Summary of Clinical Trial Results

A study comparing the use of giredestrant with doctor's choice of hormonal therapy in people with oestrogen receptor (ER)-positive, HER2-negative advanced 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 acelERA Breast Cancer clinical trial (called a 'study' in this document) – written for:

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

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

The study started in November 2020 and this summary includes the results that were collected until February 2022 and analysed thereafter. At the time of writing this summary, this study is still happening – this summary will be updated when the study ends.

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.**

Contents of the summary

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about a specific type of breast cancer that has a higher-than-normal number of oestrogen receptors (known as oestrogen receptor-positive, or ER-positive) and has spread to other parts of the body (advanced breast cancer), and the medicine studied – 'giredestrant'.

1. General information about this study

Why was this study done?

Hormone receptors are a type of protein found in some cells, including some breast 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 oestrogen receptor (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.

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. When breast cancer cells do not have a higher-than-normal number of HER2 receptors – this is called HER2-negative breast cancer.

Advanced breast cancer is when the cancer has spread to other parts of the body and is incurable. People with ER-positive, HER2-negative advanced breast cancer will receive medicines to help them live as long as possible with the disease.

Researchers want to find out how giredestrant compares with a doctor's choice of hormonal therapy, also called endocrine therapy, in people with advanced breast cancer after previous treatment has not worked. The study will measure the length of time between the start of the study and people's cancer getting worse (in other words, spread, spread further, or grew larger) or people dying.

Some people's tumours may have a change in a gene called *ESR1*; this change is also known as a mutation. This study also looked specifically into groups of people whose tumour had a mutation in the *ESR1* gene or not to see the if the benefit of giredestrant was different for people whose tumours did or did not have a mutation in the *ESR1* gene.

What were the study medicines?

This study included two groups of patients who took either:

- **Giredestrant** – the medicine that was being investigated in this study
- **Doctors' choice of hormonal therapy** – choice of existing medicines

'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) that is taken by mouth every day.
- Giredestrant blocks access to the oestrogen receptors on the surface of cells and breaks down the oestrogen receptors, therefore, there is no signalling for cells to make copies of themselves.

The study doctors had a choice of existing hormonal therapies that are routinely given to people with ER-positive, HER2-negative advanced breast cancer. These medicines were:

- Aromatase inhibitors (anastrozole, letrozole, or exemestane), these are medicines that reduce oestrogen production and reduce activation of the ER.
- Fulvestrant, this medicine works in a similar way to giredestrant but is given as monthly injections into a muscle.

What did researchers want to find out?

- Researchers did this study to compare giredestrant with doctor's choice of hormonal therapy – to see how well giredestrant worked (**see section 4 "What were the results of the study?"**).
- They also wanted to find out how safe the medicine was – by seeing how many people had side effects and seeing how serious they were, when taking each of the medicines during this study (**see section 5 "What were the side effects?"**).

The main questions that researchers wanted to answer were:

1. Could giredestrant delay the cancer getting worse?
2. In patients whose tumours had a mutation in the *ESR1* gene, could giredestrant delay the cancer getting worse?
3. Could giredestrant delay the worsening of people's pain, quality of life and ability to perform daily activities?
4. What kind of side effects were there? Which side effects were serious?

What kind of study was this?

