Summary of Clinical Trial Results

A study that measures preferences for a single injection of pertuzumab and trastuzumab under the skin or two separate infusions into a vein to treat early-stage 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 that started in December 2018 (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. It presents the results from the study up until February 2020.

At the time of writing this summary, results from the study are still being collected.

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 those of 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 have taken part and who continue to take part in this study

The people who have taken part in the study and those who continue to take part in the study are helping researchers to answer important questions about HER2-positive breast cancer and the medicines studied – 'pertuzumab' and 'trastuzumab'.

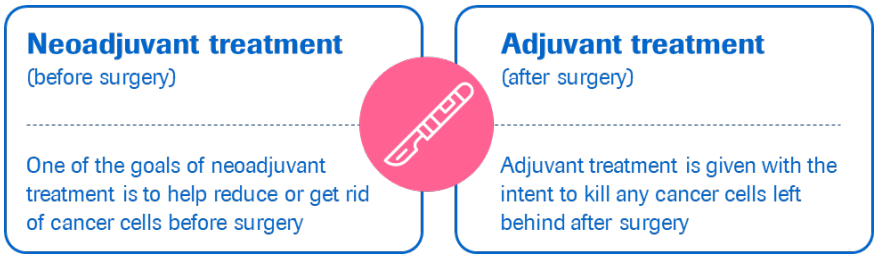
These medicines are usually given as two separate infusions into a vein. However, a new formulation means that these medicines can now be given together in one syringe by a single injection under the skin.

This new formulation is already approved and available for use in the USA and Europe. It is also being considered for approval in other countries/regions.

1. General information about this study

Why was this study done?

Some breast cancer cells have higher-than-normal levels of a receptor (a type of protein found on some cancer cells) called HER2 on their surface, which stimulates them to grow. This type of breast cancer is called 'HER2-positive breast cancer'. People in the early stages of HER2-positive breast cancer often receive several types of treatment:



People with HER2-positive breast cancer receive HER2-targeted therapies before and after surgery because these therapies give them the best chance of a cure.

HER2-targeted therapies (treatments that affect cancer cells with high levels of HER2 receptor) can be given by drip into a vein (we call this 'giving by intravenous infusion') or by an injection under the skin (we call this 'giving by subcutaneous injection').

This study was designed to find out the proportion of people with early-stage HER2-positive breast cancer who preferred having their HER2-targeted therapies (pertuzumab and trastuzumab) by a single injection under the skin rather than by two separate infusions into a vein.

When pertuzumab and trastuzumab are given intravenously, they are given one after the other. This takes 30 to 60 minutes for pertuzumab and 30 to 90 minutes for trastuzumab. After each infusion, a person typically stays in the clinic and a nurse checks on the person from time to time to see if she/he is having side effects. This 'observation period' varies according to guidelines in each country. In this study, the observation periods were 30 to 60 minutes for pertuzumab and 30 to 60 minutes for trastuzumab.

When pertuzumab and trastuzumab are given by subcutaneous injection, they are given together as a single injection in one syringe by a nurse, doctor or pharmacy technician. This single injection takes from 5 to 8 minutes. The 'observation period' lasts for 30 minutes after the injection at the first visit and 15 minutes after the injection at each additional visit.

What are 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 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 to destroy any cancer cells that could not be removed during surgery.

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

How are the HER2-targeted study medicines being given to people in the study?

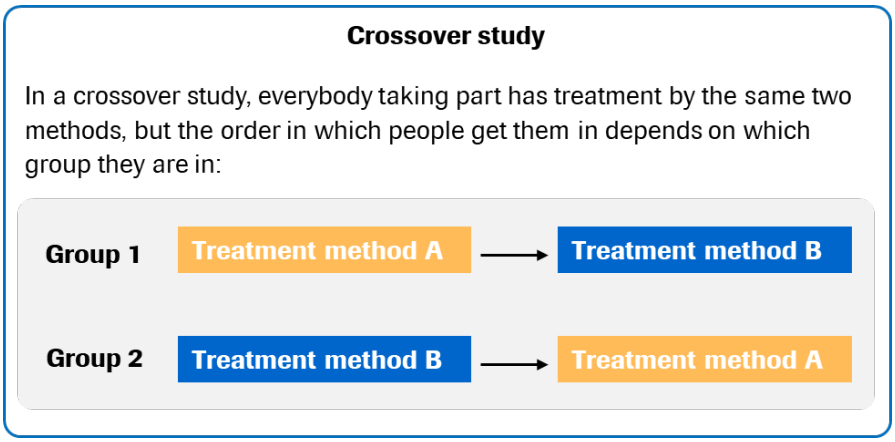
Subcutaneous injection
- Pertuzumab and trastuzumab are combined in one syringe and injected under the skin as a single injection. It takes from 5 to 8 minutes to administer the medicines like this.

