

A study of trastuzumab and docetaxel plus pertuzumab in Chinese patients with metastatic 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 (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 study started in September 2016 and finished in January 2021. This summary was written after the study had ended.

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.**

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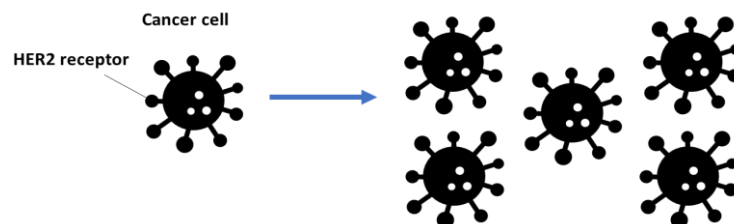
Thank you to the people who took part in this study

The people who took part in this study have helped researchers to answer important questions about Chinese people with HER2-positive, metastatic breast cancer and the HER2-targeted therapies studied – 'pertuzumab' and 'trastuzumab'.

1. General information about this study

Why was this study done?

HER2 receptors are a type of protein found on the surface of some cells, including some cancer cells, that signal the cells to grow and make copies of themselves. Breast cancer cells can sometimes have a higher-than-normal number of HER2 receptors - this is called HER2-positive breast cancer. In HER2-positive breast cancer, cancer cells will grow and make copies of themselves more often – this can be seen in the image below.



Metastatic breast cancer is when the cancer cells have spread to other parts of the body. Treatments are given to help people with the disease to live for as long as possible. Chemotherapy and HER2-targeted therapies, such as pertuzumab and trastuzumab, are the recommended treatment for people with HER2-positive, metastatic breast cancer, who have not received treatment for their metastatic breast cancer. Pertuzumab and trastuzumab target and attack cancer cells with HER2 receptors.

Researchers wanted to study pertuzumab, trastuzumab and chemotherapy in Chinese people with HER2-positive, metastatic breast cancer. Researchers wanted to find out the length of time between the start of the study and people's cancer getting worse.

What were the study medicines?

'Trastuzumab' is an existing medicine given to people with HER2-positive breast cancer.

- You say this as 'trass-too-za-mab'.
- Trastuzumab is a HER2-targeted therapy. Trastuzumab works by attaching itself to the HER2 receptor on the cancer cells which causes the HER2 receptor to stop sending signals that tell the cells to grow and copy themselves.

A medicine called 'pertuzumab' was the focus of this study.

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

'Docetaxel' is an existing chemotherapy medicine given to people with cancer.

- You say this as 'dow-suh-tak-sl'.

Trastuzumab and docetaxel plus pertuzumab were compared with trastuzumab and docetaxel plus a 'placebo'.

- You say this as 'plah-see-bo'.
- The placebo looked the same as pertuzumab but did not contain any active medicine.

What did researchers want to find out?

- Researchers did this study to look at the impact of pertuzumab in the length of time until the HER2-positive, metastatic breast cancer of Chinese people gets worse – to see how well pertuzumab worked (**see section 4 "What were the results of this study?"**).
- They also wanted to find out how safe the combination of medicines was – by checking how many people had side effects and seeing how serious they were, when taking either pertuzumab or placebo during this study (**see section 5 "What were the side effects?"**).

The main questions that researchers wanted to answer were:

1. What was the length of time between the start of the study and people's cancer getting worse? (**see section 4 "What were the results of the study?"**)
2. Did people who were given trastuzumab and docetaxel plus pertuzumab live longer, compared with those given trastuzumab and docetaxel plus a placebo? (**see section 4 "What were the results of the study?"**)
3. How many people had side effects and how serious were they (**see section 5 "What were the side effects?"**)?

What kind of study was this?

This study was a 'Phase 3' study. This means that pertuzumab has already been tested in a small group of people with HER2-positive, metastatic breast cancer. In this study, Chinese people with HER2-positive, metastatic breast cancer were given either trastuzumab and docetaxel plus pertuzumab or trastuzumab and docetaxel plus a placebo.