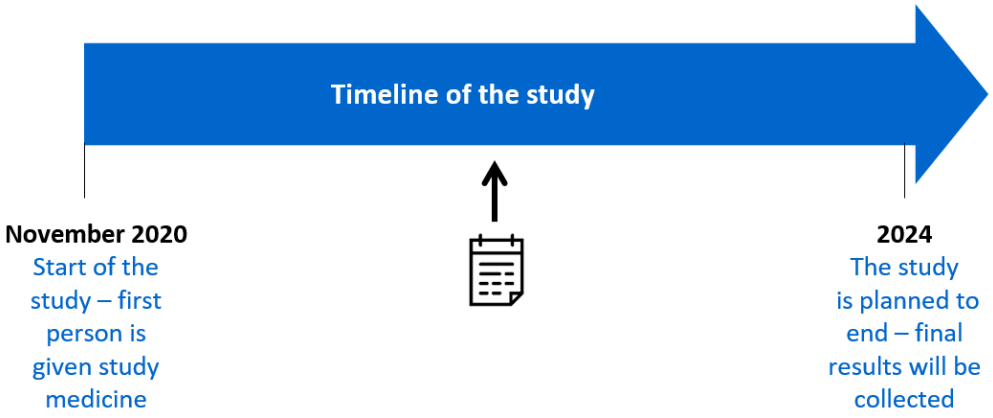
This study was a 'Phase 2' study. Giredestrant had been tested in a small number of people with ER-positive, HER2-negative advanced breast cancer before this study. In this study, people with ER-positive, HER2-negative advanced breast cancer either took giredestrant or their study doctor's choice of hormonal therapy – this was to compare their benefits in delaying their cancer getting worse and their side effects.

The study was 'randomised'. This means that it was decided by chance which of the two groups people in the study would be in. Randomly choosing which study 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, race or disease characteristics).

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.

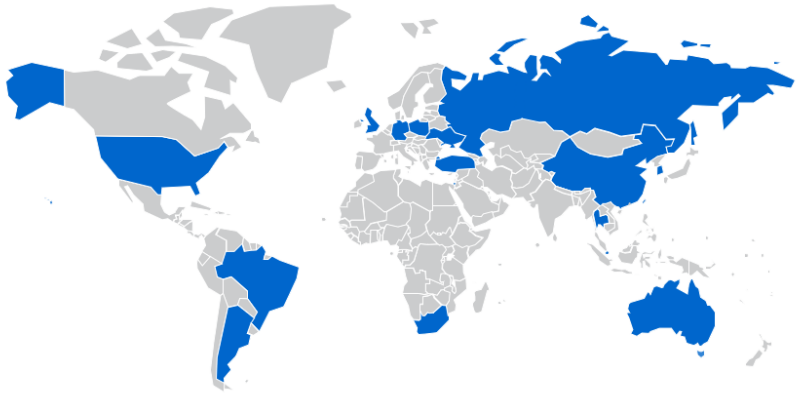
When and where did the study take place?

The study started in November 2020 and this summary includes the complete results up until February 2022. At the time of writing this summary, further safety information is being collected.



This study is still happening, and the symbol on the timeline ( ) shows when the information shown in this summary was collected – after 15 months (February 2022).

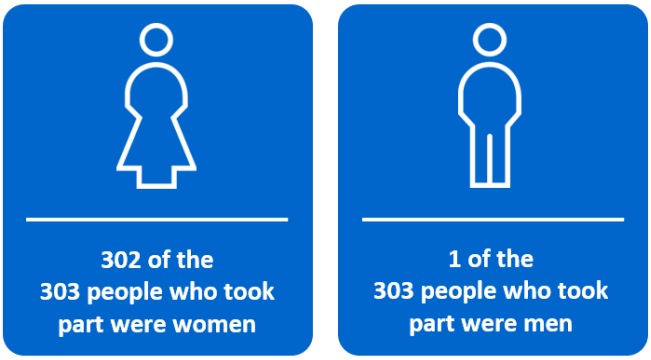
The study took place at 106 study centres – across 17 countries. The following map shows the countries where this study took place.



- Argentina
- Australia
- Brazil
- China
- Germany
- Israel
- Republic of Korea
- Poland
- Russian Federation
- Singapore
- South Africa
- Taiwan
- Thailand
- Turkey
- Ukraine
- United Kingdom
- Unites States of America

2. Who took part in this study?

In this study, 303 people with ER-positive, HER2-negative advanced breast cancer took part. People who took part in the study were between 28 and 93 years of age, 302 of the 303 people were female and 1 of the 303 people was male.



