

## Clinical Trial Results – Layperson Summary

### A study looking at heart-related side effects in people with early-stage HER2-positive breast cancer who were given pertuzumab, trastuzumab and chemotherapy

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 the results of the study up until March 2016.

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.

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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 HER2-positive early-stage breast cancer.

# 1. General information about this study

## Why was this study done?

People with the early stages of a type of breast cancer called 'HER2-positive breast cancer' are usually treated with a combination of surgery to remove the tumour and then treatment with cancer medicines to destroy any cancer cells that could not be removed during surgery.

This study was designed to look at how safe two different treatment options are when given to people with early-stage HER2-positive breast cancer who have unknown heart problems before they undergo surgery to treat their cancer. Researchers were especially interested in whether people developed any heart problems after starting to take the study medicines.

## What were the study medicines?

### HER2-targeted therapies

'Trastuzumab'

- You say this as 'trass-too-za-mab'.
- Trastuzumab works by attaching to the HER2 protein on the surface of HER2-positive cancer cells. When trastuzumab attaches to HER2, it stops the HER2 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.
- This may mean that trastuzumab helps make the tumour smaller before people have surgery.

'Pertuzumab'

- You say this as 'per-too-za-mab'.
- Pertuzumab works in the same way as trastuzumab but attaches to a different part of the HER2 protein.

### Anthracycline chemotherapies

'Doxorubicin' (generic medicine so brand names can vary)

- You say this as 'dock-so-roo-bi-sin'.

'Epirubicin' (generic medicine so brand names can vary)

- You say this as 'epp-ee-roo-bi-sin'.

These chemotherapy medicines work by going into cells and attaching to the cell DNA (deoxyribonucleic acid), which leads to cell death. This may mean that anthracycline chemotherapies help make the tumour smaller before people have surgery. This way, the tumour can be removed during surgery and there is a smaller risk of leaving any cancer behind.

### Other chemotherapies

'Docetaxel'

- You say this as 'doe-seh-tax-el'.

'Paclitaxel'

- You say this as 'pack-lih-tax-el'.

Docetaxel and paclitaxel are chemotherapy medicines that work by stopping cancer cells from growing.

‘Cyclophosphamide’

- You say this as ‘sai-klow-fos-fuh-mide’.

Cyclophosphamide works by slowing or stopping the growth of the cancer cells.

‘5-Fluorouracil’

- You say this as ‘five-floo-ruh-yoo r-uh-sil’

5-Fluorouracil works by stopping cancer cells from growing and multiplying.

## What did researchers want to find out?

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Researchers conducted this study to see how safe different treatment options were in people with early-stage HER2-positive breast cancer. This was done by checking how many people had heart problems and other side effects during the study (a side effect is an undesirable effect of a medicine or medical treatment).

**The main questions researchers wanted to answer were:**

1. During treatment before surgery, how many people treated with study medicines had severe heart failure?

Heart failure is when the heart no longer pumps blood around the body as well as it should. Severe heart failure was diagnosed based on specific criteria that looked at whether people were no longer able to perform physical activities as well as they did before, and whether they felt tired, even when resting.

2. During treatment before surgery, how many people had a decrease in the amount of blood being pumped out of the heart with each heartbeat?

When a person has problems with the left side of the heart where the heart is not able to pump as much blood out as it did previously, this is called ‘Left Ventricular Ejection Fraction (LVEF) decline’. This can be diagnosed by doctors using special types of scans to measure how much blood is pumped out of your heart every time it beats.

## What kind of study was this?

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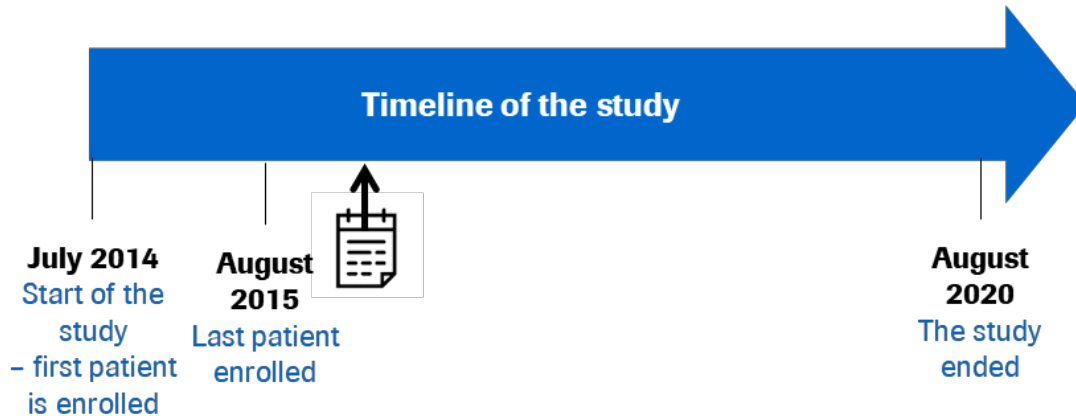
This study was a ‘Phase II’ study looking at safety. Although this was a Phase II study, some of the previous studies were Phase III, which means that all of the medicines had been tested beforehand in people with early-stage HER2-positive breast cancer.

