Summary of Clinical Trial Results

A study to compare the study medicine (GDC-0810) to another treatment (fulvestrant) in patients with 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.
- Participants – these are the patients who took part in the study.

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

The study started in December 2015 and stopped in February 2020.

The study 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 the 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.

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 patients who took part have helped researchers to answer important questions about a type of breast cancer and the study medicine (GDC-0810). The type of breast cancer that was studied was ER-positive and HER2-negative, written as, "**ER+/HER2−**".

Key information about this study

- This study was done to compare the effects of the study medicine, GDC-0810, to fulvestrant, an approved medicine.
- The study of GDC-0810 was stopped early by the sponsor. The sponsor learned more about GDC-0810 and similar medicines, and then decided to develop another study medicine.
- The decision to stop the study of GDC-0810 was not because of any side effects. Patients benefitting from the study treatment (GDC-0810 or fulvestrant) continued their treatment until their breast cancer got worse or the medicine was no longer available.
- Since the study of GDC-0810 was stopped early, there is not enough study data to compare the results of GDC-0810 to fulvestrant.
- This study enrolled 71 patients in 6 countries.
- Patients were assigned by chance (like tossing a coin) to one treatment group: GDC-0810 or fulvestrant.
- The common side effects seen in this study were tolerable (mild to moderate in severity).
- One patient (3%) taking GDC-0810 had a serious side effect thought to be caused by GDC-0810.
- No patients taking fulvestrant had any serious side effects caused by that treatment.

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 with breast cancer, the tumor produces a protein called "**estrogen receptor**" or "**ER**" for short. Another protein that tumors can produce is 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 tumor produces. This study looked at patients whose tumors 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 affect 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-0810**" could be useful for patients with ER+/HER2− breast cancer.

What was the study medicine?

The study medicine was called, "**GDC-0810**".

- GDC-0810 binds to the ER protein.
- GDC-0810 blocks the ability of estrogen (a hormone) to bind to the ER protein, and also breaks down the ER protein.
- GDC-0810 is a type of medicine known as a "hormone" or "endocrine therapy".
- GDC-0810 was taken by mouth.

GDC-0810 was to be compared to another medicine, called, "**fulvestrant**".

- Fulvestrant is a medicine that is approved for use in patients with ER+/HER2− breast cancer.
- Fulvestrant works by binding to the ER protein and also breaks down the ER protein.
- Fulvestrant was given by intramuscular injections.

What did researchers want to find out?

Researchers did this study to compare the study medicine (GDC-0810) with an existing medicine (fulvestrant).

The main questions that researchers wanted to answer were:

1. How effective was GDC-0810 in comparison to fulvestrant for patients with ER+/HER2− breast cancer?
2. How effective was GDC-0810 in comparison to fulvestrant for patients with ER+/HER2− breast cancer with *ESR1* mutation?

What kind of study was this?

Phase 2 study
This study was a "Phase 2" study. It tested one dose of GDC-0810, 600 mg, in patients. Before this study, the 600 mg dose was tested in some patients with ER+/HER2−breast cancer in a Phase 1 study.

Phase 1 studies are done to test if a new medicine is safe. The Phase 1 study for GDC-0810 tested different doses and found that 600 mg was the highest dose of GDC-0810 that did not cause bad side effects.

In this study, women with ER+/HER2− breast cancer got GDC-0810 or fulvestrant treatments. This was done to compare the effects of GDC-0810 to fulvestrant.

Randomized study
The study was '"randomized". That means that it was decided by chance which treatment group (GDC-0810 or fulvestrant) – that patients in the study would join – just like tossing a coin.

Randomly choosing which medicine patients get makes it more likely that the types of patients in both groups (for example, age, race) will be a similar mix.

Apart from the medicines being tested in each group, all other aspects of care were the same between the groups.

Open-label study
This study was "open-label" because patients and doctors knew which treatment the patients were getting, after a computer randomly decided which group each patient joined.

When and where did the study take place?

The study started in December 2015 and was stopped early by the sponsor. The sponsor learned more about GDC-0810 and similar medicines then decided to developed another study medicine.

The decision to stop the study of GDC 0810 was not because of any bad side effects. Patients benefitting from study treatment (GDC-0810 or fulvestrant) continued their treatment until their breast cancer got worse or study drug was no longer available.

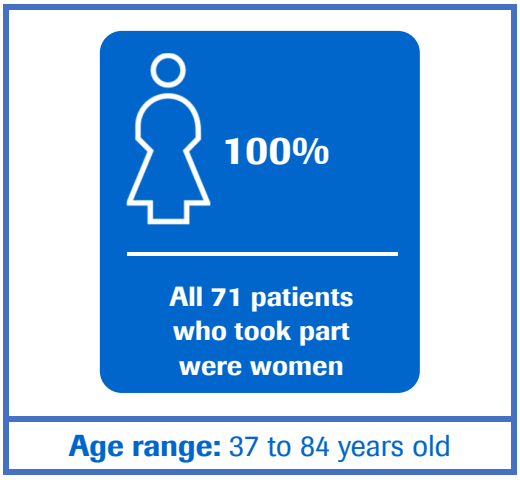
This summary presents the results of the study up until the last patient finished study treatment in February 2020.

The study took place at 26 study centers in 6 countries:

- Australia (4 centers)
- Germany (1 center)
- Korea (6 centers)
- Spain (8 centers)
- United Kingdom of Great Britain and Northern Ireland (4 centers)
- United States of America (3 centers)

2. Who took part in this study?

There were 71 patients with breast cancer who took part in this study.



