Summary of Clinical Trial Results

Study of a new medicine called "GDC-0927" in women who have a certain kind of 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 March 2015 and stopped in January 2020.

The study of GDC-0927 was stopped early by the sponsor because the sponsor learned more about GDC-0927 and similar medicines then decided to developed another study medicine.

The decision to stop was not based on any safety concerns for this medicine. Patients benefitting from study treatment continued their treatment until their breast cancer got worse or the medicine was no longer available.

This summary was written after the study had ended.

Contents of the summary

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.**

Thank you to the people who took part in this study

The patients who took part have helped researchers answer important questions about a type of breast cancer and the study medicine called, "GDC-0927". The type of breast cancer studied was ER-positive and HER2-negative, written as, "**ER+/HER2−**".

Key information about this study

- This study was done to test different doses of a study medicine. Researchers wanted to find a dose that was safe for possible future studies.
- This study stopped early because the sponsor learned more about GDC-0927 and similar medicines, then decided to develop another study medicine. This decision was not based on any safety concerns.
- In this study, everyone received a study medicine called, “GDC-0927”.
- This study included 42 women in 2 countries.
- Thirty of 42 patients (70%) in this study had at least one side effect from the study medicine.
- The side effects seen in this study were tolerable (mild to moderate in severity).
- No one had any serious (life-threatening) side effects caused by the study medicine.
- The cancer in 14 patients (39%) showed a response of stable disease (disease that did not get better or worse).

1. General information about this study

Why was this study done?

Breast cancer is the most common type of cancer in women. In many patients, the cancer produces a protein in cancer cells called "**estrogen receptor**" or "**ER**" for short. The cancer can also produce another protein called "**HER2**". Both of these proteins help cancer cells to live and grow.

Treatments for breast cancer can depend on the types of protein that the patient's cancer produces.

This study looked at patients whose cancers had the ER protein but not HER2. This type of breast cancer is called, "ER-positive and HER2-negative", written as, "**ER+/HER2−**".

- ER+/HER2− breast cancer grows in response to a protein in the body, called "**estrogen**, which is a type of hormone.
- Estrogen binds to the ER protein found in ER+ breast cancer, and causes the cancer cells to grow and spread.

Treatments for ER+ breast cancers include medicines - that block the "**estrogen bound to the ER protein**" structure and reduce the amount estrogen in the body - which can slow or stop the growth of cancer cells.

There are many treatments for patients with ER+/HER2− breast cancer. However, over time, the cancer can come back (**relapse**). The tumor proteins can also change (**mutate**) and stop responding to treatments (tumor becomes **resistant**).

Certain genes affect response to treatment. One such gene is called *ESR1*. A mutation in the *ERS1* gene called an "***ESR1* mutation**" can happen in the gene for the ER protein. The ESR1 mutation may make tumors resistant to some treatments for ER+ cancers. Not all patients will have tumors with *ESR1* mutations.

There is a need for new treatments for patients with ER+/HER2− breast cancer. This study was done because researchers wanted to find out if a new experimental medicine (that health authorities have not approved for the treatment of breast cancer) called "**GDC-0927"** might be useful for patients with ER+ breast cancer.

This study was done to find out if GDC-0927 was safe for patients with ER+/HER− breast cancer.

What was the study medicine?

The study medicine was called, "**GDC-0927**".

- GDC-0927 is a study medicine that binds to the ER protein.
- GDC-0927 blocks the ability of estrogen (a hormone) to bind to the ER protein and breaks down the ER protein.
- GDC-0927 is a type of study medicine known as a "hormone" or "endocrine therapy".
- GDC-0927 is taken by mouth.
- GDC-0927 may be useful for patients with ER+/HER− breast cancer.

What did researchers want to find out?

The main questions that researchers wanted to answer were:

1. What was the highest dose of GDC-0927 that was safe for patients with ER+/HER− breast cancer?
2. What was the recommended dose of GDC-0927 for possible further studies?

Other questions that researchers wanted to answer included:

3. Was GDC-0927 safe for patients with ER+/HER− breast cancer?

What kind of study was this?

This was a "**Phase 1**" study. Phase 1 studies test a new medicine to see if it is safe for patients. This was the first time GDC-0927 was given to patients.

The study was divided into two parts, a "**dose-escalation**"part (where different doses were tested) and a "**dose-expansion**"part (where one dose was tested).

This study was done to find out what effects, good and/or bad, GDC-0927 had on patients and their ER+/HER−breast cancer.

In the first part of the study (dose escalation), the dose started low and slowly increased as new patients joined the study. The dose kept increasing for new groups of patients as as long as it did not cause bad side effects.

In the second part of the study (dose-expansion), researchers tested one dose of the study medicine in a larger group of patients. Researchers agreed upon this dose after looking at results from the dose-escalation study that showed this dose was safe for future studies.

When and where did the study take place?

The study started in March 2015 and stopped early because the Sponsor decided not to investigate GDC-0927 any further. This decision was not related to safety.