In this study, people with early-stage HER2-positive breast cancer were given one of two treatment options before surgery, including chemotherapy and HER2-targeted medicines – this was to find out about the safety of the two different treatment options tested (see Section 3 for more details on the combinations of medicines given).

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

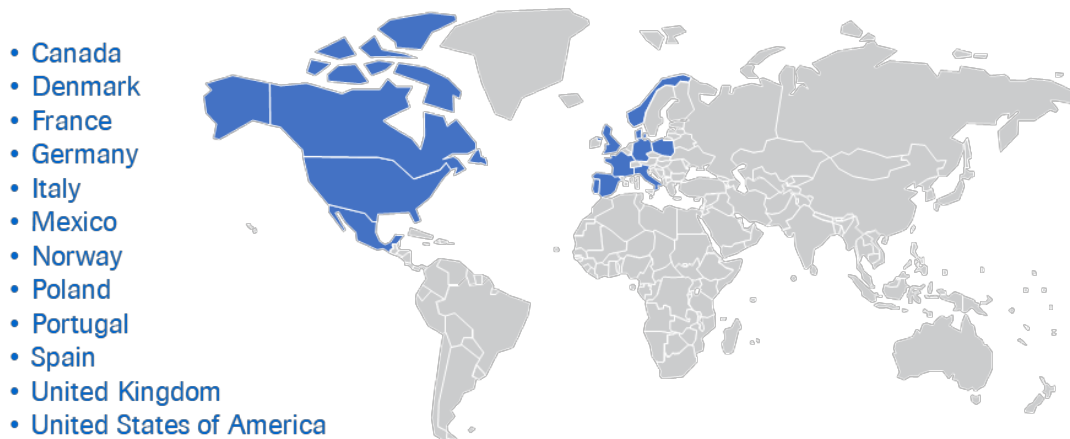
## When and where did the study take place?

The study started in July 2014 and ended in August 2020. This summary includes the results up until March 2016, the date when information was collected on how safe different treatment options were.



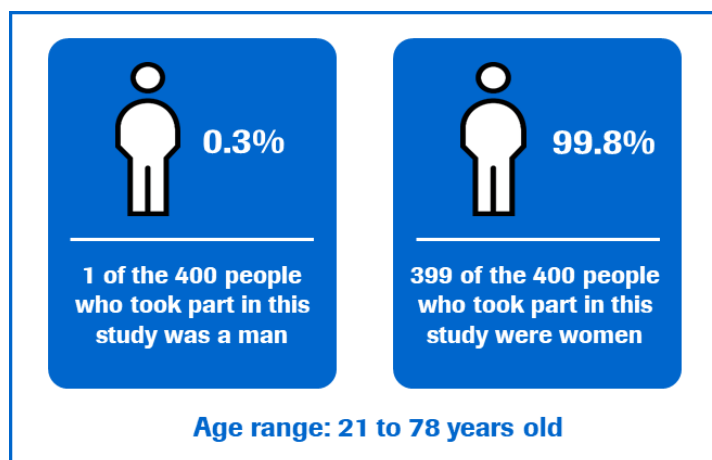
This study is still happening, so the symbol on the timeline (📅) shows when the information shown in this summary was collected (March 2016).

The study took place at 75 study centres – across 12 countries in Europe, Central and North America.



## 2. Who took part in this study?

In this study, 400 people with early-stage HER2-positive breast cancer took part.



