Clinical Trial Results Summary

The safety and effects of LJN452 in participants with liver disease when taken in the evening or morning

Thank you

Thank you to the participants who took part in the clinical trial for the trial drug LJN452. All of the participants helped the researchers learn more about the safety of LJN452 and how it works.

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.

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

Research Sponsor: Novartis
Drug Studied: LJN452 (Tropifexor)
Trial Number: CLJN452A2113

Overview of this trial

What was the purpose of this trial?

The researchers studied the safety of a trial drug called LJN452. They also wanted to find out if taking LJN452 in the evening compared to the morning had a different effect on blood levels of:

- 2 types of fat called LDL and HDL
- Markers of liver health

Who was in the trial?

87 men and women participated in this clinical trial.

The participants were 28 to 74 years old and had liver disease.

What treatments did the participants take?

All the participants in this trial took both LJN452 and a placebo for a total of 4 weeks. The placebo looked like the trial drug but had no trial drug in it.

The participants either took:

- LJN452 in the **morning** and the placebo in the **evening** OR
- LJN452 in the **evening** and the placebo in the **morning**

The trial staff, sponsor staff, and participants did not know when each participant took LJN452 or the placebo.

What were the main results of the trial?

Overall, the researchers learned that both the morning and evening LJN452 groups had a similar:

- Increase in LDL and decrease in HDL
- Change in markers of liver health

Most of the participants had medical problems during this trial. None were serious.

The most common medical problem was itchy skin (pruritus). There were 9 participants who left the trial due to itchy skin. Overall, the researchers found no safety concerns.

More details about the results of this trial are included later in this summary.

What was the purpose of the trial?

Before a drug can be approved for patients to take, researchers do clinical trials to find out how safe it is and how it works. LJN452 is being developed as a possible treatment for a type of liver disease where fat builds up in the liver. This build-up can lead to liver damage.

LJN452 works by helping the body make specific proteins in the liver. These proteins help the liver break down fats that can lead to liver damage.

LJN452, and other treatments like it, have been found to be associated with changes in certain types of fat in the blood. In this trial, the researchers wanted to see if there was a difference in the amount of these fats in the blood when LJN452 was taken in the evening compared to the morning.

In this trial, the researchers looked at 2 types of fats in the blood:

- **LDL:** a type of fat which can collect in the walls of the blood vessels. This can increase the chances of serious conditions like heart attacks and strokes.
- **HDL:** sometimes called a “good” kind of fat because it helps remove other fats from the blood.

The main questions the researchers wanted to answer:

- Was there a difference in LDL levels when participants took LJN452 in the evening compared to the morning for 2 weeks?
- What medical problems did the participants have during this trial?

Keeping track of the medical problems helped to learn about the safety of LJN452.

Other questions the researchers wanted to answer:

- Was there a difference in LDL and HDL levels when people took LJN452 in the evening compared to the morning for 4 weeks?
- Was there a difference in markers of liver health when people took LJN452 in the evening compared to the morning for 4 weeks?

How long was the trial?

This trial started in May 2020 and ended in November 2020. Each participant was in the trial for up to about 13 weeks.

Who was in the trial?

There were 87 participants in this trial—60 women and 27 men. The participants were 28 to 74 years old. Their average age was 55 years old. All of the participants had a type of liver disease where fat builds up in the liver.

What trial treatments did the participants take?

All the participants in this trial took both LJN452 and a placebo.

The clinical trial team used a computer program to randomly assign each participant to take either:

LJN452 in the **morning** and the placebo in the **evening**

OR

LJN452 in the **evening** and the placebo in the **morning**

The placebo looked like LJN452 but had no trial drug in it. Using a placebo ensured the trial staff and the participants did not know when the participants were taking LJN452.

Not knowing when the participants took LJN452 and using a computer program to assign treatments helped make sure the results were looked at fairly.

The participants in this trial took LJN452 and the placebo as a pill by mouth. The doses of LJN452 were measured in micrograms, also known as µg.

