Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis

Drug Studied: LJN452 (tropifexor)

Protocol Number: CLJN452X2202

Thank you!

Thank you for taking part in the clinical trial for the study drug LJN452, also called tropifexor. You and all of the participants helped researchers learn more about how LJN452 works in people with primary bile acid diarrhea, also called PBAD.

Novartis sponsored this trial and believes it is important to share the results of the trial with you and the public. An independent non-profit organization called CISCRP prepared this summary of the trial results for you. We hope it helps you understand your important role in medical research.

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

What has happened since the trial ended?

You were in this trial for up to about 3 months. The entire trial lasted about 1 year and 9 months. This is because participants started and stopped at different times. The trial started in April 2016 and ended in January 2018.

The researchers planned to include 30 participants in the trial. But, after reviewing the initial results, they found that LJN452 did not lower PBAD symptoms as much as the researchers expected. It was also challenging for the researchers to find enough participants with PBAD suitable to join the trial. So, the researchers decided to stop the trial early.

The trial included 20 participants from 4 trial sites in the United Kingdom and the United States. After the trial ended, the sponsor reviewed the data and created a report of the results. This is a summary of that report.

Why was the research needed?

Researchers are looking for a better way to treat participants with PBAD. Before a drug can be approved for participants to take, researchers perform clinical trials to find out how safe it is and how well it works. The information collected from many clinical trials is needed to find out if LJN452 improves the health of participants with PBAD.

The liver makes a substance called bile acid that helps people digest their food. Usually, the bile acid is taken up in the small intestine during digestion. But in people with PBAD, not all the bile acid gets taken up by the small intestine. So, the bile acid ends up in the large intestine. This causes diarrhea.

LJN452 helps reduce the amount of bile acid that is produced by the liver. Researchers think that by reducing the amount of bile produced by the liver, less bile should reach the large intestine. The researchers think this may help lessen diarrhea in participants with PBAD.

In this trial, the researchers wanted to find out if LJN452 works in a small number of participants with PBAD. They also wanted to find out about the safety of LJN452 in participants with PBAD. To do this, the researchers compared LJN452 with a placebo. A placebo looks like the trial drug but does not have any medicine in it. Using a placebo helps researchers to understand the actual effect of a trial drug better.

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

- Did LJN452 change how often the participants had bowel movements?
- Did LJN452 change the form of the participants' stools?
- How much LJN452 got into the participants' blood?
- Did LJN452 change how much rescue medicine the participants used?
- What medical problems did the participants have?

What kind of trial was this?

To answer the questions in this trial, the researchers asked for the help of men and women with PBAD. The participants in this trial were 30 to 75 years old.

This was a “double-blind” trial. This means none of the participants or trial staff performing the tests knew what treatment each participants took. Some trials are done this way because knowing what treatment the participants are taking can affect the results of the trial. Doing a trial this way helps make sure the results are looked at fairly.

A computer program was used to randomly assign the treatment each participant took. Researchers do this so that comparing the results of each treatment is done as fairly as possible.

When the trial ended, the research sponsor created a report of the trial results. The sponsor staff did not know the identity of any of the participants.

What happened during the trial?

This trial was done in 2 parts. In each part, each participant took LJN452 or the placebo. By the end of the trial, each participant had taken both treatments.

Before treatment started, the trial doctors did tests and checked the health of the participants to make sure they could take part in the trial.

The participants could take rescue medicine during this time, if needed. This is medicine participants could take to treat their PBAD symptoms right away.