### People who could take part in this study:

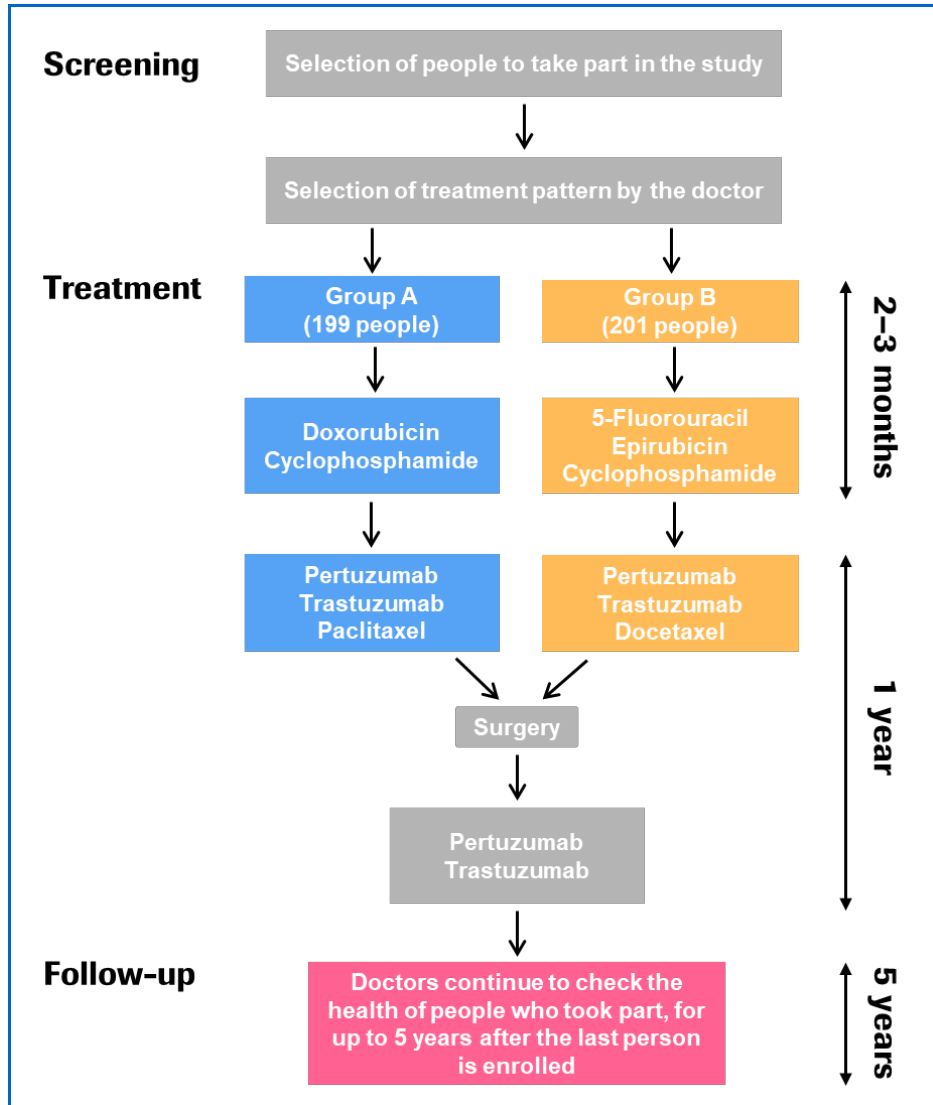
- People aged 18 years or older
- People diagnosed with early breast cancer that had not spread to other parts of the body
- People with HER2-positive breast cancer confirmed by a specific test
- People with normal heart function

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

- Breast cancer that had spread to other parts of the body
- A small section of the cancer removed (a 'biopsy')
- Another form of cancer within the previous 5 years
- History or evidence of a heart condition

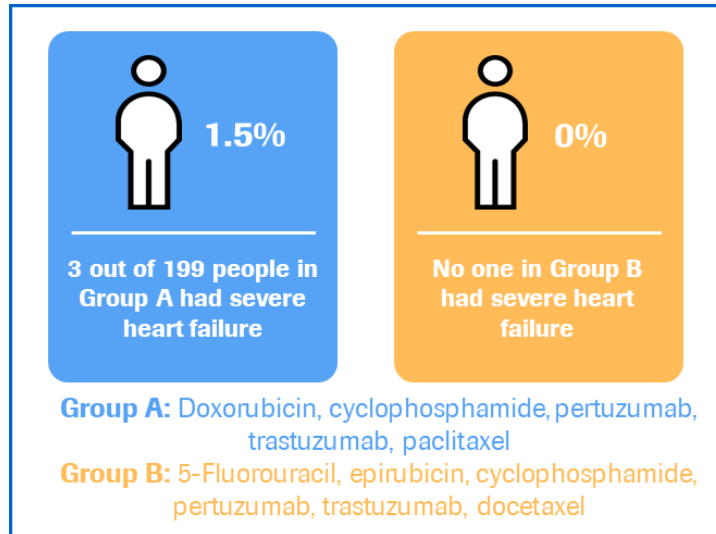
### 3. What happened during the study?

