Clinical Trial Results Summary

Research Sponsor: Novartis

Drug Studied: Tropifexor (LJN452)

Trial Number: CLJN452X2201

Plain Language Title: A trial to learn about the effects of LJN452 on the liver and about its safety in participants with primary biliary cholangitis

Thank you!

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

Note: 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?

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.

In this clinical trial, the researchers studied how a drug called tropifexor affected liver health in participants with a liver disease called primary biliary cholangitis. This disease is also known as PBC.

The researchers also learned more about the safety of tropifexor in these participants.

What treatments did the participants take?

The participants took either tropifexor or a placebo. A placebo looks like a drug but does not have any medicine in it.

Who took part in the trial?

There were 61 adult women and men with PBC who participated in this clinical trial. These participants had already tried treatments that did not help their PBC.

What did the researchers want to learn?

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

- How did the level of liver enzymes change after treatment?
- 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 tropifexor.

What were the main results of the trial?

Overall, the researchers learned that:

- The level of liver enzymes decreased in all treatment groups. Higher doses of tropifexor caused a bigger decrease in liver enzymes compared to the placebo.
- Most of the participants had medical problems during this trial, and none of the medical problems were serious. The most common medical problem was itching.

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

Why was the research needed?

Researchers are looking for a better way to treat patients with primary biliary cholangitis, also known as PBC. 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. In this trial, the researchers studied how the trial drug called tropifexor affected liver health in participants with PBC. The researchers also wanted to learn more about the safety of tropifexor.

PBC is a disease that destroys the bile ducts in the liver. The liver makes bile, which is a fluid that helps the body break down fats. When bile ducts cannot send bile to the gut, bile builds up in the liver and damages it.

There are treatments for PBC, but these may not help some patients. In this trial, the researchers wanted to learn more about tropifexor as a possible treatment. The researchers already did trials with tropifexor in healthy people. In this trial, they wanted to study its effects on liver health in participants with PBC.

Tropifexor works by preventing new bile acids from being made and helping more bile acids leave the liver. This helps to decrease the overall buildup of bile acids in the liver.

What was the purpose of the trial?

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

- How did the level of liver enzymes change after treatment?
- What medical problems did the participants have during the trial?

What treatments did the participants take?

During this trial, the participants took tropifexor or the placebo. Tropifexor was measured in milligrams, also known as mg. The participants took 1 of the following treatments once a day for 28 days:

- 0.03 mg tropifexor
- 0.06 mg tropifexor
- 0.09 mg tropifexor
- 0.15 mg tropifexor
- the placebo

The researchers used a computer program to randomly choose the treatment each participant took. This helped make sure that comparing the results of the treatments was as fair as possible.

The chart below shows the treatments the participants took.

	• 11 participants	• 9 participants	• 12 participants	• 8 participants	• 21 participants
	• 0.03 mg tropifexor	• 0.06 mg tropifexor	• 0.09 mg tropifexor	• 0.15 mg tropifexor	• the placebo
	• Through a capsule by mouth				
	• Once a day for 28 days				

Who took part in the trial?

To answer the questions in this trial, the researchers asked for the help of adult participants with PBC who had tried other treatments that did not help. The average age of the participants was about 56 years. All who joined the trial were between 31 to 80 years old when they joined.

The trial included 61 participants in 6 countries: Canada, Germany, Poland, Russia, the United Kingdom, and the United States.

What type of trial was this?

This trial studied the trial drug's safety by giving different amounts of the drug to a small number of people.

In this trial, none of the participants, trial staff, or sponsor staff knew what treatment each participant took.

Some trials are done this way because knowing what treatment the participants are taking can influence the results. Not knowing what treatment the participants take helps make sure the results are looked at fairly.

What happened during the trial?

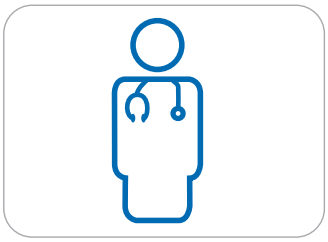
Each participant was planned to be in the trial for up to about 24 weeks. The trial started in September 2015 and ended in August 2018.

There were 2 parts planned for this trial. In July 2018 the researchers made the decision to stop this trial early before starting Part 2. This was because the sponsor had enough data to understand how tropifexor worked in people with PBC. The decision to stop was not related to the safety of the treatment.

The chart below shows what happened during the trial.

Before the participants took the trial treatment

- The trial doctors checked to make sure the participants could join the trial.