Intravenous infusion
- Pertuzumab and trastuzumab are put in separate infusion bags containing fluid and slowly infused by drip into a vein with a pump. It takes up to two-and-a-half hours to administer the medicines one after the other.

What did researchers want to find out?

1. How did the people in the study prefer to have their treatment?

Researchers did this study to see if people with HER2-positive early-stage breast cancer preferred having their pertuzumab and trastuzumab treatment together as a single injection under the skin. This was done by performing a 'crossover study'.



After having treatment by both methods, people were asked to fill in a questionnaire about which method they preferred and why they preferred it.

The different treatment methods used in this study are shown below:
- Method A: Having the pertuzumab and trastuzumab as two separate infusions into a vein;
- Method B: Having the pertuzumab and trastuzumab together in one syringe by a single injection under the skin.

A separate questionnaire was used to ask how satisfied people were with each treatment method. This included asking people if they had enough time to speak to their doctor or nurse during their treatment.

2. What benefits did the single injection under the skin have according to the doctors, nurses and pharmacists?
The doctors, nurses and pharmacists involved in the study were given a different questionnaire. They were asked to estimate how much time people could save by having their treatment as one single injection under the skin, among other things.

3. What side effects were seen in the study?
The researchers also wanted to know if there were any differences in side effects after injecting pertuzumab and trastuzumab together under the skin as a single injection or infusing them into a vein separately. Side effects were recorded by the investigators using a standard system.

What kind of study is this?

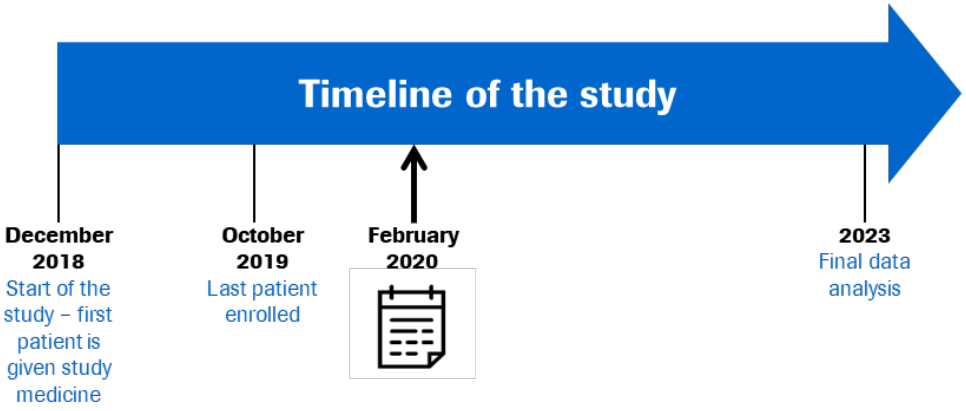
In this study, people with early-stage HER2-positive breast cancer are given pertuzumab and trastuzumab by both an injection under the skin as a single injection and by separate infusions into a vein. This was to find out which administration method people preferred and how satisfied they were with each method.

This is an 'open-label' study. This means that both the people taking part in the study and the study doctors know how the HER2-targeted therapy is being administered.

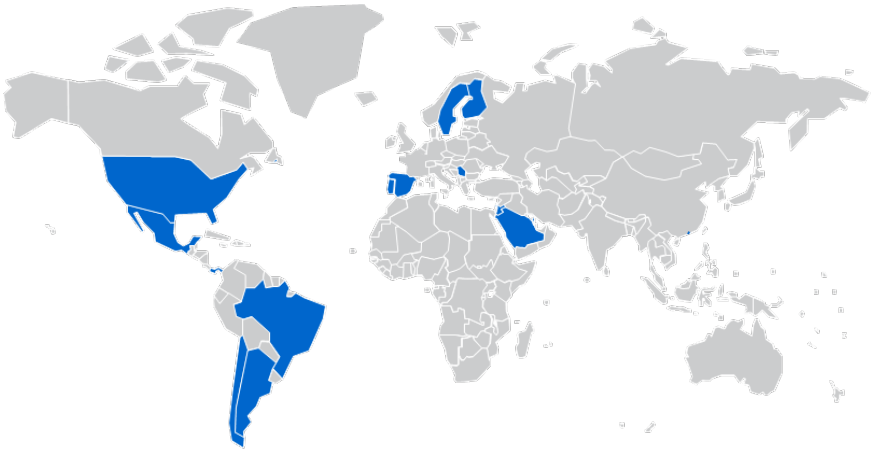
The study is 'randomised'. This means that it was decided by chance which order the medicines are given to people in the study. Randomly choosing which way to give the medicines makes it more likely that the types of people in both groups (for example, age) will be similar. Apart from the way the medicines were given in each group, all aspects of care are the same in both groups.

