NOVARTIS

Clinical Trial Results Summary

A trial to learn more about the safety of LJN452 when taken with cenicriviroc in participants with nonalcoholic steatohepatitis and liver fibrosis

Trial Number: CLJC242A2201J

Thank you

Thank you to the participants who took part in the clinical trial for the trial drug LJN452, also called tropifexor, when given together with cenicriviroc. All of the participants helped the researchers learn more about how LJN452 and cenicriviroc work and how safe it is to take the combination treatment.

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.

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 on the last page of this summary.

What was the purpose of the trial?

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 and cenicriviroc are being developed as possible treatments for people with "steatohepatitis", also known as **fatty liver disease**, who also have liver fibrosis.

In people with **fatty liver disease**, fat builds up in the liver, which leads to liver damage and liver fibrosis. Liver fibrosis means that there is an increased amount of scarred tissue in the liver, which can keep the liver from working as well as it should.

The trial drug, LJN452, works by helping specific proteins in the intestines and liver. These proteins help keep the liver working as well as it should.

Researchers think that another potential treatment known as cenicriviroc may also help people with fatty liver disease and liver fibrosis. Cenicriviroc works by blocking a specific protein that can increase the levels of swelling and scarring to the liver and liver tissue.

Other trials have been done to learn about the safety of LJN452 or cenicriviroc and how they individually affected liver health when they were taken on their own. In this trial, the researchers wanted to learn more about how safe LJN452 and cenicriviroc were and how they affected the liver when taken together, compared to when they were taken on their own.

The main question the researchers wanted to answer in this trial was:

- What medical problems happened during this trial?

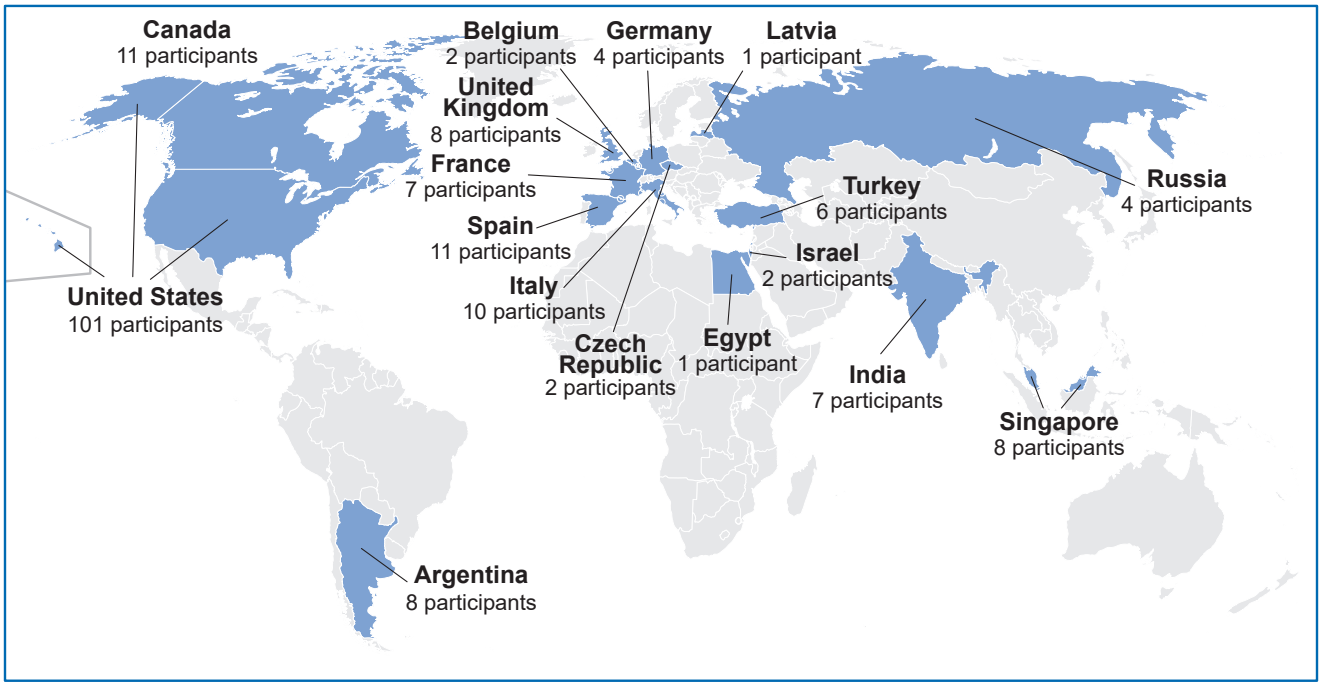
Other questions the researchers wanted to answer were:

