A study, named PERUSE, to look at how safe and effective pertuzumab, trastuzumab and taxane chemotherapy is in people with HER2-positive metastatic 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:

- people who took part in the study, and
- members of the public.

This summary is based on information known at the time of writing.

The PERUSE study started in May 2012 and ended in September 2019, with the last results collected in January 2020. This summary was written after the study had ended and includes results up until January 2020.

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 what 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 in the PERUSE study have helped researchers to find out and understand more about HER2-positive metastatic breast cancer and the medicines studied.

1. General information about this study

What is HER2-positive breast cancer?

- Receptors are a type of protein found on cells. Some breast cancer cells have higher-than-normal levels of a receptor called 'HER2' (human epidermal growth factor receptor 2) on their surface, which causes them to grow.
- This type of breast cancer is called HER2-positive breast cancer.
- The cancer is known as 'metastatic' when it has spread to other parts of the body.

How can HER2-positive breast cancer be treated?

- Anti-cancer medicines that block the HER2 receptor are known as 'HER2-targeted therapies' and include medicines such as 'pertuzumab' and 'trastuzumab'.
- HER2-targeted therapies are often given in combination with chemotherapy, to help stop the cancer from growing as much as possible.
- The combination of pertuzumab, trastuzumab and 'docetaxel' (a chemotherapy medicine belonging to a group called 'taxanes') was previously investigated in a study called 'CLEOPATRA'.
- Results from the CLEOPATRA study showed that pertuzumab, trastuzumab and docetaxel helped people with HER2-positive metastatic breast cancer to live longer without their cancer getting worse, compared with placebo (a substance that looked the same as pertuzumab but did not contain any real medicine), trastuzumab and docetaxel.
- Based on these results, the combination of pertuzumab, trastuzumab and docetaxel was approved in Europe and the United States for use as the first treatment given to people with HER2-positive metastatic breast cancer.
- 'Paclitaxel' and 'nab-paclitaxel' are also taxane chemotherapy medicines. Some studies have shown that people given paclitaxel and nab-paclitaxel may have fewer, or milder, side effects compared with docetaxel, while finding they have similar effectiveness against their cancer cells.

Why was this study done?

- In the PERUSE study, researchers wanted to know how safe and effective the three different taxanes (docetaxel, paclitaxel and nab-paclitaxel) were, in combination with pertuzumab and trastuzumab in people with HER2-positive metastatic breast cancer.

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 messages 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.

'Pertuzumab'

- You say this as 'per-too-za-mab'.

Pertuzumab is the medicine being studied in PERUSE. It works together with trastuzumab but attaches to a different part of the HER2 protein.

In the PERUSE study, pertuzumab was given in combination with trastuzumab and one of the following taxane chemotherapy medicines: docetaxel, paclitaxel or nab-paclitaxel.

What did researchers want to find out?

- Researchers looked at how safe and effective the pertuzumab, trastuzumab and taxane treatment combinations were (see section 4, “What were the results of this study?” and section 5, “What other side effects were seen?”).

The main question that researchers wanted to answer was:

1. How many side effects did people get, and how well did they cope with the study medicines?

Other questions that researchers wanted to answer included:

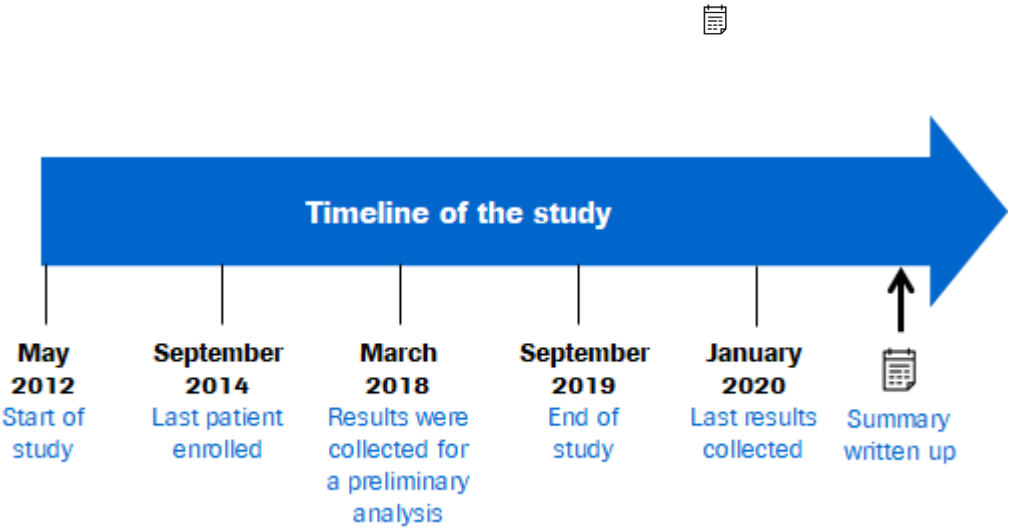
2. How much time was there between the start of treatment and people’s cancer getting worse?
3. How long did people live in this study?
4. Did the study medicines affect people’s wellbeing?