Patients could take part in the study if:

- They had ER+/HER2– breast cancer that had metastasized (spread to other parts of the body), or had remained in the breast tissue and got worse with other cancer treatments.
- They could not get pregnant - because of age or because of medical reasons.
- They were at least 18 years old.

Patients could not take part in the study if:

- They had received fulvestrant treatment before joining this study.
- They had received or were receiving cancer treatments for their current disease.
- Their cancer had metastasized to the brain and was not treated. Patients whose brain cancers were treated could join this study under some circumstances.
- They had certain other health issues.

3. What happened during the study?

Patients joined the study at different times. There were two treatment groups. It was decided at random by a computer - which treatment group each patient joined.

Treatment Groups:

Group A Total patients = 36 Patients with *ESR1* mutation = 14	**Group B** Total patients = 35 Patients with *ESR1* mutation = 11
Treatment: **GDC-0810** 600 mg, taken by mouth once daily, within 30 minutes of eating.	**Treatment:** **Fulvestrant** 500 mg given by injection into the muscle once every 4 weeks. Fulvestrant is an approved treatment. (The first treatment was split into two 250 mg injections given two weeks apart.)
Patients were treated until one of the following happened: • Their disease became worse. • They could not tolerate the side effects. • They decided to stop participating in the study (withdrew consent). • The Sponsor stopped the study.	**Patients were treated until one of the following happened:** • Their disease became worse. • They could not tolerate the side effects.

During the study, patients were seen at the clinic to check their overall health. They got medical tests throughout the study. They were treated for side effects when it was needed.

The study was stopped early by the sponsor because researchers had developed a newer medicine. The decision to stop the study of GDC-0810 was not because of any side effects. Patients benefitting from study treatment (GDC-0810 or fulvestrant) continued their treatment until their breast cancer got worse or study drug was no longer available.

4. What were the results of the study?

Question 1: How effective was GDC-0810 in comparison to fulvestrant for patients with ER+/HER2− breast cancer?

Since the study of GDC-0810 was stopped early, there is not enough study data to compare the results of GDC-0810 to fulvestrant.

Question 2: How effective was GDC-0810 in comparison to fulvestrant for patients with ER+/HER2− breast cancer with *ESR1* mutation?

Since the study of GDC-0810 was stopped early, there is not enough study data to compare the results of GDC-0810 to fulvestrant.

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 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 patients in this study had all of the side effects.
- Side effects may be mild to 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, results regarding serious side effects were available for 35 patients in each treatment group.

Serious side effects	**Group A** Treatment: **GDC-0810**	**Group B** Treatment: **fulvestrant**
How many patients had serious side effects related to the treatment?	1 out of 35 patients (3%)	None of the 35 patients (0%)
What was the serious effect?	Feeling sick to stomach (nausea)	None

Deaths

There were 12 patient deaths (34%) in the GDC-0810 treatment group and 4 patient deaths (11%) in the fulvestrant treatment group.

The main cause of death for 15 patients was worsening of patient's cancer (disease progression). One patient death was due to getting foreign material (food, liquid, or something else) into the lungs. This condition is known as "aspiration", and can happen when a person has difficulty swallowing. This death was not caused by the study medicine.

Most common side effects

During this study, 41 of 70 patients (59%) reported they had a side effect that was not considered serious, but was caused by the treatment.

- **Group A** (GDC-0810)**:** 26 out of 35 patients (74%) had a side effect thought to be caused by the treatment.
- **Group B** (fulvestrant)**.:** 15 of 35 patients (43%) had a side effect thought to be caused by the treatment

The most common side effects are shown in the following table – these happened in at least 5% of the patients. Some patients had more than one side effect – that means that they are included in more than one row in the table

Group A (GDC-0810)		**Group B (fulvestrant)**	
Common side effects	**Number of patients with side effect**	**Common side effects**	**Number of patients with side effect**
Diarrhea	12 patients (34%)	Feeling tired (fatigue)	6 patients (17%)
Feeling sick to stomach (nausea)	11 patients (31%)		
Feeling weak (asthenia)	7 patients (20%)		
Vomiting	6 patients (17%)		

During the study, some patients stopped taking their medicine for a while or took a lower dose - because of side effects. This included:

- Group A (GDC-0810): 13 patients (37%).
- Group B (fulvestrant): 1 patient (3%).

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 GDC-0810 in patients with ER+/HER2− breast cancer.

These results helped researchers learn more about GDC-0810 and ER+/HER2− breast cancer.

The study was stopped early. There is not enough study data to compare the results of GDC-0810 to fulvestrant. Results from this study would have been more meaningful if there were more patients in the treatment groups (larger treatment 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 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?

At the time of writing this summary, no more studies looking at GDC-0810 are planned at the current time.

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/NCT02569801

https://www.clinicaltrialsregister.eu/ctr-search/search?query=2015-000106-19

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 II, Open-Label, Randomized Study of GDC-0810 versus fulvestrant in Postmenopausal Women with Advanced or Metastatic ER+/HER2− Breast Cancer Resistant to Aromatase Inhibitor".

- The study is known as "**HydranGea**".
- The protocol number for this study is **GO29689**.
- The ClinicalTrials.gov identifier for this study is **NCT02569801**.
- The EudraCT number for this study is **2015-000106-19**.