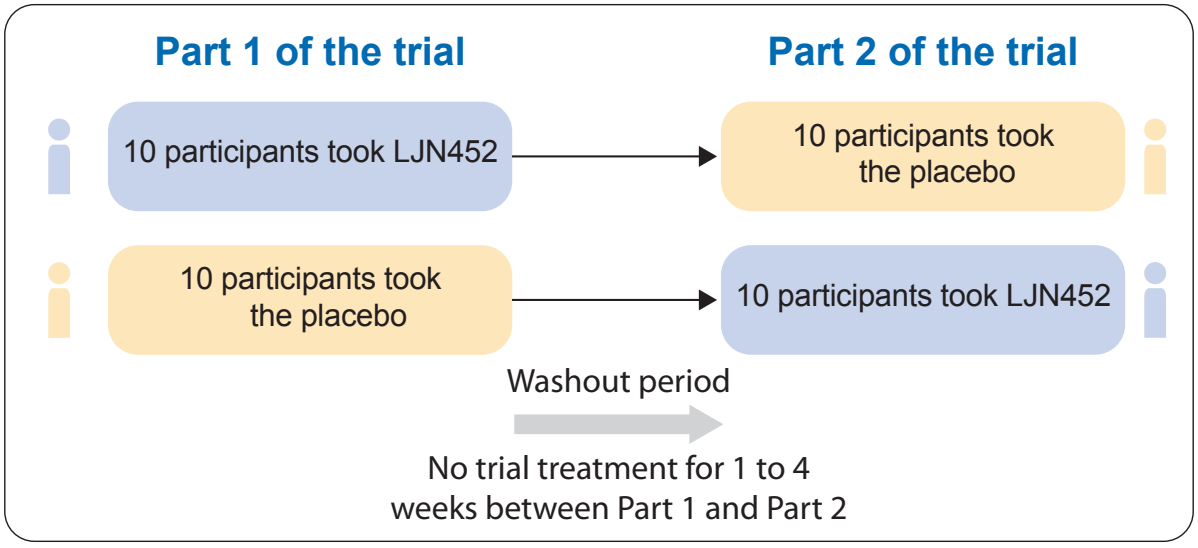
Before treatment started, the trial doctors gave the participants a diary to keep track of their bowel movements and when they took the rescue medicine.

During treatment, the trial doctors took blood, urine, and stool samples. They also checked the participants’ diaries and asked questions about the participants’ PBAD symptoms.

In both parts of the trial, the participants took a single dose of either the trial drug or the placebo once a day for 14 days. The participants took both the trial drug and the placebo in pill form by mouth.

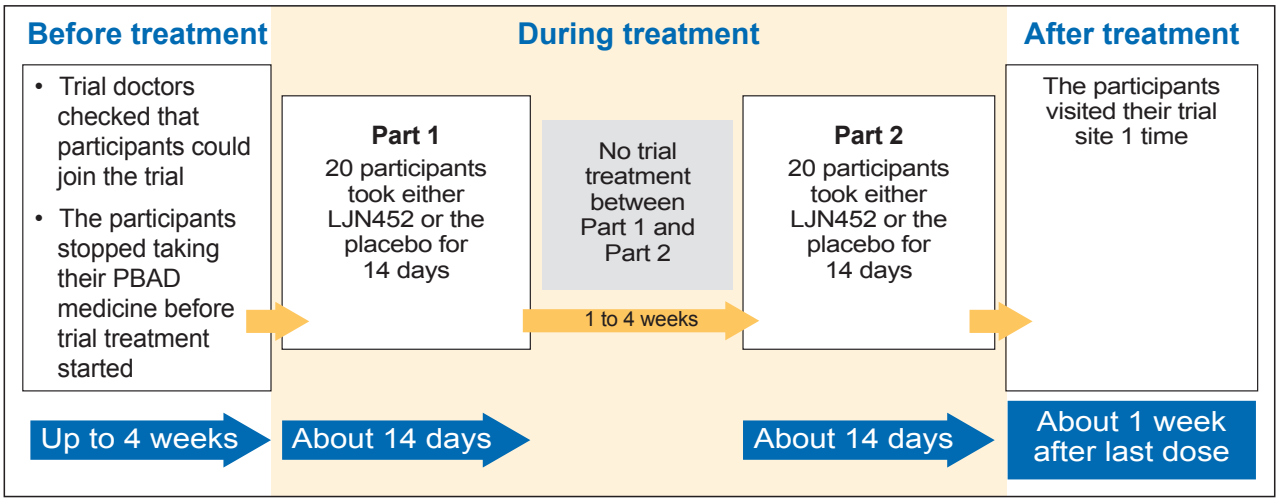
Participants used their diary to keep track of their bowel movements, when they took rescue medicine, and when they took the treatment.

There were 1 to 4 weeks between Part 1 and Part 2. During this time, the participants did not take any treatment. This was done to make sure any effects the researchers saw during each part were due to the treatment taken in that part. The graphic below shows how the participants took their treatment during this study.



After treatment, the trial doctors took blood, urine, and stool samples. They also collected the participants' diaries and asked questions about the participants' PBAD symptoms.

The chart below shows how the trial was done.



What were the results of the trial?

This is a summary of the overall results of your trial, not your individual results. The results presented here are for a single trial. Other trials may provide new information or different results. You should not make medical decisions based on the results of a single trial. Always talk to a doctor before making any changes to your medications or treatment plans.

All 20 participants took at least 1 dose of LJN452. But, 3 participants stopped taking the trial drug, so not all of their results are included below.

For more information about the questions researchers wanted to answer, please check the websites listed at the end of this summary. If a full report of the study results is available, it can be found on those websites.

