Summary of Clinical Trial Results

A study of a new medicine (fazpilodemab) in people with a type of liver disease called non-alcoholic steatohepatitis or NASH

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 September 2020 and finished in January 2023. 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.

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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 non-alcoholic steatohepatitis (NASH) and the study medicine (fazpilodemab).

Key information about this study

- This study was done to find out if a new study medicine (fazpilodemab) was effective for people with a type of liver disease: non-alcoholic steatohepatitis or NASH.
- People joined one of four treatment groups. It was decided by chance which group they joined. Three groups were treated with fazpilodemab. One group was treated with placebo.
- This study included 46 people in two countries – the USA and France.
- There were some improvements with fazpilodemab treatments – in comparison to placebo treatments. The study results were not as clear because not enough people joined the study. This was because the study stopped early due to a business decision made by the sponsor.
- Sixteen people (35%) reported side effects that were not serious but study doctors thought they were caused by the study treatment.

1. General information about this study

Why was this study done?

The fatty liver disease called non-alcoholic steatohepatitis or "**NASH**" happens if your liver has too much fat, combined with swelling and cell damage. It is seen in about 2% to 6% of the people. The name of this disease has changed from the time the study occurred. It is now called "metabolic dysfunction-associated steatohepatitis" (MASH). In this summary, we will continue to call it "NASH."

People with NASH often also have other health problems. These include being overweight (obese), type 2 diabetes, and high cholesterol. With the high rate of obesity in the United States, the number of NASH cases is expected to rise in the coming years

If left untreated, NASH can turn into other worse diseases. However, the currently available treatment options for NASH have not been very helpful. Some medicines do not work well and other medicines have undesirable side effects.

Fazpilodemab is a new medicine that may be effective for treating NASH. This medicine can make the body more responsive to insulin, increase energy usage, and reduce the amount of fat stored in the wrong places. (Your body makes insulin naturally unless you have type 1 diabetes.)

So far, studies on fazpilodemab have shown that its side effects could be tolerated. However, higher dose were more difficult for people to tolerate because they caused more stomach problems.

This study was done to follow up on the earlier studies. Researchers wanted to find out how well fazpilodemab worked, how safe it was, and how it moved within the body – in people with NASH.

What was the study medicine?

Fazpilodemab is a type of medicine known as a "bispecific antibody." It is also known as **BFKB8488A** and **RO7040551**.

Fazpilodemab was designed to bind to two different proteins in the "FGFR1/KLB complex" – found in fat tissues in our bodies.

When fazpilodemab is bound to the FGFR1/KLB complex, it flips a switch in the "on" position. Researchers believe this may help our bodies make better use of insulin, burn more energy, and get rid of unwanted fat.

Some people in the study were treated with a "**placebo**." It looked like the real medicine but it did not contain any medicine.

Researchers wanted to compare the results of fazpilodemab and placebo treatments.

What did researchers want to find out?

The main question that researchers wanted to answer was:

1. Were treatments with fazpilodemab effective in comparison to treatments with the placebo?

What kind of study was this?

Phase 2 study
In Phase 1 studies, researchers learn about how much medicine people can tolerate and what the side effects are. Then, if it is safe to do so, they move on to Phase 2 studies. In Phase 2 studies, the medicine is given to a larger group and to those who have the disease. Researchers want to find out if the treatment is effective for the disease and take a further look at its safety.

Randomized study
People are randomly assigned – by chance – to one of several study groups. Each group gets a different treatment, and then doctors can compare the results.

Parallel-Group study
In a parallel-group study, two or more groups of people receive different treatments at the same time for comparison.

Double-blind study
In this type of study, neither the doctors nor the people in the study know who is getting the real medicine and who is getting a fake treatment without any medicine (placebo), until the study is over.

Placebo-controlled study
In this type of study, some groups are treated with the real medicine while other groups are treated with the placebo treatment without any medicine. The idea is to find out if people who get the real medicine do better than those who receive the placebo.

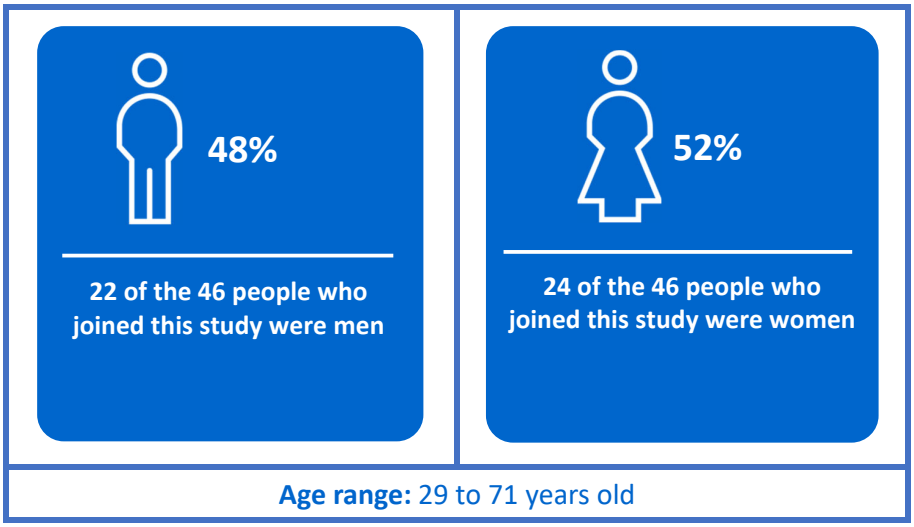
When and where did the study take place?

