Summary of Clinical Trial Results

A study comparing the use of palbociclib with giredestrant or anastrozole in women with oestrogen receptor (ER)-positive, HER2-negative untreated early 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 the coopERA Breast Cancer 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 coopERA Breast Cancer study started in September 2020 and finished in November 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 treatment.

- **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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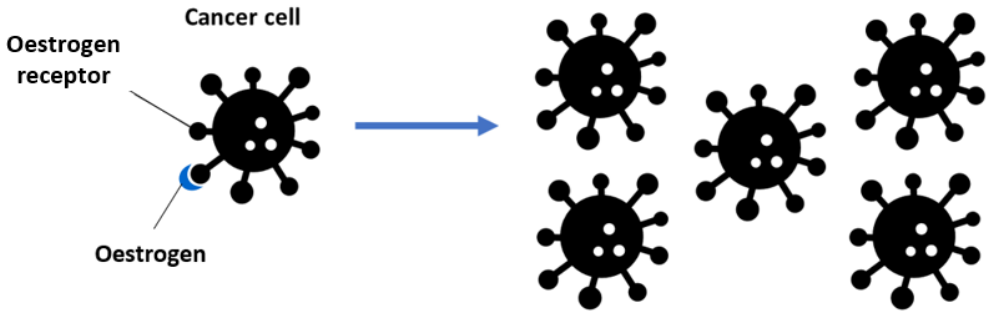
Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about breast cancer that has not spread to other parts of the body (early breast cancer) and has a higher-than-normal number of oestrogen receptors (known as oestrogen receptor-positive, or ER-positive), and the medicine studied – 'giredestrant'.

1. General information about this study

Why was this study done?

Hormone receptors are a type of protein found on the surface of some cells, including some cancer cells. Hormones in the blood will attach to the hormone receptor, which tells the cell to perform a specific function. This is called hormone signalling. Oestrogen is a type of hormone in the body. When oestrogen attaches to an ER on a cell's surface, the cell will be told to make copies of themself. In ER-positive breast cancer there is a higher-than-normal number of ER on the cancer cells. This means the cancer cells are signalled more often so they grow and copy themselves more, meaning the tumour will grow.



Early breast cancer is when the cancer has not spread to other parts of the body. People with ER-positive, HER2-negative early breast cancer often receive several types of treatments including:

- Surgery to remove the tumour
- Chemotherapy
- Radiation
- Hormonal therapy

All people will need to receive hormonal therapy after surgery. This is a type of medicine that changes the levels of hormones, or the amount of hormonal signalling, in the body.

This study was carried out to compare two different types of hormonal therapy, 'giredestrant' and 'anastrozole', that were taken with another medicine, 'palbociclib', for a period of time followed by surgery in people with ER-positive, HER2-negative early breast cancer. The main purpose of taking these medicines is to reduce or prevent cancer cell growth. This study measured the amount of a protein in people's tumours that is associated with cell growth, Ki67. High levels of this protein will mean that more cell growth is happening therefore, if the medicines are working, the amount of Ki67 should reduce.

What were the study medicines?

This study looked at three medicines:

- **Giredestrant** – the medicine that was being investigated in this study
- **Anastrozole** – existing medicine
- **Palbociclib** – existing medicine

‘Giredestrant’ is the medicine that was studied here.

- You say this as ‘Gee-Red-Est-Rant’.
- It is a type of hormonal therapy called a selective oestrogen receptor degrader (SERD).
- Giredestrant blocks access to the oestrogen receptors on the surface of cells and breaks down the oestrogen receptors. This means that the hormone oestrogen cannot attach to the receptors and therefore there is no signalling for cells to make copies of themselves.

‘Anastrozole’ is an existing medicine given to people with ER-positive breast cancer.

- You say this as ‘An-Ass-Troh-Zoll’.
- It is a type of hormonal therapy called an aromatase inhibitor (AI).
- Anastrozole reduces the amount of oestrogen being produced. This means there are lower levels of oestrogen in the blood to attach to oestrogen receptors on cancer cells, and therefore fewer signals are sent to instruct the cancer cells to grow and make copies of themselves.