What kind of study was this?

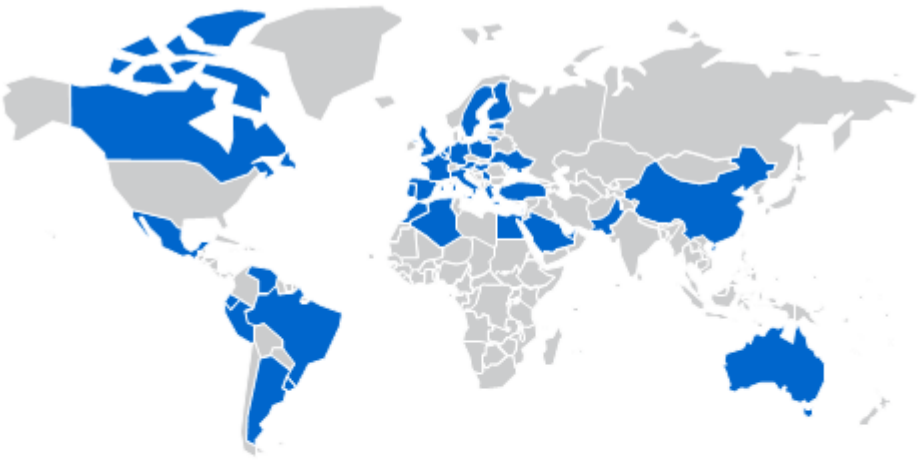
This was a ‘Phase 3’ study. This means that the combination of pertuzumab, trastuzumab and a taxane (docetaxel) has already been tested in people with HER2-positive metastatic breast cancer before this study. In this study, a larger number of people with this cancer took the combination of pertuzumab, trastuzumab and a taxane (docetaxel, paclitaxel or nab-paclitaxel). This was to find out how safe and effective these treatment combinations were. This could then help doctors decide whether paclitaxel, nab-paclitaxel or docetaxel could be combined with pertuzumab and trastuzumab for people with HER2-positive metastatic breast cancer.

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 took place at 229 study centres across 39 countries worldwide. The following map shows the countries where this study took place.



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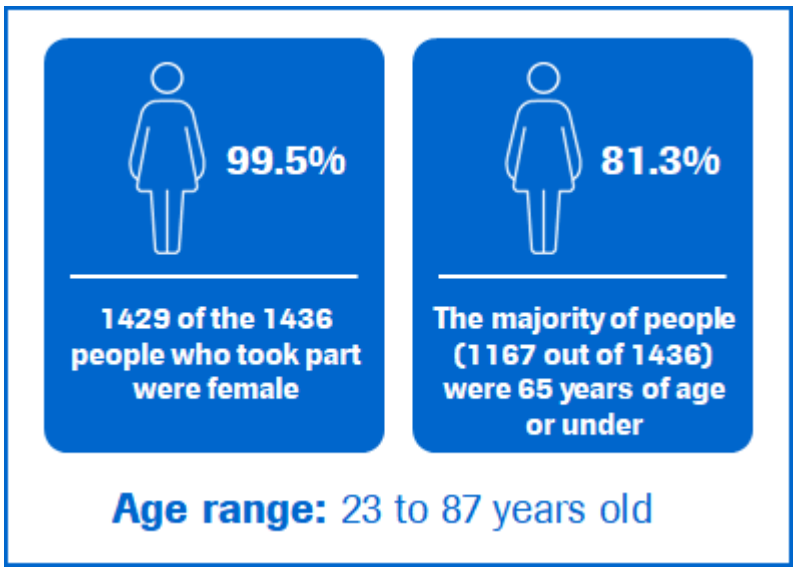
- Portugal
- Saudi Arabia
- Serbia
- Slovenia
- Spain
- Sweden
- Turkey
- Ukraine
- United Arab Emirates
- United Kingdom
- Uruguay
- Venezuela

2. Who took part in this study?

In this study, 1436 people (1429 women) with HER2-positive metastatic breast cancer took part. More information on the people who took part is given below.