Age range: 28 to 93 years old

People could take part in the study if they had:

- Advanced breast cancer
- ER-positive, HER2-negative breast cancer (confirmed by testing)
- Received one or two previous treatments for their advanced breast cancer

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

- Previously received certain anti-cancer treatments
- Certain other medical conditions, such as heart or liver disease, or certain infections

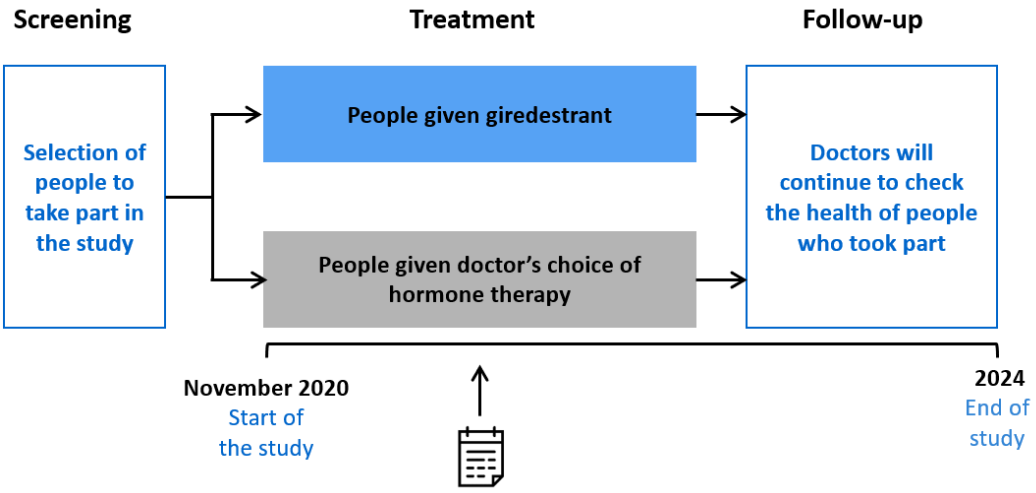
3. What happened during the study?

During the study, people were assigned randomly by a computer to be in either of the treatment groups. The treatments were given until their cancer got worse or they experienced significant side effects.

The treatment groups were:

- **Giredestrant** (the medicine being studied) – was taken by mouth every day.
- **Doctor's choice of hormonal therapy** was given as stated in local prescribing guidelines.
- In both groups, women who were not post-menopausal and men also took a medication known as an LHRH-agonist.

This study is still happening so some people are still being treated with the study medicines or being monitored after finishing the study treatment. Look below to see more information about what has happened in the study so far – and what the next steps are.



This study is still happening, so the symbol on the timeline (📋) shows when the information shown in this summary was collected – after 15 months (February 2022).

4. What were the results of the study?

Question 1: Could giredestrant delay the cancer getting worse?

At the time these results were collected, people had been participating in the study for 8 months on average. The main objective of the study was to find if giredestrant reduced the risk of the cancer getting worse or people dying compared with doctor's choice of hormone therapy.

People who had been given giredestrant had a 20% lower risk of their cancer getting worse or them dying than people who had been given doctor's choice of hormone therapy, but this was not statistically significant and therefore a definite conclusion cannot be made.

Question 2: In patients with a mutation in the *ESR1* gene, could giredestrant delay the cancer getting worse?

People who had been given giredestrant and whose tumours had a mutation in the *ESR1* gene had a 40% lower risk of their cancer getting worse or them dying than people who had been given doctor's choice of hormone therapy and had a mutation in the *ESR1* gene. The study was not designed to make any definite conclusions about whether this was a significant difference.

Question 3: Could giredestrant delay the worsening of people's pain, quality of life and ability to perform daily activities?

People who had been given giredestrant had reduced risk of worsening of pain, quality of life and ability to perform daily activities compared with people who had been given doctor's choice of hormone therapy. The study was not designed to make any definite conclusions about whether this was a significant difference.

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**).

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).