‘Palbociclib’ is an existing medicine given to people with ER-positive breast cancer.

- You say this as ‘Pal-Boh-Sic-lib’.
- Palbociclib stops specific proteins called cyclin-dependent kinase 4 and 6 from working, and so stops the cell making copies of itself.

What did researchers want to find out?

- Researchers wanted to find out how effective giredestrant was at slowing cancer cell growth compared with anastrozole after taking either giredestrant or anastrozole for 2 weeks and then taking giredestrant or anastrozole with palbociclib for 16 weeks **(see section 4, “What were the results of the study?”)**.
- They also wanted to find out how safe the medicines were – by seeing how many people had side effects and how serious these were, when taking the medicines during this study **(see section 5, “What were the side effects?”)**.

The main question that researchers wanted to answer was:
How much does each medicine lower the amount of Ki67, a protein associated with cell growth, in the cancer cells after taking the medicine for 2 weeks and at the time just before people had surgery?

What kind of study was this?

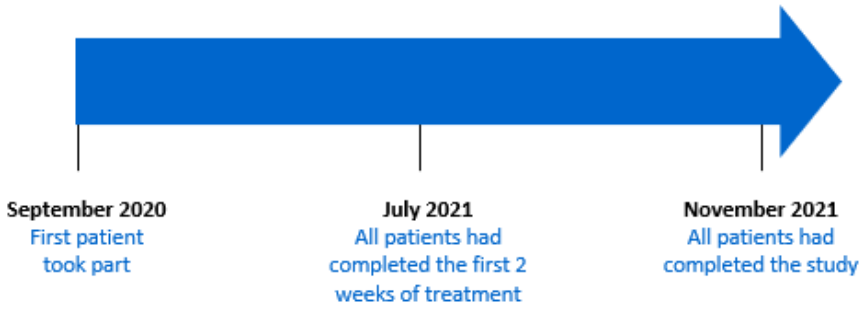
This was a ‘Phase 2’ study. This means that giredestrant had been tested in a small number of people with or without ER-positive breast cancer before this study. In this study, people with ER-positive breast cancer took either giredestrant or anastrozole – this was to find out if giredestrant worked to lower the amount of Ki67. The study had two treatment periods; the first period was 2 weeks when people took either giredestrant or anastrozole (after this period people had a sample of the tumour taken) the second period was 16 weeks and people continued to take either giredestrant or anastrozole with palbociclib before surgery.

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 will be a similar mix (for example, with regard to age or race). Apart from the exact medicines being tested in each group, all other 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?

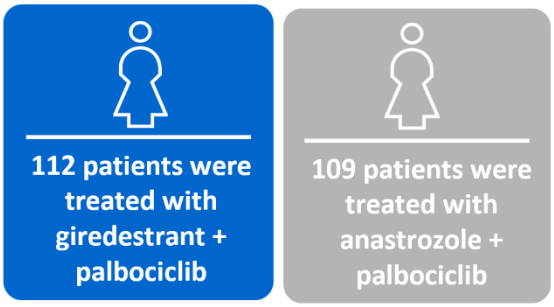
The study started in September 2020 and finished in November 2021. This summary was written after the study had ended.



The study took place at 59 study centres – across 11 countries. The following map shows the countries where this study took place.

2. Who took part in this study?

In this study, 221 people with ER-positive, HER2-negative early breast cancer took part. People who took part in the study were between 23 and 83 years of age and were all female.



Age range: 23 to 83 years old

People could take part in the study if they had:

- Early breast cancer (breast cancer that had not spread to other parts of the body)
- ER-positive, HER2-negative breast cancer (confirmed by testing)
- At least 5% of cancer cells containing the protein Ki67

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

- Breast cancer that had spread to other parts of the body
- Previous treatment for breast cancer

3. What happened during the study?

During the study, people were selected by chance to receive one of two treatments regimens. The treatments were selected at random – by a computer.

