# Summary of Clinical Trial Results

## A study to look at how safe was it to give people with blood cancer (non-Hodgkin's lymphoma and chronic lymphocytic leukemia) – different doses of a study medicine (fenebrutinib)

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 December 2013 and finished in March 2022. 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 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.

- **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 people who took part have helped researchers answer important questions about blood cancers (B-cell non-Hodgkin's lymphoma and B-cell chronic lymphocytic leukemia) – and fenebrutinib, the study medicine.

## Key information about this study

- This study was done to find out if it was safe to give a new medicine – called "fenebrutinib" – to people with blood cancer.
- People in this study had B-cell non-Hodgkin's lymphoma (B-NHL) or B-cell chronic lymphocytic leukemia (B-CLL).
- This study included 24 people in two countries.
- Two out of 24 people (8%) had a serious side effect that researchers thought was caused by the study medicine.
- Fourteen out of 24 people (58%) had a non-serious side effect that researchers thought was caused by the study medicine.
- The Sponsor decided to stop the study and not develop the study medicine for B-NHL or B-CLL any further. This decision had nothing to do with the safety of the medicine.

## 1. General information about this study

### Why was this study done?

Several different blood cancers are in a type of white blood cells known as "**B-cells**". These include several subtypes of B-cell non-Hodgkin's lymphoma (**B-NHL**), and B-cell chronic lymphocytic leukemia (**B-CLL**).

Currently available medicines have brought improvements to the lives of many people who have B-NHL or B-CLL. The "**median survival**" for people with these diseases is 8 to 10 years. That means half of the people live for less than 8 to 10 years and the other half live for more than 8 to 10 years after diagnosis.

However, not everyone benefits from available treatments, and there is no cure for B-NHL or B-CLL. Therefore, there is a need for new treatments that are safe and effective.

This study was done to find out if a new medicine was safe to give to people with B-NHL and B-CLL.

## 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 B-cells and other blood cells (except T-cells) in the body.
- Here is what BTK does in B-cells:
    - Helps B-cells become active (activation)
    - Helps in the production of more B-cells (proliferation)
    - Helps B-cells mature into other cells (differentiation)
- Researchers believe that blocking BTK will be useful for controlling the growth and activity of cancerous B-cells – such as those found in people with B-NHL and B-CLL.
- Researchers have already tested different doses of fenebrutinib in humans.

## What did researchers want to find out?

**The main questions that researchers wanted to answer were:**

1. Was fenebrutinib safe and tolerable for people with B-NHL and B-CLL?
2. What was the highest dose of fenebrutinib that was tolerable? What were the side effects that stopped researchers from giving people higher doses?

**Other questions that researchers wanted to answer included:**

3. How was fenebrutinib processed in the body?
4. Did fenebrutinib have any effect on cancer in people with B-NHL or B-CLL?

## What kind of study was this?

Here are some features of this study.

**Phase 1 study**
This was a "Phase 1" study, which means that this was an early study looking at fenebrutinib in B-NHL and B-CLL. A small number of people with B-NHL and B-CLL got treatments. Researchers did medical tests on the people to find out more about the treatments.

**Dose-escalation study**
Each new group of people who joined the study received the next higher dose of the treatment. The decision to increase the dose level – "dose escalation" – was made after reviewing safety results from people who had already been treated at the lower dose levels.

**Open-label study**
Researchers and people in the study knew which medicine the people were getting. That made it an "open-label" study.

### When and where did the study take place?

The study started in December 2013 and finished in May 2022. This summary was written after the study had ended.