Did LJN452 change how often participants had bowel movements?

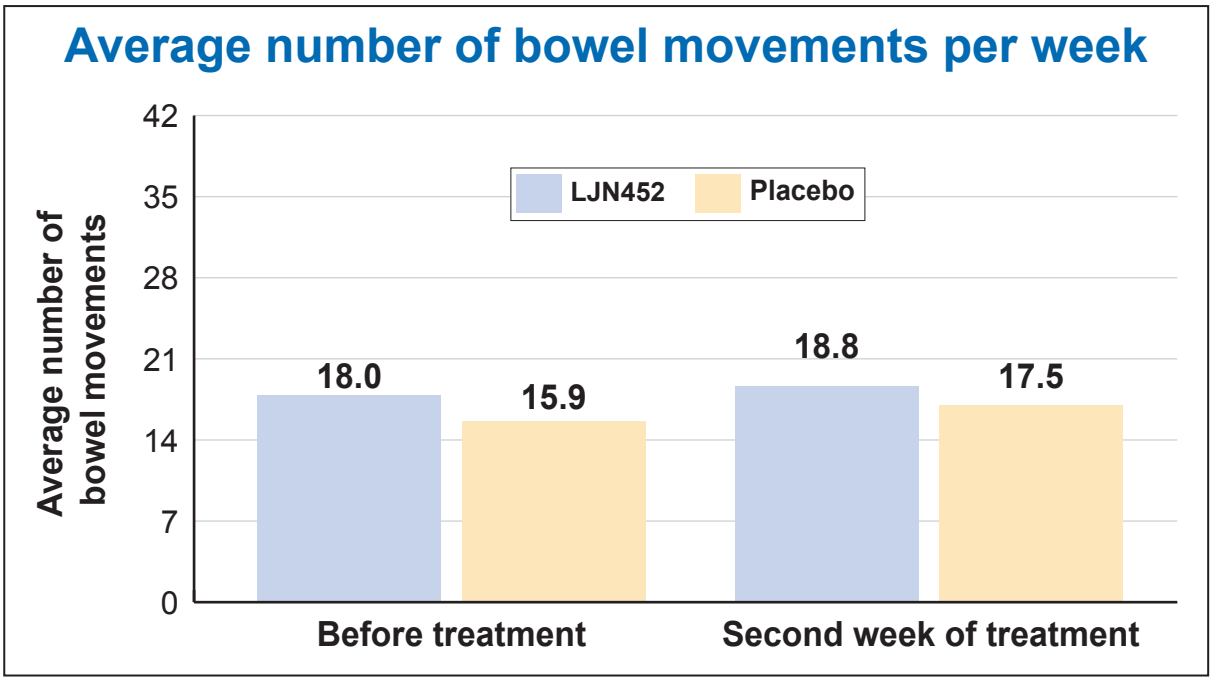
After 2 weeks of trial treatment, the difference between the trial drug and the placebo was too small to know if LJN452 changed how often the participants had bowel movements.

To answer this question, the researchers used the participants' diaries to count how many times the participants had bowel movements. They counted the participants' bowel movements before they started treatment and during the 2 weeks of trial treatment.

The researchers learned that the participants had an average of:

- 18.8 bowel movements per week after taking LJN452 compared to an average of 18.0 bowel movements per week before taking LJN452.
- 17.5 bowel movements per week after taking the placebo compared to an average of 15.9 bowel movements per week before taking the placebo.

The chart below shows these results.

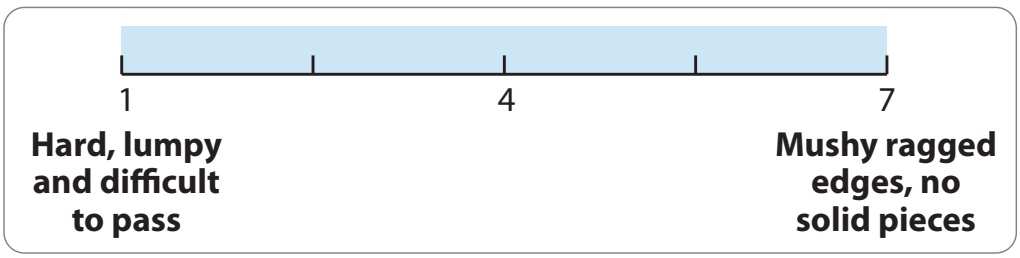


Did LJN452 change the form of participants' stools?

The number of participants in each treatment group was too small for the researchers to know if LJN452 changed the form of the participants' stools.