Up to 84 days before taking treatment

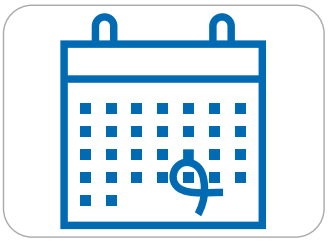
While the participants were taking the trial treatment

- The participants took tropifexor or the placebo once a day.
- The trial doctors took blood and urine samples from each participant once a week.
- The trial doctors checked each participant's health and asked about their medical problems.

Up to 28 days

After taking the last trial treatment

- The participants had final visits 1 month and 2 months after taking the last dose.



What did researchers learn from the 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.

Other trials may provide new information or different results. Always talk to a doctor before making any treatment changes.

How did the level of liver enzymes change after treatment?

The researchers found that higher doses of tropifexor decreased the participants' liver enzymes more than the placebo did.

To answer this question, the trial doctors measured the level of a liver enzyme known as gamma-glutamyl transferase, also called GGT. Enzymes are found in cells and help speed up chemical reactions in the body. In this trial, the researchers were most interested in GGT because it shows how well bile is flowing out of the liver. The amount of GGT in the blood is usually higher in people with liver disease. The researchers wanted to learn if the level of GGT decreased more in the participants who took tropifexor than in the participants who took the placebo.

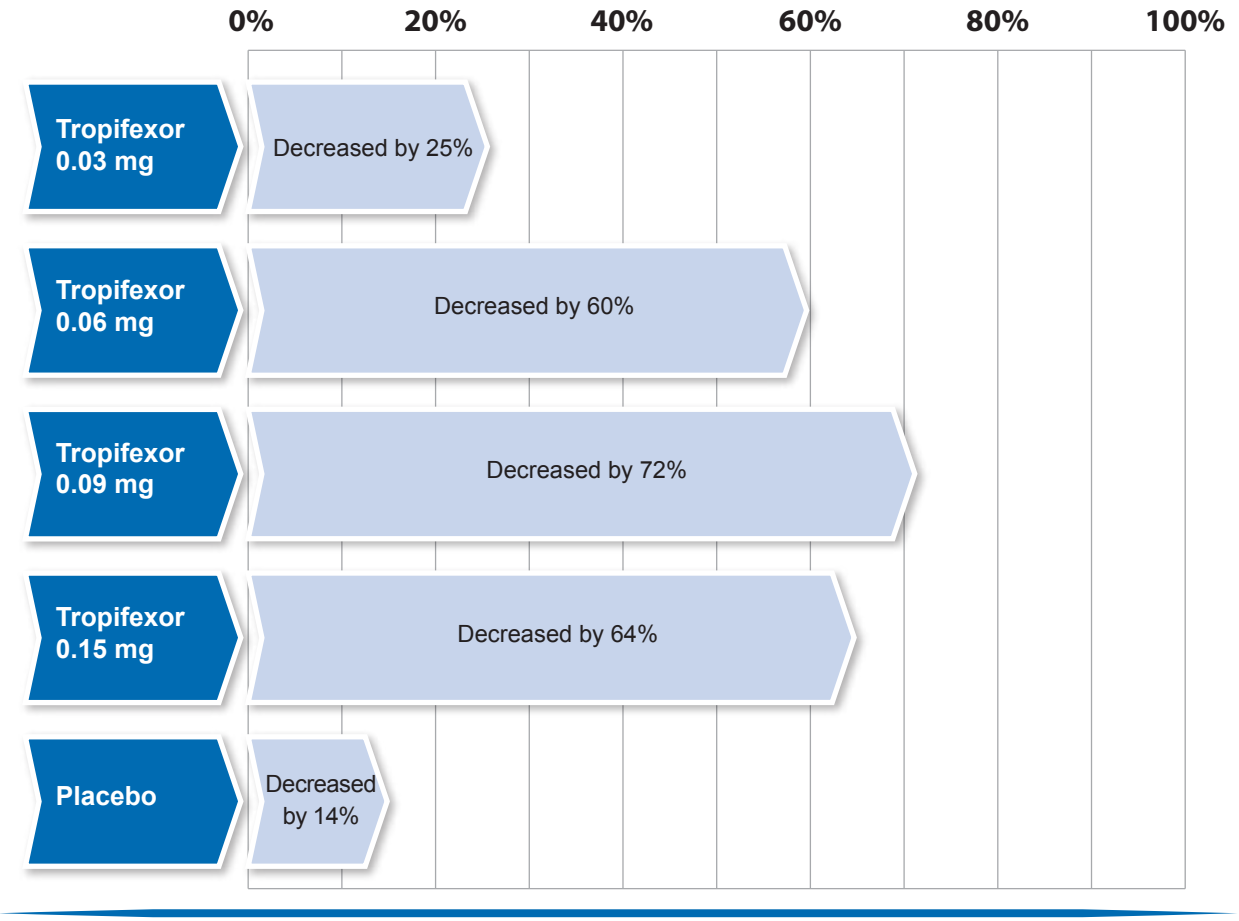
The researchers found that after 28 days of taking trial treatment:

