Summary of Clinical Trial Results

A study to find out what happens to a new medicine inside women's bodies – and to look at different forms of the medicine (giredestrant)

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).

This summary is written for:

- Members of the public
- People who took part in the study

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

The study started in December 2020 and finished in April 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 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 the medicine that was studied – "giredestrant".

Key information about this study

- This study was done to find out what happens to a new medicine inside women's bodies.
- People in this study were given the study medicine, giredestrant, in different forms.
- This study included 16 healthy women in one country.
- One of the findings was that giredestrant is excreted mainly in the feces and very little is removed in urine.
- A comparison of two different capsule formulations of giredestrant showed both deliver approximately the same amount of medicine in the body. This was about 60% of the amount compared to when giredestrant was given intravenously.
- There were no serious side effects in this study.

1. General information about this study

Why was this study done?

Breast cancer is the most common type of cancer in women. About 80% of breast cancers express a protein called "**estrogen receptor**", or "**ER**" for short.

- If the ER protein is present on cancer cells, the disease is known as "ER+ breast cancer".
- A protein in the body called "**estrogen**", which is a type of hormone, can bind to the ER protein.
- When estrogen is bound to ER, the cancer cells are able to grow and spread.

Treatments for ER+ breast cancers include medicines that interfere with the formation of estrogen or with its activity. Many patients' cancers come back after the treatments work for a while – the cancer "**relapses**". In some patients, the cancer stops responding to treatment – the cancer becomes "**resistant**".

The gene for the ER-alpha protein is called "***ESR1***". Changes (**mutations**) in the *ESR1* gene can make the cancer cells grow and spread without the need for estrogen. This makes cancer medicines that work on estrogen become ineffective.

Giredestrant is a new type of medicine that may be useful for treating ER+ breast cancer. It works on ER+ breast cancers with mutations in the *ESR1* gene as well on those that do not have these mutations.

Giredestrant has been studied in several clinical trials for ER+ breast cancer. This study was done to take a detailed look at what happens to giredestrant in the body of healthy women who were not pregnant, unable to have children, and were not breastfeeding.

What were the study medicines?

Giredestrant is a study medicine taken by mouth. It is also known as "**GDC-9545**".

- Giredestrant binds to the ER protein in cancer cells and blocks estrogen from binding the ER protein.
- Giredestrant also breaks down the ER protein. This is another way to interfere with estrogen binding to the ER protein.
- When estrogen cannot bind the ER protein (because of giredestrant), it leads to a stop or slowdown of cancer cell growth.
- Giredestrant is a type of study medicine known as a "hormone therapy" or "endocrine therapy". It is also known as a "**SERD**", which stands for "selective estrogen receptor degrader".

In Part 1 of the study, people got the study medicine in the form of **[^{14}C]-giredestrant**. The [^{14}C] is a **radiolabel**.

- Radiolabeling is a technique used for tracking a medicine. Even if the medicine breaks down or undergoes a chemical change in the body, the radiolabel will still be present.
- Using a radiolabel allowed researchers to study how [^{14}C]-giredestrant was removed from the body (**excreted**).

In Part 2 of the study, people got giredestrant in three different forms (formulations).

- Giredestrant as a solution given intravenously (via IV).
- Giredestrant in capsule form – F12.
- Giredestrant in capsule form – F18.

What did researchers want to find out?

The main questions that researchers wanted to answer were:

1. What happens to giredestrant in the body?
2. How do different formulations of giredestrant compare to each other?

What kind of study was this?

Several phrases can be used to describe this study:

- **Phase 1 study**
  This was one of the early studies to look at giredestrant. A small number of healthy people were given treatments. Information from this study will be used in other studies with more people.
- **Open-label study**
  This study was open label which means all the people in this study knew which medicine they were getting.
- **Randomized study**
  Part of the study included joining one of two groups – each group got the medicine in a different sequence. People were randomly assigned to the groups – that means a computer decided who joined which group.

