Clinical Trial Results Summary

NOVARTIS

The effects and safety of LMB763 for people with NASH (non-alcoholic steatohepatitis)

Thank you!

Thank you to the participants who took part in the clinical trial for the drug **LMB763**, also called nidufexor. All of the participants helped the researchers learn more about how LMB763 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: CLMB763X2201
Drug studied: LMB763
Sponsor: Novartis

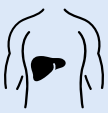
You can find **more information** about this trial by going to the websites listed on **page 11** of this summary.

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

This trial at a glance

What was the purpose of this trial?

Read more on **page 3**



This trial was designed to learn if the trial drug LMB763 worked to treat a severe type of fatty liver disease called NASH, or non-alcoholic steatohepatitis. To find this out, the trial staff looked at the levels of a protein in the blood called alanine aminotransferase (ALT). Higher ALT levels in the blood can be a sign of liver damage. This trial was also designed to learn about the safety of LMB763.

This trial was designed to answer these questions:

- Did LMB763 lower ALT levels in the participants' blood?
- What medical problems did the participants have in this trial?
  Keeping track of the medical problems helped to learn about the safety of LMB763.

Who was in this trial?

Read more on **page 3**

- 121 men and women were in this trial
- Every participant in this trial had NASH or signs of liver damage

What treatments did the participants take?

Read more on **page 4**

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

- High dose of LMB763
- Low dose of LMB763
- 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 **page 6**

On average, the participants who took either dose of LMB763 had lower ALT levels at the end of the trial compared to the participants who took the placebo.

The clinical trial team concluded that LMB763 was safe for the participants in this trial. Fewer participants who took the low dose reported medical problems compared to those who took the high dose. Some of the medical problems were serious. The most common medical problem was itchiness.

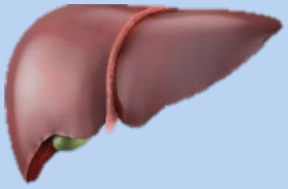
This trial had other results along with the main results. Read more on **page 9**

What was the purpose of this clinical trial?

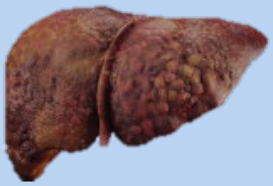
Researchers are looking for better ways to treat **NASH**, which stands for non-alcoholic steatohepatitis. NASH is a severe type of fatty liver disease, which happens when there is too much fat in the liver. It causes liver damage and inflammation.

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 and high cholesterol. The disease is not caused by drinking too much alcohol, 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, feeling tired, and unexplained weight loss.

LMB763, also called nidufexor, is a trial drug designed to possibly help treat NASH by preventing the buildup of fat that damages the liver. To find out if LMB763 had an effect on liver damage, the clinical trial team looked at the levels of a protein found in the liver and blood called alanine aminotransferase or **ALT**. As liver damage happens, the liver leaks ALT into the blood, causing ALT levels to go up.

LMB763 has not yet been approved for use. Before a drug can be approved for people to take, researchers do many trials to find out how safe it is and how it works.

This trial was designed to answer these questions:

- Did LMB763 lower ALT levels in the participants' blood?
- What medical problems did the participants have in this trial? Keeping track of the medical problems helped to learn about the safety of LMB763.

Who was in this trial?

121 participants were in this trial – 69 women and 52 men. Everyone was 18 to 75 years old. Their average age was 51.

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

Every participant in this trial either:

- Had been diagnosed with NASH after doctors did a liver biopsy, which is when doctors take a small piece of the liver to check under a microscope
- Was overweight and had type 2 diabetes

A person couldn't be in this trial if they regularly drank too much alcohol or took certain medicines.

Partway through the trial, the sponsor changed the ranges of ALT levels the participants had to have to let more people take part in the trial.

This trial took place in Australia, Georgia, Jordan, New Zealand, Switzerland, the United Kingdom, and the United States.

For more information about who could and could not be in this trial, and the participants in this trial, visit novctrd.com. Use trial number **CLMB763X2201** to find the scientific summary.

What treatments did the participants take?

A computer program was used to randomly assign each participant the treatment they took:

- **High dose LMB763**: 100 mg (milligrams)
- **Low dose LMB763**: 50 mg
- **Placebo**: A 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 clinical trial team compared the results as fairly as possible.

The participants took their assigned treatment as pills one time a day every day for 12 weeks.

