Clinical Trial Results – Layperson Summary

A study to compare different doses of fenebrutinib with a "placebo" – in patients with lupus

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 lupus patients who took part in the study

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

The study started in January 2017 and finished in July 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 lupus 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 lupus.
- 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 260 patients in 12 countries.
- This study found that fenebrutinib was not effective in lupus patients at the highest dose tested in this study in comparison to the placebo.
- Side effects were similar in groups that got the study medicine or the placebo.
- This report was written after the study was completed.

1. General information about this study

Why was this study done?

Systemic lupus erythematosus (lupus) is an "autoimmune" disease, where your own immune system damages your body.

This disease has many symptoms that include joint pain, swelling, skin rashes, sores in your mouth, and feeling extremely tired. Some patients get a very serious form of the disease that involves the brain and kidney.

There are several medicines available for treating lupus. However, some patients still die from the disease, or become disabled. 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 lupus.

Researchers carried out this study to compare treatments with fenebrutinib against a placebo. The placebo did not have any medicine; it was only made to look like medicine.

Researchers wanted to find out what effect, good or bad, fenebrutinib caused in comparison to the placebo.

What was the study medicine?

Fenebrutinib, also known as **GDC-0853**, is a medicine that has been given to people in other studies. 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.
- Researchers wanted to find out if fenebrutinib could be useful for patients with lupus.

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

- In this study, some patients got fenebrutinib while others got a 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 lupus patients?

Another question that researchers wanted to answer was:

2. Can fenebrutinib reduce the number of flare-ups of the disease?

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. This study was testing two different doses of the study medicine that researchers thought might be useful.
- **Placebo-controlled study**
  Some people got fenebrutinib while others got a placebo. This was done so that all patients got a treatment, and the real effect of the medicine could be compared against the placebo.
- **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 January 2017 and finished in July 2019. The study took place in:

- Argentina
- Brazil
- Bulgaria
- Chile
- Columbia
- Germany
- Great Britain
- Korea
- Mexico
- Spain
- Taiwan
- United States

This summary was written after the study had ended.

2. Who took part in this study?

Patients were required to have moderate to severe lupus. There were 260 patients who received treatment.

The majority of the patients were female (97%). Most of the patients were white (66%). Half of the patients were below 41 years old (median age). The youngest patient was 18 years old. The oldest patient was 72 years old.

There were 3 treatment groups:

Placebo	Fenebrutinib (150 mg once daily)	Fenebrutinib (200 mg twice daily)
Total = 84 patients 67% white 99% women Average age = 40 years	Total = 87 patients 71% white 94% women Average age = 43 years	Total = 88 patients 59% white 97% women Average age = 40 years

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

1. Provide written consents to volunteer in this study.
2. Be between 18 and 75 years old.
3. Agree to use family planning methods to prevent pregnancies while participating in this study.
4. Have lupus that is documented by a doctor.
5. Have evidence of lupus in your blood sample.
6. Must use prescription medicines to control lupus (corticosteroids, anti-malarials, and/or immunosuppressants).

What conditions disqualified patients from participating in this study

1. Lupus disease in the kidney or the brain.
2. Lupus disease that required a high dose of medicine to control it.
3. Blood test results that were out of the range specified for this study.
4. Patients with infectious diseases, cancer, and several other diseases.
5. Patients who were taking certain medicines.
6. Women who were breast-feeding, pregnant, or intended to get pregnant.

3. What happened during the study?

The study treatment was given to patients **in addition to their regular lupus medicine**.

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.
- Patients did not know whether they were getting placebo or medicine pills.
- The mixture of pills was given to patients so that:
    - One group of patients got all placebo pills. These patients were randomly assigned to the "**placebo group**" at the start of the study.
    - One group of patients got a low dose of fenebrutinib. These patients were randomly assigned to the "**fenebrutinib 150 mg once daily group**".
    - One group of patients got a high dose fenebrutinib. These patients were randomly assigned to the "**fenebrutinib 200 mg twice a day group**".

What happened after treatment started?

Patients got their treatment for 48 weeks. 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 8 weeks after the 48 weeks of treatment was over.

4. What were the results of the study?

Two hundred and fifty-nine patients got at least one treatment; 195 patients completed the 48-week study.

Question 1: Is fenebrutinib effective in lupus patients?

