NOVARTIS

The safety and effects of LYS006 and LJN452 for people with a type of fatty liver disease

Thank you!

Thank you to the participants who took part in the clinical trial for the trial drugs LYS006 and LJN452, also called tropifexor. Every participant helped the researchers learn more about these drugs for people with **a type of fatty liver disease.**

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.

Trial information

Trial number: CADPT02A12001
Drugs studied: LYS006 and LJN452
Sponsor: Novartis

What was the main purpose of this trial?

The purpose of this trial was to help researchers learn about the safety of LYS006 taken alone or with LJN452. This trial was in people with a type of fatty liver disease. The researchers also wanted to learn if LYS006 with LJN452 could lower liver fat, inflammation, and scarring of the liver more than taking LYS006 alone.

Fatty liver disease happens when there is a buildup of fat in the liver that can cause inflammation and can lead to fibrosis.

- **Inflammation** involves many cells and proteins that work to remove harmful things and protect the body while it heals. Too much inflammation can harm the body.
- **Fibrosis** is scarring of the liver.

LYS006 is a trial drug that blocks a certain protein related to inflammation. Researchers think blocking this protein may lower liver inflammation.

LJN452 is a trial drug that turns on a certain protein that may lower liver fat, inflammation, and fibrosis.

The main question this trial was designed to answer:

- What medical problems did the participants have during this trial?
  Keeping track of the medical problems helped to learn about the safety of LYS006, taken alone or with LJN452.

Main results: Most of the participants (31 of 41) had medical problems. The most common medical problems were itching and headache. None of the participants had medical problems that were considered serious. The researchers concluded there were no new safety concerns for LYS006 alone or with LJN452 in this trial.

Other results: The researchers also learned that LYS006 alone or with LJN452 was unlikely to have a meaningful effect on liver fat, inflammation, and fibrosis.

How long was this trial?

The trial began in June 2020 and ended in January 2022. The participants joined the trial on different dates. It was planned for each participant to be in the trial for about 4 months after starting treatment.

In December 2021, the sponsor decided to stop this trial early. The sponsor reviewed the data and concluded that there was enough data to know if taking LYS006 with LJN452 had an effect in people with a type of fatty liver disease. The sponsor concluded that LYS006 alone or when taken with LJN452 was unlikely to have a meaningful effect on liver fat, inflammation, and fibrosis. The decision to stop was not related to safety.

Who was in this trial?

41 participants were in this trial – 22 women and 19 men. The participants were 34 to 69 years old. Their average age was 54.

The participants reported their race as:

- White – 36 participants
- Black or African American – 2 participants
- Asian – 1 participant
- Multiple – 1 participant
- Native Hawaiian or Other Pacific Islander – 1 participant

Every participant in this trial had NAFLD that could have been NASH.

- **NAFLD**, also called non-alcoholic fatty liver disease, happens when there is a buildup of fat in the liver. NAFLD is not caused by drinking too much alcohol.
- **NASH**, also called non-alcoholic steatohepatitis, is a severe type of NAFLD that causes inflammation and damage in the liver. It can sometimes lead to fibrosis. Without treatment, the inflammation and fibrosis from NASH can make the liver not work as well and it may stop working.

None of the participants:

- Could be taking certain medicines, such as weight loss medicines
- Had severe liver damage or any other type of liver disease

This trial took place in Argentina (2 participants), Germany (3 participants), and the United States (36 participants).

Visit **novctrd.com** for more information about:

- Who could and could not be in this trial
- Which medicines they could or could not take
- Reasons why the participants did not complete the trial

Use trial number **CADPT02A12001** to find the scientific summary.

What trial treatments did the participants take?

