Clinical Trial Results – Layperson Summary

A study to compare different doses of fenebrutinib with a "placebo" – in patients with an autoimmune disease called "chronic spontaneous urticaria"

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 patients who took part in the study

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

The study started in May 2017 and finished in October 2019. This summary was written after the study ended.

No single study can tell us everything about the risks and benefits of a medicine. Many people volunteer in several studies to help us 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 chronic spontaneous urticaria and different doses of the study medicine.

Key information about this study

- In this study, participants were given different doses of a treatment.
- The treatment was a medicine (fenebrutinib) or no medicine (placebo).
- This study was done to find out if fenebrutinib could be effective for patients with chronic spontaneous urticaria (CSU).
- Researchers wanted to see what the results would be if treatments were given with fenebrutinib in comparison to treatments with the placebo.
- This study included 134 patients in 3 countries.
- This study found that fenebrutinib showed an improvement in CSU signs and symptoms in patients at 2 out of 3 doses tested in this study, in comparison to the placebo.
- There were more side effects in patients who got fenebrutinib in comparison to those who got the placebo.
- This report was written after the study was completed.

1. General information about this study

Why was this study done?

Chronic spontaneous urticaria (**CSU**) is an "autoimmune" disease, where your own immune system damages your body.

Patients may get hives (**urticaria**), which are swollen bumps that appear without any known reason. Other patients may get a swelling under the skin that looks puffy and can be painful (**angioedema**).

Patients are diagnosed with CSU if they get one or both symptoms without any known reason, with symptoms lasting for 6 weeks or longer.

There are several medicines available for treating CSU. However, some patients do not respond to available treatments (up to 4-times the approved dose of antihistamine therapy). Researchers are trying to find new medicines that are more effective.

Fenebrutinib is an experimental medicine that blocks a protein called "**Bruton's tyrosine kinase"** or **"BTK"** for short. This affects the immune cells that cause autoimmune diseases, such as CSU.

Researchers carried out this study to compare treatments with fenebrutinib against placebo. The placebo looked like fenebrutinib, but did not contain medicine.

Researchers wanted to find out what effect, good or bad, fenebrutinib had on patients with CSU who did not respond to available treatments.

What was the study medicine?

Fenebrutinib, also known as **GDC-0853**, is a medicine that has been given to people in other studies for other autoimmune diseases. Here is how the medicine works:

- Fenebrutinib blocks a protein called, "**BTK**".
- BTK is present in different types of immune cells in your body.
- Blocking BTK makes these immune cells unable to function normally.
- Researchers have already tested different doses of fenebrutinib in humans.
- Fenebrutinib has shown benefit in patients with other types of autoimmune disease.

Fenebrutinib was compared to "**placebo**".

- In this study, some patients got fenebrutinib while others got placebo.
- The placebo looked the same as fenebrutinib but did not contain any real medicine.

What did researchers want to find out?

Researchers did this study to compare the study medicine against the placebo.

The main question that researchers wanted to answer were:

1. Is fenebrutinib effective in CSU patients who do not respond to high doses of currently available treatments?

Another question that researchers wanted to answer was:

2. What proportion of patients are able to see improvements after a certain period on the study?

What kind of study was this?

There are several ways to describe this study.

- **Phase 2 study**
  Phase 2 studies are carried out to find out if a study medicine is effective for patients. There were two parts to this study. First, a "**pilot study**" was carried out to find out if the treatment had any effect in CSU patients. Next, patients were enrolled in a "**dose-ranging study**" to test different doses of the study medicine.
- **Placebo-controlled study**
  Some people got fenebrutinib while others got placebo. This was done to be able to compare the real effect of the medicine against a treatment with no real effect.
- **Randomized study**
  A computer randomly decided which patient joined the medicine groups and which patient joined the placebo group. Researchers and patients had no control over this.
- **Double-blind study**
  The researchers and patients did not know which patient was getting the study medicine and which patient was getting the placebo. That made this a double-blind study.

When and where did the study take place?

The study started in May 2017 and finished in October 2019. The study took place at study centers in Canada (5 centers), Germany (6 centers), and USA (10 centers).

This summary was written after the study had ended.

2. Who took part in this study?

Patients with CSU could take part in this study if they had **refractory CSU**, which means, they continued to show disease symptoms despite taking an antihistamine (up to 4-times the approved dose of anti-histamines).

The study was divided into two groups:

Group 1: Pilot Study	Group 2: Dose-Ranging Study
Total = 41 patients 83% white 81% women; 19% men Average age = 42 years	Total = 93 patients 82% white 76% women; 24% men Average age = 43 years

What was required in order for patients to participate in this study

1. Provide written consents to volunteer in this study.
2. Be 18 to 75 years old.
3. Agree to use family planning methods to prevent pregnancies while participating in this study.
4. Have skin itch and hives for more than 6 weeks straight at any time before joining the study – while on approved treatment.
5. Have had CSU disease that is diagnosed by a doctor for 6 months or longer.
6. Must test negative to tuberculosis disease.

What conditions disqualified patients from participating in this study

1. Women who were breast-feeding, pregnant, or intended to get pregnant.
2. Patients who were treated for CSU using certain types of medicines.
3. Patients who were previously treated with the study medicine, fenebrutinib.
4. Patients who had symptoms of CSU but whose disease diagnosis was something else.
5. Patients with other skin diseases.
6. Patients who needed to take medicines that were not allowed on this study.
7. Patients who had major diseases other than CSU.