To answer this question, the researchers asked the participants to keep track of the form of their stools in their diaries. Every time the participants had a bowel movement, they scored the form of their stools using the Bristol Stool Chart, also called the BSC. The BSC scores ranged from 1 to 7. A low score meant the stools were hard, lumpy, and were difficult to pass. A high score of a 6 or 7 meant the stools were mushy with ragged edges or no solid pieces.

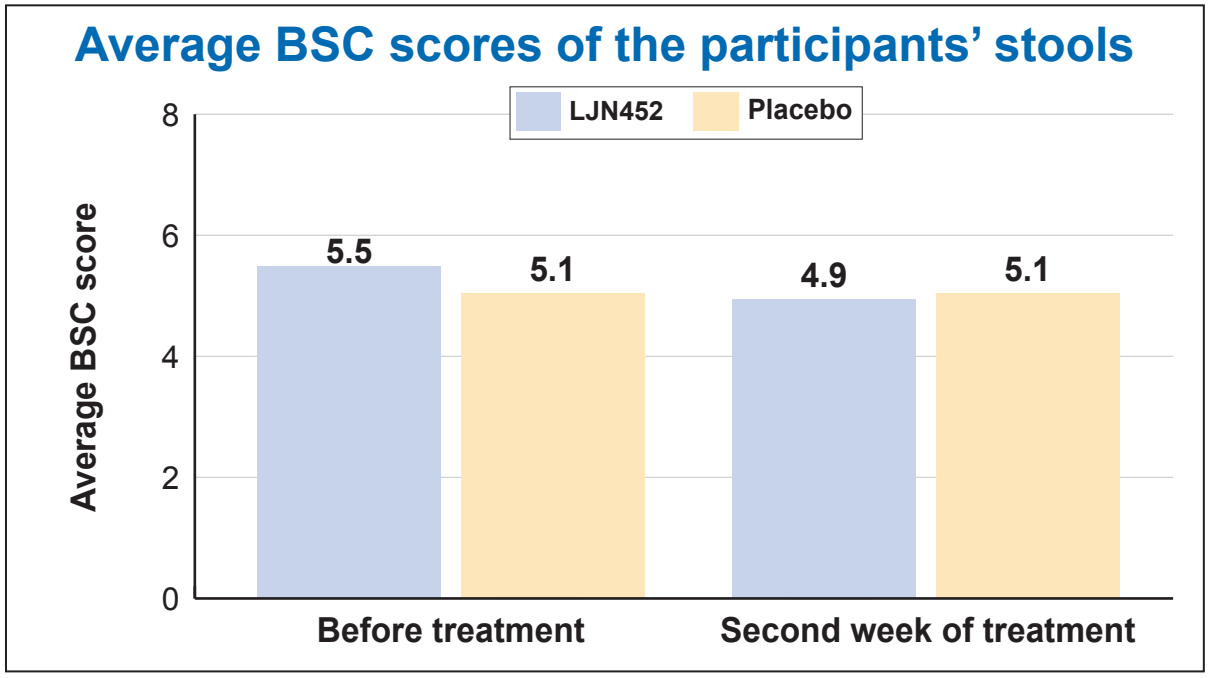
The graphic below shows the BSC.



The researchers counted the participants' average BSC scores before they started treatment and during the 2 weeks of trial treatment. They learned that:

- The participants had an average BSC score of 4.9 after taking LJN452 compared to 5.5 before taking LJN452.
- The participants had an average BSC score of 5.1 both before and after taking the placebo.

The chart below shows these results.



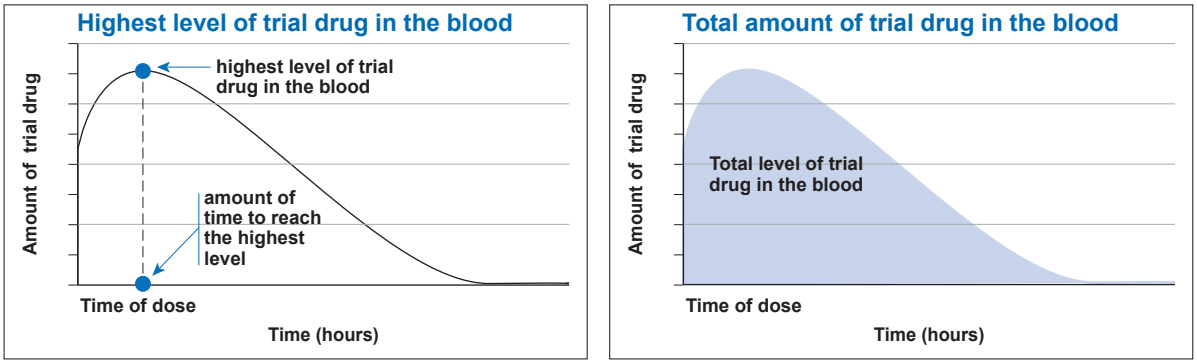
How much LJN452 got into the participants' blood?

