/trials/cancer/bc/a-study-of-trastuzumab-emtansine-versus-trastuzumab-as-adjuvant-.html

If you would like to find out more about the results of this study, the full title of the relevant scientific papers are:

Primary analysis: "Trastuzumab Emtansine for Residual Invasive HER2-Positive Breast Cancer". The authors of the scientific paper are: G. von Minckwitz, C.-S. Huang, M.S. Mano, S. Loibl, E.P. Mamounas and others. The paper is published in the journal 'The New England Journal of Medicine', volume number 380, on pages 617–628.

Final analysis: "Survival with Trastuzumab Emtansine in Residual HER2-Positive Breast Cancer". The authors of the scientific paper are: C.E. Geyer Jr, M. Untch, C.-S. Huang, M.S. Mano, E.P. Mamounas and others. The paper is published in the journal 'The New England Journal of Medicine', volume number 392, on pages 249–257.

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-versus-trastuzumab-as-adjuvant-.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: "A Randomized, Multicenter, Open-Label Phase III Study to Evaluate the Efficacy and Safety of Trastuzumab Emtansine Versus Trastuzumab as Adjuvant Therapy for Patients With HER2-Positive Primary Breast Cancer Who Have Residual Tumor Present Pathologically in the Breast or Axillary Lymph Nodes Following Preoperative Therapy".

The study is known as 'KATHERINE'.

- The protocol number for this study is: BO27938.
- The ClinicalTrials.gov identifier for this study is: NCT01772472.
- The EudraCT number for this study is: 2012-002018-37.