Summary of Clinical Trial Results

A study to see how well the body tolerates different dose levels of a new medicine for type 2 diabetes mellitus and non-alcoholic fatty liver disease called "BFKB8488A"

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
- Patients who took part in the study

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

The study started in March 2017 and finished in Dec 2019. 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 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.**

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 type 2 diabetes mellitus (T2DM), non-alcoholic fatty liver disease (NAFLD), and the study medicine.

Key information about this study

- This study was done to find out how safe different doses of a study medicine were, and how the body processed the medicine.
- Patients received the study medicine (called "BFKB8488A") or a placebo – it was decided by chance which treatment each person was given.
- This study included 153 patients in the USA who had type 2 diabetes mellitus (T2DM) or non-alcoholic fatty liver disease (NAFLD).
- The main finding was that BFKB8488A was tolerable in patients with T2DM or NAFLD at low and medium dose levels. Side effects became a problem at high doses.
- One patient taking BFKB8488A had a serious side effect thought to be caused by the study medicine.

1. General information about this study

Why was this study done?

"Type 2 diabetes mellitus" (**T2DM**) is a disease associated with high blood sugar levels and the lack of proper activity of beta cells that make insulin to regulate sugar levels.

Over time, T2DM can cause serious damage to the body, such as heart disease, kidney disease, and blindness, among others.

About 70% of patients who have T2DM may at some point also have a disease called "non-alcoholic fatty liver disease" (**NAFLD**). NAFLD is a disease where the body stores excess fat in the liver, leading to liver damage.

Diet and exercise are useful for controlling T2DM. Several medicines are also available. However, for most patients, their blood sugar levels continue to rise over time.

In spite of the many approaches for treating and managing T2DM, there is a need for additional safe and effective medicines, especially those that can improve other diseases that people with T2DM may have, such as NAFLD.

This study was done to look a new medicine, called, "BFKB8488A", in patients with T2DM or NAFLD.

What were the study medicines?

A medicine called "**BFKB8488A**" was the focus of this study.

- BFKB8488A is a type of medicine called an antibody.
- Antibodies are designed to bind to specific proteins.
- BFKB8488A binds to specific proteins in cells, causing a change in the cell function. Researchers believe this will lead to improvements for patients with T2DM or NAFLD.

BFKB8488A was compared to a "**placebo**".

- You say this as "plah-see-bo".
- The placebo looked the same as BFKB8488A but did not contain any real medicine. This means it had no medicine-related effect on the body.
- Researchers compared BFKB8488A to the placebo so they could show which benefits or side effects were actually due to the medicine.

What did researchers want to find out?

Researchers did this study to find out the effects on patients who got the medicine (BFKB8488A) in comparison those who received no medicine (placebo).

The main questions that researchers wanted to answer were:

1. How safe was BFKB8488A when given to patients at different doses?
2. What happened to BFKB8488A in the body, when given at different doses?

Other questions that researchers wanted to answer included:

3. Were there any signs of improvement for patients?

What kind of study was this?

This was a "**phase 1b, multiple ascending dose study**". Being phase 1b means it was one of the early studies. Patients received several doses of their treatment, described as "multiple doses". Each new group of patients received a higher dose of the treatment, described as "ascending dose".

This was a "**placebo-controlled study**", which means that researchers could compare results for patients who got the medicine with those who got a pill without any medicine.

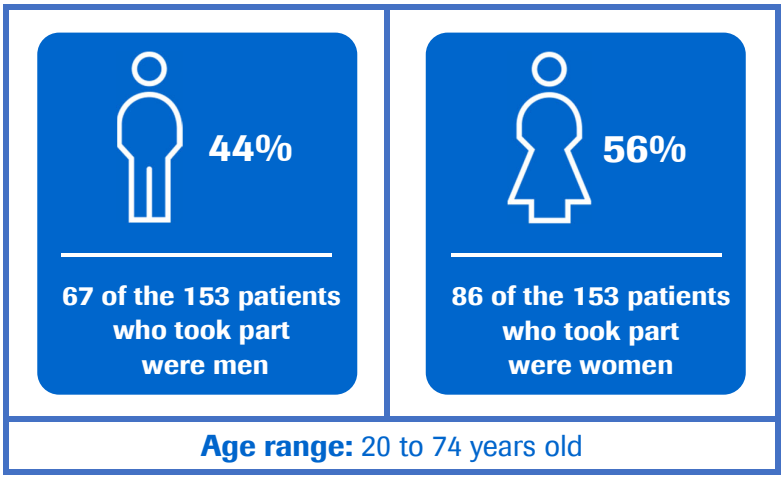
The study was "**randomized**". This means that it was decided by chance who joined the group that got the real medicine and who joined the group that got placebo. Randomly choosing which medicine people get makes it more likely that the types of people in both groups (for example, age, race) will be a similar mix.

This was a "**blinded study**" because patients and their doctors did not know who was getting the medicine and who was getting the placebo. Blinding of treatment is a way to reduce any unfairness (bias) when patients and doctors report what happened after patients got their treatments.

When and where did the study take place?

The study started in March 2017 and finished in December 2019. This summary was written after the study had ended. The study took place at 17 study centers in the USA.