When and where is the study taking place?

The study started in December 2018 and the final results will be analysed in 2023. This summary includes the results up until February 2020; this is when all the information had been analysed on which of the two ways of giving the study medicines people preferred. This study is still happening, so the symbol on the timeline (📋) shows when the information shown in this summary was analysed – after 14 months (February 2020).



The study is taking place at 39 study sites – across 16 countries and territories in Asia, Europe, and North and South America.



39 study sites

- Argentina
- Brazil
- Chile
- Finland
- Hong Kong
- Jordan
- Lebanon
- Mexico
- Panama
- Portugal
- Qatar
- Saudi Arabia
- Serbia
- Spain
- Sweden
- United States of America

2. Who is taking part in this study?

In this study, 160 women with early-stage HER2-positive breast cancer are taking part.

The people who are taking part in the study were aged between 22 and 80 years when it started.

People could take part in the study if they:

- Had early breast cancer that had not spread to other parts of the body
- Had HER2-positive breast cancer confirmed by a specific test
- Had already been treated with chemotherapy, pertuzumab and trastuzumab followed by surgery to remove their breast cancer

People could not take part in the study if they:

- Had a serious heart condition
- Were pregnant

3. What is happening during the study?

This study is split into two parts: the 'crossover' part and the 'continuation' part.

In the crossover part of the study, people had treatment by one method for a short time and then had treatment by the other method for a short time. The sequence of treatment methods that people got was selected at random – by a computer.

The treatment groups for the crossover part of the study were:

- **Group 1 (80 people):**
    - **First treatment method: Pertuzumab and trastuzumab as two separate infusions into a vein** (intravenous) once every 3 weeks;
    - **Second treatment method: Pertuzumab and trastuzumab injected under the skin as a single injection** (subcutaneous) once every 3 weeks.

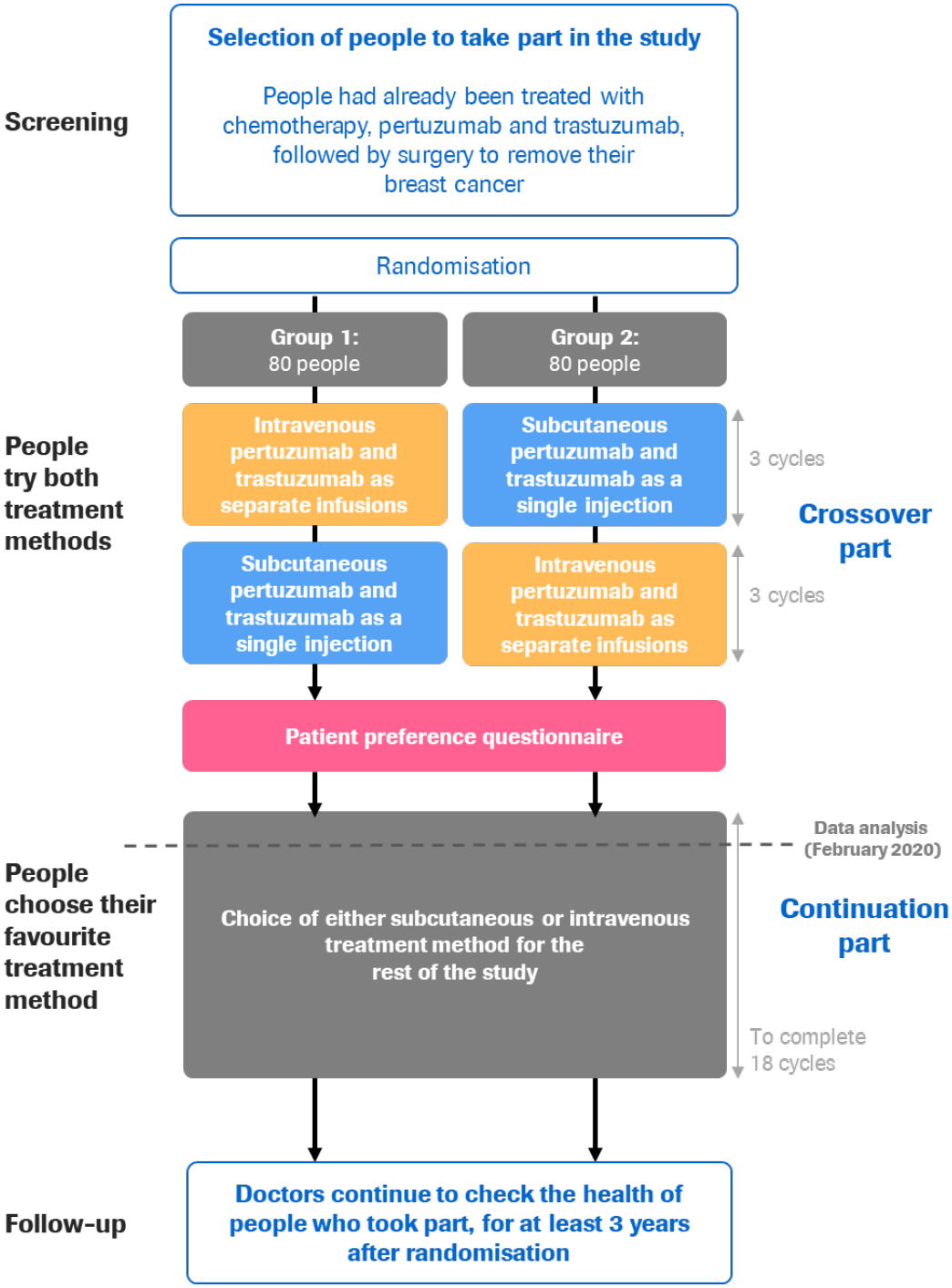
- **Group 2 (80 people):**
    - **First treatment method: Pertuzumab and trastuzumab injected under the skin as a single injection** (subcutaneous) once every 3 weeks;
    - **Second treatment method: Pertuzumab and trastuzumab as two separate infusions into a vein** (intravenous) once every 3 weeks.

