Clinical Trial Results Summary

NOVARTIS

The effects and safety of LIK066 for people with NASH (non-alcoholic steatohepatitis)

Thank you!

Thank you to the participants who took part in the clinical trial for the trial drug **LIK066**, also called **licogliflozin**.

All of the participants helped the researchers learn more about how LIK066 works and how safe it is to take.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public. An independent organization prepared this summary of the trial results.

We hope this helps the participants understand their important role in medical research.

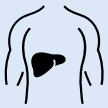
Trial information

Trial number: CLIK066X2204
Drug studied: LIK066 (licogliflozin)
Sponsor: Novartis

This clinical trial at a glance

What was the purpose of this trial?

Read more on **page 3**



The purpose of this trial was to learn:

- Did LIK066 lower ALT levels in the participants' blood?
- What medical problems did the participants have during this trial? Keeping track of the medical problems helped to learn about the safety of LIK066.

Who was in this trial?

Read more on **page 4**

- 107 men and women began this trial
- The participants were 22 to 77 years old and had signs of NASH

What trial treatments did the participants take?

Read more on **page 5**

Each participant was assigned one of these trial treatments to take as pills:

- High dose of LIK066
- Low dose of LIK066
- Placebo – looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.

What were the main results of this trial?

Read more on **pages 5-7**

- On average, the participants who took either dose of LIK066 had lower ALT levels compared to the participants who took the placebo. The participants who took the high dose of LIK066 had a more meaningful change in ALT levels than those who took the low dose.
- Most of the participants had medical problems during this trial. A total of 3 participants, one from each treatment group, left the trial because of medical problems. The most common medical problem was diarrhea.

Read about other results of this trial on **page 9**

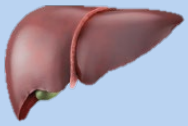
You can find **more information** about this trial by going to the websites listed on **pages 10-11**.

What was the purpose of this trial?

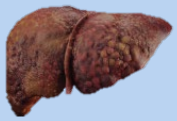
Researchers are looking for better ways to treat **NASH**, which stands for non-alcoholic steatohepatitis. NASH is a severe type of liver disease that happens when there is a buildup of fat in the liver. Over time, this buildup leads to liver damage.

What does the liver do?

The liver is a large organ inside the belly that helps digest food, stores energy, and removes waste from the body.



If the liver is damaged, it cannot work as well.



NASH often happens in people who are overweight and have other health issues, such as diabetes. Drinking too much alcohol does not cause NASH, but the liver damage can look similar to alcohol-related liver damage. In the early stages of NASH, many people have few or no symptoms. In the later stages, the symptoms can include belly pain, weakness, and feeling tired.

Previous research found that the trial drug called **LIK066** can lead to weight loss in people who are overweight. Researchers wanted to find out if LIK066 could also reduce the buildup of fat that leads to liver damage in people with NASH.

When the liver is damaged, it leaks a protein called **ALT** (alanine aminotransferase) into the blood, causing ALT levels to go up. The clinical trial team looked at the levels of ALT in the participants' blood to find out if LIK066 had an effect on liver damage.

Before a drug can be approved for doctors to prescribe for people with NASH, researchers do many trials to find out how safe it is and how well it works.

The main questions this trial was designed to answer:

- Did LIK066 lower ALT levels in the participants' blood?
- What medical problems did the participants have during this trial? Keeping track of the medical problems helped to learn about the safety of LIK066.

How long was this trial?

This trial started in October 2017 and ended in November 2019. Each participant was in this trial for about 6 months. 11 participants did not complete this trial.

Who was in this trial?

107 participants were in this trial – 59 women and 48 men. The participants were 22 to 77 years old. Their average age was 51.

