Clinical Trial Results Summary

Research Sponsor: Novartis

Drug Studied: LJN452

Trial Number: CLJN452A2109

Plain Language Title: A trial to learn how much LJN452 gets into the blood and about its safety in participants with liver disease and in healthy participants without liver disease

Thank you

Thank you to the participants who took part in the clinical trial for the trial drug LJN452, also known as tropifexor. All of the participants helped the researchers learn more about how LJN452 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.

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 on the last page of this summary.

Overview of this trial

What was the purpose of this trial?

In this clinical trial, the researchers studied how much and how quickly a trial drug called LJN452 got into the blood in participants with liver disease and in healthy participants without liver disease.

The researchers also studied the safety of LJN452 in these participants.

The main questions the researchers wanted to answer in this trial were:

- Did the severity of liver disease affect how much and how quickly LJN452 got into the participants' blood?
- What medical problems did the participants have during the trial?

Keeping track of the participants' medical problems helped the researchers learn about the safety of LJN452.

Who was in the trial?

42 men and women participated in this clinical trial. Some of the participants had different severities of liver disease. Some were healthy participants with no liver disease.

What treatments did the participants take?

All of the participants in this trial took LJN452.

What were the main results of the trial?

Overall, the researchers learned that:

- The severity of liver disease did not affect how much LJN452 got into the blood. But, they found the severity of liver disease did affect how quickly LJN452 got into the blood.
- 11.9% of the participants had medical problems during this trial. This was 5 out of 42 participants. Some of the medical problems were serious. None of the participants left the trial due to a medical problem.

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

Why was the research needed?

Before a trial 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 fatty liver disease. In people with fatty liver disease, fat builds up in the liver. This can lead to liver damage. So, it is important for researchers to know if LJN452 is processed by the body differently in people with liver damage compared to healthy people without liver damage.

One of the ways the body removes drugs from the blood is through the liver. The liver breaks down waste, nutrients, and some drugs from the blood. So, when the liver is not working normally, the amount of some drugs in the blood can increase. If this happens, a different dose of the drug could be needed.

In this trial, the researchers wanted to learn if participants with different severities of liver disease would need different doses of LJN452 compared to healthy participants without liver disease.

The main questions the researchers wanted to answer in this trial were:

- Did the severity of liver disease affect how much and how quickly LJN452 got into the participants' blood?
- What medical problems did the participants have during the trial?

Other questions the researchers wanted to answer were:

- Were the results of different liver health measurements related to how much LJN452 was in the participants' blood?
- How much LJN452 was attached to protein in the participants' blood?

Who was in the trial?

To answer the questions in this trial, the researchers asked for the help of men and women with mild, moderate, or severe liver disease. They also asked for the help of healthy participants without liver disease. The participants did not need to have fatty liver disease to be included in the trial.

The participants in this trial were 26 to 68 years old when they joined. The average age of the participants was 51 years.

The trial included 42 participants in the United States.

What treatments did the participants take?

All of the participants in this trial took LJN452 as a pill by mouth.

The doses of LJN452 were measured in micrograms, also known as µg.

During this trial, each participant knew what they were taking. The trial staff and sponsor staff also knew what each participant was taking.

The participants were in different treatment groups based on the severity of their liver disease. The chart below shows the treatment that each group of participants took.

	Group 1	Group 2	Group 3	Group 4
	18 healthy participants	8 participants	8 participants	8 participants
	No liver disease	Mild liver disease	Moderate liver disease	Severe liver disease
	200 µg LJN452			
	1 time			

What happened during the trial?

The trial started in September 2018 and ended in September 2019. Each participant was in the trial for up to about 8.5 weeks.

The chart below shows what happened during the trial.

Before the participants took the treatment

The trial doctors checked the participants' health to make sure they could be in the trial.

Up to 3 weeks

While the participants took the treatment

The participants took LJN452 1 time.

The participants:

- had their overall health checked and answered questions about any medical problems they were having
- had blood and urine samples taken

Up to 8 days

After the participants took the treatment

The trial doctors called the participants and asked them about any medical problems they were having.

30 days after their last visit

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.

Did the severity of liver disease affect how much and how quickly LJN452 got into the participants' blood?

Overall, the researchers found that the severity of liver disease:

- **Did <u>not</u> affect how much LJN452 got into the participants' blood.**
- **Did affect how quickly LJN452 reached the highest level in the participants' blood.**

The researchers wanted to know how much and how quickly LJN452 got into the participants' blood and whether this varied depending on the severity of liver disease. To find this out, the trial staff took blood samples at different times over a period of 7 days before and after the participants took LJN452. The researchers studied:

- the total amount of LJN452 in the blood
- the highest level of LJN452 in the blood
- the average time it took to reach the highest level of LJN452 in the blood

They combined the results of the participants from each group. Then, they calculated the average of the measurements above after the participants took LJN452.