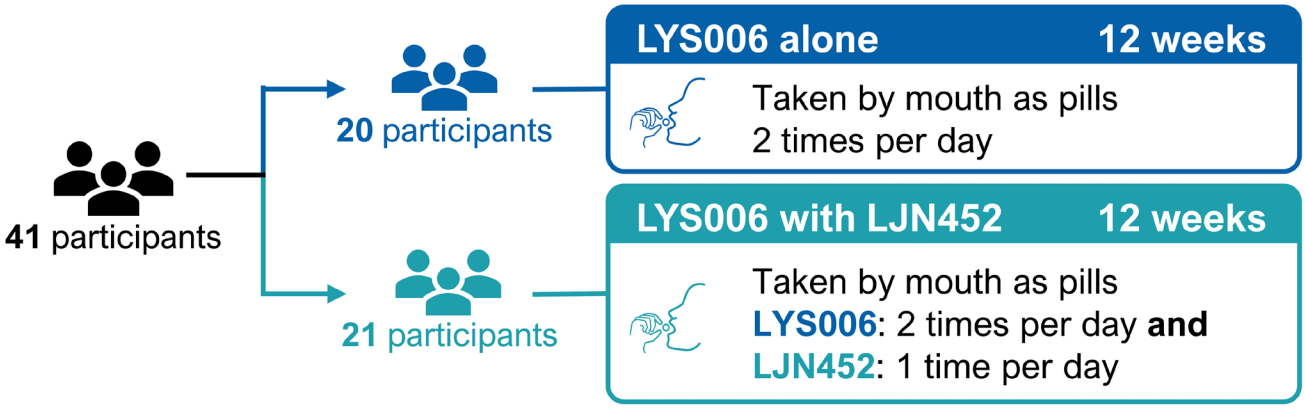
Participants were randomly assigned to take one or both of these treatments:

- **LYS006** – 20 milligrams (mg) 2 times per day
- **LJN452** – 200 micrograms (µg) 1 time per day

A computer program was used to randomly assign the treatments. This helped make sure the researchers compared the results as fairly as possible.

All the participants in this trial took LYS006 **or** LYS006 with LJN452 as pills for up to 12 weeks. Everyone knew which treatment the participants took.

The graphic below shows how many participants were assigned each treatment.



What were the main results of this trial?

This is a summary of the overall results of this trial. Individual results from each participant may be different and are not included in this summary.

Researchers need many trials to learn if a drug or other treatment is safe and works well. Other trials may provide new information or different results.

Always talk to a doctor before making any changes to your health care.

What medical problems did the participants have during this trial?

Medical problems that happen during trials are called “adverse events”.

Trial doctors keep track of **all** adverse events that happen in trials, even if they think the adverse events are **not** related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

An adverse event is:

- Any **unwanted sign or symptom** that the participants have during a trial.
- 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 treatments in the trial.

The adverse events in this section include any that happened during treatment and up to 28 days after treatment.

Most of the participants (31 of 41) had adverse events. The most common adverse events were itching and headache. Besides itching, the number of participants who had adverse events was similar for those who took LYS006 alone or with LJN452. None of the participants had adverse events that were considered serious. 3 participants left the trial due to adverse events. The researchers concluded there were no new safety concerns for LYS006 alone or with LJN452 in this trial.

What serious adverse events did the participants have?

None of the participants had serious adverse events, including no deaths.

What other adverse events did the participants have?

LYS006 alone: 14 of 20 participants or 70% had an adverse event.

LYS006 with LJN452: 17 of 21 participants or 81% had an adverse event.

The table below shows the adverse events that happened in **3 or more participants**. Additional adverse events happened in fewer participants. Based on past trials with LJN452, itching was expected in participants who took LYS006 with LJN452.

	LYS006 alone 20 participants	LYS006 with LJN452 21 participants
Itching Pruritus	0% 0 of 20	62% 13 of 21
Headache	20% 4 of 20	19% 4 of 21
Feeling sick to the stomach Nausea	15% 3 of 20	10% 2 of 21
High blood sugar Hyperglycemia	5% 1 of 20	14% 3 of 21
Pain in the upper belly Abdominal pain upper	5% 1 of 20	10% 2 of 21
Diarrhea	15% 3 of 20	0% 0 of 21
Possible sign of liver damage Blood alkaline phosphatase increased	0% 0 of 20	14% 3 of 21

What other results were learned?

Did the participants who took LYS006 with LJN452 have lower signs of liver fibrosis?