After people had received three lots of treatment by each method, they were asked to choose which method they wanted to use for the continuation part of the study.

People received a total of 18 lots of pertuzumab and trastuzumab treatment before and after surgery.

When the data from this study were analysed (February 2020), some people were still being treated with the study medicines. The people taking part in the study are still going back to their study centre regularly. When the treatment finishes, the people will continue to go back for more visits – to check their overall health.

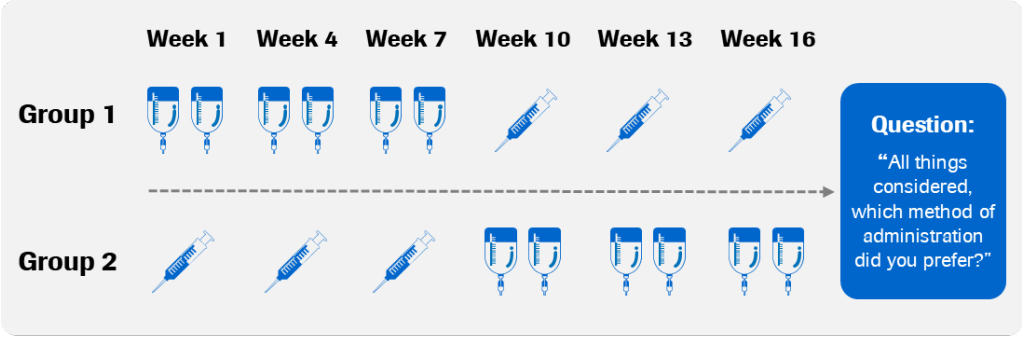
Look below to see more information about what has happened in the study so far – and what the next steps are. The dashed line shows when the information presented in this document was analysed.


Screening
Selection of people to take part in the study
People had already been treated with chemotherapy, pertuzumab and trastuzumab, followed by surgery to remove their breast cancer
Randomisation
Group 1: 80 people
Group 2: 80 people
People try both treatment methods
Intravenous pertuzumab and trastuzumab as separate infusions
Subcutaneous pertuzumab and trastuzumab as a single injection
3 cycles
Crossover part
Subcutaneous pertuzumab and trastuzumab as a single injection
Intravenous pertuzumab and trastuzumab as separate infusions
3 cycles
Patient preference questionnaire
Data analysis (February 2020)
People choose their favourite treatment method
Choice of either subcutaneous or intravenous treatment method for the rest of the study
Continuation part
To complete 18 cycles
Follow-up
Doctors continue to check the health of people who took part, for at least 3 years after randomisation

4. What are the results of the study so far?

Do people prefer being treated with pertuzumab and trastuzumab together in the same syringe by a single injection under the skin?