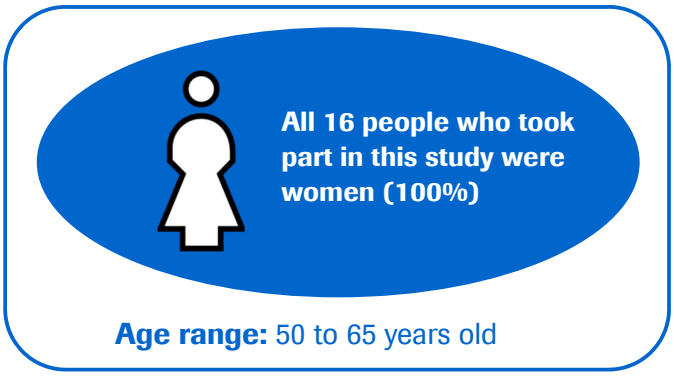
When and where did the study take place?

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

The study took place at one study center – in one country – The United Kingdom.

2. Who took part in this study?

Sixteen healthy women took part in this study.



People could take part in this study if all of the following were true:

- They were healthy women between 30 and 65 years old.
- They were not pregnant or breastfeeding, and could not get pregnant.
- They had a certain height-weight ration (BMI of 18.5 to 32.0 kg/m^2).
- They had regular daily bowel movements.

People could not take part in this study if any of the following were true:

- They had received another study medicine in the last 90 days.
- Their health or health history did not meet the study requirements.
- They were related to study center staff to any employee of the Sponsor.
- People who took part in Part 1 were not allowed to join Part 2.
- They had a history of or currently used drugs, excessive amounts of alcohol, cigarettes, or nicotine products.
- Their past radiation exposure exceeded allowed limits for the study.
- They did not have good veins for blood draws.
- They had donated more than 400 mL of blood of plasma in the last 3 months.
- They were taking medicines or had previously taken medicines that were not allowed.

3. What happened during the study?

There were 4 treatments that could be given to people in this study:

- **Treatment A**
  [14C]-giredestrant capsule, 30 mg. Taken by mouth with a glass of water.
- **Treatment B**
  Giredestrant solution, 30 mg. Given intravenously – by IV over 30 minutes.
- **Treatment C**
  Giredestrant F12 capsule, 30 mg. Taken by mouth with a glass of water.
- **Treatment D**
  Giredestrant F18 capsule, 30 mg. Taken by mouth with a glass of water.

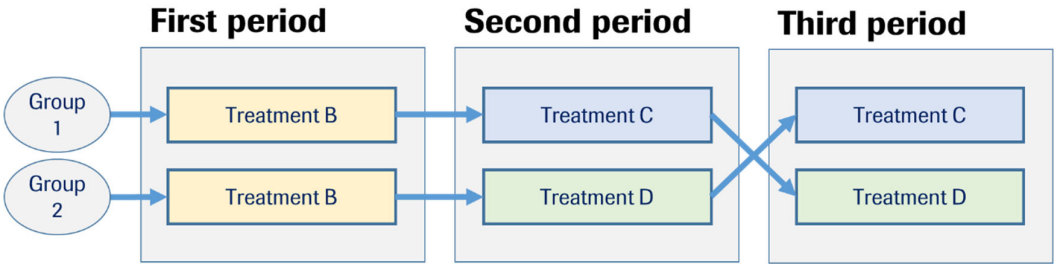
Part 1 of the study:

- Six people joined Part 1 after "**screening**" – which was a check-up to find out if they qualified for the study.
- Day -1: They checked into the clinic one day before they day they got their treatment. They provided "**baseline samples**" – before treatment. Samples included blood, urine, and feces.
- Day 1: They got **Treatment A** in the morning on Day 1 after fasting overnight (10 hours).
- During Day 1 to Day 21, they provided "**post-treatment samples**" – samples taken after treatment.
- Day 21: They checked out of the clinic on Day 21.
- Days 28, 35, and 42: After checking out, they returned to the clinic every 7 days for 24 hours to collect more samples.
- During Part 1, doctors checked the people on the study for any side effects.

Part 2 of the study:

- Ten people joined Part 2 after screening.
- In Part 2, there were **three treatment periods**: First, second, and third.
  - Each treatment period lasted from Day 1 to Day 8.
  - People got their treatment on Day 1 in each treatment period.
  - Blood samples were collected before treatment and from Day 1 to Day 8, in each period.
  - There was a "10-day washout" between periods. That means 10 days passed going from when one treatment was given to when the next one started.