Every participant had ALT levels that the trial doctors considered higher than healthy levels. Every participant was either:

- Diagnosed with NASH after doctors did a liver biopsy, which is when doctors take a small piece of liver tissue to look at it under a microscope
- Overweight and had controlled type 2 diabetes

A person couldn't be in this trial if they:

- Regularly drank too much alcohol
- Took certain medicines
- Had another liver disease besides NASH

This trial took place in Argentina, Canada, Israel, the Netherlands, Russia, Taiwan, Thailand, and the United States.

Visit novctrd.com for more information about:

- Who could and could not be in this trial
- The participants in this trial, such as their age, gender, and race

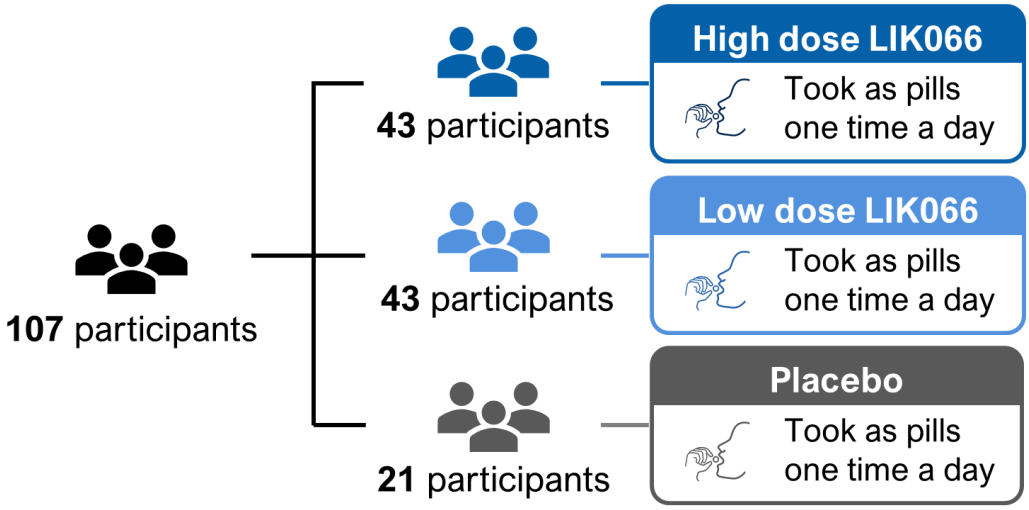
Use trial number **CLIK066X2204** to find the scientific summary.

What trial treatments did the participants take?

A computer program was used to randomly assign each participant the treatment they took as pills for 12 weeks:

- **High dose LIK066**: 150 mg (milligrams)
- **Low dose LIK066:** 30 mg
- **Placebo:** Looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.

Using a computer program to assign the treatments helped make sure the team compared the results as fairly as possible.



The participants and trial staff did not know what treatment each participant took during the trial. Some trials are done this way because knowing what treatment participants took can influence the results. Not knowing what treatment participants took helps make sure the results are looked at fairly.

The trial doctors asked the participants to follow a healthy eating plan and exercise regularly during this trial.

What were the main results of this trial?

This is a summary of the overall results of this trial. Individual results from each participant may be different and are not included in this summary.

Researchers need many trials to learn if a drug or other treatment is safe and works well. Other trials may provide new information or different results.

Always talk to a doctor before making any changes to your health care.