During the study, people were selected by the doctor treating them to join one of two study groups (Group A and Group B). Each study group followed a different treatment option as shown in the diagram below.

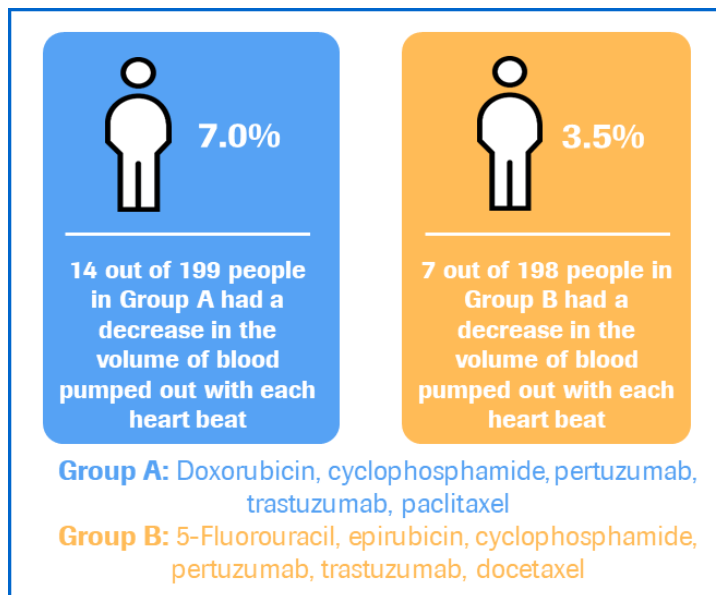


## 4. What were the results of the study at this point?

**Question 1:** During treatment before surgery, how many people treated with study medicines had severe heart failure?



**Question 2:** During treatment before surgery, how many people had a decrease in the amount of blood being pumped out of the heart with each heart beat?



This section only shows the key results 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 in the treatment period before surgery?

Side effects (also known as 'adverse reactions') are undesirable effects of a medicine or medical treatment (such as a headache) that happen during the study.