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

Researchers compared results for each group of patients using a measure for lupus (SRI-4 response) after 48 weeks of study treatment:

- Placebo group had 44% of patients who responded.
- Fenebrutinib 150 mg once daily group had 51% of patients who responded.
- Fenebrutinib 200 mg twice daily group had 52% of patients who responded.

There was not much improvement in the outcome by giving patients the experimental study treatment, in comparison to the placebo.

Question 2: Can fenebrutinib reduce the number of flare-ups of the disease?

Here are the results for patients and the number of flares:

- Placebo group: 6 patients (7%) experienced 11 flares.
- Fenebrutinib 150 mg once daily group: 7 patients (8%) experienced 19 flares.
- Fenebrutinib 200 mg twice daily group: 12 patients (14%) experienced 30 flares.

There was not much improvement in the outcome by including the new medicine as part of the treatment for lupus patients.

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

There were 82 patients (32%) who reported a side effect thought to be related to the study treatment. The side effects caused by the treatment that happened in two or more patients are listed in the following table:

Placebo	Fenebrutinib (150 mg once daily)	Fenebrutinib (200 mg twice daily)
Low white blood cell count (**lymphopenia**) 4 patients, (5%)	**Urinary tract infection** 3 patients (3%)	Low white blood cell count (**lymphopenia**) 4 patients, (5%)
Feeling sick (**nausea**) 4 patients (5%)	Inflammation of the nose & throat (**nasopharyngitis**) 3 patients (3%)	Feeling sick (**nausea**) 4 patients (5%)
Urinary tract infection 3 patients (4%)	Feeling sick (**nausea**) 3 patients (3%)	Low cell count for immune cells (**neutropenia**) 2 patients (2%)
Infection of the airway (**upper respiratory tract infection**) 2 patients (2%)	Low cell count for immune cells (**neutropenia**) 3 patients (3%)	Low white blood cell count (**leukopenia**) 2 patients (2%)
Diarrhea and vomiting (**gastroenteritis**) 2 patients (2%)	Infection of the airway (**upper respiratory tract infection**) 2 patients (2%)	Stomach ache (**upper abdominal pain**) 2 patients (2%)
Dry mouth 2 patients (2%)	Tuberculosis infection (**latent tuberculosis**) 2 patients (2%)	**Diarrhea** 2 patients (2%)
Low cell count for immune cells (**neutropenia**) 2 patients (2%)	Stomach ache (**upper abdominal pain**) 2 patients (2%)	**Urinary tract infection** 2 patients (2%)
		Flu (**influenza**) 2 patients (2%)
		Abnormal lab tests (**alanine aminotransferase increased**) 2 patients (2%)
		Abnormal lab tests (**lipase increased**) 2 patients (2%)
		Feeling **dizzy** 2 patients (2%)

Serious side effects

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

Nine patients (4%) reported a total of 16 serious side effects that were considered to be related to the study treatment. The 9 patients were in the fenebrutinib group (5 patients) as well as the placebo group (4 patients). Two patients had urinary tract infection, one

each in the placebo and fenebrutinib 200 mg twice daily group. The other 7 patients had 14 serious side effects that were reported one time each.

There were 3 deaths during this study due to:

- Respiratory failure – in the placebo group – considered related to the treatment by the investigator.
- Respiratory failure – in the placebo group – considered not related to the treatment by the investigator.
- Growth in the salivary gland (neoplasm) – in the fenebrutinib 150 mg once daily group – considered related to treatment by the investigator. This growth was found to be cancerous (parotid tumor).

6. How has this study helped research?

This study investigated 2 different doses of fenebrutinib. Researchers found out that adding fenebrutinib to the medicines that patients already took for lupus did not provide further improvements. The Sponsor decided not to continue developing this treatment for lupus patients.

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/NCT02908100

- EU clinical trials registry:
  https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-001039-11

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 randomized, double-blind, placebo-controlled, multi-center study to evaluate the safety and efficacy of multiple doses of GDC-0853 [BTKi] in patients with moderately to severely active systemic lupus erythematosus”.

- The protocol number for this study is GA30044.
- The study is known by a short name, which is “ATHOS”.
- The ClinicalTrials.gov identifier for this study is NCT02908100.
- The EudraCT number for this study is 2016-001039-11.