To answer this question, the trial doctors measured how much LJN452 got into the participants' blood during the 2 weeks of treatment with LJN452. They measured how much LJN452 was in the blood over the course of 24 hours after the first dose. They also measured how much LJN452 was in the blood 8 hours after the last dose.

This helped the researchers to find:

- The average highest level of LJN452 that got into the participants' blood. This is measured in nanograms per milliliter, also called ng/mL.
- The average amount of time it took LJN452 to reach the highest level in the participants' blood. This is measured in hours.
- The average total amount of LJN452 measured in the participants' blood from the first dose to the last dose. This is measured in hours multiplied by nanograms per milliliter, also called hr•ng/mL.

The graphs below show an example of how the amount of a trial drug in the blood can change over time. They do not show actual results from this trial.



The researchers found that:

- The average highest level of LJN452 that got into the participants' blood was 1.6 ng/mL after the first dose and 1.8 ng/mL after the last dose.
- The average amount of time it took LJN452 to reach its highest level in the blood was 5.0 hours after the first and last dose.
- The average total amount of LJN452 that got into the participants' blood was 23.6 hr•ng/mL after the first dose and 22.1 hr•ng/mL after the last dose.

Did LJN452 change how much rescue medicine participants used?

No. LJN452 did not change how much rescue medicine the participants used. To answer this question, the researchers used the participants' diaries to count how many participants took rescue medicine during each trial treatment. But, the difference between the treatment groups was too small for the researchers to know if LJN452 changed how much rescue medicine the participants used.

What medical problems did the participants have?

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. These problems may or may not be caused by the trial drug.

A lot of research is needed to know whether a drug causes an adverse event. During a trial, all adverse events are reported and written down, whether or not they are caused by the trial drug. So when new drugs are being studied, researchers keep track of all adverse events that participants have.

This section is a summary of the adverse events that happened during this trial. All 20 participants are included in these results because they all took at least 1 dose of trial drug.

How many participants had adverse events?

Fewer participants had adverse events while taking LJN452 than while taking the placebo. None of the participants stopped taking treatment because of adverse events. The table below shows how many participants had adverse events during this trial.

Adverse events during this trial

	LJN452 (Out of 17 participants)	Placebo (Out of 19 participants)	Total (Out of 20 participants)
How many participants in this trial had adverse events?	52.9% (9)	73.7% (14)	90.0% (18)

What were the most common serious adverse events?

None of the participants had serious adverse events during this trial.

None of the participants died during this trial.

What were the most common adverse events?

The most common adverse event that happened in participants during this trial was headache. This adverse event happened in a similar number of participants in both treatment groups.

The table below shows the most common adverse events that happened in 2 or more total participants. There were other adverse events, but these happened in fewer participants.

Most common adverse events during this trial

Adverse event	LJN452 (Out of 17 participants)	Placebo (Out of 19 participants)	Total (Out of 20 participants)
Headache	11.8% (2)	21.1% (4)	30.0% (6)
Abdominal pain	5.9% (1)	5.3% (1)	10.0% (2)
Chest pain not related to the heart	11.8% (2)	0.0% (0)	10.0% (2)
Congestion in the nose	5.9% (1)	5.3% (1)	10.0% (2)

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

How has this trial helped patients and researchers?

The results of this trial helped researchers better understand if LJN452 works in patients with PBAD. The results from many trials are needed to find out which treatments can be used for patients with PBAD. This summary shows only the main results from this 1 trial. This trial was done in a small number of participants with a short treatment period. Other trials may provide new information or different results.

If other trials with LJN452 in participants with PBAD are planned, you will be able to find them on the websites listed below.

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 (www.novctrd.com). Once on the site, click **"READ MORE"** under **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **"CLJN452X2202"** into the keyword search box and click **"Search"**. If you have questions about the results, please speak with the trial doctor or trial 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 **"NCT02713243"** into the **"Other terms"** search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2015-003192-30"** in the 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 **"LJN452"**.

Full trial title: A double blind, randomized placebo controlled crossover multiple dose study of LJN452 to assess safety, tolerability and efficacy in participants with primary bile acid diarrhea (pBAD)

Thank you!

As a clinical trial participant, you belong to a large community of participants around the world. You helped researchers answer important health questions and test new medical treatments.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation.

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