People could take part in this study if they had:

- HER2-positive breast cancer, confirmed by a specific test
- Breast cancer that could not be removed by surgery or had spread to other parts of the body
- Normal pumping of blood by their heart
- A life expectancy of at least 12 weeks

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

- Previously been treated with anti-cancer medicines for metastatic breast cancer (up to two 'hormonal therapy'* medicines were allowed)
- Previously been treated with any HER2-targeted therapies (except with 'trastuzumab' and/or 'lapatinib' for early breast cancer)
- Uncontrolled cancer that had spread to the brain or spinal cord

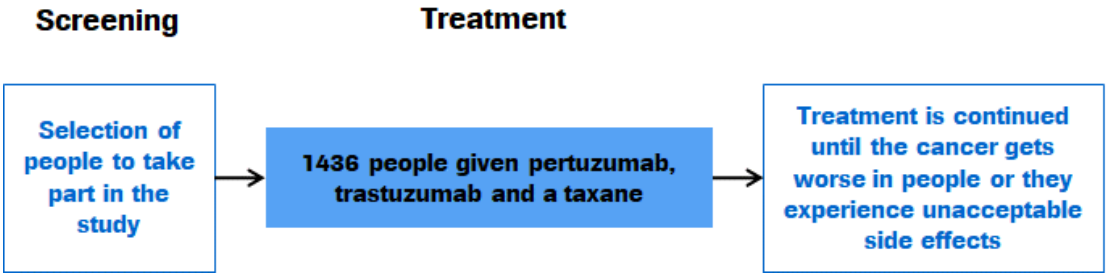
* Hormonal therapies are medicines that target 'hormone receptors' on cancer cells (hormone receptors are proteins that bind to hormones in the body that can make cancer cells grow).

3. What happened during this study?

All the people in the study were given pertuzumab and trastuzumab, which were infused into a vein (intravenous) every 3 weeks for 1 year.

People in the study were also given a taxane – these were given according to standard clinical guidelines or the local prescribing information for each medicine. The choice of taxane (docetaxel, paclitaxel or nab-paclitaxel) was decided by the study doctors.

Look below to see more information about what happened in the study.



4. What were the results of this study?

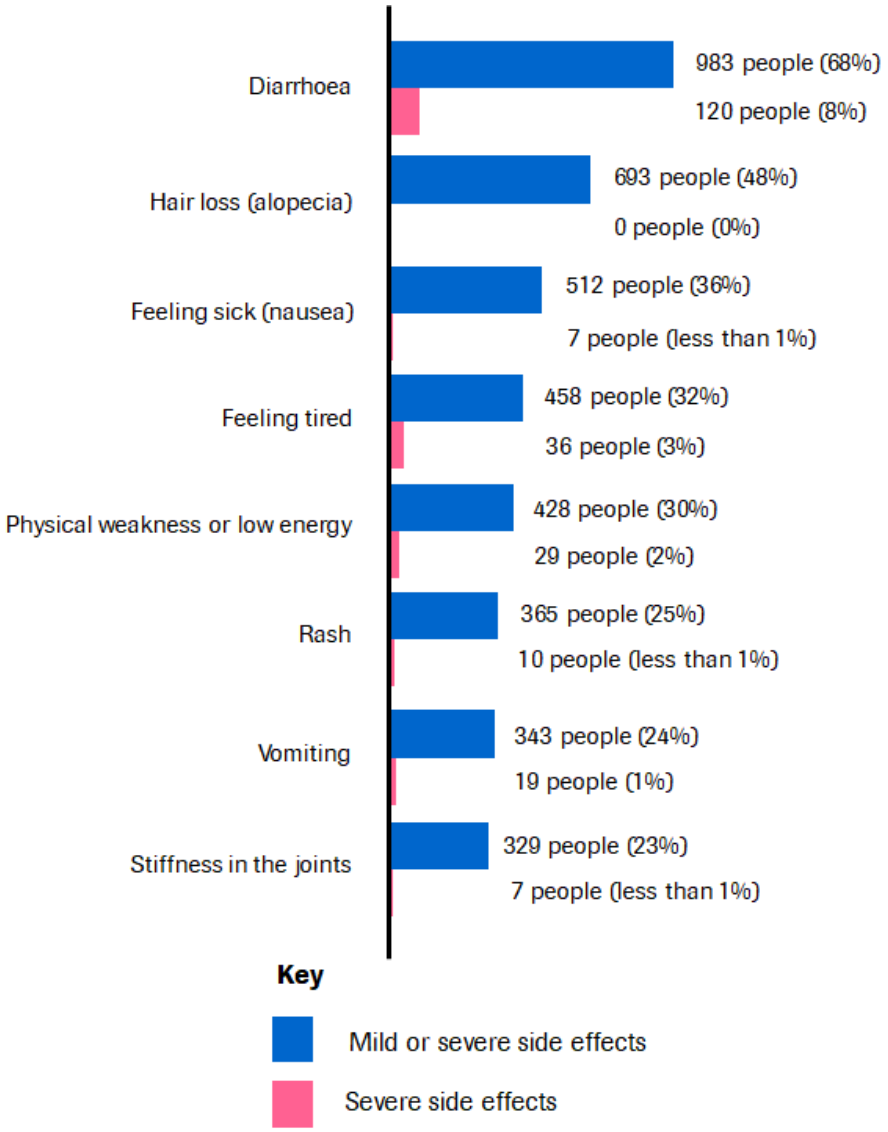
Question 1: How many side effects did people get, and how well did they cope with the study medicines?