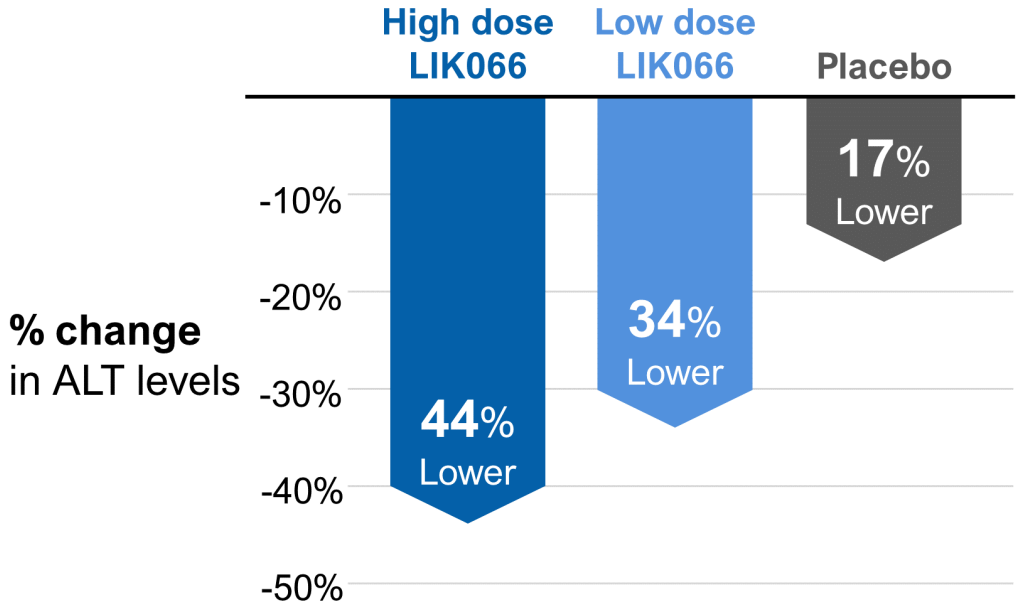
Did LIK066 lower ALT levels in the participants' blood?

On average, the participants who took either dose of LIK066 had lower ALT levels compared to those who took the placebo. The participants who took the high dose of LIK066 had a more meaningful change in ALT levels than those who took the low dose.

To find this out, the trial staff measured each participant's ALT levels before and after 12 weeks of treatment. As liver damage happens, the liver leaks ALT into the blood, causing ALT levels to go up. The chart below shows the average change in the participants' ALT levels.

Percent change in ALT levels

The average change in ALT levels from before treatment to after 12 weeks of treatment



What medical problems did the participants have during this trial?

Medical problems that happen during trials are called “adverse events”. An **adverse event** is any unwanted sign or symptom that participants have during a trial. An adverse event is considered “**serious**” when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death.

Adverse events may or may not be caused by treatments in the trial. Many trials are needed to know if a drug or treatment causes an adverse event. Trial doctors keep track of all adverse events that happen in trials, even if they think the adverse events might not be related to the trial treatments.

Most of the participants had adverse events during this trial. A total of 3 participants, one from each treatment group, left the trial because of adverse events. The most common adverse event was diarrhea.

Trial doctors looked for adverse events when they checked the participants’ health at the trial site. The participants also reported adverse events. This section includes the adverse events that happened during and after trial treatment.

Participants who had adverse events

Participants who had:	High dose LIK066 43 participants	Low dose LIK066 43 participants	Placebo 21 participants
Serious adverse events	0% 0 of 43	0% 0 of 43	5% 1 of 21
Non-serious adverse events	84% 36 of 43	72% 31 of 43	86% 18 of 21
Left this trial due to adverse events	2% 1 of 43	2% 1 of 43	5% 1 of 21

What serious adverse events did the participants have?

No participants who took either dose of LIK066 had serious adverse events.

One participant who took the placebo had a serious adverse event which was **the stomach flu** (gastroenteritis viral).

During and after trial treatment, no other serious adverse events were reported, including deaths.

What non-serious adverse events did the participants have?

Most of the participants had adverse events that were not serious. The table below shows the adverse events that happened to **8 or more participants**. Other adverse events were reported by fewer participants.