The chart below shows the treatments that each group of participants took:

	Morning LJN452 group	Evening LJN452 group
	42 participants	45 participants
	• 200 µg of LJN452 in the morning • placebo in the evening	• placebo in the morning • 200 µg of LJN452 in the evening
	As a pill by mouth	
	Each day for up to 4 weeks	

What were the main results of the trial?

This is a summary of the overall results from this trial. The individual results of each participant might be different and are not in this summary.

The results from several trials are needed to decide which treatments are safest and work best. Other trials may provide new information or different results. Always talk to a doctor before making changes to your healthcare.

Was there a difference in LDL levels when participants took LJN452 in the evening compared to the morning for 2 weeks?

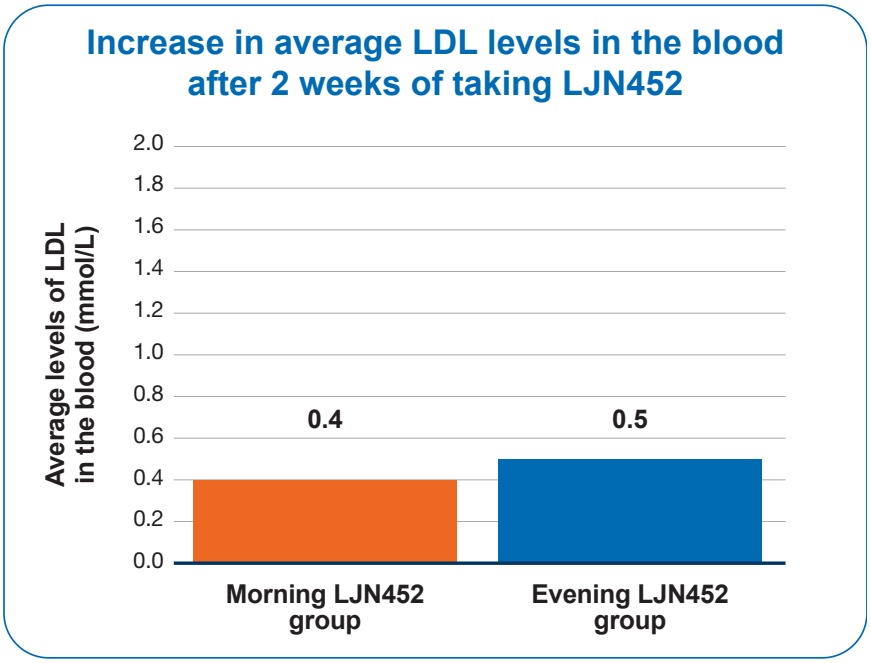
No. Overall, there was **no meaningful difference** in LDL levels when the participants took LJN452 in the evening compared to the participants who took it in the morning.

After 2 weeks of treatment, both groups showed a similar increase in LDL levels.

To find this out, the trial doctors took blood samples from the participants at different times for up 2 weeks after treatment started. The researchers measured how much LDL was in the blood before and after the participants took treatment. Then, they calculated the average change in LDL levels after 2 weeks of treatment for the evening and morning LJN452 groups.

The researchers found that both groups had a similar increase in LDL levels after 2 weeks of treatment. They concluded that taking LJN452 in either the evening or the morning for 2 weeks did not have a meaningful difference in LDL levels.

The chart below shows these results.



The levels of LDL were measured in millimoles per each liter of blood, also known as mmol/L.

What other results were learned?

The researchers also wanted to see if there was a difference between taking LJN452 in the evening compared to the morning for 4 weeks. To find this out, the trial doctors took blood samples at different times before and after the participants took LJN452. They measured LDL, HDL, and markers of liver health. The researchers compared these results from the evening and morning LJN452 groups.

Was there a difference in LDL and HDL levels when people took LJN452 in the evening compared to the morning for 4 weeks?

No. Overall, there was **no meaningful difference** in LDL and HDL levels when the participants took LJN452 in the evening compared to taking it in the morning.

After 4 weeks of treatment, both groups had a similar increase in LDL levels and a similar decrease in HDL levels.