The study was 'randomised'. This means that people were randomly selected by chance to take either trastuzumab and docetaxel plus pertuzumab or trastuzumab and docetaxel plus a placebo. Randomly choosing which medicine people are given makes it more likely that characteristics (for example, age and race) of people in both groups will be similar.

This was a 'double-blind' study. This means that neither the people taking part in the study, nor the study doctors knew which of the study medicines people were being given. 'Blinding' of a study is done to reduce the chance of bias.

When and where did the study take place?

The study started in September 2016 and finished in January 2021. The study took place at 15 study centres in China. This summary was written after the study had ended.

2. Who took part in this study?

In this study, 242 people with HER2-positive, metastatic breast cancer took part and were given either trastuzumab and docetaxel plus pertuzumab or trastuzumab and docetaxel plus a placebo. People who took part in the study were between 25 and 74 years of age and all were female and Asian.

People could take part in the study if they had:

- HER2-positive breast cancer (confirmed by a specific test) which had spread to other parts of the body;
- Normal heart function.

People could not take part in the study if they had:

- Previously been given HER2-targeted therapies or other anti-cancer medicines for their metastatic breast cancer.

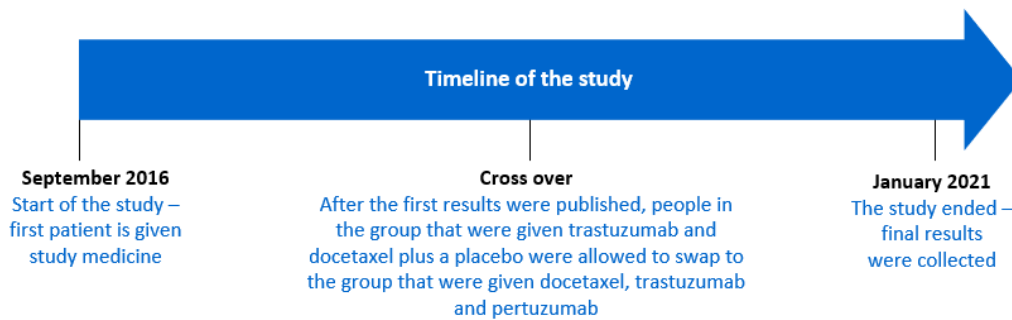
3. What happened during this study?

During the study, people were selected by chance to get one of 2 treatment combinations. The treatments were selected at random – by a computer.

The treatment groups were:

- Trastuzumab and docetaxel plus pertuzumab
- Trastuzumab and docetaxel plus a placebo.

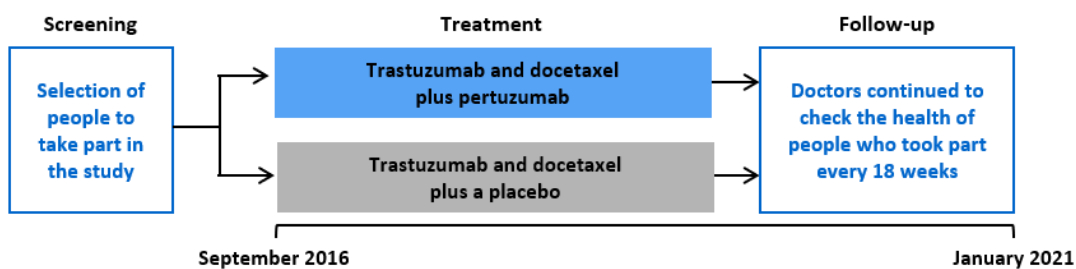
The first results of this study that were published showed that trastuzumab and docetaxel plus pertuzumab was more effective than trastuzumab and docetaxel plus a placebo. Therefore, people in the group that were given trastuzumab and docetaxel plus a placebo were allowed to swap to the group that was given trastuzumab and docetaxel plus pertuzumab. See below for a timeline of the study:



People received the medicines via an injection into a vein known as intravenous or IV every 3 weeks in the following order:

1. Pertuzumab or placebo
2. Trastuzumab
3. Docetaxel

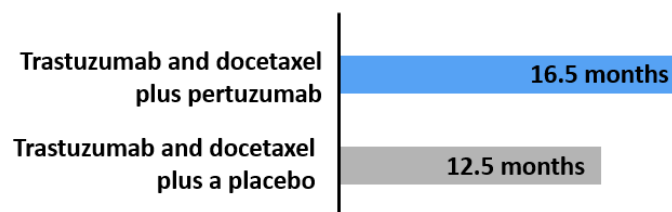
People in the study were given the treatment combinations until their disease worsened or they had to stop taking the medicines because of safety reasons. When the study finished, the people who took part were asked to go back to their study centre for more visits – to check on their overall health. More information about what happened in the study can be found in the image below:



4. What were the results of this study?

Question 1: What was the length of time between the start of the study and people’s cancer getting worse?