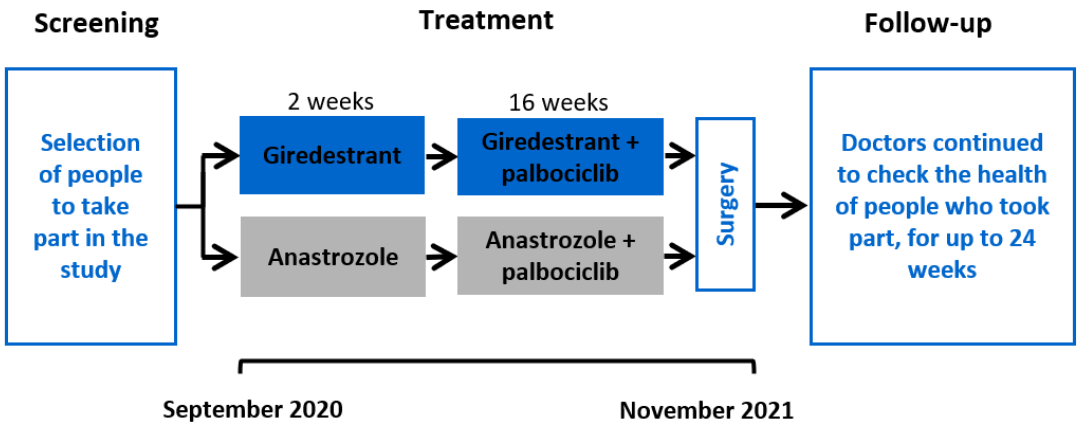
The treatment groups were:

- **Giredestrant and palbociclib** – giredestrant was taken by mouth once a day for 18 weeks. After the first 2 weeks of taking giredestrant, people then completed 4 treatment cycles of palbociclib. Surgery was performed within 2 weeks of the last time taking the medicines. See in the image below.
- **Anastrozole and palbociclib** – anastrozole was taken by mouth once a day for 18 weeks. After the first 2 weeks of taking anastrozole, people then completed 4 treatment cycles of palbociclib. Surgery was performed within 2 weeks of the last time taking the medicine. See in the image below.

The medicine palbociclib was given in 'treatment cycles'.

- Each treatment cycle lasted for 28 days.
- People took the study medicine for 21 days – they then had a break where they took no palbociclib for 7 days.

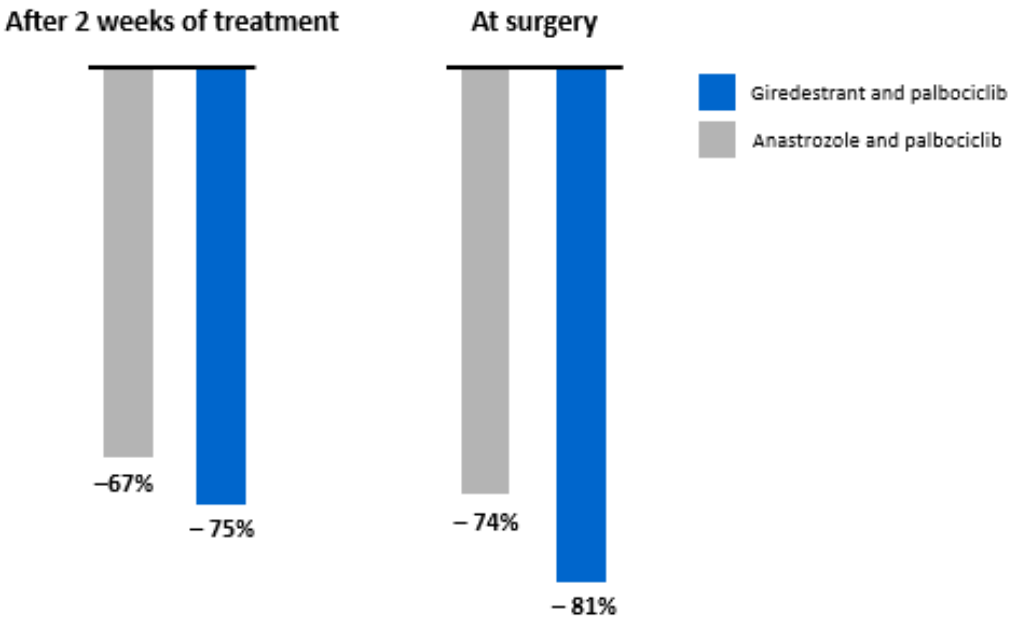
When the study finished, the people who took part were asked to go back to their study centre for more visits – to check their overall health.