- Did the number of participants with a decrease in the severity of their **liver fibrosis** differ between participants who took LJN452 with cenicriviroc compared to participants who took only 1 of them?
- Did the number of participants with a decrease in the severity of their **fatty liver disease** differ between participants who took LJN452 with cenicriviroc compared to participants who took only 1 of them?

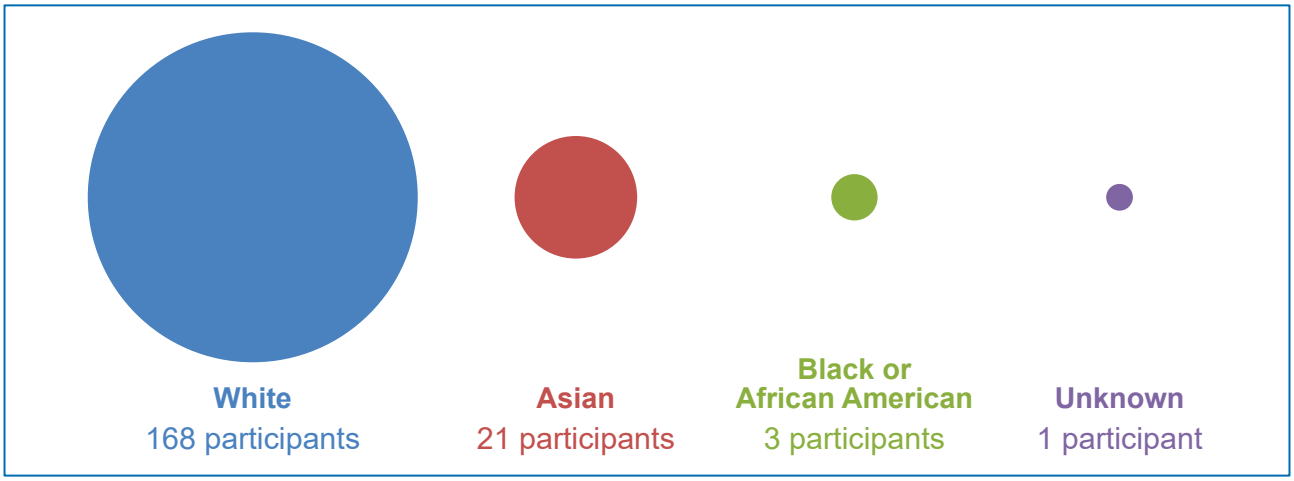
Who was in this trial?

To answer the questions in this trial, the researchers asked for the help of men and women who had fatty liver disease not related to alcohol with liver fibrosis. This trial included 113 women and 80 men. Of these participants, 149 were 22 to 64 years old, and 44 were 65 to 81 years old.

Participants' countries (out of 193 participants)



Participants' race (out of 193 participants)



What treatments did the participants take?

The participants in this trial took 1 of the following treatments:

- LJN452 with cenicriviroc
- LJN452 with a placebo that looked like cenicriviroc
- cenicriviroc with a placebo that looked like LJN452

The placebo looked like either LJN452 or cenicriviroc, but had no trial drug in it. This was done so all the participants took the same number of tablets or capsules. Using a placebo ensured that the trial staff and the participants did not know if they were taking LJN452 with cenicriviroc, or taking 1 of the drugs by itself.

There were 2 different doses of LJN452 in this trial. These doses were measured in micrograms, also known as µg. There was 1 dose of cenicriviroc. The dose of cenicriviroc was measured in milligrams, also known as mg.

The researchers used a computer program to randomly assign the treatment each participant took. This helped make sure the treatments were chosen fairly and comparing the results of the treatments was as accurate as possible.

This was a “double-blind” trial. This means none of the participants, trial staff, or sponsor staff knew what treatment each participant took.