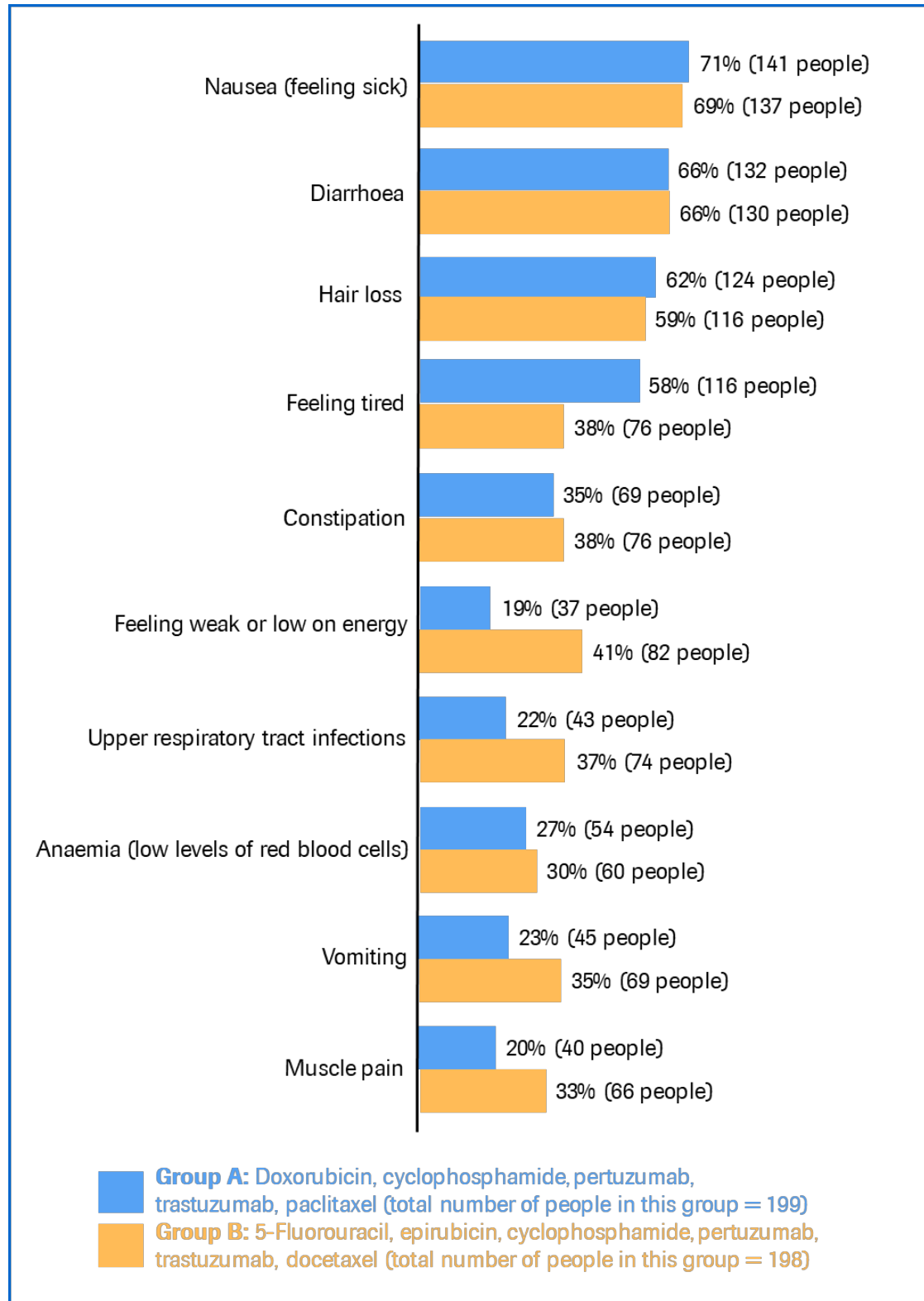
- Not all of the people in this study had all of the side effects.

Common and serious side effects are listed in the following sections.

### Most common side effects

During this study, almost all people had at least one side effect that was not considered serious (around 99% of people in Group A and 100% of people in Group B).

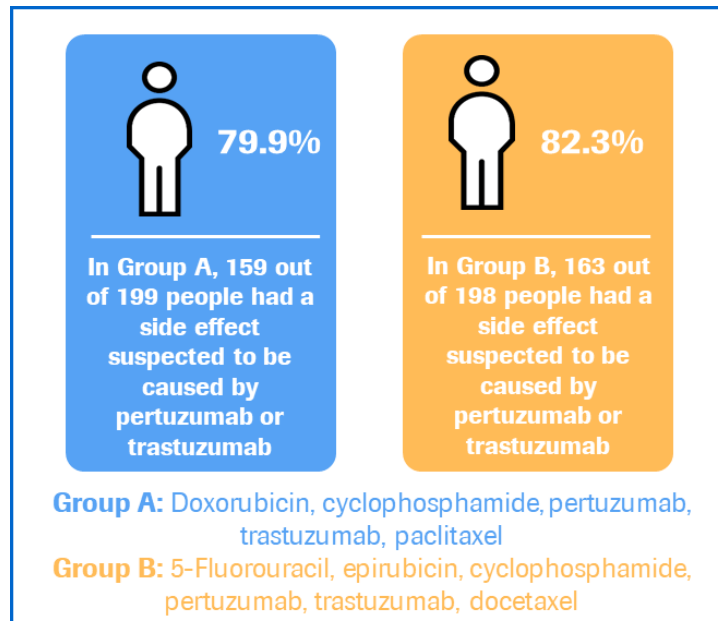
The ten most common side effects across both treatment groups are shown below.





