Summary of Clinical Trial Results

The effect of a new medicine (giredestrant or GDC-9545) in patients with ER+ 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).

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 July 2019 and finished in May 2021. This summary was written after the study 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.

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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 ER+ breast cancer and the medicine that was studied, "giredestrant".

Key information about this study

- This study was done to find out if giredestrant could slow down the growth of ER+ breast cancer cells in patients.
- In this study, biopsies were taken before and after patients got the study medicine.
- This study included 75 patients in 5 countries.
- The main finding was that taking giredestrant once daily for about 2 weeks caused a slow-down in the growth of cancer cells.
- None of the patients had any serious side effects thought to be caused by giredestrant.

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 protein is called "***ESR1***". Changes (**mutations**) in the *ESR1* gene are common in breast cancer that has spread throughout the body (**metastasized**). Mutations 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.

Giredestrant works on ER+ breast cancers that have mutations in the *ESR1* gene. Giredestrant also works on ER+ breast cancers that do not have these mutations.

This study was done to find out whether giredestrant was effective in slowing down ER+ breast cancer cell growth in patients. Researchers also wanted to find out if it was safe and if patients could tolerate this medicine.

What was the study medicine?

The study medicine was "**giredestrant**". It is also known as "**GDC-9545**".

- Giredestrant is a study medicine taken by mouth.
- Giredestrant binds to the ER protein in cancer cells. This reduces the ability of estrogen to bind to the ER protein. This stops or slows down cancer cell growth.
- Giredestrant also breaks down the ER protein. This removes the "fuel" for the cancer to grow.
- Giredestrant is a type of study medicine known as a "hormone therapy" or "endocrine therapy".
- Giredestrant is also known as a "**SERD**", which stands for "selective estrogen receptor degraders".
- Giredestrant may be useful for patients with ER+ breast cancer.

What did researchers want to find out?

The main question that researchers wanted to answer was:

1. Does giredestrant slow down the growth of cancer cells in patients with ER+ breast cancer?

Other questions that researchers wanted to answer included:

2. What dose of giredestrant was safe and tolerable for patients with ER+ breast cancer?
3. What happens to giredestrant in the body of patients with ER+ breast cancer?

What kind of study was this?

This was a "**Phase 1**" study, which means that this was one of the early studies for giredestrant. A small number of patients with ER+ breast cancer took giredestrant. The researchers did medical tests on them to find out more about the effect of giredestrant.

This study was "**open label**", which means that the patients and the researchers knew which medicine and what dose the patients were getting.

When and where did the study take place?

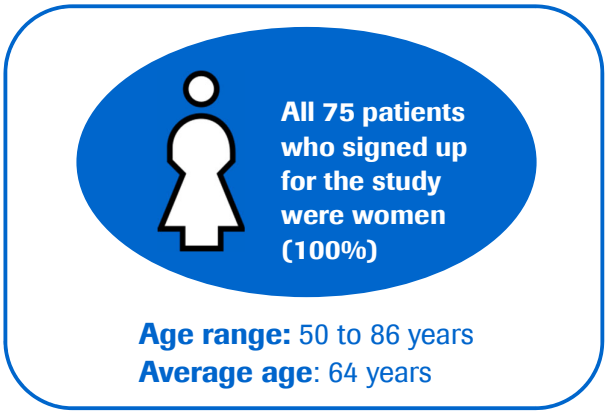
The study started in July 2019 and finished in May 2021. This summary was written after the study ended.

The study took place at 15 study centers across 5 countries:

- Australia
- Belgium
- Spain
- United Kingdom
- United States

2. Who took part in this study?

Seventy-five patients with HER+ breast cancer signed up for the study. The cancer was Stage 1, 2, or 3, and could be operated on.



People could take part in the study if:

1. They were at least 18 years old.
2. They had a main (primary) tumor that was at least 1.5 cm. They did not have any metastasized tumors away from the primary tumor – no distant metastasis.
3. They had ER-positive and HER-2 negative tumor confirmed through lab tests. That means the tumor had ER protein present and HER2 protein absent.
4. They had sufficient functioning organs in their bodies.
5. They were confirmed to be postmenopausal women.
6. They had submitted a tumor biopsy before the study began.