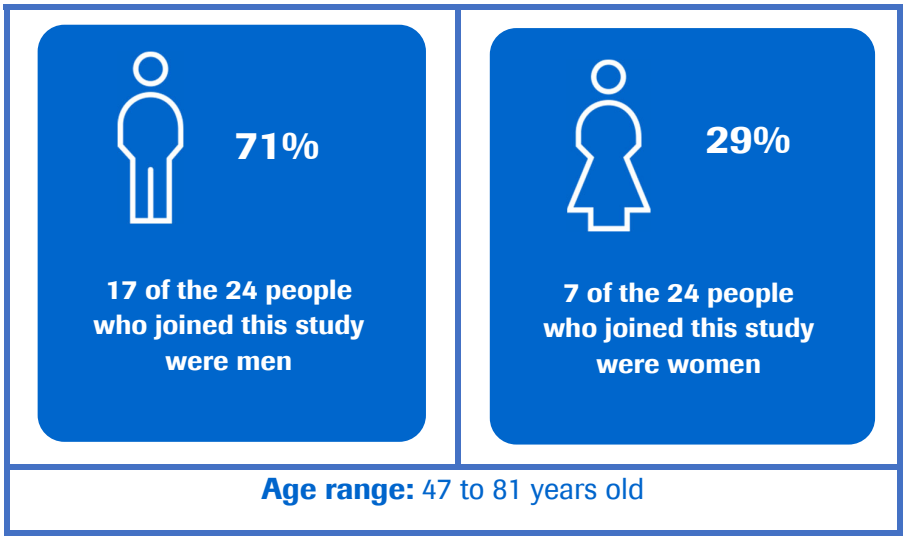
The study took place at nine study centers in two countries:

- USA (7 study centers)
- Australia (2 study centers)

## 2. Who took part in this study?

Twenty-four people with B-NHL or B-CLL – that had come back (**relapsed**) or did not respond to medicine (**refractory**) – where the disease had gotten worse (**progressed**) even after getting available medicines – and for which no other effective medicine was available – took part in this study.

The "median age" of people in the study was 67.5 years. That means half of the people were younger than 67.5 years – and the other half were older than 67.5 years.




**People could take part in the study if they met all of the following:**

- At least 18 years old.
- They were able to perform activities as well or almost as well as they could before they had the illness (ECOG score of 0 to 1).
- Doctors had done tests to confirm they had B-NHL or B-CLL that could not be cured with available medicines.
- They had cancer that could be seen by imaging (CT scan) so that it could be measured before and after the study treatment.
- The organs in their bodies were healthy enough for this study (blood production, liver and kidney function).

**People could not take part in the study if they met any of the following:**

- They were not healthy enough to survive the next 12 weeks.
- They had received certain medicines for their disease less than 3 weeks ago.
- They had a major surgery in the last 4 weeks.
- They had other active health conditions or a history of health conditions.
- Women who were pregnant, breast-feeding, or intended to become pregnant – were not allowed.

## 3. What happened during the study?

There were 3 treatment groups in this study.

| | Group 1 | Group 2 | Group 3 |
|---|---|---|---|
| **Fenebrutinib dose** | 100 mg | 200 mg | 400 mg |
| **Number of people** | 6 | 9 | 9 |

**Here is what happened during the study**

- People took their medicine by mouth with water in the morning – on an empty stomach.
- Food was not allowed for at least two hours after taking the pills.
- Day 1 – they got their first dose of the study medicine.
- Day 2 to Day 7 – this was the "washout period". The medicine was not taken during this period.
- Day 8 – starting on Day 8, everyone got a dose of the study medicine every day.
- Day 1 to Day 35 – this was the first cycle, "**Cycle 1**".
- After Cycle 1, every cycle was 28-days long.
- People took their medicine at home most days. They got their medicine at the study center on certain days so that blood samples could be collected before dosing – and several times after dosing.
- People took their medicine for as long as the researchers thought it was safe and useful to do so.
- People came back to the study center within a month of taking their last dose to be checked by the researchers.

**The study stopped early**

- The Sponsor decided to stop the study early and not develop the study medicine for B-NHL and B-CLL. This had nothing to do with the safety of the study medicine.

## 4. What were the results of the study?

In this study, people received treatments for an average of 738 days. Nine people received treatments for more than one year (more than 365 days).