## Side effects suspected to be caused by pertuzumab or trastuzumab

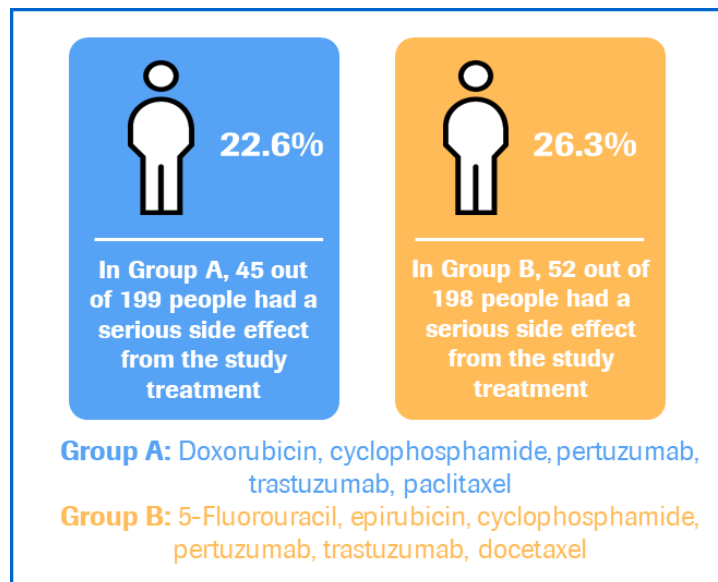
The proportion of people who had a least one side effect suspected to be caused by pertuzumab or trastuzumab is shown below.



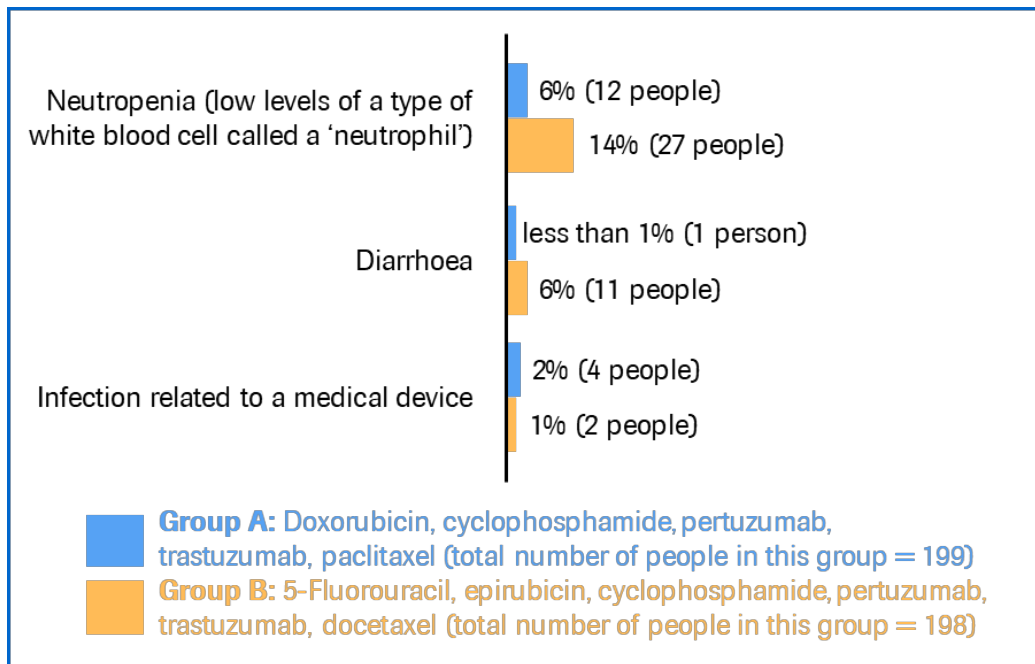
## Serious side effects

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

- Deaths are also considered a serious side effect, but no people died during the treatment period.

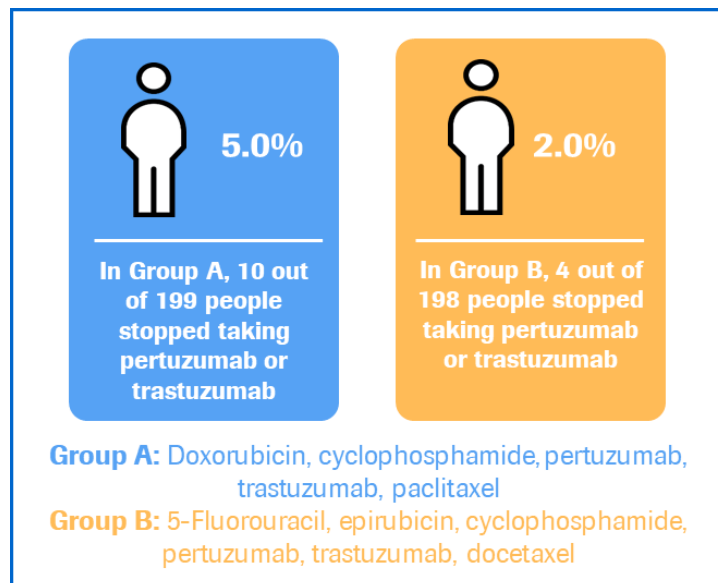


The three most common serious side effects are shown below.

