Summary of Clinical Trial Results

A study medicine (fenebrutinib) manufactured in different ways – how do different fenebrutinib formulations move through the body

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 August 2022 and finished in September 2023. This summary was written after the study had ended.

A single study cannot tell us all there is to know about the risks and benefits of a medicine. It takes many people in several studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

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Contents of the summary

Thank you to the people who took part in this study

The people who took part in this study have helped researchers answer important questions about the medicine studied, "fenebrutinib."

Key information about this study

- In this study, people took a medicine called "fenebrutinib." Researchers made this medicine in different ways.
- Researchers wanted to know how much of the medicine got into the body from each different version.
- Thirty people joined this study, and it took place in the United Kingdom.
- The main result was that Treatments A, B, and C all worked similarly and moved through the body at about the same speed. Treatments D, E, and F also moved through the body at similar speeds, but Treatment F reached a level in blood that was 26% higher than other treatments.
- There were no serious side effects in this study.
- Five out of the 30 people (17%) had side effects that were not serious but were thought to be caused by the study medicine.

1. General information about this study

Why was this study done?

Multiple sclerosis (MS) is a long-term disease. It happens when the immune system makes a mistake and attacks the protective covering of nerve fibers in the brain and spinal cord, which are parts of the central nervous system.

People with MS might feel weak in their arms and legs, have trouble seeing, forget things easily, feel muscle pain, and have other problems.

There are treatments that can decrease how often the symptoms happen and how bad they are, but they do not cure or completely stop it from getting worse. MS symptoms can come back after getting better for a while.

The treatments available now do not work for everyone and can have serious side effects. We need new medicines that are safer, work better, and help people with MS live better lives.

Fenebrutinib is a medicine being studied to treat MS. Different versions (**formulations**) of the medicine are made in different ways, but they all have the same active ingredient.

This study looked at how different versions of fenebrutinib affect how much of the medicine gets into the blood and how fast the medicine moves through the body.

What was the medicine being studied?

Fenebrutinib is also known by other names:

- G02599853
- RO7010939
- GDC-0853

Fenebrutinib works by stopping the action of a protein in immune cells called "**BTK**." BTK helps certain immune cells (B cells and myeloid cells) that are involved in inflammation, which causes MS.

By blocking BTK, fenebrutinib aims to reduce the activity of these immune cells. This could help lower inflammation and slow the progression of MS.

What did researchers want to find out?

Researchers did this study to compare fenebrutinib made in different ways – fenebrutinib was available in different "formulations." The new formulations were compared to the "reference," which was a formulation that was used in other studies.

The main questions that researchers wanted to answer were:

1. How much medicine got into the blood – when comparing two new formulations to the reference?
2. How fast did the medicine move through the body – when comparing two new formulations to the reference?

What kind of study was this?

These are some ways to explain this study.

Phase 1 study
This was a "Phase 1" study to learn about a new medicine. A small group of healthy people took the medicine. The information from this study might be used in larger studies with more people.

Open-label study
Both the researchers and people in the study knew which medicine was given. That made it an "open-label" study.

Randomized study
A computer randomly chose who went into which treatment group. Neither the researchers nor the people in the study had any control over this.

Three-period crossover study
There were 3 groups in Part 1, and each group received 3 different treatments (A, B, C) in three different orders. This is called a "three-period crossover study."

- Group 1: A→B→C.
- Group 2: B→C→A.
- Group 3: C→A→B.

In Part 2, there were 3 more groups, and they received 3 different treatments (D, E, F).

- Group 4: D→E→F.
- Group 5: E→F→D.
- Group 6: F→D→E.

When and where did the study take place?

The study started in August 2022 and finished in September 2023. This summary was written after the study had ended.

The study took place at one study center in the United Kingdom.

2. Who took part in this study?

Fifteen healthy people joined Part 1 of this study. There were 10 males (67%) and 5 females (33%). They were between 26 and 59 years old.

Fifteen healthy people joined Part 2 of this study. There were 13 males (87%) and 2 females (33%). They were between 21 and 60 years old.