The participants and most trial staff did not know what treatment each participant took during the trial. The trial pharmacists knew the treatment assigned to each participant so they could supply them with the right treatment. Some trials are done this way because knowing what treatment participants take can influence the results. Not knowing what treatment participants take helps make sure the results are looked at fairly.

What happened during this trial?

The trial began in October 2016 and ended in March 2019.
27 of the 121 participants did not complete this trial.

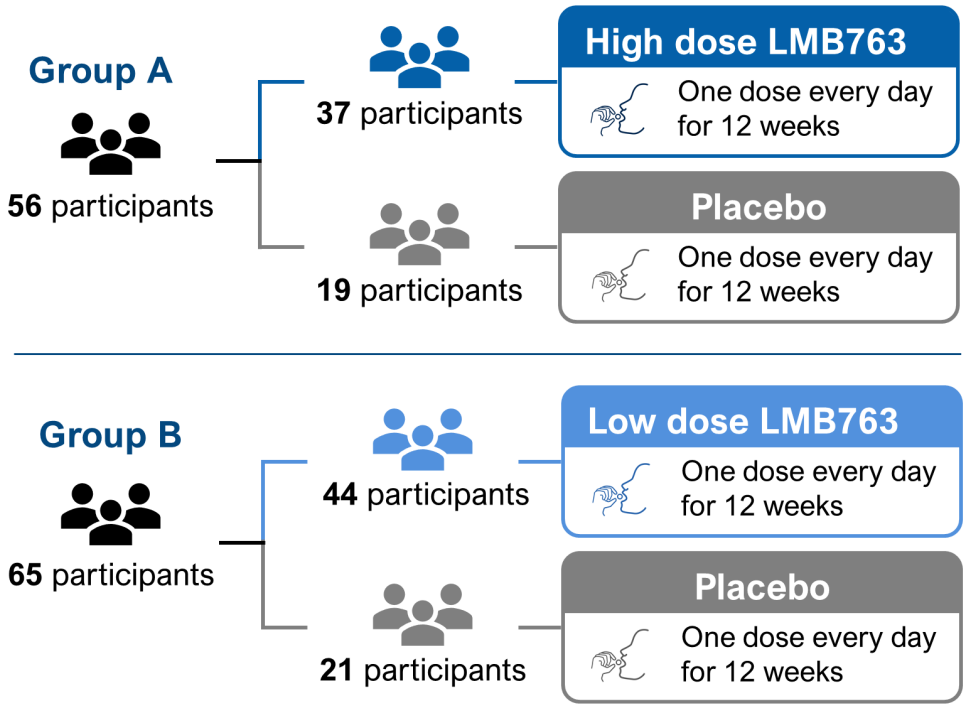
This trial ended early because the clinical trial team had collected enough data about the safety of the low dose of LMB763 and how well it worked.

Here's how this trial was done:

Before treatment

- The trial doctors checked each participant's health, ALT levels, and other NASH symptoms to make sure they could be in this trial

During treatment



For Group A and Group B:

- The trial doctors could lower a participant's dose if needed
- The trial doctors asked each participant to follow a healthy eating plan
- The trial staff took blood and urine samples and checked each participant's health during visits to the trial site

After treatment

- About 4 weeks after their last dose, each participant visited the trial site for the trial doctors to check their health
- 30 days after each participant's last visit, the trial staff called to check their health

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.