Once people had tried both treatment methods, researchers asked them which method they preferred and why they preferred it.

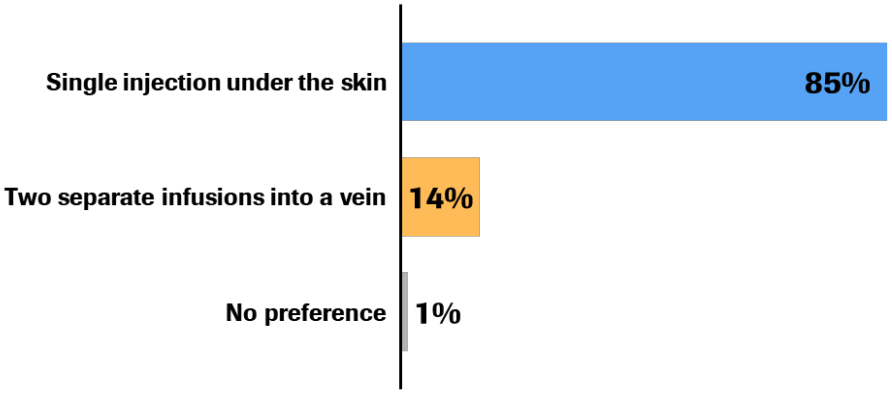


Two separate infusions of pertuzumab and trastuzumab into a vein

Single injection of pertuzumab and trastuzumab under the skin

- Most people (85%) preferred having their treatment by a single injection under the skin (subcutaneous).
- Some people (14%) preferred having their treatment by two separate infusions into a vein (intravenous).
- A small number of people (1%) had no preference.

Which treatment method did people prefer?



The main reasons people preferred the **single injection under the skin** were:

Less time in the clinic for treatment

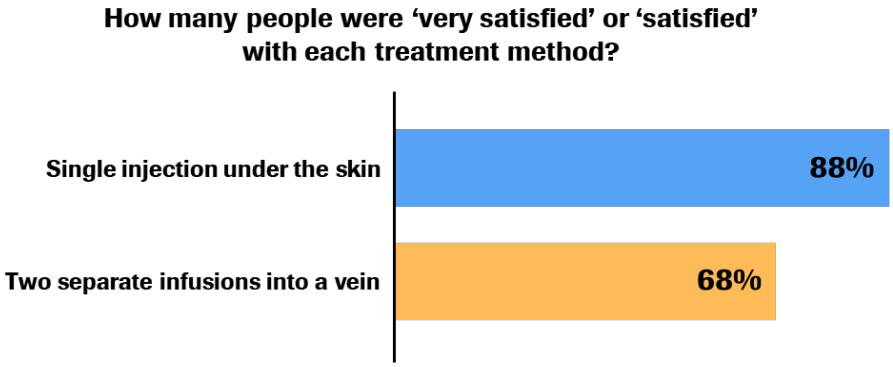
More comfortable during treatment

- Most people (87%) chose to have their pertuzumab and trastuzumab by a single injection under the skin for the rest of their treatment in the continuation part of the study.

How satisfied were people with each treatment method?

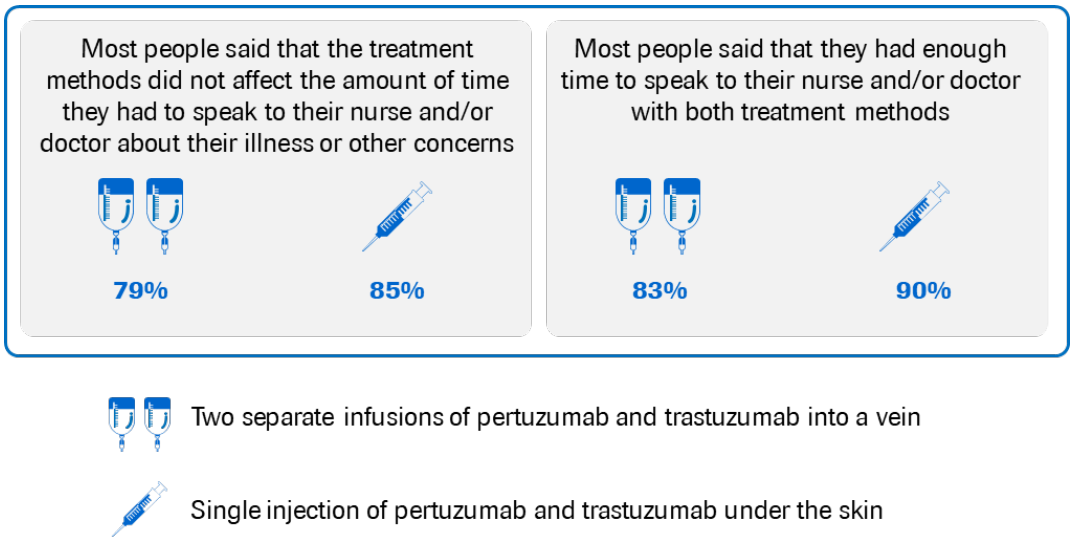
After having pertuzumab and trastuzumab by each different treatment method, researchers asked people how satisfied or dissatisfied they were with each one.