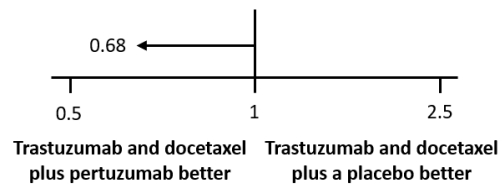
Researchers looked at how long people lived with the disease without it worsening. Pertuzumab increased the length of time people lived with the disease without it worsening, compared with the placebo, from 12.5 months to 16.5 months. This can be seen in the image below.



Question 2: Did people who were given trastuzumab and docetaxel plus pertuzumab live longer, compared with those given trastuzumab and docetaxel plus a placebo?

Another piece of information that researchers collected was how long people lived in this study, when given either trastuzumab and docetaxel plus pertuzumab or trastuzumab and docetaxel plus a placebo.

Researchers measured how often patients lived with the disease until the end of the study, when given either trastuzumab and docetaxel plus pertuzumab or trastuzumab and docetaxel plus a placebo; this is called a hazard ratio. In this study the hazard ratio was a value less than 1 (0.68), meaning survival was better in people given trastuzumab and docetaxel plus pertuzumab compared with those given trastuzumab and docetaxel plus a placebo. This can be seen in the image below.



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 7).

5. What were the side effects?

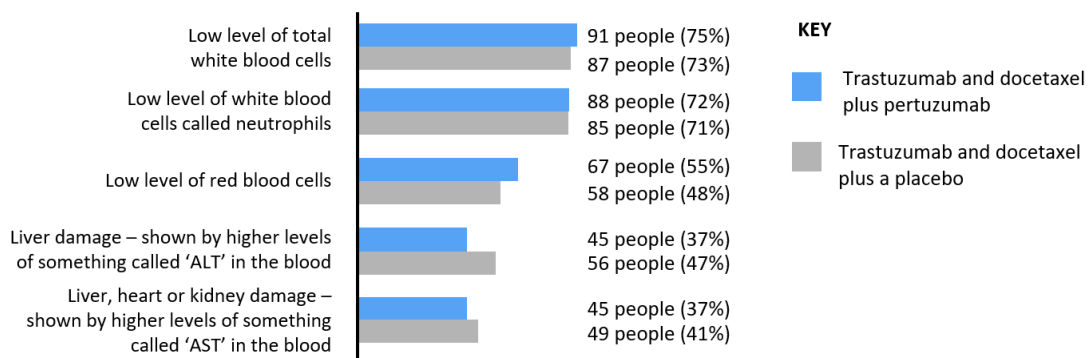
Side effects are medical problems (such as feeling dizzy) that happen during the study.

- Not all of the people in this study had all of the side effects.
- 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, and may be different from those seen in other studies, or those that appear on the medicine leaflets.
- Most common and serious side effects are listed in the following sections.

Most common side effects

During this study, 236 out of 242 people (98%) had a side effect that was not considered serious. Around 99% of people given trastuzumab and docetaxel plus pertuzumab had a side effect that was not considered serious, compared with around 96% of people given trastuzumab and docetaxel plus a placebo. In the group that swapped from placebo to pertuzumab, 5 out of 12 people (42%) had a side effect.

The most common side effects are shown in the following image – these are the 5 most common side effects across both treatment groups. Some people had more than one side effect – this means that they are included in more than one row in the image.