People could join the study if they met all the following conditions:

- Could talk and follow directions, and signed a consent form
- Between 18 and 60 years old
- Healthy male or female
- Females were not pregnant, could not get pregnant, and were not breastfeeding
- Met the height to weight ratio (BMI 18-32 kg/m^2)
- Fully vaccinated against COVID-19 virus
- All sexually-active males agreed to use a condom during the study and for one month after taking the last dose of the study medicine
  Any female partners who could get pregnant agreed to use birth control during this time
  Males agreed not to donate sperm during this time
- All females in the study agreed not to donate eggs during the study and for one month after taking the last dose of fenebrutinib

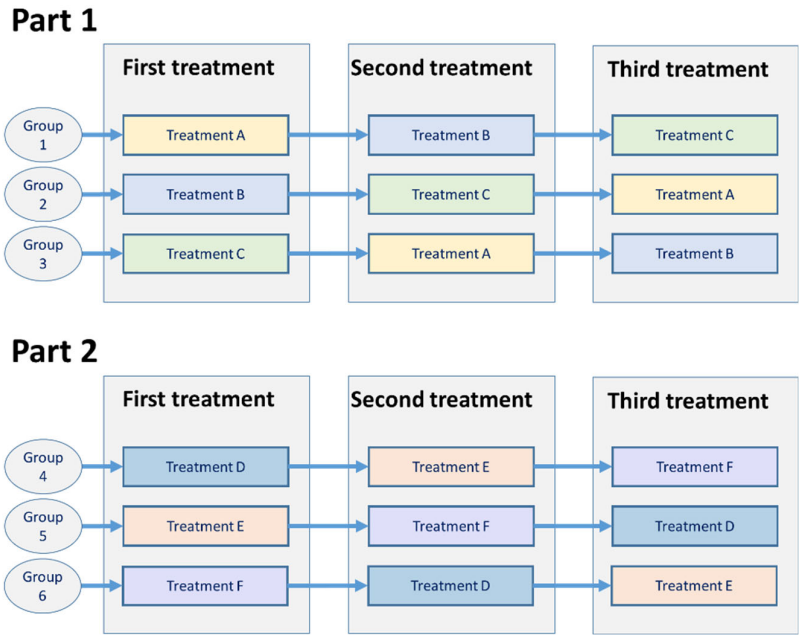
People could not join the study if they met any one of the following conditions:

- Did not meet any one of the medical, surgical, or mental health requirements for this study
- Did not have good veins for multiple blood samples during the study
- Failed any one of several laboratory tests
- Took part in another study in the last 3 months
- Donated more than 400 mL of blood or plasma in the last 3 months
- Received blood transfusions, vaccinations, medicines, or over-the-counter products that were not allowed
- Had a history of drug or alcohol abuse in the past year or failed current drug test
- Used alcohol more than the allowed limit
- Used nicotine products in the last 6 months
- Males with female partners who were pregnant or breastfeeding

3. What happened during the study?

Screening
Study staff asked questions and did medical tests to see if people interested in the study met the study requirements before they were allowed to join. This happened up to 28 days before the study started.

Treatments
People who joined the study came to the study center one day before their first treatment. This was "Day -1." They were randomly put into one of three treatment groups in Part 1 and another one of three treatment groups in Part 2.



People got their treatments with a glass of water on an empty stomach after not eating for about 10 hours. The study treatments were:

- **A.** Fenebrutinib reference tablets
- **B.** Fenebrutinib instant release (IR) Tablet 1
- **C.** Fenebrutinib IR Tablet 3
- **D.** Fenebrutinib reference tablets
- **E.** Fenebrutinib IR Tablet 3
- **F.** Fenebrutinib IR Tablet 4

People got their treatments on Day 1. There was a "**washout**" period of at least 3 days between treatments. This allowed the previous dose to leave the body before the next dose.

Study procedures
Several blood samples were collected, people were asked questions, and they had medical tests in the clinic. This happened before, during, and after each treatment dose.