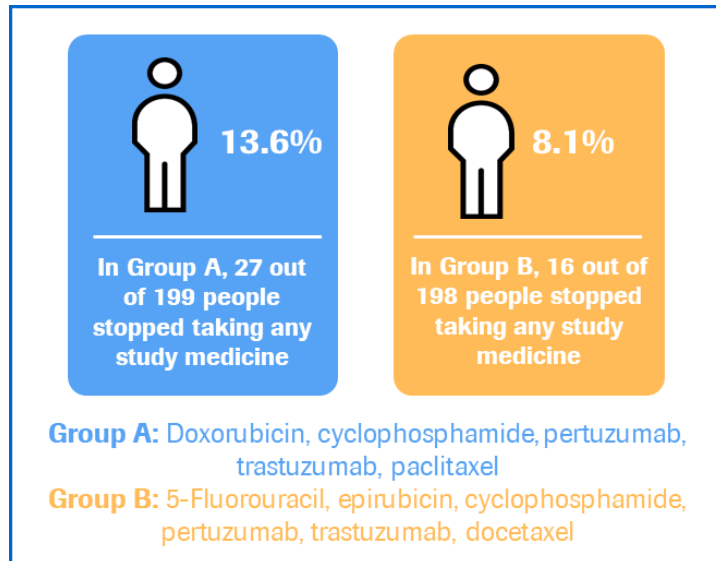


## People who stopped taking their medicine

During the study, the doctor could decide that someone should stop taking their medicine because of side effects – a person taking part in the study could also decide this.



The most common reason that people stopped taking pertuzumab or trastuzumab was due to the heart not being able to pump as much blood out as it did previously.



## 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 400 people with early-stage HER2-positive breast cancer. This study helped researchers learn more about how safe it is to combine specific chemotherapy drugs with pertuzumab and trastuzumab to improve treatment options and increase the chance of a cure for these people.

As both treatment options included pertuzumab, trastuzumab and an anthracycline, it is not possible to establish the impact that each individual medicine had on the heart problems or side effects reported in this study.

## 7. Are there plans for other studies?

At the time of writing this summary, no more studies are planned to look at pertuzumab and trastuzumab in treatment options that also include anthracycline chemotherapies. All medicines given to people in this study are already available for use in some countries.

This study is going on and study doctors are still collecting information.

## 8. Where can I find more information?

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

- <https://forpatients.roche.com/en/trials/cancer/bc/a-study-evaluating-pertuzumab--perjeta--combined-with-t-50414.html>
- <https://clinicaltrials.gov/ct2/show/results/NCT02132949>
- <https://www.clinicaltrialsregister.eu/ctr-search/trial/2014-000156-28/results>

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “Pertuzumab, trastuzumab, and standard anthracycline- and taxane-based chemotherapy for the neoadjuvant treatment of patients with HER2-positive localized breast cancer (BERENICE): a Phase II, open-label, multicenter, multinational cardiac safety study”. The authors of the scientific paper are: Sandra M. Swain, Michael S. Ewer, Giuseppe Viale, Suzette Delaloge, Jean-Marc Ferrero and others. The paper is published in the journal ‘Annals of Oncology’ in 2018, volume number 29, on pages 646–653.

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

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If you have any further questions after reading this summary:

- <https://forpatients.roche.com/en/trials/cancer/bc/a-study-evaluating-pertuzumab--perjeta--combined-with-t-50414.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?**

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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**

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The full title of this study is: “A Multicenter, Multinational, Phase II Study to Evaluate Perjeta in Combination With Herceptin and Standard Neoadjuvant Anthracycline-Based Chemotherapy in Patients With HER2-Positive, Locally Advanced, Inflammatory, or Early-Stage Breast Cancer”.

The study is known as ‘BERENICE’.

- The protocol number for this study is: WO29217.
- The ClinicalTrials.gov identifier for this study is: NCT02132949.
- The EudraCT number for this study is: 2014-000156-28.