The trial staff took the participants' blood samples before and at the end of treatment. They did this to test for signs of liver fibrosis in participants.

The participants who took LYS006 with LJN452 had about the same signs of liver fibrosis compared to those who took LYS006 alone. Both groups' signs of liver fibrosis stayed about the same compared to before treatment.

The researchers concluded LYS006 alone or with LJN452 did not meaningfully lower signs of liver fibrosis.

Did the participants who took LYS006 with LJN452 lose more liver fat?

The trial staff measured the fat in the participants' livers before and at the end of treatment using an MRI, also called magnetic resonance imaging. An MRI uses magnets to create a detailed picture of the inside of the body.

At the end of treatment, the participants who took LYS006 with LJN452 lost a higher percent of liver fat than those who took LYS006 alone. Researchers concluded this higher percent was mostly due to LJN452 based on past trial results and was not considered meaningful for this trial.

The researchers concluded the participants who took LYS006 with LJN452 lost a higher percent of liver fat than those who took LYS006 alone.

Did LYS006 with LJN452 affect common measures of body weight, blood sugar, and metabolism?

Before and at the end of treatment, the trial staff measured the participants' weight. They also did blood tests to measure the participants' **metabolism**, which is how the body processes food into energy. These tests included:

- Insulin resistance, which is how well the body responds to insulin, a protein that controls blood sugar
- Levels of cholesterol, sugar, and insulin in the blood after fasting, which is not eating for at least 8 hours
- Average blood sugar level

Compared to the participants who took LYS006 alone, the participants who took LYS006 with LJN452 had:

- Lost more body weight
- Higher "bad" cholesterol and lower "good" cholesterol
- Higher blood sugar levels after fasting

Between the two groups, there were no meaningful changes in insulin resistance or average blood levels of insulin and sugar.

The researchers concluded that there weren't meaningful differences in the blood sugar or metabolism measures in participants who took LYS006 alone or with LJN452.

There was no meaningful difference in body weight in participants who took LYS006 alone. The researchers concluded the body weight loss in participants who took LYS006 with LJN452 was mostly due to LJN452, based on past trial results.

Did the participants who took LYS006 with LJN452 have lower signs of inflammation?

Before and at the end of treatment, the trial staff did blood tests to measure 2 signs of inflammation:

- ALT (alanine aminotransferase)
- hsCRP (high-sensitivity C-reactive protein)

Higher levels of ALT and hsCRP are signs of more inflammation. Compared to the participants who took LYS006 alone, the participants who took LYS006 with LJN452 had:

- Lower blood levels of ALT
- About the same blood levels of hsCRP

The researchers concluded participants who took LYS006 with LJN452 had lower blood levels of ALT and about the same blood levels of hsCRP.

What was learned from this trial?

This trial helped researchers to learn about the effects and safety of LYS006 alone and with LJN452 in people with NAFLD that could be NASH. The researchers concluded there were no new safety concerns for the participants in this trial.

The researchers also learned that LYS006 alone or with LJN452 was unlikely to have a meaningful effect on liver fat, inflammation, and fibrosis. Because of this, the sponsor decided to stop this trial early.

These are the results of a single trial. Other trials may have different results. This was one of many trials a drug goes through. This type of trial helped researchers learn about the safety of a trial drug in a small number of participants.

Where can I learn more about this and future trials?

For more information about this trial, go to any of these websites:

- **novctrd.com** – search using the study number **CADPT02A12001**
- **clinicaltrials.gov** – search using the number **NCT04147195**
- **clinicaltrialsregister.eu/ctr-search** – search using the number **2019-000440-10**

If more trials are planned, they will appear on the public websites above. When there, search for **LYS006, LJN452, tropifexor, NAFLD,** or **NASH**.

Full trial title:
NASH EXploratory Single and COmbination Treatment (NEXSCOT): An open label, multicenter, platform study to evaluate the safety, tolerability, pharmacokinetics and efficacy of various single and combination treatments in patients with non-alcoholic fatty liver disease (NAFLD) who manifest a non-alcoholic steatohepatitis (NASH)-like biomarker phenotype

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

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