- The participants in every treatment group had a decreased level of GGT.
- The participants who took 0.06 mg, 0.09 mg, or 0.15 mg of tropifexor had a bigger decrease in GGT levels compared to the participants who took the placebo.
- The difference in the decrease between the participants who took 0.03 mg of tropifexor and those who took the placebo was smaller. It was too small for the researchers to know if 0.03 mg of tropifexor decreased GGT levels more than the placebo.

The researchers concluded that higher doses of tropifexor decreased the participants' GGT levels more than the placebo did.

The chart below shows the decrease in the average GGT levels that each treatment group had after 28 days of treatment.

Percent decrease in the average GGT levels after 28 days of treatment



What medical problems happened during the trial?

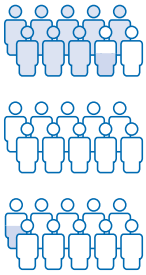
Medical problems that happen in clinical trials are called “adverse events”. An adverse event is any unwanted sign or symptom that participants have during a trial. An adverse event is considered “serious” when it is life-threatening, causes lasting problems, or the participant needs hospital care.

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 medical problems during this trial, and none of the medical problems were serious. The most common medical problem was itching.

How many participants had adverse events?



- 85.2% of participants had adverse events. This was 52 out of 61 participants.
- None of the participants had serious adverse events.
- 4.9% of participants stopped treatment because of adverse events. This was 3 out of 61 participants.

What were the most common serious adverse events?

During this trial, none of the participants had serious adverse events or died due to serious adverse events.

What were the most common adverse events?

The most common adverse event during this trial was itching.

The adverse events below happened in more than 2 participants during the trial. There were other adverse events, but these happened in fewer participants.

Most common adverse events during this trial

	0.03 mg of tropifexor (Out of 11 participants)	0.06 mg of tropifexor (Out of 9 participants)	0.09 mg of tropifexor (Out of 12 participants)	0.15 mg of tropifexor (Out of 8 participants)	Placebo (Out of 21 participants)
Itching	27.3% (3)	66.7% (6)	41.7% (5)	87.5% (7)	28.6% (6)
Nausea	9.1% (1)	11.1% (1)	16.7% (2)	0.0% (0)	14.3% (3)
Headache	0.0% (0)	0.0% (0)	16.7% (2)	12.5% (1)	14.3% (3)
Upper stomach pain	9.1% (1)	0.0% (0)	8.3% (1)	0.0% (0)	14.3% (3)
Indigestion	9.1% (1)	22.2% (2)	0.0% (0)	12.5% (1)	0.0% (0)
Common cold	18.2% (2)	0.0% (0)	8.3% (1)	0.0% (0)	4.8% (1)
Decreased appetite	0.0% (0)	0.0% (0)	0.0% (0)	12.5% (1)	9.5% (2)
Tiredness	0.0% (0)	0.0% (0)	8.3% (1)	12.5% (1)	4.8% (1)
Being unable to sleep	9.1% (1)	0.0% (0)	8.3% (1)	12.5% (1)	0.0% (0)
Rash	9.1% (1)	0.0% (0)	0.0% (0)	12.5% (1)	4.8% (1)
Sleep disorder	9.1% (1)	0.0% (0)	0.0% (0)	12.5% (1)	4.8% (1)
Vomiting	9.1% (1)	0.0% (0)	0.0% (0)	0.0% (0)	9.5% (2)

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.

How has this trial helped patients and researchers?

The information described above helped researchers learn more about how LJN452 affects liver health in participants with PBC. The information also helped researchers learn how safe tropifexor is to take.

More research is needed to find out which treatments can be used for patients with PBC. This summary shows only the main results from this one trial. Other trials may provide new information or different 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 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 **"CLJN452X2201"** 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 websites listed below.

- www.clinicaltrials.gov Once you are on the website, type **"CLJN452X2201"** into the **"Other terms"** search box, and click **"Search"**.

If you would like to search by trial title, please use the full trial title listed below.

- www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search"**, then type **"2015-001590-41"** in the search box, and click **"Search"**.

Full trial title: A multi-part, randomized, double-blind, placebo-controlled study to assess the safety, tolerability and efficacy of tropifexor (LJN452) in patients with Primary Biliary Cholangitis

Protocol number: CLJN452X2201

Thank you!

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

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