- More people said that they were 'very satisfied' or 'satisfied' with treatment by a single injection under the skin (88%) than with the two separate infusions into a vein (68%).



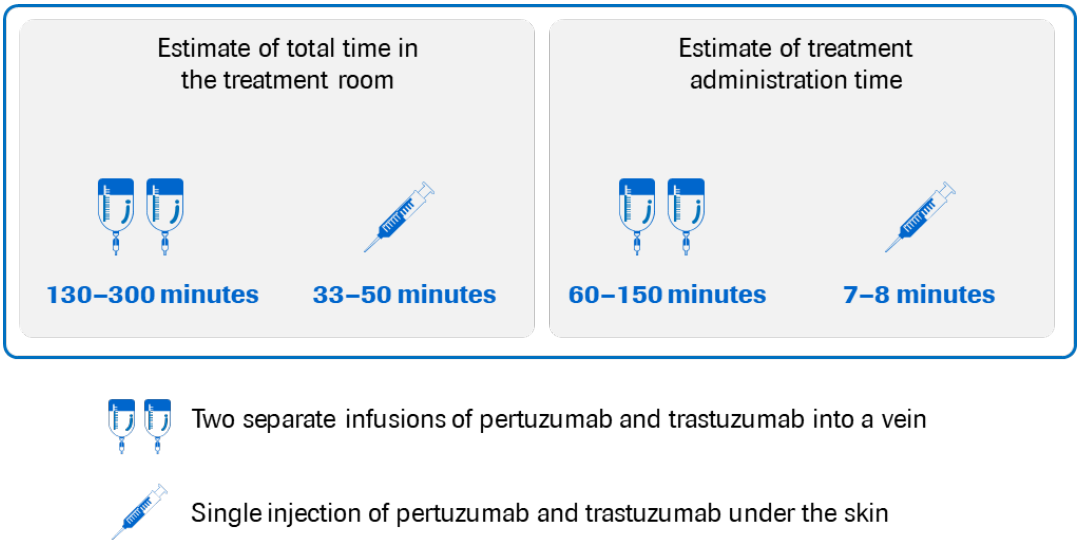
Did people have enough time to speak to their doctor or nurse during their treatment?

After having pertuzumab and trastuzumab by each different treatment method, researchers asked people if they'd had enough time to speak to their doctor or nurse about their illness.



How much time did the healthcare professionals involved in the study think that people saved by using a single injection of pertuzumab and trastuzumab under the skin?

Researchers asked the nurses and doctors involved in the study to estimate how much time people spent in the treatment room, and how much of this was spent having treatment for each method.



The nurses and doctors thought that changing the treatment method from separate infusions into a vein to a single injection under the skin would save time during treatment.

5. What are the side effects so far?

Side effects are unwanted effects of a drug or medical treatment (such as feeling dizzy) that happen during the study.

- Not all of the people in this study experienced all of the side effects that were seen in the study.
- 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 single study. This means that the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflet.
- Serious and common side effects are listed in the following sections.

The safety results discussed here are from the crossover part of the study. The side effects people had with each treatment method were recorded and combined.