Side effects (also known as 'adverse reactions') are unwanted medical problems (such as feeling dizzy) that happen during the study. Not all of the people in this study had all of the side effects.

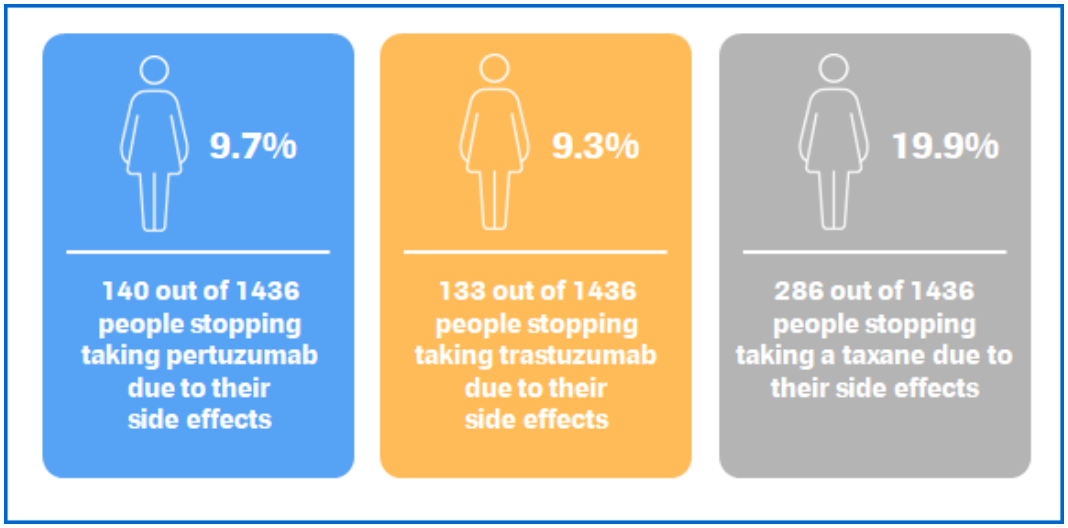
Researchers looked at how many side effects people had when given pertuzumab, trastuzumab and a taxane. They also wanted to know how well people coped with the study medicines, by looking at how many people had to stop taking a study medicine because of their side effects.

Overall, almost everyone (99%) in the study had at least one side effect. The most common side effects were diarrhoea, hair loss and feeling sick, as shown below.