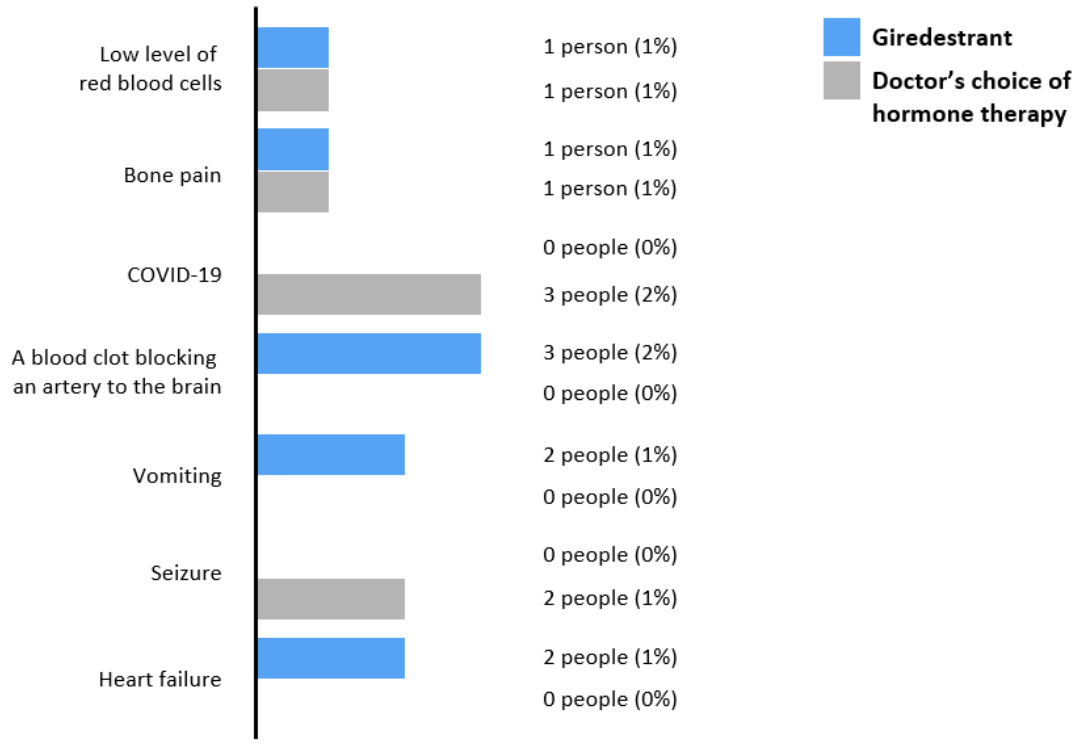
- Not all of the people in this study had all of the side effects.
- Side effects may be mild to very serious; and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different 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 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, 26 out of 302 people (9%) who received study treatment had at least one serious side effect. Around 9% of people taking giredestrant had a serious side effect, and around 8% of people taking doctor's choice of hormone therapy had a serious side effect.

Serious side effects that occurred in two or more people across both treatment groups are shown in the following picture. Some people had more than one side effect – this means that they are included in more than one row in the picture.



One person in the study died because of a side effect that may have been related to giredestrant.