Was there a difference in markers of liver health when people took LJN452 in the evening compared to the morning for 4 weeks?

No. Overall, there was **no meaningful difference** in markers of liver health when the participants took LJN452 in the evening compared to taking it in the morning.

After 4 weeks of treatment, both groups showed a similar difference in markers of liver health.

The researchers measured the blood levels of 3 liver proteins. Doctors use these as markers of liver health:

- alanine aminotransferase, also known as ALT
- aspartate aminotransferase, also known as AST
- gamma-glutamyl transferase, also known as GGT

If the levels of these proteins are too high, this can be a sign of poor liver health. People with liver disease usually have high levels of ALT, AST, and GGT.

Overall, both LJN452 groups had a similar decrease in ALT, AST, and GGT levels after 4 weeks of treatment. The researchers concluded that taking LJN452 in the evening compared to the morning did not make a meaningful difference in changing markers of liver health.

What medical problems happened during the trial?

Medical problems that happen in clinical 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 the treatments in the trial.

A lot of research is needed to know whether a treatment causes an adverse event. Doctors keep track of all the adverse events that happen in trials, even if they do not think the adverse events might be related to the treatments.

This section is a summary of the adverse events that happened during this trial.

Most of the participants had adverse events during this trial. None were considered serious. The most common adverse event was itchy skin. There were 9 participants who left the trial due to itchy skin (pruritus).

Overall, the researchers found no safety concerns.

Serious adverse events

There were no serious adverse events reported, including no deaths.

What were the other adverse events?

The adverse events in the table below happened in **5.0% or more of the participants. This is about 4 or more participants.** There were additional adverse events, but these happened in fewer participants.

Most common other adverse events

Adverse events	Morning LJN452 group (42 participants)	Evening LJN452 group (45 participants)
Itchy skin Pruritus	**47.6%** 20 out of 42	**55.6%** 25 out of 45
Nausea	**11.9%** 5 out of 42	**11.1%** 5 out of 45
Constipation	**9.5%** 4 out of 42	**13.3%** 6 out of 45
Decreased appetite	**7.1%** 3 out of 42	**2.2%** 1 out of 45
Dry mouth	**2.4%** 1 out of 42	**6.7%** 3 out of 45
Vomiting	**2.4%** 1 out of 42	**8.9%** 4 out of 45

For more information about the adverse events in this trial, please see the scientific summary that can be found on the website noted at the end of the summary.

What was learned from this trial?

The clinical trial helped the researchers learn that taking LJN452 in the evening compared to the morning did not make a difference in LDL, HDL, and markers of liver health. It also helped the researchers learn more about the safety of LJN452.

The results presented are for a single trial. Other trials may have different results. This summary shows only the main results from this one trial in a small number of participants. Additional research is needed to confirm these results.

Where can I learn more about this trial?

More information about the results of this trial can be found in the scientific results summary available on the Novartis Clinical Trial Results website.

- Go to www.novctrd.com.
- Once on the site, click **"Clinical Trial Results"** at the top right of the page.
- After accepting the terms, look for the drop-down menu on the left of the page. Click **"Study number"** from the drop-down menu.
- Type **"CLJN452A2113"** into the keyword 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 participated in the trial and have questions about the results, please speak with the trial doctor or staff at your trial site.

You can find more information about this trial on the website listed below.

- www.clinicaltrials.gov Once you are on the website, type **"CLJN452A2113"** into the **"Other terms"** search box and click **"Search"**.

If more clinical trials are planned, they will be listed on the above public websites or at www.novartisclinicaltrials.com. Search for **"LJN452"** or **"tropifexor"** or **"liver disease"** or **"non-alcoholic steatohepatitis"** or **"NASH"**.

Full trial title: A randomized, investigator and subject blinded, multi-center, parallel-arm study to determine the safety and tolerability of tropifexor administered in the morning or in the evening to patients with non-alcoholic steatohepatitis (NASH)

Protocol number: CLJN452A2113

Thank you

Clinical trial participants belong to a large community of participants around the world. They help researchers answer important health questions and study new medical treatments.

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