2. Who took part in this study?



Patients with T2DM or NAFLD could take part in the study if:

- They were between 18 and 75 years of age.
- They had agreed to use birth control methods.
- Patients with T2DM needed to have:
    - A stable treatment for diabetes before joining this study.
    - Body mass index between 27 kg/m^2 and 40 kg/m^2.
    - A certain level of diabetes (HbA1b between 6.8% and 9.0%).
- Patients with NAFLD needed to have:
    - Body mass index between 25 kg/m^2 and 40 kg/m^2.
    - Liver fat confirmed by ultrasound or calculated using NAFLD liver fat variables to be greater than 10%.

Patients with T2DM or NAFLD could not take part in the study if:

- They were breastfeeding, pregnant, or intending to get pregnant.
- They were taking or had taken certain medicines.
- They had type 1 diabetes or other certain other medical problems.
- They had a history of liver disease other than NAFLD.
- They smoked heavily or used drugs and alcohol.
- They were on a weight loss program or had weight loss surgery.

3. What happened during the study?

Patients were randomized to receive the study medicine or the placebo:

- **121 patients got the study medicine.**
- **32 patients got the placebo**.

The treatment groups and number of patients were:

BFKB8488A dose	Patients with T2DM	Patients with NAFLD	All patients in each dose group
Once a week:			
20 mg	8	-	8
30 mg	8	-	8
50 mg	9	-	9
100 mg	12	-	12
Once every 2 weeks:			
40 mg	8	-	8
50 mg	-	8	8
75 mg	-	8	8
100 mg	-	8	8
130 mg	-	8	8
150 mg	8	-	8
Dose*	-	7	7
Once a month:			
100 mg	8	-	8
250 mg	12	9	21
All BFKB8488A doses:	**73**	**48**	**121**
All placebo doses:	**18**	**14**	**32**

All patients enrolled in the study continued taking their regular treatment for diabetes and associated conditions.

Patients on the study got their study treatments for 12 weeks. They were examined and got medical tests throughout the study. They were treated for side effects when it was needed. When the study ended, patients were asked to return to their study center for more tests to check their overall health.

4. What were the results of the study?

Question 1: How safe was BFKB8488A when given to patients at different doses?

Researchers found that in general, patients who had T2DM or NAFLD could tolerate BFKB8488A in the low and medium dose ranges.

The higher doses became intolerable for patients due to side effects affecting the stomach (such as diarrhea).

The higher doses included 100 mg once a week, 250 mg once a month, 130 mg twice a week, and 150 mg twice a week.

Question 2: What happened to BFKB8488A in the body, when given at different doses?

Researchers found that BFKB8488A levels in the body were not proportional to the dose given to the patients. For example, 100 mg given once a week resulted in more than twice the level of medicine in the body in comparison to 50 mg given once a week.

Question 3: Were there any signs of improvements for patients?

BFKB8488A did not have any effect on insulin levels or blood sugar levels. However, there were improvements seen in liver function, heart health, and how the body stores and uses energy.

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 happen 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.
- Side effects can vary from mild to very serious and may vary from person to person.
- 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.

One patient on the study had gastritis, which was a serious side effect thought to be related to study medicine.

There were no deaths on the study.

Most common side effects

During this study, around 74 out of 153 patients (48%) had a side effect that was thought to be caused by the treatments but was not considered serious. This included:

- 8 patients (25%) who received placebo treatment.
- 66 patients (55%) who received BFKB8488A treatment.

The most common side effects are shown in the following table. These are the side effects experienced by more than 5% of patients in the entire study.

Most common side effects	Patients taking placebo	Patients taking BFKB8488A
Feeling sick to your stomach (nausea)	1 patient (3%)	31 patients (26%)
Diarrhea	0	14 patients (12%)
Vomiting	1 patient (3%)	13 patients (11%)
Feeling tired (fatigue)	0	9 patients (7%)
Weight loss	1 patient (3%)	7 patients (6%)

During the study, some patients stopped taking their treatment.

- 19 patients (16%) who received BFKB8488A stopped taking the study medicine because of side effects related to the medicine.

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 153 patients. These results helped researchers learn more about T2DM, NAFLD, and BFKB8488A.

Treatments with BFKB8488A led to improvements in heart health and in how the body stores and uses energy (cardiometabolic profile). Liver health (liver transaminase levels and liver fat fraction) also showed signs of improvement in patients who got medium and high doses BFKB8488A.

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?

Studies with BFKB8488A are still happening and can be found at:

https://clinicaltrials.gov/ct2/results?cond=&term=BFKB8488A&cntry=&state=&city=&dist=

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/NCT03060538

https://forpatients.roche.com/en/trials/metabolic-disorder/t2d/a-multiple-ascending-dose-study-to-evaluate-safety-and-tolerabil.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 Ib, Randomized, Blinded, Placebo-Controlled, Multiple Ascending-Dose Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of Subcutaneous BFKB8488A in Patients with Type 2 Diabetes Mellitus and Patients with Non-Alcoholic Fatty Liver Disease.
- The protocol number for this study is:
  GC39547.
- The ClinicalTrials.gov identifier for this study is:
  NCT03060538.