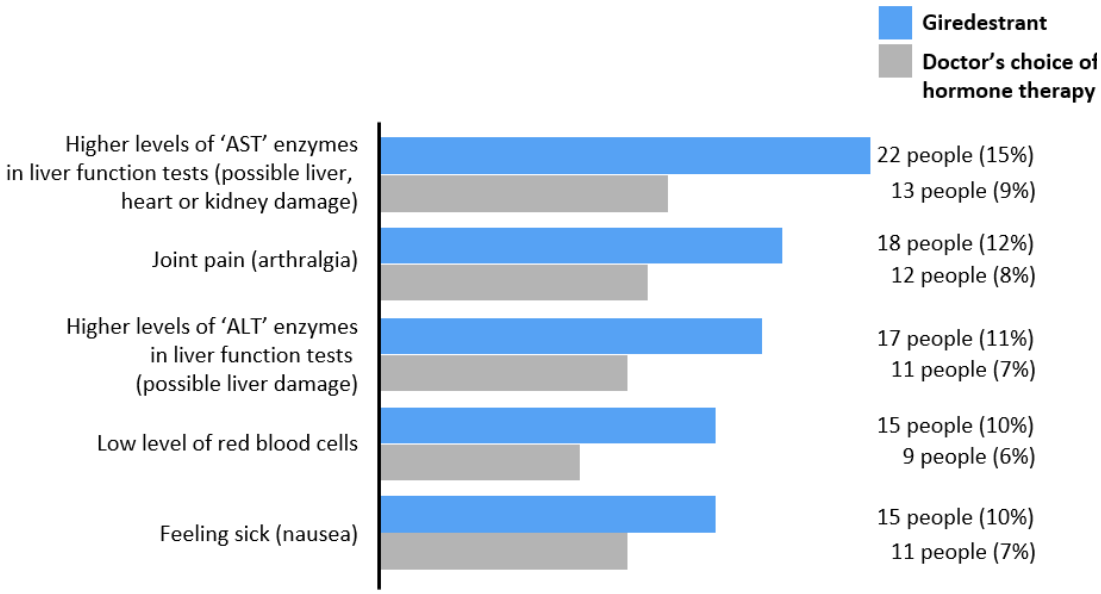
During the study, some people decided to stop taking their medicine because of the side effects:

- 2 out of 150 people (1%) stopped taking giredestrant.
- 3 out of 152 people (2%) stopped taking doctor's choice of hormone therapy.

Most common side effects

During this study, 235 out of 302 people (78%) had at least one side effect whilst they were taking the study treatment. Around 85% of people who were given giredestrant had a side effect, compared with around 71% of people who were given doctor's choice of hormone therapy.

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



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?

These results presented here are from a single study of 303 people and helped researchers learn more about the effect of giredestrant in people with ER-positive, HER2-negative advanced breast cancer.

Giredestrant lowered the risk of the cancer getting worse or people dying compared with doctor's choice of hormonal therapy, but the result was not statistically significant. In people whose tumour had mutations in a gene called *ESR1*, giredestrant lowered even more the risk of the cancer getting worse or people dying compared with doctor's choice of hormonal therapy. The numbers and types of side effects were comparable for giredestrant and doctor's choice of hormonal therapy.

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.**

7. Are there plans for other studies?

Studies with giredestrant are happening:

- 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)
- pionERA Breast Cancer: giredestrant in combination with palbociclib, ribociclib, or abemaciclib in ER-positive, HER2-negative, breast cancer that has spread to other parts of the body (NCT06065748)

8. Where can I find more information?

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

- https://www.clinicaltrials.gov/study/NCT04576455
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001984-10
- https://forpatients.roche.com/en/trials/cancer/bc/a-study-evaluating-the-efficacy-and-safety-of-gdc-9545--37336.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “Giredestrant for Estrogen Receptor-Positive, HER2-Negative, Previously Treated Advanced Breast Cancer: Results From the Randomized, Phase II acelERA Breast Cancer Study”. The authors of the scientific paper are: Miguel Martín, Elgene Lim, Mariana Chavez-MacGregor, Aditya Bardia, Jiong Wu, and others. The paper is published in the journal ‘Journal of Clinical Oncology’, volume number 42, on pages 2149–2160.

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-and-safety-of-gdc-9545--37336.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 Study Evaluating the Efficacy and Safety of Giredestrant Compared With Physician's Choice of Endocrine Monotherapy in Participants With Previously Treated Estrogen Receptor-Positive, HER2-Negative Locally Advanced or Metastatic Breast Cancer”.

The study is known as ‘acelERA Breast Cancer’.

- The protocol number for this study is: WO42312.
- The ClinicalTrials.gov identifier for this study is: NCT04576455.
- The EudraCT number for this study is: 2020-001984-10.