Eight most common side effects in people taking part in the study

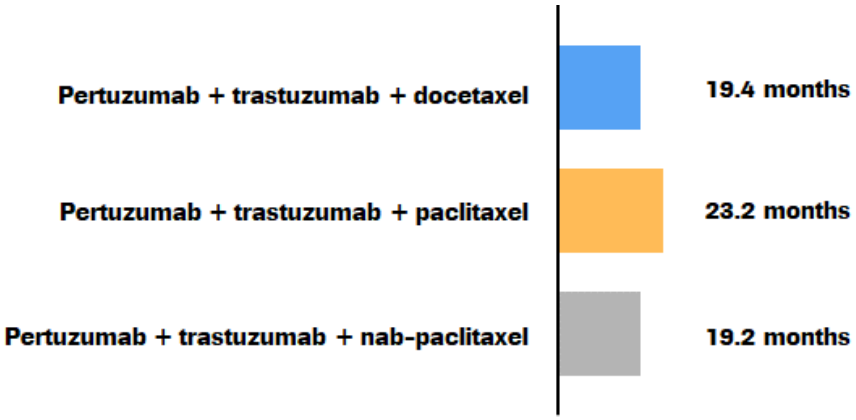


During the study, some people stopped taking their study medicine permanently because of their side effects, as shown below.



Question 2: How much time was there between the start of treatment and people's cancer getting worse?

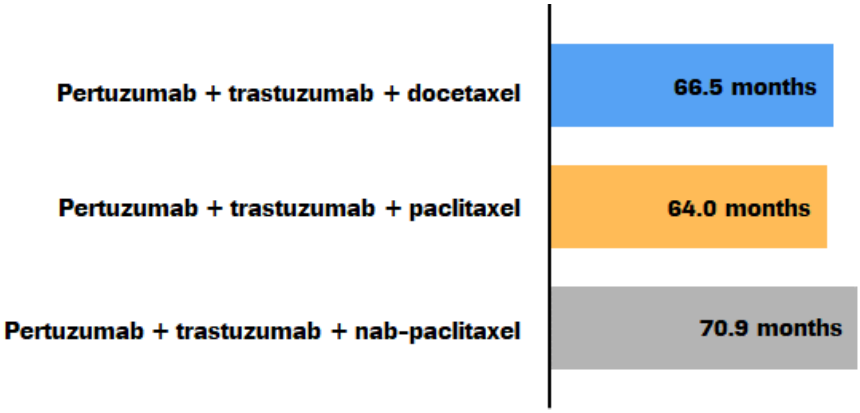
Researchers looked at the time between the start of treatment and when the cancer worsened. The median or middle time (when all values were ordered by rank) for all the people in the study was 20.7 months. The type of taxane that people were given did not seem to affect this median or middle time, as shown below.



Question 3: How long did people live in this study?

Breast cancer is not curable when it has spread to other parts of the body (metastatic disease). People with HER2-positive metastatic breast cancer are given treatments to help them live as long as possible. Researchers therefore wanted to know how long people lived in this study when given the combination of pertuzumab, trastuzumab and a taxane. Overall, by September 2019, 658 people (46%) in the study had died. The median or middle time (when all values were ordered by rank) for how long people lived in the study was around 65 months (almost 5 and a half years).

The type of taxane people were given did not appear to affect this median or middle time, as shown below.



Following the end of this study in September 2019, people who were still alive could continue their anti-cancer treatment in other ways (for example, through hospitals, oncology clinics, or taking part in other studies).

679 people (47%) who took part in PERUSE were continuing their anti-cancer treatment after the study. The most common HER2-targeted therapies that people were given were trastuzumab (25%), 'trastuzumab emtansine' (19%), lapatinib (16%) and pertuzumab (7%).

Question 4: Did the study medicines affect people's wellbeing?

Researchers wanted to know how people's wellbeing was affected during the study. People who took part in the study were asked to fill in questionnaires about their physical, social, emotional and functional (ability to continue with everyday life) wellbeing, as well as their breast cancer-specific wellbeing. The questionnaires were filled in by people before they started their study treatment, and then at regular time points throughout the study.

Researchers compared the 'baseline' scores (before people had received their first study medicine) with the scores throughout the study. Overall, people did not feel that their wellbeing was affected during the study.