Most common side effects

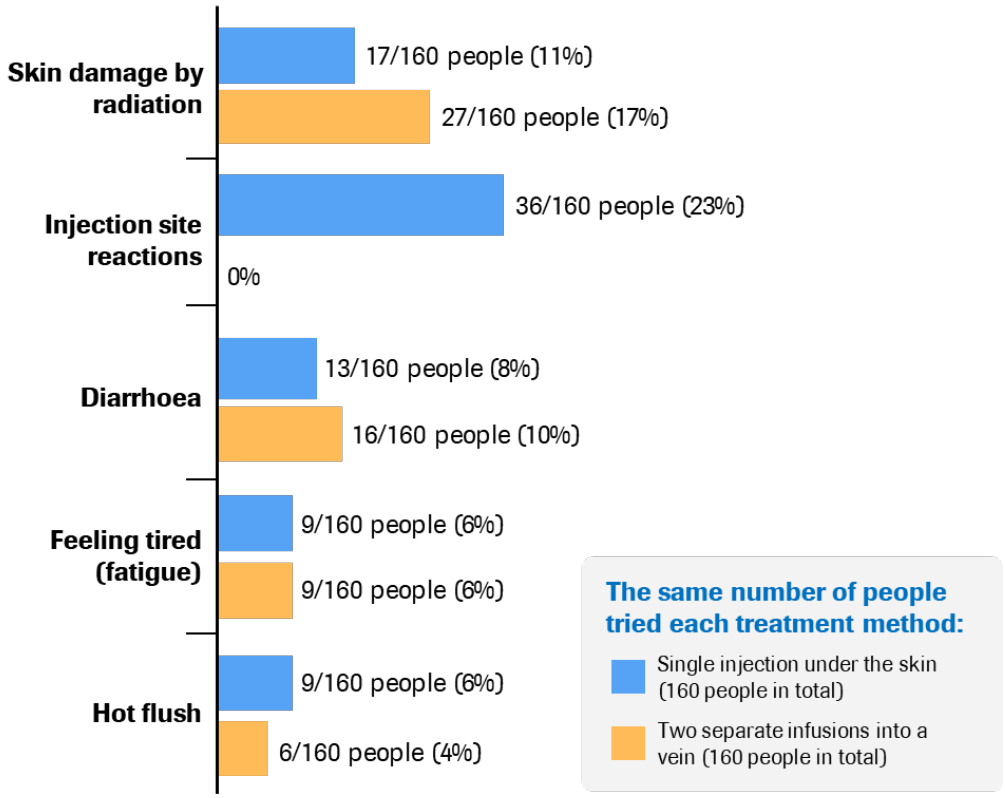
During this study, the majority of the people taking part have had a side effect so far.

Around 71% of people had a side effect that was not considered serious when they had the pertuzumab and trastuzumab by separate infusions into a vein, compared with around 75% of people when they had the pertuzumab and trastuzumab by a single injection under the skin.

The most common side effects from the **crossover part of the study** are shown in the following graph. These are the five most common side effects seen when having each treatment method. Some people had more than one side effect – this means that they are included in more than one bar in the picture.

Injection site reactions (which can include redness, itching, pain, swelling and bruising) were only seen when people had their treatment by a single injection under the skin. This is because the needle causes mild irritation when injected under the skin. No-one on the study had a serious reaction at the injection site and nobody stopped treatment because of this side effect.