### **Question 1:** Was fenebrutinib safe and tolerable for people with B-NHL and B-CLL?

Two people had a serious side effect that researchers thought was caused by the study medicine.

Fourteen people had a non-serious side effect that researchers thought was caused by the study medicine.

Researchers thought that fenebrutinib was tolerated well enough – at the doses tested by the people in this study.

### **Question 2:** What was the highest dose of fenebrutinib that was tolerable? What were the side effects that stopped researchers from giving people higher doses?

The Sponsor stopped the study early. Researchers did not get to a high enough dose – to find a dose where many people had side effects. Researchers were not able to determine the intolerable dose.

### **Question 3:** How was fenebrutinib processed in the body?

At the 100 mg dose, it took 19 hours to drop to half of the highest concentration reached in the body after one dose. At 200 and 400 mg doses, this took about 17 and half hours.

For people who got the same dose, the highest concentration reached was different for different people – there was "high inter-individual variability".

### **Question 4:** Did fenebrutinib have any effects on cancer in people with B-NHL and B-CLL?

Twenty people remained in the study long enough for assessments.

- Eleven people (55%) had cancer that was not getting worse or better – they had "stable disease".
- Seven people (35%) had a decrease in the size of the tumor that was confirmed by a follow-up scan – they had "confirmed partial response".
- Two people (10%) did not show any response to the study medicine.

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.

- 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 people in this study had all of 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.

### Serious side effects

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

During this study, 2 out of 24 people (8%) had serious side effects that researchers thought were caused by the study medicine. One person had three and the other person had one:

- Infection in the airways (respiratory tract infection)
- Fever and low white blood cells (febrile neutropenia)
- Infection in the lungs
- Influenza (H1N1)

Three people in the study died. Researchers thought these deaths were not related to the study medicine. Two people died from complications due to influenza and one person's cancer became worse (progressed) leading to death.

One person stopped taking the study medicine because of side effects (influenza) – thought to be caused by the study medicine.

### Most common side effects

During this study, 14 people (58%) had a side effect that was not considered serious – but was thought to be caused by the study medicine.

Some people had more than one side effect – there were 64 side effects among the 14 people. The most common side effects – seen in more than one person – are listed:

| Side effect | Number of people |
|---|---|
| Feeling tired (fatigue) | 6 people (25%) |
| Low platelet count in the blood (thrombocytopenia) | 4 people (17%) |
| Feeling sick to stomach (nausea) | 3 people (13%) |
| Abnormal blood test (increased amylase) | 2 people (8%) |
| Abnormal blood test (increased blood creatine phosphokinase) | 2 people (8%) |
| Bruising (contusion) | 2 people (8%) |
| Diarrhea | 2 people (8%) |
| Difficult to breath (dyspnea) | 2 people (8%) |

### 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 24 people with B-NHL or B-CLL. These results helped researchers learn more about blood cancer and fenebrutinib, the study medicine.

The results presented in this study are only applicable to the people in this study. The results will be different for people with other types of diseases who use the same medicine.

The Sponsor decided not to develop fenebrutinib as a medicine for B-NHL or B-CLL. This decision was not based on any safety concerns. Fenebrutinib may be developed for other diseases.

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, the Sponsor decided to discontinue the development of fenebrutinib for B-NHL and B-CLL.

Others clinical trials are ongoing to find out if fenebrutinib is useful for the treatment of autoimmune diseases.

## 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/NCT01991184

https://forpatients.roche.com/en/trials/cancer/non-hodgkins-lymphoma/a-study-of-gdc-0853-in-patients-with-resistant-b-cell-l-94923.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:

An open-label, phase 1, dose-escalation study evaluating the safety and tolerability of GDC-0853 in patients with relapsed or refractory B-cell non-Hodgkin's lymphoma and chronic lymphocytic leukemia

- The protocol number for this study is GO29089.
- The ClinicalTrials.gov identifier for this study is NCT01991184.