Follow-up
People in this study went home two days after the third treatment. They received a phone call 7-10 days after the last dose. If they reported a side effect that happened after going home, they were called back to the study center for a checkup.

4. What were the results of the study?

Researchers measured how much fenebrutinib was in the blood. Here are some key terms:

- **Peak concentration** (C_{max}) is the highest amount of medicine in the blood after you take it. It shows the maximum level the body gets exposed to, and can affect how well the medicine works and its side effects.
- **Half-life** is the time it takes for half of the total amount of medicine that got into blood to leave. It helps determine how often you need to take the medicine and how long it stays active in the body.
- **Overall exposure** (AUC) is the total amount of medicine that reaches the blood over a certain time. It shows how much medicine is present for how long, which tells us how well the body absorbs it.

PART 1

Question 1: How much medicine got into the blood – when comparing two new formulations to the reference?

- The peak concentration and overall exposure from Treatments B and C were not significantly different from Treatment A.

Question 2: How fast did the medicine move through the body – when comparing two new formulations to the reference?

- It took about 1 hour for fenebrutinib to reach its peak concentration in the blood after taking the tablets with water on an empty stomach. This was the same for Treatments A, B, and C.
- The half-life was similar for Treatments A, B, and C, taking about 8.2 to 9.3 hours for half of the total amount of fenebrutinib that got into the blood to leave the body.

PART 2

Question 1: How much medicine got into the blood?

- The peak concentration for Treatment E was similar to Treatment D. However, Treatment F had a 26% higher peak concentration than Treatment D, and this difference was statistically significant.
- There was a large difference in peak concentrations among people in the study.
- Overall exposure was not significantly different across Treatments D, E, and F.

Question 2: How fast did the medicine move through the body?

- It took about 1.5 hours for fenebrutinib to reach its peak concentration in the blood after taking the tablets with water on an empty stomach. This was the same for Treatments D, E, and F.
- The half-life was similar across Treatments D, E, and F, taking about 8.0 to 8.7 hours for fenebrutinib to drop to half its peak concentration.

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 happened during the study.

- If they were seen in this study, they are described in this summary because the study doctor believes the side effects were related to the treatments in the study.
- Not everyone in a study gets all 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.
- Serious and common side effects are listed in the following sections if they were seen in this study.

Serious side effects

A side effect is considered "serious" if it is life-threatening, needs hospital care, or causes lasting problems. There were no serious side effects in Part 1 and Part 2 of this study that were caused by the study treatments.

There were no deaths in this study due to side effects caused by the study treatments. During the study, nobody dropped out of the study because of side effects that were caused by the study treatments.

Most common side effects

PART 1

Four out of 15 people (27%) reported a total of 4 side effects that were not serious but were thought to be caused by the study treatment.

Treatment	Side effect	Number of people with side effect
A	Queasy feeling in the stomach that gives the sensation of wanting to throw up (nausea)	2 (13%)
B	Nausea	1 (7%)
C	Throwing up (vomiting)	1 (7%)

PART 2

One out of 15 people (7%) reported one side effect that was not serious but was thought to be caused by the study treatment.

Treatment	Side effect	Number of people with side effect
E	Changes in the sense of taste, making food taste strange or causing a strange taste in the mouth (dysgeusia)	1 (7%)

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 30 healthy people. These results helped researchers learn more about the different formulations of fenebrutinib.

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7. Are there plans for other studies?

At the time of writing this summary, other studies on fenebrutinib were ongoing.

8. Where can I find more information?

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

- https://www.isrctn.com/ISRCTN17780768
- https://forpatients.roche.com/en/trials/healthy-volunteers/a-study-medicine--fenebrutinib--manufactured-in-different-ways--.html

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 1, single center, randomized, open-label study investigating the effect of formulation, and active pharmaceutical ingredient particle size on the pharmacokinetics of fenebrutinib in healthy subjects
- The protocol number for this study is GP43970.
- The International Standard Randomized Controlled Trial Number for this study is: ISRCTN17780768