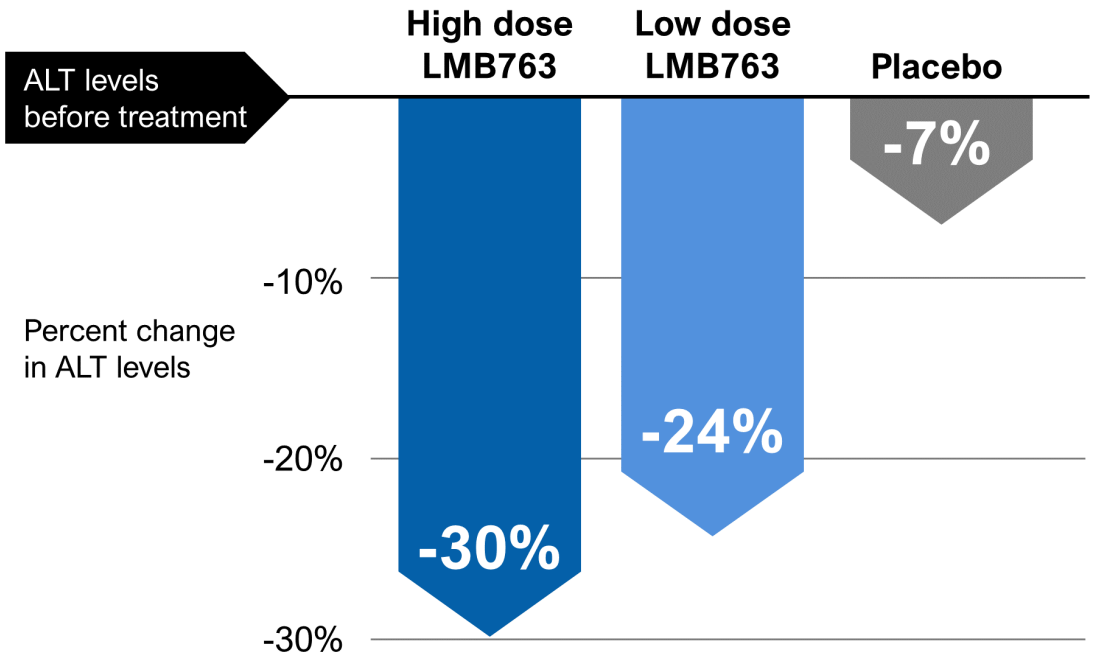
Did LMB763 lower ALT levels in the participants' blood?

On average, the participants who took either dose of LMB763 had lower ALT levels compared to the participants who took the placebo.

To find this out, the trial doctors measured the levels of a protein found in the liver and blood called alanine aminotransferase or **ALT**. As liver damage happens, the liver leaks ALT into the blood, causing ALT levels to go up.

The trial staff measured each participant's ALT levels before and after 12 weeks of treatment. The chart below shows the average change in the participants' ALT levels. A negative percent means their ALT levels went down after treatment.

Average percent change in ALT levels after 12 weeks of treatment



What medical problems did the participants have during the 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 do not think the adverse events might be related to the trial treatments.

The clinical trial team concluded that LMB763 was safe for the participants in this trial. The most common adverse event was itchiness.

The trial doctors looked for adverse events when they checked the participants’ health at the trial site and when they checked their blood and urine samples. The participants also reported adverse events.

Participants who had adverse events

Participants who had:	High dose LMB763 37 participants	Low dose LMB763 44 participants	Placebo 40 participants
Serious adverse events	5% 2 of 37	7% 3 of 44	0% 0 of 40
Other adverse events	95% 35 of 37	84% 37 of 44	83% 33 of 40
Left this trial due to adverse events	30% 11 of 37	0% 0 of 44	10% 4 of 40

What serious adverse events did the participants have?

High dose of LMB763 **37** participants	Low dose of LMB763 **44** participants
2 participants (5%) had a serious adverse event. These were: • **A non-cancerous tumor in the small intestine** (benign small intestinal neoplasm) • **A condition where the liver cannot clear waste properly** (cholestatic jaundice)	3 participants (7%) had a serious adverse event. These were: • **Cough** • **Gallstones** (cholelithiasis) • **Middle ear infection** (otitis media)

None of the participants who took the placebo reported serious adverse events. None of the participants died.

What other types of adverse events did the participants have?

Most participants reported adverse events that were not serious. The table on the next page show the adverse events that happened to **10 or more participants**. Other adverse events were reported by fewer participants.

For more information about the adverse events, including those that happened to fewer participants in this trial, visit novctrd.com. Use clinical trial number **CLMB763X2201** to find the scientific summary.

Types of adverse events reported during this trial

Participants who had:	High dose LMB763 37 participants	Low dose LMB763 44 participants	Placebo 40 participants
Itchiness Pruritus	54% 20 of 37	30% 13 of 44	15% 6 of 40
Headache	8% 3 of 37	16% 7 of 44	20% 8 of 40
Protein leak into urine Urine protein/creatinine ratio increased	19% 7 of 37	18% 8 of 44	8% 3 of 40
Feeling sick to the stomach Nausea	19% 7 of 37	11% 5 of 44	5% 2 of 40
Diarrhea	11% 4 of 37	9% 4 of 44	10% 4 of 40
Protein leak into urine Urine albumin/creatinine ratio increased	5% 2 of 37	9% 4 of 44	13% 5 of 40

What other results were learned?

Did LMB763 affect the fats in the participants' bodies?

The clinical trial team also learned that, compared to the participants who took the placebo, the participants who took LMB763 lost more weight and liver fat.

