Clinical Trial Results – Layperson Summary

A study of long-term effects of fenebrutinib treatment in patients with rheumatoid arthritis

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 rheumatoid arthritis patients who participated in the current study

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

The study started in November 2016 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 rheumatoid arthritis and long-term effects of the study medicine.

Key information about this study

- In this study, patients with rheumatoid arthritis (RA) received an experimental medicine (fenebrutinib).
- Patients in this study had previously participated in another study that investigated treatment with fenebrutinib and placebo.
- Researchers wanted to find out if fenebrutinib was safe and effective when used long-term.
- This study included 496 patients in 10 countries.
- This study found that fenebrutinib was safe and effective when used long-term by the RA patients who enrolled in this study.
- This report was written after the study was completed.

1. General information about this study

Why was this study done?

Rheumatoid arthritis (**RA**) is an "autoimmune" disease, where your own immune system damages your body.

This disease has many symptoms, including joint pain, swelling, and feeling extremely tired. Some patients become disabled due to the damage caused to their joints by the disease.

There are several medicines available for treating RA. However, some patients still have significant pain and disability from the disease. 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 RA.

Researchers carried out this study to look at the long-term effects of fenebrutinib, whether good or bad, on patients with RA.

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.
- Researchers believe that blocking BTK makes immune cells less able to contribute to the RA disease.
- Researchers have already tested different doses of fenebrutinib in humans.
- Fenebrutinib has shown benefit in patients with RA.

What did researchers want to find out?

Researchers did this study to find out the long-term effects of fenebrutinib in RA patients.

The main question that researchers wanted to answer were:

1. Is the long-term use of fenebrutinib safe for RA patients?

Another question that researchers wanted to answer was:

2. Can fenebrutinib provide improvements to RA symptoms in patients when used long-term?

What kind of study was this?

There are several ways to describe this study.

- **Phase 2 study**
  This Phase 2 study was carried out to find out if the study medicine (fenebrutinib) was safe and effective for patients. This medicine had already been studied in Phase 1 studies to find the safe dose for human use.
- **Open-label extension study**
  Researchers and patients knew that all patients were getting the study medicine – this made it an "open-label" study.
  This was an "extension" study because patients had already participated in a prior study investigating fenebrutinib. This study continued to study RA patients on fenebrutinib treatment for a longer time than the previous study.

When and where did the study take place?

The study started in November 2016 and finished in July 2019. The study took place in:

- Argentina
- Brazil
- Bulgaria
- Columbia
- Mexico
- Poland
- Russia
- Serbia
- Ukraine
- United States

This summary was written after the study had ended.

2. Who took part in this study?

Patients with moderate to severe active RA who were taking a medicine for RA (methotrexate) were allowed to participate in this study.

Patients could also take corticosteroids, another medicine for RA, on this study.

All patients were required to have previously participated in another fenebrutinib study.

There were two groups of patients who received treatment in this study:

Group 1	Group 2
Patients with RA disease who did not respond well to one medicine they were treated with previously: 1) Methotrexate therapy	Patients with RA disease who did not respond well to two medicines they were treated with previously: 1) Methotrexate therapy 2) Tumor necrosis factor inhibitors
410 patients 19 to 75 years old 82% female; 18% male	86 patients 20 to 71 years old 74% female; 26% male

In this study (including both groups), the majority of the patients were female (80%). Most of the patients were white (88%). Half of the patients were below 51 years old (median age). The youngest patient was 19 years old. The oldest patient was 75 years old.

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 76 years old.

3. Agree to use family planning methods to prevent pregnancies while participating in this study.
4. Complete your participation in another study investigating fenebrutinib prior to this one.
5. Must use prescription medicines to control RA (methotrexate with or without corticosteroids).

What conditions disqualified patients from participating in this study

1. Patients who took certain experimental (unapproved) medicines during or after the prior study.
2. Female patients who were breast-feeding, pregnant, or intended to get pregnant.
3. Patients who developed certain new diseases in addition to RA.
4. Patients who got a severe infection or who got a tumor during the prior study.
5. Patients whose blood tests showed certain components of the results were not normal.

3. What happened during the study?

The study treatment was given to patients in addition to their regular RA medicine (methotrexate).

The "treatment" was **fenebrutinib 200 mg taken twice daily**.

What happened after treatment started?

- Patients got their treatment for 52 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 treatment.
- Patients were followed for 8 weeks after the 52 weeks of treatment was over.

4. What were the results of the study?

Four hundred and twenty-three patients (85%) completed the study through Week 52. This included 351 patients (86%) in Group 1 and 72 patients (84%) in Group 2.

Question 1: Is the long-term use of fenebrutinib safe for RA patients?

Fenebrutinib was thought to have a favorable benefit versus the risk of side effects for the RA patients who enrolled in this study. The treatment was well tolerated. Patients could be taken off the treatment to control the side effects.

Question 2: Can fenebrutinib provide improvements to RA symptoms in patients when used long-term?

Long-term treatment with fenebrutinib showed an improvement for patients with RA disease who were enrolled in this study. The number of patients who experienced an

improvement increased with time on treatment, although this study did not include a placebo (no medicine) group for comparison.

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 142 patients overall (29%) who reported a side effect thought to be related to the study treatment. Among these patients, 20 withdrew from the treatment and 37 had their treatment dose changed or stopped for a while.

The side effects thought to be caused by the treatment that happened in four or more patients in the entire study are listed in the following table:

No. of patients with side effects in the entire study		Group 1 (410 patients)	Group 2 (86 patients)
Abnormal lab tests (alanine aminotransferase increased)	12	11	1
Feeling sick to stomach (nausea)	9	9	0
Urinary tract infection	9	7	2
Low red blood cells in the body (anemia)	7	7	0
Infection in the airway (upper respiratory tract infection)	7	6	1
Abnormal lab tests (aspartate aminotransferase increased)	6	6	0
Headache	5	4	1
Low no. of white blood cells (neutropenia)	5	5	0
Abnormal lab tests (high density lipoprotein increased)	4	4	0
Low no. of white blood cells (leukopenia)	4	4	0
Lung infection (pneumonia)	4	3	1
Slow heartbeat (sinus bradycardia)	4	4	0

Serious side effects

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

There were 15 serious side effects; 11 patients (2%) experienced at least one serious side effect.

There were 3 deaths during this study due to:

- Cardio-respiratory failure. A patient died from heart problems and breathing difficulties almost a year after starting fenebrutinib treatment. The investigators thought this was related to the study medicine.
- Acute kidney injury. A patient died from kidney failure about a year after starting fenebrutinib treatment. The investigators thought this was related to the study medicine.
- Ischemic stroke. A patient died after experiencing a stroke about 7 months after starting the study medicine. The investigators did not think this was related to the study medicine.

6. How has this study helped research?

This study investigated fenebrutinib treatment for RA patients over 52 weeks. Researchers found out that the long-term use of fenebrutinib was safe and effective for the RA patients who were enrolled in this study.

7. Are there plans for other studies?

Fenebrutinib is being studied for several 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/NCT02983227

- EU clinical trials registry:
  https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-000498-19

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
  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: “Phase 2 open-label extension (OLE) study of patients previously enrolled in study GA29350 to evaluate the long-term safety and efficacy of fenebrutinib in patients with moderate to severe rheumatoid arthritis”.

- The protocol number for this study is GA30067.
- The ClinicalTrials.gov identifier for this study is NCT02983227.
- The EudraCT number for this study is 2016-000498-19.