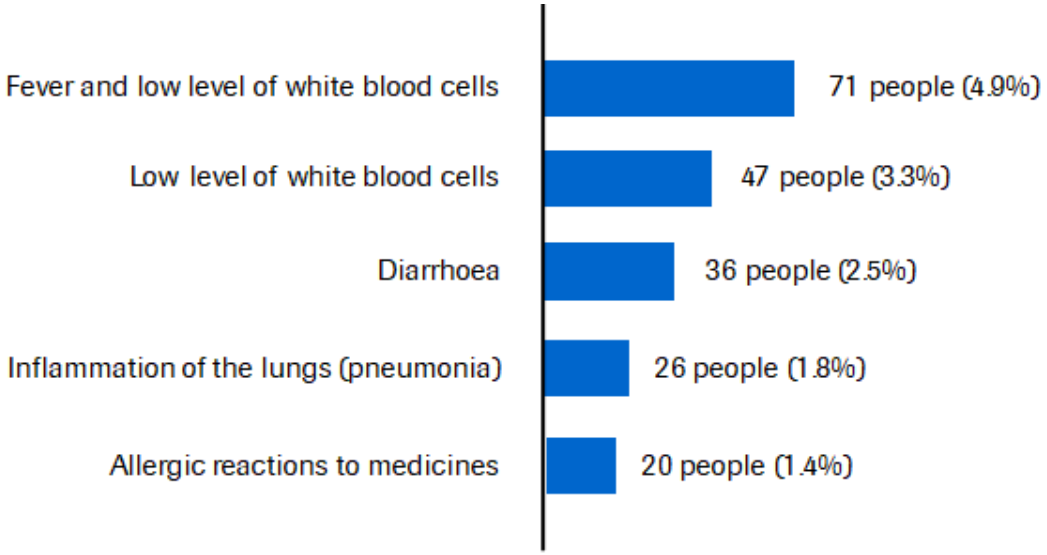
This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see section 8, "Where can I find more information?").

5. What other side effects were seen?

Serious side effects

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

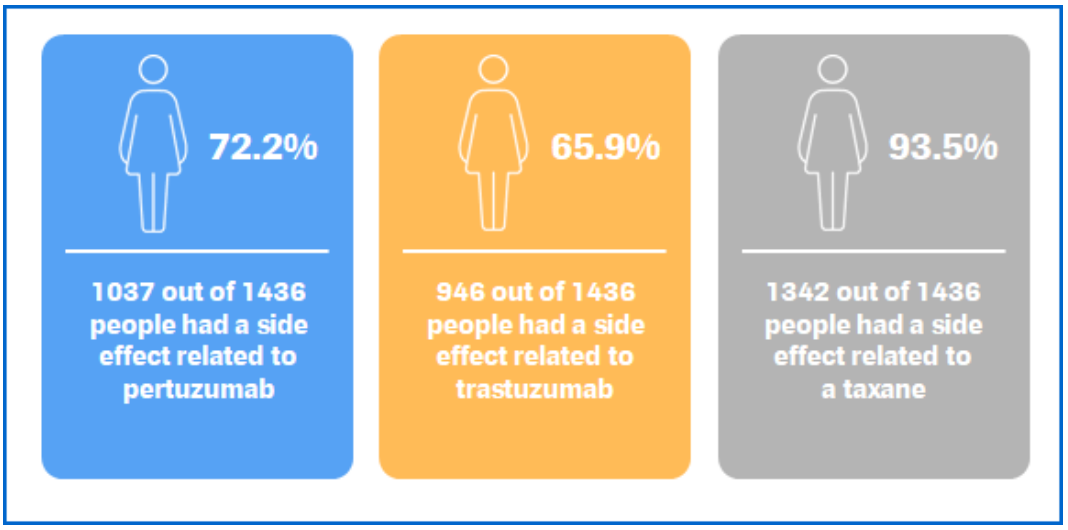
During this study, around 37% of people had at least one serious side effect. The five most common serious side effects in all the people who took part in the study are shown below.