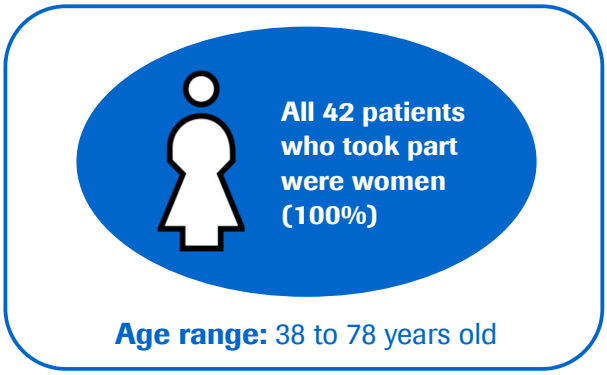
This summary presents the results of the study up until it was stopped in January 2020.

The study took place at 14 study centers in the USA (6 sites) and Spain (8 sites).

2. Who took part in this study?

Forty-two women took part:

- The women were postmenopausal, which means their menstrual period had stopped due to age or medical reasons.
- They had ER+/HER– breast cancer.
- Some women had cancers that had **advanced** in the original site or had spread to other parts of the body (**metastasized**).



Women could take part in the study if:

- They were at least 18 years old.
- Their disease had become worse after at least 6 months of therapy for ER+ breast cancer.
- They had no more than 2 chemotherapy treatments after their disease became worse.
- Enough time had passed since they had received certain previous cancer treatments.
- They did not have side effects from their previous treatments,

Women could not take part in the study if:

- Their cancer had metastasized to the brain and was not under control.
- They were currently receiving treatment for their cancer.
- They were taking certain medicines for other causes.
- They had heart disease within the last 12 months.
- They had liver disease, diseases of the stomach, or HIV infection.
- They had surgery in the 4 weeks prior to this study.

Dose-expansion part of the study

- Patients were allowed to join the dose-expansion if their breast cancer became worse after 1 chemotherapy treatment.

3. What happened during the study?

Patients who joined the dose escalation study were in 1 of 3 groups. The doses tested were 600 mg, 1000 mg, and 1400 mg.

After dose escalation was finished, patients who joined the dose-expansion study got GDC-0927 1400 mg once daily.

Study	Dose groups	Number of patients
Dose-escalation	600 mg	3
	1000 mg	3
	1400 mg	6
Dose-expansion	1400 mg	30

Treatments
Patients took their GDC-0927 tablets by mouth once daily, after fasting for at least 6 hours overnight and for 2 hours after taking the tablets.

What was done during the study
Patients were seen by their doctors on a regular basis. Doctors collected blood and urine samples from patients for lab analyses and did other tests. Doctors found out how patients were reacting to the treatment. They noted and treated any side effects that the patients got.

How much medicine did patients get
Patients and their doctors could decide to stop their treatments at any time. The number of days that patients took their medicine varied from 32-1127 days, with half of the patients receiving more than 99 days of treatment.

What happened to patients on the study
Most patients stopped the study when their disease became worse (38 patients, 90%). The Sponsor stopped the study, and 4 patients (10%) came off the study that way. These four patient got other study medicine after this study finished.

4. What were the results of the study?

Question 1: What was the highest dose of GDC-0927 that was safe for patients with ER+/HER– breast cancer?

None of the doses that were tested caused bad or unmanagable side effects. All the doses were considered safe.

Question 2: What was the recommended dose of GDC-0927 for possible future studies?

Researchers decided that GDC-0927 1400 mg taken once daily was the recommended dose for future studies.

Question 3: Was GDC-0927 safe for patients with ER+/HER– breast cancer?

Researchers found that GDC-0927 1400 mg taken once daily was considered safe for patients. At this dose, the best tumor response seen was stable disease (disease that did not get better or worse) in 14 patients (39%).

Section 4 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 happen 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 leaflet.
- Side effects can vary from mild to very serious and may vary from person to person.
- 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, there were no serious side effects thought to be caused by the study medicine.

There were no deaths reported in this study.

Most common side effects

During this study, 30 out of 42 patients (71%) had a side effect considered not serious, but was thought to be caused by the study medicine.

The most common side effects (seen in more than 10% of the patients) 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.

Common side effects in this study	Number of patients with side effect
Feeling sick to your stomach (nausea)	8 patients (19%)
Suddenly feeling very warm (hot flashes)	8 patients (19%)
Constipation	6 patients (14%)
Diarrhea	5 patients (12%)
Feeling tired (fatigue)	5 patients (12%)

During the study, none of the patients stopped taking their medicine because of side effects, but 2 patients (5%) changed or interrupted their dose due to 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 42 patients. These results helped researchers learn more about ER+/HER– breast cancer.

GDC-0927 is a type of hormone therapy and researchers were able to gather information about its safety and usefulness in patients with ER+/HER– breast cancer that had advanced or had metastasized.

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7. Are there plans for other studies?

At the time of writing this summary, there are no more studies planned for testing GDC-0927 any further.

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/NCT02316509

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the For Patients 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:

"An Open-Label, Phase I Study of GDC-0927 in Postmenopausal Women with Locally Advanced or Metastatic Estrogen Receptor Positive Breast Cancer".

- The protocol number for this study is **GO29656**.
- The ClinicalTrials.gov identifier for this study is **NCT02316509**.
- The EudraCT number for this study is **2015-000272-95**.