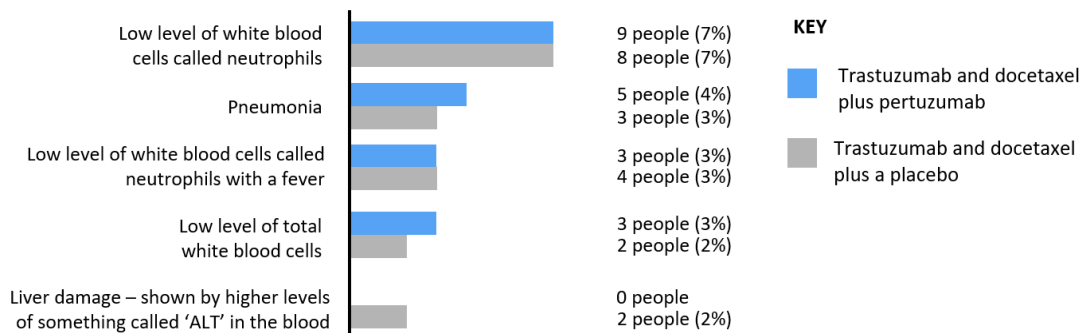


The most common side effect experienced by people who swapped from the placebo group to the pertuzumab group was liver, heart or kidney damage, shown by higher levels of something called 'AST' in the blood (2 out of 12 people [17%]).

Serious side effects

Serious side effects are side effects that are life-threatening or require immediate treatment or hospitalisation. During this study, 53 out of 242 people (22%) had at least one serious side effect. More people who received trastuzumab and docetaxel plus pertuzumab had a serious side effect (25%), compared to those who received trastuzumab and docetaxel plus placebo (19%). Among those that swapped groups, 1 out of 12 people (8%) had a serious side effect; this patient had small growths on the inner lining of the large intestine and blockage or narrowing of an artery in the legs.

The 5 most common serious side effects are shown in the following image. Some people had more than one side effect – this means that they are included in more than one row in the image.



There were some people in the study who died due to side effects that may have been related to one of the study medicines. These were:

- 4 out of 122 people (3%) given trastuzumab and docetaxel plus pertuzumab
- 2 out of 120 people (2%) given trastuzumab and docetaxel plus a placebo.

During the study, some people decided to stop taking pertuzumab or placebo because of their side effects:

- 7 out of 122 people (6%) given trastuzumab and docetaxel plus pertuzumab stopped taking pertuzumab
- 2 out of 120 people (2%) given trastuzumab and docetaxel plus a placebo stopped taking the placebo.

Other side effects

You can find out more information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – **see section 7**.

6. How has this study helped research?

The information presented here is from a single study of 242 Chinese people with HER2-positive, metastatic breast cancer. These results have helped researchers learn more about pertuzumab in combination with trastuzumab and docetaxel in Chinese people with HER2-positive, metastatic breast cancer, and showed that it is just as safe and effective when given to Chinese people, compared with to people from rest of the world.

Studies with pertuzumab are still happening, and further studies are planned in China and in other countries.

7. Where can I find more information?

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

- <https://clinicaltrials.gov/ct2/show/results/NCT02896855>
- <https://forpatients.roche.com/en/trials/cancer/bc/a-study-to-evaluate-the-efficacy-and-safety-of-pertuzum-08881.html>

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 docetaxel for Chinese patients with previously untreated HER2-positive locally recurrent or metastatic breast cancer (PUFFIN): final analysis of a phase III, randomized, double-blind, placebo-controlled study”. The authors of the scientific paper are: Binghe Xu, Wei Li, Qingyuan Zhang, Qiao Li, Xiaojia Wang and others. The paper is published in the journal ‘Breast Cancer Research and Treatment’, volume number 197, on pages 503–513.

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-to-evaluate-the-efficacy-and-safety-of-pertuzum-08881.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 phase 3, randomised, double blind, placebo controlled clinical trial to evaluate the efficacy and safety of pertuzumab + trastuzumab + docetaxel versus placebo + trastuzumab + docetaxel in previously untreated human epidermal growth factor receptor 2-positive metastatic breast cancer”.

The study is known as ‘PUFFIN’.

- The protocol number for this study is: YO29296.
- The ClinicalTrials.gov identifier for this study is: NCT02896855.