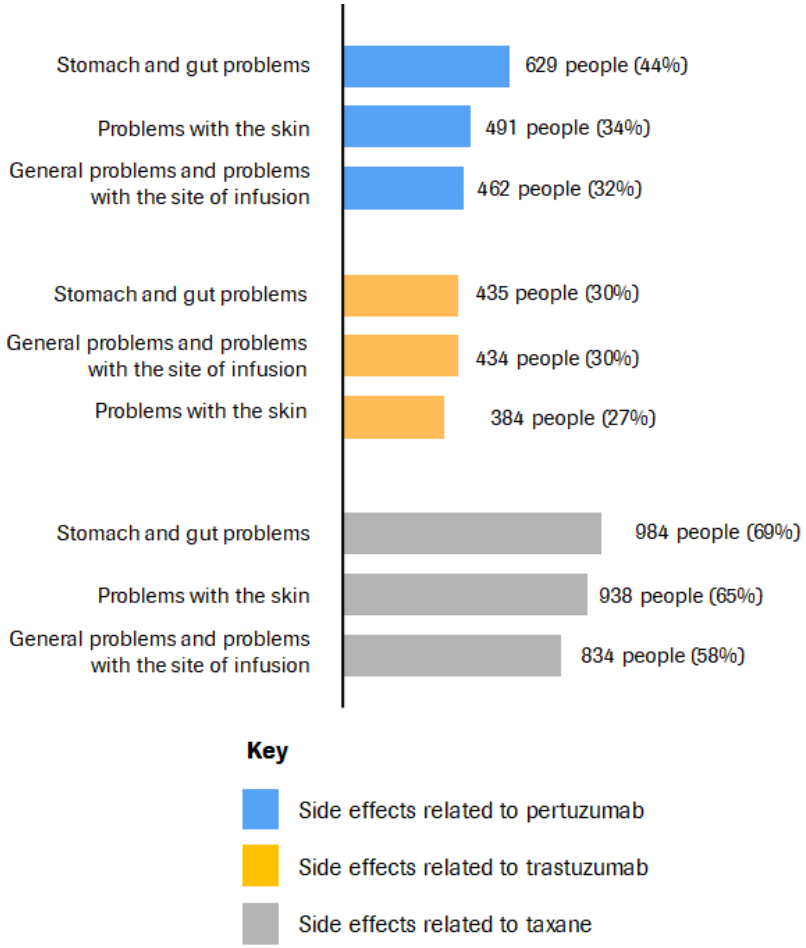
There were some people in the study who died due to side effects that may have been related to one of the study medicines. During the study, 35 people (2.4%) died due to their side effects. Of these side effects, ten were considered to be related to one of the study medicines by the study doctors. The most common side effects leading to death were pneumonia, 'sepsis' (a serious reaction to an infection, also called 'blood poisoning') and heart problems. These happened in less than 1% of people in the study.

Most common side effects related to a study medicine

Around 72% of people had a side effect related to pertuzumab, compared with around 66% for trastuzumab and 94% for a taxane, as shown below.



The most common types of side effects related to each study medicine are shown below.



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, "Where can I find more information?").

6. How has this study helped research?

The information presented here is from a single study of 1436 people with HER2-positive metastatic breast cancer. The results from the PERUSE study are similar to those seen for pertuzumab, trastuzumab and docetaxel in the earlier CLEOPATRA study, which showed that this treatment combination helped people with HER2-positive metastatic breast cancer to live longer, without their cancer getting worse. The PERUSE study therefore further supports the use of this combination as the first treatment for people with HER2-positive metastatic breast cancer.

The results from the PERUSE study also showed that using other taxanes such as paclitaxel or nab-paclitaxel, instead of docetaxel, was just as safe and effective. This may provide alternative, and potentially more tolerable, chemotherapy options for people given pertuzumab and trastuzumab for HER2-positive metastatic breast cancer.

7. Are there plans for other studies?

Studies with pertuzumab are still happening, and further studies are planned.

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-of-pertuzumab-in-combination-with-trastuzumab---50542.html
- https://clinicaltrials.gov/ct2/show/results/NCT01572038
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2011-005334-20/results

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: "Final results from the PERUSE study of first-line pertuzumab plus trastuzumab plus a taxane for HER2-positive locally recurrent or metastatic breast cancer, with a multivariable approach to guide prognostication". The authors of the scientific paper are: David Miles, Eva Ciruelos, Andreas Schneeweiss, Fabio Puglisi, Tamar Peretz-Yablonski and others. The paper is published in the journal 'Annals of Oncology', volume number 32, on pages 1245–1255.

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-pertuzumab-in-combination-with-trastuzumab---50542.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 Multicenter, Open-Label, Single-Arm Study of Pertuzumab in Combination With Trastuzumab and a Taxane in First Line Treatment of Patients With HER2-Positive Advanced (Metastatic or Locally Recurrent) Breast Cancer".

The study is known as 'PERUSE'.

- The protocol number for this study is: MO28047.
- The ClinicalTrials.gov identifier for this study is: NCT01572038.
- The EudraCT number for this study is: 2011-005334-20.