Non-serious adverse events

Participants who had:	High dose LIK066 43 participants	Low dose LIK066 43 participants	Placebo 21 participants
Diarrhea	77% 33 of 43	49% 21 of 43	43% 9 of 21
Passing gas Flatulence	19% 8 of 43	5% 2 of 43	10% 2 of 21
Headache	12% 5 of 43	5% 2 of 43	14% 3 of 21
Feeling sick to the stomach Nausea	7% 3 of 43	9% 4 of 43	14% 3 of 21
Throwing up Vomiting	5% 2 of 43	12% 5 of 43	10% 2 of 21
Bloating in the belly Abdominal distension	14% 6 of 43	5% 2 of 43	0% 0 of 21
Belly pain Abdominal Pain	12% 5 of 43	2% 1 of 43	10% 2 of 21

For more information about the adverse events the participants in this trial had, visit novctrd.com. Use trial number **CLIK066X2204** to find the scientific summary.

What other results were learned?

Did LIK066 lower the participants' liver fat?
The trial staff measured the fat in participants' livers before and after trial treatment using an MRI, also called magnetic resonance imaging. An **MRI** uses magnets to create a detailed picture of the inside of the body.

The participants who took the high dose of LIK066 lost more liver fat after the trial treatment than those who took the low dose or the placebo.

Did LIK066 lower other signs of NASH?
The trial staff measured the participants' weight and body measurements before and after the trial treatment. They also looked for other signs of NASH in the participants' blood samples.

Compared to the participants who took the placebo, the participants who took either dose of LIK066:

- Lost more body weight
- Had lower levels of a protein called AST (aspartate aminotransferase) in their blood. Higher AST levels are a sign of liver damage.

Did LIK066 lower the participants' signs of liver fibrosis?
Over time, NASH can lead to liver fibrosis, which is when large amounts of scar tissue form in the liver. Liver fibrosis can cause serious, permanent liver damage and can be life-threatening. The trial staff checked for signs of liver fibrosis in the participants' blood samples before and after the trial treatment.

LIK066 may have lowered signs of liver fibrosis in some of the participants, but more research is needed to know if this change was meaningful.

What was learned from this trial?

This was the first trial to learn about how well LIK066 works for people with NASH. The clinical trial team found that on average, the participants who took either dose of LIK066 had lower ALT levels than those who took the placebo. The participants who took the high dose of LIK066 had a more meaningful change in ALT levels than those who took the low dose. The clinical trial team also found no new safety concerns for LIK066.

This was one of many trials a drug must go through before it can be approved for doctors to prescribe. This type of trial learned about the safety of a trial drug and how well it works in a small number of participants.

The results presented here are for one trial. One trial cannot give a complete picture of the benefits and risks of a trial drug. The results of many trials are needed to find out which treatments can be used for people with NASH. This summary shows only the main results from this trial. Other trials may provide new information or different results.

Where can I learn more about this and future clinical trials?

This is a summary of the results for one trial.

You can find detailed results and more information about this clinical trial on the Novartis Clinical Trial Results website:

1. Visit novctrd.com
2. Click on “Clinical trial results” at the top right of the page
3. Read and scroll down, then click “I accept” to agree to use the information and the website
4. Select “Study number” from the drop-down menu
5. Type **“CLIK066X2204”** in the search box and click search

If you would like to view the website in a language other than English, you can click the “Google Translate” button on the top right of the page.

This trial was registered on the following websites:

- ClinicalTrials.gov – https://clinicaltrials.gov/
  To find this trial, type **CLIK066X2204** in the **Other terms** search box
- European Union Clinical Trials Register – https://www.clinicaltrialsregister.eu/ctr-search
  To find this trial, type **CLIK066X2204** in the search box

Full trial title:

A 12-week randomized, patient and investigator blinded, placebo-controlled, parallel group study to investigate the efficacy of LIK066 in obese patients with non-alcoholic steatohepatitis (NASH)

If more trials are planned, they will appear on the public websites listed above. When there, search for **LIK066** or **licogliflozin.**

? If you participated in the trial and have **questions** about the results, please speak with the trial doctors or staff at your trial site.

Thank you!

Novartis would like to thank all of the people who participated in this clinical trial. The participants made this clinical trial possible and helped researchers answer important health questions and learn about a possible medical treatment. Many volunteers and many clinical trials are needed to advance medical science.

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