Knowing how much and how quickly LJN452 got into the blood and whether this varied depending on the severity of liver disease will help researchers decide what dose to give participants in future trials.

Overall, the researchers found that:

- The severity of liver disease did not affect the total amount of LJN452 in the participants' blood.
- The severity of liver disease did not affect the highest level of LJN452 in the participants' blood.
- The average time it took to reach the highest level of LJN452 in the blood was longer for the participants with more severe liver disease.

What other results were learned?

Were the results of different liver health measurements related to how much LJN452 was in the participants' blood?

The researchers wanted to find out if the results of different types of liver health measurements were related to how much LJN452 was in the participants' blood.

To find this out, the researchers used different types of measurements at the start of the trial to measure how well each participant's liver was working. They then compared the results of the different types of liver health measurements to how much LJN452 was in the participants' blood.

Overall, the researchers found that the results of the different types of liver health measurements did not affect the amount of LJN452 in the participants' blood.

How much LJN452 was attached to protein in the blood?

Overall, the researchers found:

- **Most of the LJN452 in the blood was attached to protein. This was true for all the groups.**
- **The amount of LJN452 in the blood that was not attached to protein increased slightly with liver severity.**

The researchers wanted to find out how much LJN452 was attached to protein in the participants' blood. When a person takes a drug, some of that drug attaches to the proteins in the blood and some does not. The amount of drug that is not attached to protein is usually the amount of drug that is available to treat the condition. Knowing the amount attached and not attached to protein helps researchers find out the right dose for people with and without liver disease.

The researchers in this trial found that:

- Most of the LJN452 in the blood was attached to protein. This was true for the participants with liver disease and the healthy participants without liver disease.
- Overall, the amount of LJN452 not attached to protein in the participants' blood increased with severity of liver disease. But, this amount was much lower than what researchers have found in healthy participants in other trials. In those trials, the healthy participants could handle higher amounts of LJN452 not attached to protein in the blood.

So, changing the dose of LJN452 may not be needed in participants with liver disease. More research is needed to know for sure.

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.

11.9% of the participants had adverse events during this trial. Some of the adverse events were serious. None of the participants left the trial due to an adverse event.

Summary of adverse events

Treatment group	Participants who had any adverse events	Participants who had serious adverse events
No liver disease Out of 18 healthy participants	11.1% 2 of 18	0.0% 0 of 18
Mild liver disease Out of 8 participants	0.0% 0 of 8	0.0% 0 of 8
Moderate liver disease Out of 8 participants	12.5% 1 of 8	0.0% 0 of 8
Severe liver disease Out of 8 participants	25.0% 2 of 8	25.0% 2 of 8

None of the participants left the trial due to adverse events.

What were the serious adverse events?

There were 4.8% of participants who had a serious adverse event. This was 2 out of 42 participants. The serious adverse events were:

- multiple broken bones in a participant who had severe liver disease
- decreased brain function because of liver disease in a participant who had severe liver disease

No other serious adverse events were reported, including death.

What were the non-serious adverse events?

All of the adverse events in this trial happened in 1 participant each. The table below shows the adverse events that happened during this trial.

	No liver disease (Out of 18 healthy participants)	Mild liver disease (Out of 8 participants)	Moderate liver disease (Out of 8 participants)	Severe liver disease (Out of 8 participants)
Abnormal build-up of fluid in the belly area (Ascites)	0.0% 0 of 18	0.0% 0 of 8	12.5% 1 of 8	0.0% 0 of 8
Constipation	0.0% 0 of 18	0.0% 0 of 8	12.5% 1 of 8	0.0% 0 of 8
Leaking of fluids from a vein because of a needle put into the vein (Infusion site extravasation)	5.6% 1 of 18	0.0% 0 of 8	0.0% 0 of 8	0.0% 0 of 8
Complications during a blood vessel procedure (Vascular procedure complications)	5.6% 1 of 18	0.0% 0 of 8	0.0% 0 of 8	0.0% 0 of 8

For 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 information described above helped researchers learn more about how much LJN452 gets into the blood in participants with liver disease and healthy participants with no liver disease. It also helped researchers learn about how safe LJN452 is in these participants.

The results presented here are for a single trial. This summary shows only the main results from this one trial in a small number of participants.

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 and trial summary for patients"** at the top right of the page.
- After accepting the terms, go to the bottom left of the page and click **"Search by study number"**.
- Type **"CLJN452A2109"** 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 **"CLJN452A2109"** 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 www.novartisclinicaltrials.com. Search for **"Tropifexor"**, **"LJN452"**, **"Fatty liver disease"** or **"NASH"**.

Full trial title: A Phase 1, open-label, single-dose, multi-center, parallel group study to evaluate the pharmacokinetics of tropifexor (LJN452) in subjects with mild, moderate or severe hepatic impairment compared to healthy control subjects

Protocol number: CLJN452A2109

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.

NOVARTIS

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