4. What were the results of the study?

How much does each medicine lower the amount of Ki67, a protein associated with cell growth, in the cancer cells after taking the medicine for 2 weeks and at the time just before people had surgery?

People who were given giredestrant had a bigger reduction in the amount of Ki67 protein when compared with people who were given anastrozole after 2 weeks of treatment. This was also seen later on in the study at surgery where people who took giredestrant and palbociclib had a bigger reduction than people who took anastrozole and palbociclib.



This section only shows the key results from this study. You can find more information about the results via the website links at the end of this summary **(see section 8)**.

5. What were the side effects?

Side effects are effects that happen in addition to the intended effect of a medicine; these can be medical problems (such as feeling dizzy).

- 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. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflets.
- Side effects may or may not be related to the study medicine, or they might have happened to people even if they were not taking part in this study.
- Serious and common side effects during the 18 weeks of treatment are listed in the following sections.

Serious side effects

A side effect is considered 'serious' if it is life-threatening, needs hospital care or causes long-lasting problems. During this study, seven of the 221 people who took part (3%) had at least one serious side effect. Around 4% of people taking giredestrant and palbociclib had a serious side effect, compared with around 2% of people taking anastrozole and palbociclib.

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

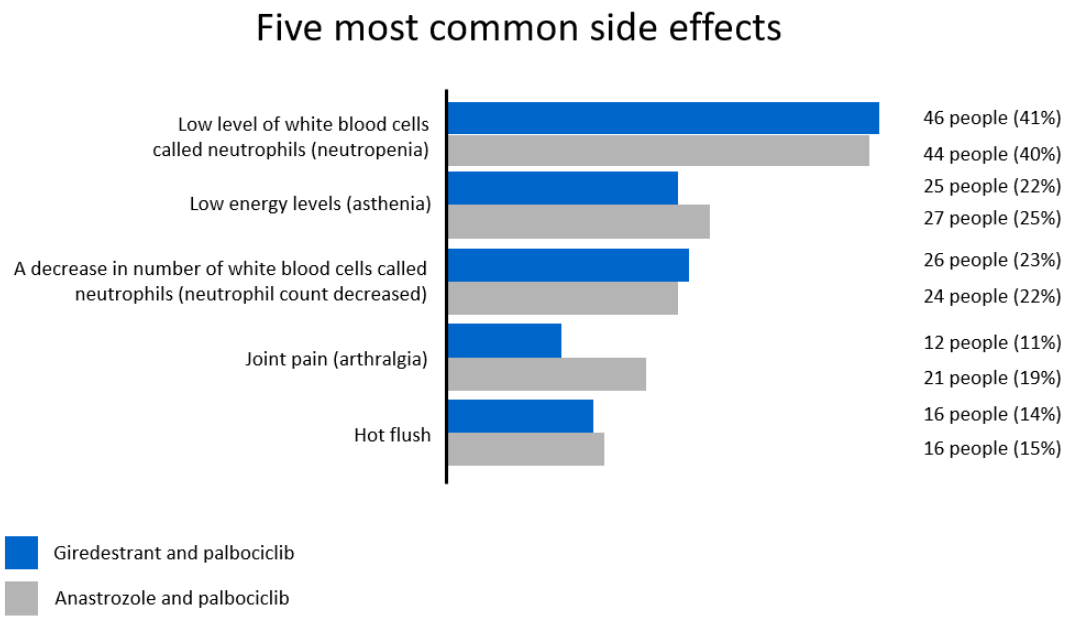
Serious side effects reported in this study	**People taking giredestrant and palbociclib** (112 people total)	**People taking anastrozole and palbociclib** (109 people total)
Broken hip bone (hip fracture)	1% (1 out of 112)	0% (0 out of 109)
Pain during medical procedure	0% (0 out of 112)	1% (1 out of 109)
Damage to the wall of the uterus (uterine perforation)	1% (1 out of 112)	0% (0 out of 109)
Heart attack (myocardial infarction)	1% (1 out of 112)	0% (0 out of 109)
Fever (pyrexia)	1% (1 out of 112)	0% (0 out of 109)
COVID-19	1% (1 out of 112)	0% (0 out of 109)
Low oxygen levels (hypoxia)	0% (0 out of 112)	1% (1 out of 109)