On average, the participants had no change in the levels of most of the fats in their blood while fasting during this trial.

Did LMB763 affect 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.

At trial visits before and after treatment, the trial staff checked for signs of liver fibrosis in the participants. On average, the treatments in this trial had no effect on participants' signs of liver fibrosis.

Did LMB763 affect participants' itchiness?

The participants also rated their itchiness before and at the end of treatment. The participants who took the high dose of LMB763 rated their itchiness slightly higher compared to the participants who took the low dose or placebo. However, more trials are needed to know if this difference was meaningful.

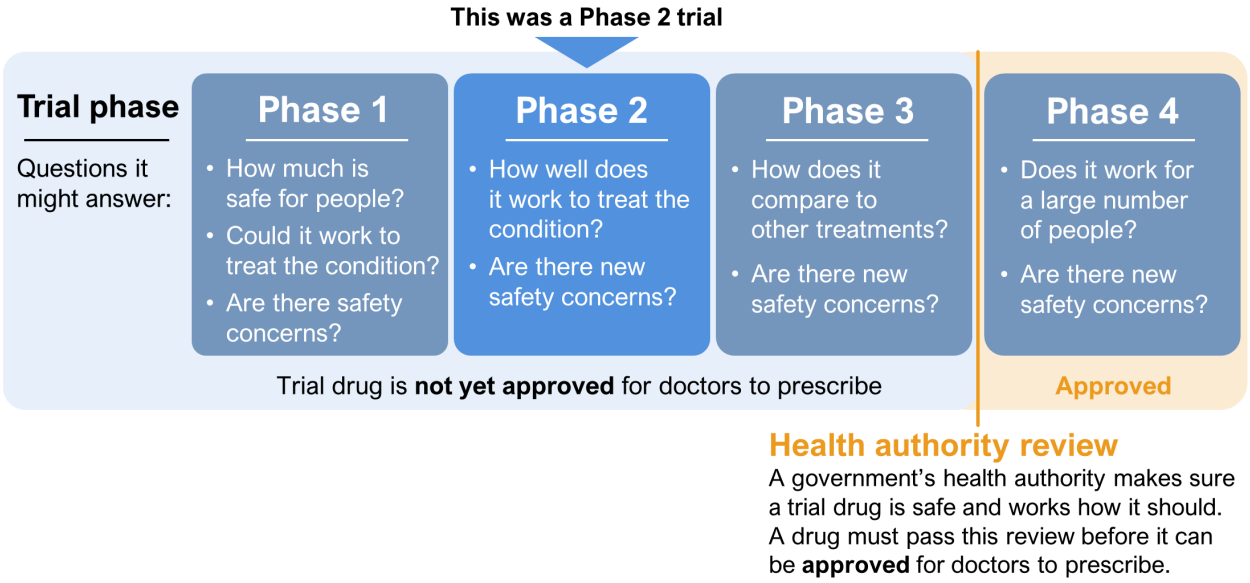
What was learned from this trial?

This was the first trial to learn about how well LMB763 works for people with NASH. The clinical trial team found:

- Lower ALT levels in the blood of participants who took either dose of LMB763 compare to those who took placebo.
- Less adverse events were reported by those that took the low dose of LMB763 compared to those who took the high dose.

The team concluded that LMB763 was safe for the participants in this trial.

This was a Phase 2 trial, which learns about the safety of a trial drug and how well it works in a small number of participants. This was one of many trials a drug must go through before it can be approved for doctors to prescribe. The chart below shows these phases and the questions they're designed to answer.



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 and trial summary for patients” 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 “Search by study number” on the bottom left of the page
5. Type **“CLMB763X2201”** 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.

If you were in this trial and have questions about the results, please speak with the doctor or staff where you took part in this clinical trial.

This trial was registered on the following websites:

- ClinicalTrials.gov – https://clinicaltrials.gov/
  To find this trial, type **CLMB763X2201** in the **Other terms** search box
- European Union Clinical Trials Register – https://www.clinicaltrialsregister.eu/ctr-search
  To find this trial, type **CLMB763X2201** in the search box

Full trial title:

A randomized, patient and investigator blinded, placebo-controlled, multicenter study to assess the safety, tolerability, pharmacokinetics and efficacy of LMB763 in patients with non-alcoholic steatohepatitis (NASH)

If more trials are planned, they will appear on the public websites listed on the previous page. When there, search for **LMB763**.

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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