- In Part 2, one day before the first treatment period: People checked into the study center and were randomized into two groups – it was decided by chance who joined Group 1 and who joined Group 2.
    - Group 1 got **Treatments B, C, and D**, in that order.
    - Group 2 got **Treatments B, D, and C**, in that order.



- All 10 people in Part 2 received a follow up call about 13 to 15 days after getting their last treatment.
- During Part 2, doctors checked the people on the study for any side effects.

4. What were the results of the study?

Question 1: What happens to giredestrant in the body?

After taking a 30 mg [^{14}C]-giredestrant capsule in Part 1 of the study:

- A large portion (67%) of the radiolabel was removed from the body (excreted) in the feces over several days. A smaller portion (9%) was excreted in the urine – measured over several days.
- The highest concentration of the radiolabel found in plasma - was reached at about 5 hours after dosing. (Plasma is the liquid part of blood without the blood cells). That means, it takes about 5 hours for giredestrant in combination with any breakdown products to reach their highest concentration in the body.
- The concentration of the radiolabel found in plasma dropped to half of its maximum – at about 48 hours after dosing. This information can help researchers figure out dosing times for patients.

Once in the body, [^{14}C]-giredestrant could undergo a chemical reaction – and change to a different molecule. The radiolabel would still be detected in the same way – whether it remained on giredestrant or was found on a different molecule.

- Researchers were able to find seven different radiolabeled molecules in plasma. That means, there was giredestrant – and there were six other new molecules that giredestrant formed in the body.

- Among all the radiolabeled molecules found in plasma, about 57% of the radiolabel was associated with giredestrant. That means a lot of giredestrant remained in its useful form – as a medicine in the body.

Question 2: How do different formulations of giredestrant compare with each other?

Researchers found all 3 formulations of giredestrant given to people in Part 2 of the study behaved similarly in the body. The time it took for giredestrant in plasma to drop to half of the highest (peak) concentration was:

- About 38 hours for the solution formulation given via IV.
- About 35 hours for F12 capsules.
- About 36 hours for F18 capsules.

Researchers found that both capsule formulations of giredestrant behaved similarly in the body:

- About 58-59% of the 30 mg giredestrant in F12 and F18 capsules became available in the body (in plasma).
- It took about 4-5 hours after taking F12 and F18 capsules for giredestrant to reach its peak concentration in the body.

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 medical problems (such as feeling dizzy) that happened during the study.

- They are described in this summary because the study doctor believes the side effects were related to the treatments in 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. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflets.
- 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 lasting problems.

There were no serious side effects reported in this study. There were no deaths reported in this study.

Most common side effects

Common side effects – those that were not considered serious but were thought to be caused by the study medicine – were absent in Part 1. In Part 2, three of 10 people (30%) had a side effect that was not considered serious, but was thought to be caused by giredestrant.

The 3 people with side effects in Part 2 of the study included:

- One person who got giredestrant solution via IV experienced night sweats.
- One person who got giredestrant F12 capsule experienced feeling tired (fatigue).
- One person who got giredestrant F18 capsule experienced a headache.

No one in this study stopped taking part in the study because of side effects.

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?

The information presented here is from a single study of 16 healthy women. These results helped researchers learn more about what happens to giredestrant in the bodies of women.

Researchers found the 2 different capsule formulations of giredestrant resulted in similar amounts of medicine in the bodies of healthy women.

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.

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7. Are there plans for other studies?

Several studies with giredestrant are ongoing and others are planned.

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/NCT04680273

https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-004650-29/results

https://forpatients.roche.com/en/trials/healthy-volunteers/study-to-investigate-the-absorption--metabolism--and-ex-28355.html

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/About.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 organized and paid for this study?

This study was organized and paid for by Genentech, Inc., South San Francisco, CA, USA. Genentech is part of F. Hoffmann-La Roche Ltd., with headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is:

A phase 1, single center, open-label, partially randomized, two part study to investigate the absorption, metabolism, and excretion of [^{14}C]-GDC-9545 following a single oral dose (Part 1) and to evaluate the absolute bioavailability of oral capsule formulations of GDC-9545 F12 and F18 and the relative bioavailability of F18 compared to F12 (Part 2) in healthy female subjects of non-childbearing potential

- The protocol number for this study is GP42662.
- The ClinicalTrials.gov identifier for this study is NCT04680273.
- The EudraCT number for this study is 2020-004650-29.