There was one death in the study in the giredestrant and palbociclib group. For this case, the treating doctor (independent from the study sponsor) determined that the person's death was not related to taking the study drug.

Most common side effects

During this study, 202 out the 221 people who took part (91%) had a side effect that was not considered serious.

The most common side effects are shown in the following image – these are the five 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.



During the study, some people stopped taking their medicine because of the side effects:

- In the giredestrant and palbociclib group,
  - 2 out of 112 people (2%) stopped taking giredestrant
  - 2 out of 112 people (2%) stopped taking palbociclib.
- In the anastrozole and palbociclib group,
  - 1 out of 109 people (1%) stopped taking anastrozole
  - 1 out of 109 people (1%) stopped taking palbociclib.

Other side effects

You can find more information about other side effects (not shown in the sections above) via the website links 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 221 people with ER-positive, HER2-negative early breast cancer. These results helped researchers learn more about the effect of giredestrant in people with ER-positive early breast cancer.

The purpose of the study was to find out how far the medicines giredestrant and anastrozole taken with palbociclib reduce the growth and copying of cancer cells. In this study 221 people in 11 countries took part. These people were put into two groups randomly; one group took giredestrant and palbociclib and the other group anastrozole and palbociclib. People who were given giredestrant and palbociclib had a larger reduction in the amount of Ki67, a protein associated with cell growth, compared to people given anastrozole and palbociclib. The most common side effects experienced by people were similar between the two groups.

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?

Studies with giredestrant are still happening, and further studies are planned:

- lidERA Breast Cancer: giredestrant after surgery in ER-positive, HER2-negative, breast cancer that has not spread to other parts of the body (NCT04961996)
- persevERA Breast Cancer: giredestrant plus palbociclib in ER-positive, HER2-negative, breast cancer that has spread to other parts of the body (NCT04546009)
- evERA Breast Cancer: giredestrant plus everolimus in ER-positive, HER2-negative, breast cancer that has spread to other parts of the body (NCT05306340)
- heredERA Breast Cancer: giredestrant plus PHESGO in ER-positive, HER2-positive, breast cancer that has spread to other parts of the body (NCT05296798)
- MORPHEUS Breast Cancer: giredestrant alone and in combination with other medicines in breast cancer that has spread to other parts of the body (NCT04802759)

8. 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/NCT04436744
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001007-16/results
- https://forpatients.roche.com/en/trials/cancer/bc/a-study-evaluating-the-efficacy--safety--and-pharmacoki-19834.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “Neoadjuvant palbociclib plus either giredestrant or anastrozole in oestrogen receptor-positive, HER2-negative, early breast cancer (coopERA Breast Cancer): an open-label, randomised, controlled, phase 2 study”. The authors of the scientific paper are: Sara A Hurvitz, Aditya Bardia, Vanesa Quiroga, Yeon Hee Park, Isabel Blancas and others. The paper is published in the journal ‘The Lancet Oncology’, volume number 24, on pages 1029–1041.

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-evaluating-the-efficacy--safety--and-pharmacoki-19834.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 with 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 which has its headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: “A Study Evaluating the Efficacy, Safety, and Pharmacokinetics of Giredestrant Plus Palbociclib Compared With Anastrozole Plus Palbociclib for Postmenopausal Women With Estrogen Receptor-Positive and HER2-Negative Untreated Early Breast Cancer”.

The study is known as ‘coopERA Breast Cancer’.

- The protocol number for this study is: WO42133.
- The ClinicalTrials.gov identifier for this study is: NCT04436744.
- The EudraCT number for this study is: 2020-001007-16.