People could not take part in the study if:

1. They had a diagnosis of inflammatory or bilateral breast cancer.
2. They had been previously treated for primary breast cancer.
3. They were using hormone replacement therapy.
4. They were getting approved or experimental cancer treatments.
5. They had a medical condition or lab test results that could make it difficult to understand the effect of the study medicine.

3. What happened during the study?

Patients were examined (screened) before the study began. The tumors that patients had were graded – Grades 1, 2, or 3. In addition, patients were recorded as nodal positive or nodal negative – based on whether the lymph nodes in the underarm area contained cancer.

A computer program made sure that patients with different tumor grades and nodal status were spread evenly in three different dose groups.

One patient took back (withdrew) her agreement (consent) to the study. Therefore, 74 patients were treated.

The treatment dose groups for giredestrant were:

- 10 mg, 17 patients.
- 30 mg, 40 patients.
- 100 mg, 18 patients.

Treatment started on Day 1 of the study and lasted for about 14 days. Patients took their pills by mouth once daily at about the same time each day, with or without food.

Biopsy was done before treatment started – these were the pre-treatment samples. For post-treatment samples, biopsy was done on Day 14 for some patients. For others, tissue was collected during surgery. Surgery took place between days 13 and 17. Patients were required to take their medicine up to the day of surgery.

When the treatment period was over, patients were asked to go back to see their doctor anytime after 4 weeks from the day they stopped the treatment. Patients could keep seeing their doctor periodically up to 30 months.

4. What were the results of the study?

Question 1: Does giredestrant slow down the growth of cancer cells in patients?

Researchers looked at tissue samples placed on a glass slide. Samples were stained with a dye (Ki67 antibody) to mark cells that were actively growing.

In comparing pre-treatment and post-treatment tissue, researchers found that growth slowed down. This means that giredestrant was working. The average reduction in growth rate was:

- 80% for the 10 mg group.
- 76% for the 30 mg group.
- 78% for the 100 mg group.

Question 2: What dose of giredestrant was safe and tolerable for patients with ER+ breast cancer?

Researchers found that all 3 dose levels that were studied were safe and tolerable for patients.

Question 3: What happens to giredestrant in the body of patients with ER+ breast cancer?

Researchers found that the amount of giredestrant increased in the body with increasing doses of the medicine. The results for patients with ER+ breast cancer were in agreement with other studies of giredestrant in people.

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.

During this study, none of the 74 patients who received giredestrant reported any serious side effect thought to be caused by giredestrant.

There were no deaths reported during the study.

Most common side effects

During this study, around 32 of the 74 patients (43%) who received the treatment experienced a total of 60 side effects that was thought to be caused by the study medicine but not considered serious.

The most common side effects –not all – across all treatment groups are shown. Some people had more than one side effect – this means that they are included in more than one row in the table below.

Side effect	Number of patients
Feeling sick to stomach (nausea)	7 patients (10%)
Feeling tired (fatigue)	6 patients (8%)
Feeling dizzy	5 patients (7%)
Feeling hot (hot flush)	4 patients (5%)
Feeling weak (asthenia)	3 patients (4%)
Joint pain (arthralgia)	3 patients (4%)
Diarrhea	2 patients (3%)
Eye floaters and flashes (photopsia)	2 patients (3%)
Having eyesight problems (blurred vision)	2 patients (3%)
Headache	2 patients (3%)
Stomach discomfort (dyspepsia)	2 patients (3%)

One patient interrupted her treatment because of the side effect of vomiting thought to be related to giredestrant. After 2 days, she went back to taking her pills.

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 75 people with ER+ breast cancer who could have an operation – 74 people took their pills and were analyzed. These results helped researchers learn more about this disease and giredestrant.

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7. Are there plans for other studies?

Other studies with giredestrant are ongoing and still 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/NCT03916744

https://www.clinicaltrialsregister.eu/ctr-search/trial/2018-003798-85/results

https://forpatients.roche.com/en/trials/cancer/bc/a-study-of-gdc-9545-in-postmenopausal-women-with-stage--78587.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 I, Multi-Center, Open-Label, Preoperative Short-Term Window Study of GDC-9545 In Postmenopausal Women With Stage I-III Operable, Estrogen Receptor-Positive Breast Ca”.

- The protocol number for this study is GO40987.
- The ClinicalTrials.gov identifier for this study is NCT03916744.
- The EudraCT number for this study is 2018-003798-85.