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

	LJN452 140 µg and cenicriviroc 150 mg	**LJN452 90 µg and cenicriviroc 150 mg**	**LJN452 140 µg and a placebo**	**Cenicriviroc 150 mg and a placebo**
	• LJN452 as capsules by mouth • cenicriviroc as tablets by mouth	• LJN452 as capsules by mouth • cenicriviroc as tablets by mouth	• LJN452 as capsules by mouth • A placebo as tablets by mouth	• cenicriviroc as tablets by mouth • A placebo as capsules by mouth
	Once a day for up to 48 weeks			
	47 participants	48 participants	50 participants	48 participants

What happened during this trial?

The trial started in September 2018 and ended in October 2020. Each participant was in the trial for up to 62 weeks.

The chart below shows what happened during this trial to find the main results.

Before the participants took the treatment

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

Within 10 weeks before treatment

While the participants took the treatment

The participants:

- took their assigned treatments
- had blood and urine samples taken
- had a tissue sample of their liver taken
- had an ultrasound of their liver to check their liver fibrosis
- had their overall health checked and answered questions about any medical problems they were having

Up to 48 weeks

After the participants took the treatment

The participants visited their trial site to have more blood samples taken. The doctors also asked them questions about any medical problems they were having and about the medications they were taking.

4 weeks after their last dose

What were the main results of this 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.

What medical problems happened during this 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.

85.5% of the participants had adverse events during this trial. This was 165 out of 193 participants. Some of the adverse events were serious. Some of the participants left the trial due to an adverse event.

Summary of adverse events

	LJN452 140 µg and cenicriviroc 150 mg (percentage and number of participants)	LJN452 90 µg and cenicriviroc 150 mg (percentage and number of participants)	LJN452 140 µg and a placebo (percentage and number of participants)	Cenicriviroc 150 mg and a placebo (percentage and number of participants)
Participants who had any adverse events	85.1% 40 of 47	87.5% 42 of 48	84.0% 42 of 50	85.4% 41 of 48
Participants who had any serious adverse events	8.5% 4 of 47	20.8% 10 of 48	10.0% 5 of 50	6.3% 3 of 48
Participants who left the trial due to an adverse event	17.0% 8 of 47	2.1% 1 of 48	18.0% 9 of 50	6.3% 3 of 48

What were the most common serious adverse events?

The serious adverse events below happened in 2 participants each. There were other serious adverse events, but these happened in fewer participants. The participants who had a stroke did not have COVID-19.

Most common serious adverse events

Serious adverse event	LJN452 140 µg and cenicriviroc 150 mg (percentage and number of participants)	LJN452 90 µg and cenicriviroc 150 mg (percentage and number of participants)	LJN452 140 µg and a placebo (percentage and number of participants)	Cenicriviroc 150 mg and a placebo (percentage and number of participants)
A stroke	2.1% 1 of 47	2.1% 1 of 48	0.0% 0 of 50	0.0% 0 of 48
A type of virus called coronavirus known as COVID-19	0.0% 0 of 47	4.2% 2 of 48	0.0% 0 of 50	0.0% 0 of 48

None of the participants died due to serious adverse events during this trial.

What were the most common adverse events?

The table below shows the adverse events that happened in at least 5.0% of the participants overall. There were other adverse events, but these happened in fewer participants.