The study started in September 2020 and finished in January 2023. This summary was written after the study had ended.

The study took place at 24 study centers at 22 study sites in two countries – the USA (23) and France (1).

2. Who took part in this study?

There were 46 people with NASH who joined the study.



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

- Between the ages of 18 and 75 years
- Signed the informed consent form and were able to do what was asked of them in the study
- Liver disease was documented via imaging (MRI) and confirmed by testing a sample taken from the liver (liver biopsy)
- Men and women treated in the study agreed to use birth control for a specified time

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

- Unable to undergo an MRI
- With a medical condition or medical history that was not allowed in this study
- Taking medications that were not allowed in this study
- Having an eating disorder, in a weight loss program, or had a procedure for weight loss
- Planned a medical procedure or surgery during the study
- Recent treatment with an experimental medicine, biological therapy, or vaccination that was not allowed in this study
- Use of herbal or nutritional supplements that were not allowed
- Illegal drug use or marijuana use
- Current use or history of alcohol abuse
- Cigarette use exceeding what was allowed
- History of blood loss or donation exceeding what was allowed in this study
- Women who were breastfeeding, pregnant, or intended to get pregnant

3. What happened during the study?

Screening: There was a "screening" period when people were checked to see if they met the conditions for joining the study. This happened up to 8 weeks before study start.

Treatments: People were randomly assigned to one of four treatment groups. One group received placebo treatment. Three groups received fazpilodemab – a different dose in each group – low, medium, and high dose. People got their treatments by injection once every two weeks for 52 weeks (about 1 year).

Follow-up: There was a 6-week follow-up period after the last treatment. People went back to the study center for follow-up questions and study procedures.

Study design: This was a double-blind, parallel-group, and placebo-controlled study as described in Section 1, "What kind of study was this."

4. What were the results of the study?

Researchers wanted to know how many people got better after 52 weeks (about 1 year) of treatment. They used a scale to grade the liver disease, paying attention to inflammation, ballooning, fat build-up in liver cells (steatosis), and scarring (fibrosis).

Question 1: Were treatments with fazpilodemab effective in comparison to treatments with the placebo?

This study ended early because of a business decision made by the sponsor. Instead of having over 200 people join the study as planned, there were only 46 people. This means that the study results might not be as clear or as reliable.

If you only test a few people (such as 46), you might get results that do not truly reflect what would happen in a larger group (such as a million people). This is why researchers prefer to test new medicines on lots of people (such as over 200 people) before deciding if they work. It helps to make sure that the results are not just by chance, and the medicine truly is effective.

Here are some things researchers saw in the group of 46 people – which may have been different if the study was done with over 200 people:

- There was no real difference in how much fat was reduced in the liver – with fazpilodemab treatment compared to the placebo.
- More people saw an improvement in the features of their disease in their liver when looked at under a microscope – in the groups that got fazpilodemab treatment compared to the placebo treatments.
- Researchers looked at liver samples under the microscope and measured substances found in blood samples. With these methods, more people saw an improvement in fibrosis, another type of liver problem, in the low and medium dose groups than the placebo. But this was not the case for the high dose group.

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 will be described in this summary if they happened in this study and the doctor thought the side effects were related to the treatments in the study.
- Not all people in any one study have all of the side effects seen in the study.
- 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 will be 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.

No one in this study reported any serious side effects that doctors thought were related to the study treatments.

There were no deaths in this study resulting from side effects.

Some people stopped their treatment because of side effects that study doctors believed were related to the study treatment:

- 2 people who got placebo treatments
- 2 people who got fazpilodemab treatments

Some people changed or interrupted – stopped and then restarted – their treatment because of side effects that study doctors believed were related to the study treatment:

- 4 people who got fazpilodemab treatments

Most common side effects

During this study, 16 out of 46 people (35%) reported at least one side effect that was thought to be caused by the study treatment but was not serious. There were 39 of these common side effects because some people got more than one side effect.

Common side effects (that were seen in two or more people in this study)

Side effects	Among 13 people with placebo treatments	Among 33 people with fazpilodemab treatments
Queasy feeling in the stomach that gives the sensation of wanting to vomit (nausea)	1 person (8%)	7 people (21%)
Diarrhea	0	6 people (18%)
Feeling less hungry than usual (decreased appetite)	0	3 people (9%)
Vomiting	0	2 people (6%)
Swelling (erythema) at the injection site	0	2 people (6%)
Feeling tired or weak (fatigue)	1 person (8%)	1 person (3%)
Blood test showing a decrease in a protein (insulin-like growth factor decreased)	1 person (8%)	1 person (3%)

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 46 people. These results helped researchers learn more about fazpilodemab and NASH.

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.

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7. Are there plans for other studies?

At the time of writing this summary, no more studies looking at fazpilodemab were planned.

8. Where can I find more information?

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

- https://clinicaltrials.gov/study/NCT04171765
- https://forpatients.roche.com/en/trials/kidney-disorder/ckd/a-study-to-evaluate-the-efficacy--safety--and-pharmacok-56434.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 2 randomized, parallel-group, double-blind, placebo-controlled, multicenter study to evaluate the efficacy, safety, and pharmacokinetics of BFKB8488A compared with placebo in patients with non-alcoholic steatohepatitis

- The protocol number for this study is GC41033.
- The ClinicalTrials.gov identifier for this study is NCT04171765.