3. What happened during the study?

The study was divided into two treatment groups:

- Group 1 – This was a "**Pilot Study**", which means that patients in Group 1 started first to find out if the treatment was effective for CSU patients prior to enrolling more patients in Group 2.
- Group 2 – This was a "**Dose-finding Study**", which means that patients got different doses of fenebrutinib to find a dose that was effective.

The treatment was given to patients **in addition to their regular CSU medicine** (up to 4-times the approved dose of antihistamine therapy).

The "**treatment**" was either the study medicine or the placebo. Patients did not know what they were getting:

- All patients took 4 pills in the morning and 4 pills at night.
- The mixture of pills was given to patients so that:
    - In Groups 1 and 2, some patients were randomly assigned to "placebo treatment" which means they got all placebo pills.
    - Other patients were randomly assigned to "**fenebrutinib treatment**". They got a mixture of placebo and medicine pills.
      Group 1 - Patients got 200 mg of fenebrutinib twice a day.
      Group 2 – Patients were placed in "dose groups" within Group 2. Each dose group received a different dose of fenebrutinib:
        - 50 mg once daily
        - 150 mg once daily
        - 200 mg twice daily

What happened after treatment started?

- Patients got their treatment for 8 weeks.
- Patients wrote down their symptoms in a journal every day.
- There were some days when patients came in to the clinic to get their treatment. During the visit, patients gave blood samples and underwent other tests for the study.
- Patients answered questions so researchers could learn about the effects of the treatments.
- Patients were followed for 4 weeks after the treatment was over.

4. What were the results of the study?

Question 1: Is fenebrutinib effective in CSU patients who do not respond to high doses of currently available treatments?

Remember, the study treatment (fenebrutinib or placebo) was given to patients together with each patient's regular medicine (antihistamines) for CSU.

Patients were assessed after 8 weeks of treatment. All patients who got any dose of fenebrutinib had greater improvements to their disease symptoms than patients who got placebo.

Question 2: What proportion of patients are able to see improvements after a certain period on the study?

Group 1
Patients who reported that their symptoms were under control after 8 weeks of treatment:

- 16 of 28 patients (57%) who received fenebrutinib 200 mg twice daily
- 4 of 13 patients (31%) who received placebo

Group 2
Patients who reported that their symptoms were under control after 8 weeks of treatment:

- 13 of 23 patients (57%) who received fenebrutinib 200 mg twice daily
- 11 of 24 patients (46%) who received fenebrutinib 150 mg once daily
- 8 of 23 patients (35%) who received fenebrutinib 50 mg once daily
- 5 of 23 patients (22%) who received placebo

5. What were the side effects?

Side effects are unwanted medical problems (such as a headache) that happen during the study and are related to the treatment given during the study.

- Not every patient in a study has all or any of the side effects seen in the study.
- Common side effects and serious side effects are listed in the following sections.

Most common side effects

Here are the common side effects that occurred in 2 or more patients in each group. These side effects were thought to be related to the treatment.

Side effects in Group 1	Placebo treatment (13 patients)	Fenebrutinib treatment (28 patients)
Headache	3 patients (23%)	2 patients (7%)
Abnormal blood test (ALT increased)	0	2 patients (7%)
Abnormal blood test (AST increased)	0	2 patients (7%)
CSU	0	2 patients (7%)

Side effects in Group 2	Placebo treatment (22 patients)	Fenebrutinib treatment (71 patients)
Diarrhea	2 patients (9%)	1 patient (1%)
Hives (urticaria)	0	3 patients (4%)
Nausea	0	3 patients (4%)
Fatigue	2 patients (9%)	0
Discomfort in stomach (abdominal discomfort)	1 patient (5%)	1 patient (1%)
Headache	1 patient (5%)	1 patient (1%)

Serious side effects

A side effect is considered "serious" if it is life threatening, needs hospital care, or causes lasting problems.

Group 1: Two of 41 patients (5%) reported serious side effects that were considered to be related to the study treatment. One patient had infection and swelling around eye (periorbital cellulitis) and another had an abnormal blood test (increased liver enzymes).

Group 2: There were no serious effects for this group.

There were no patient deaths during this study in either group.

6. How has this study helped research?

Researchers found that adding higher doses (150 mg once daily and 200 mg twice daily) fenebrutinib to the medicines that patients already took for CSU provided improvements to CSU – for patients who were enrolled in this study.

Researchers also found that side effects thought to be caused by the treatment were seen in more patients who got fenebrutinib 200 mg twice a day compared to those who got placebo – for patients who were enrolled in this study.

7. Are there plans for other studies?

Fenebrutinib is being studied for other indications and studies can be found at:

https://clinicaltrials.gov/ct2/results?cond=&term=fenebrutinib&cntry=&state=&city=&dist=

Fenebrutinib is also known as "GDC-0853" and studies can be found at:

https://clinicaltrials.gov/ct2/results?cond=&term=GDC-0853&cntry=&state=&city=&dist=

8. Where can I find more information?

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

- USA clinical trials registry:
  https://clinicaltrials.gov/ct2/show/NCT03137069

- EU clinical trials registry:
  https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-004624-35

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
  or 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.

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, Multicenter, Randomized, Double-Blind, Placebo-Controlled Pilot and Dose-Ranging Study of GDC-0853 in Patients with Refractory Chronic Spontaneous Urticaria (CSU)”.

- The protocol number for this study is GS39684.
- The ClinicalTrials.gov identifier for this study is NCT03137069.
- The EudraCT number for this study is 2016-004624-35.