The five most common side effects seen in the crossover part of the study



Side effects when switching between one treatment method to the other

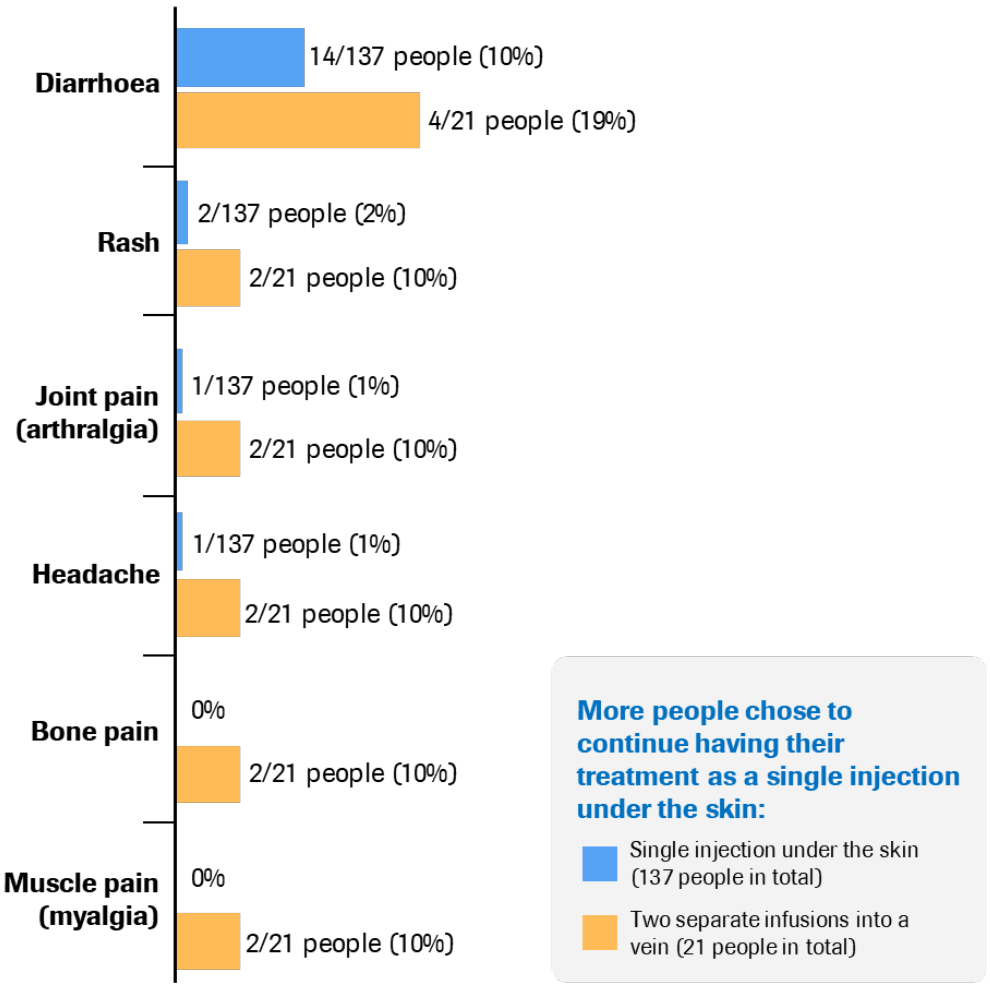
People did not experience any new side effects when the way they received their treatment was switched (from treatment by infusion to treatment by injection, or from treatment by injection to treatment by infusion).

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.

Side effects during the continuation part of the study

When the data from this study were analysed (February 2020), 87 people were having treatment in the continuation part of the study and 70 people had finished their treatment. So far, no unexpected or serious side effects have been seen in these people.
The most common side effects from the **'continuation' part of the study** are shown in the following graph. These are the six most common side effects seen when having each treatment method. When the data from this study were analysed (February 2020), some people were still having treatment in the continuation part of the study.

The six most common side effects seen in the continuation part of the study so far



6. How has this study helped research?

The information presented here is from a single study of 160 people with early-stage HER2-positive breast cancer. This study helped researchers learn if people with HER2-positive breast cancer preferred to receive their treatment with pertuzumab and trastuzumab as a single injection under the skin or as two separate IV infusions into a vein.

In this study, most people (85%) preferred to have their treatment with pertuzumab and trastuzumab as a single injection under the skin. People said that they preferred this treatment method because it meant they spent less time in the clinic and because it felt more comfortable when having the treatment.

The study also gave researchers important information about the safety of switching from one treatment method to the other. The people taking part did not see any new side effects when switching treatment methods.
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 those of 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?

At the time of writing this summary, more studies are looking at treating people with breast cancer by injecting pertuzumab and trastuzumab under the skin as a single injection.

This study is ongoing 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-to-evaluate-patient-preference-and-satisfaction-26388.html
- https://clinicaltrials.gov/ct2/show/study/NCT03674112
- https://www.clinicaltrialsregister.eu/ctr-search/search?query=MO40628
- https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761170s000lbl.pdf
- https://www.ema.europa.eu/en/documents/product-information/phesgo-epar-product-information_en.pdf

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “Preference for the fixed-dose combination of pertuzumab and trastuzumab for subcutaneous injection in patients with HER2-positive early breast cancer (PHranceSCa): A randomized, open-label phase II study”. The authors of the scientific paper are Joyce O'Shaughnessy, Susana Sousa, Josefina Cruz, Lesley Fallowfield, Päivi Auvinen and others. The paper has been submitted to the ‘*European Journal of Cancer*’, for consideration.

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

If you have any further questions after reading this summary:

- https://forpatients.roche.com/en/trials/cancer/bc/a-study-to-evaluate-patient-preference-and-satisfaction-26388.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.

Full title of the study and other identifying information

The full title of this study is: "A Study to Evaluate Patient Preference and Satisfaction of Subcutaneous Administration of the Fixed-Dose Combination of Pertuzumab and Trastuzumab in Participants With HER2-Positive Early Breast Cancer (PHranceSCa)".

The study is known as 'PHranceSCa'.

- The protocol number for this study is: MO40628.
- The ClinicalTrials.gov identifier for this study is: NCT03674112.
- The EudraCT number for this study is: 2018-002153-30.