Most common adverse events

Adverse event	LJN452 140 µg and cenicriviroc 150 mg (percentage and number of participants)	LJN452 90 µg and cenicriviroc 150 mg (percentage and number of participants)	LJN452 140 µg and a placebo (percentage and number of participants)	Cenicriviroc 150 mg and a placebo (percentage and number of participants)
Itchy skin	31.9% 15 of 47	20.8% 10 of 48	40.0% 20 of 50	20.8% 10 of 48
Nausea	14.9% 7 of 47	12.5% 6 of 48	4.0% 2 of 50	12.5% 6 of 48
Tiredness	10.6% 5 of 47	8.3% 4 of 48	14.0% 7 of 50	8.3% 4 of 48
Joint pain	12.8% 6 of 47	2.1% 1 of 48	12.0% 6 of 50	6.3% 3 of 48
Urinary tract infection	4.3% 2 of 47	8.3% 4 of 48	14.0% 7 of 50	6.3% 3 of 48
Constipation	12.8% 6 of 47	6.3% 3 of 48	10.0% 5 of 50	4.2% 2 of 48
Stomach pain	10.6% 5 of 47	4.2% 2 of 48	10.0% 5 of 50	6.3% 3 of 48
Upper respiratory tract infection	10.6% 5 of 47	10.4% 5 of 48	6.0% 3 of 50	4.2% 2 of 48
Feeling weak	10.6% 5 of 47	6.3% 3 of 48	8.0% 4 of 50	4.2% 2 of 48
Diarrhea	8.5% 4 of 47	0.0% 0 of 48	4.0% 2 of 50	14.6% 7 of 48
Back pain	10.6% 5 of 47	8.3% 4 of 48	2.0% 1 of 50	6.3% 3 of 48
Upper stomach pain	10.6% 5 of 47	4.2% 2 of 48	6.0% 3 of 50	4.2% 2 of 48
Swelling of the stomach, also known as distension	2.1% 1 of 47	8.3% 4 of 48	4.0% 2 of 50	6.3% 3 of 48
Infection of the sinuses, the small empty spaces behind the forehead and cheekbones	8.5% 4 of 47	6.3% 3 of 48	4.0% 2 of 50	2.1% 1 of 48

What other results were learned?

Did the number of participants with a decrease in the severity of their liver fibrosis differ between participants who took LJN452 with cenicriviroc compared to participants who took only 1 of them?

No. Overall, the researchers found that there was no difference in the number of participants who had a decrease in the severity of their liver fibrosis between those who took LJN452 with cenicriviroc compared to those who took only 1 of them.

The researchers wanted to know if there was a decrease in the severity of the participants' liver fibrosis after treatment. To find this out, the trial doctors took tissue samples of the participants' livers before and after the treatment period. They did this to see how much of the liver tissue was scarred. They counted how many participants had a decrease in the amount of scarred liver tissue after 48 weeks of treatment. Then, they compared the results in the participants who took LJN452 with cenicriviroc to the participants who took only 1 of the treatments.

Overall, the researchers found that there was no difference in the number of participants who had a decrease in the amount of scarred liver tissue in those who took LJN452 with cenicriviroc compared to those who took only 1 of them.

Did the number of participants with a decrease in the severity of their fatty liver disease differ between participants who took LJN452 with cenicriviroc compared to participants who took only 1 of them?

No. Overall, the researchers found that there was no difference in the number of participants who had a decrease in the severity of their fatty liver disease between those who took LJN452 with cenicriviroc compared to those who took only 1 of them.

The researchers wanted to know if there was a decrease in the severity of the participants' fatty liver disease after treatment. To find this out, the trial doctors took tissue samples of the participants' livers before and after treatment. They counted how many participants had a decrease in the severity of their fatty liver disease after 48 weeks of treatment. Then, they compared the results in the participants who took LJN452 with cenicriviroc to the participants who took only 1 of the treatments.

Overall, the researchers found that there was no difference in the number of participants who had a decrease in the severity of their fatty liver disease between those who took LJN452 with cenicriviroc compared to those who took only 1 of them.

What was learned from this trial?

The information described above helped the researchers learn that the safety of LJN452 when taken with cenicriviroc was similar to the safety results when the participants took only 1 of them. They learned that there was no difference in the the severity of the participants' liver fibrosis between participants who took LJN452 with cenicriviroc and participants who took only 1 of them. The researchers also learned that there was no difference in the severity of the participants' fatty liver disease between participants who took LJN452 with cenicriviroc and participants who took only 1 of them.

The results presented here are for a single trial. This summary shows only the main results from this one trial. If you have any questions, please talk to the doctor or staff at your trial site.

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, go to the bottom left of the page and click **"Study number"** from the drop-down menu.
- Type **"CLJC242A2201J"** 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 **"CLJC242A2201J"** 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", "Tropifexor", "Cenicriviroc", "Fatty liver disease"** or **"NASH".**

Full trial title: A randomized, double-blind, multicenter study to assess the safety, tolerability, and efficacy of a combination treatment of tropifexor (LJN452) and cenicriviroc (CVC) in adult patients with nonalcoholic steatohepatitis (NASH) and liver fibrosis (TANDEM)

Protocol number: CLJC242A2201J

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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Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

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