NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects and safety of LNP023 in people with membranous nephropathy

Thank you!

Thank you to the participants who took part in the clinical trial for **membranous nephropathy.** Every participant helped the researchers learn more about the trial drug **LNP023**, also called iptacopan.

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: CLNP023D12201
Drug studied: LNP023
Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings.

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects and safety of LNP023 compared to rituximab in people with membranous nephropathy.

Membranous nephropathy, or **MN**, is a kidney disease in which the kidney's glomeruli are damaged. **Glomeruli** are the tiny filters in the kidney. When these tiny filters are damaged, the kidneys don't work as well to filter blood. This can cause too much protein to go into the urine, which may lead to kidney failure.

MN can be caused when part of the immune system doesn't work the way it should. This might involve the **complement system**, which is made up of many different proteins that help the body fight off infections. In MN, the complement system attacks and damages the glomeruli.

The **immune system** is made up of many different cells and proteins that help the body fight off infections.

LNP023 is a trial drug designed to block a protein in the complement system. Researchers think blocking complement protein may prevent or slow down more kidney damage.

Rituximab is a drug that is often used to treat people with MN. It is approved in certain countries to treat other conditions that are related to the immune system.

The trial's purpose was to answer these main questions:

- Did LNP023 lower protein levels in participants' urine more than rituximab?
- What adverse events did the participants have during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial.

How long was this trial?

The trial began in November 2019 and ended in January 2023.

In November 2022, the sponsor decided to stop this trial early. The trial sponsor reviewed the data and concluded that there was enough data to know that LNP023 did not lower protein levels in the urine more than rituximab. The decision to stop was not related to the safety of LNP023.

Who was in this trial?

37 participants with MN received treatment in this trial. Participants' ages ranged from 22 to 78 years. Their average age was 49 years. The number of participants by sex and race are shown below.

Sex

31 Men	6 Women

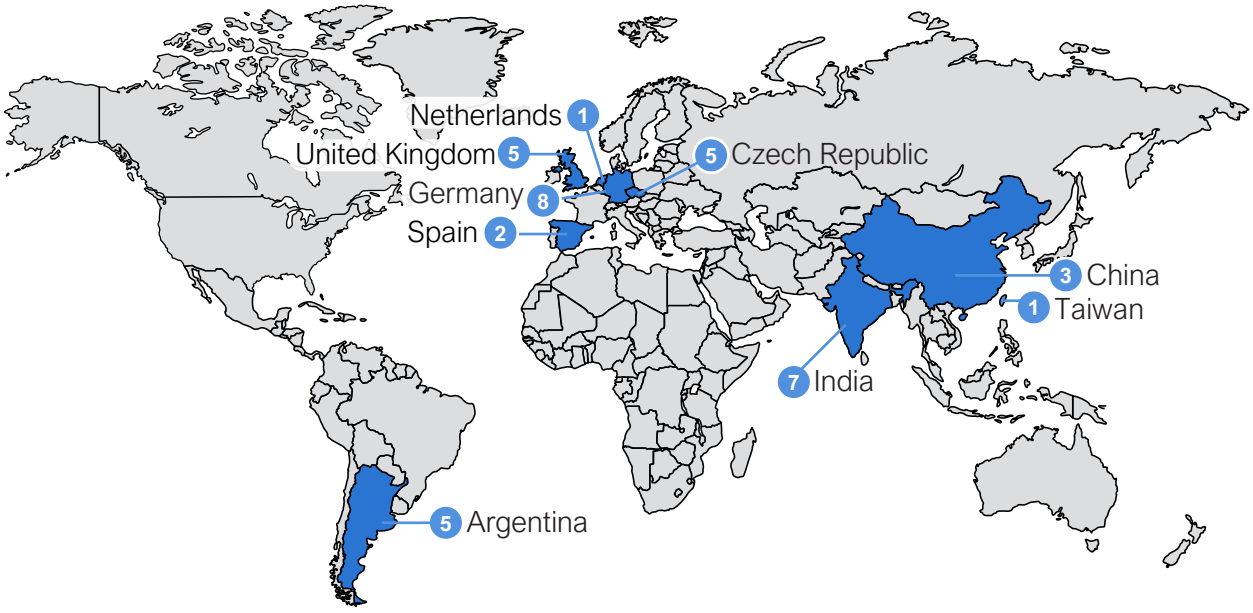
Race

10 Asian	1 Black or African American	25 White
1 Unknown		

The participants could take part in this trial if they:

- Had idiopathic, also known as primary MN, which means that MN was not caused by another health condition or treatment
- Had received certain vaccines recommended for people with weak immune systems
- Had not previously received certain drugs for the immune system

37 participants from 9 countries received treatment. The map below shows the number of participants who took part in each country.



What treatments did the participants receive?

The treatments in this trial were:

LNP023: The participants took LNP023 by mouth as capsules 2 times a day during treatment. This trial planned to look at 2 dose levels of LNP023:

- **Lower dose**: For the 1st 4 weeks, participants took 10 milligrams (mg) of LNP023 2 times per day. Then, they took 50 mg of LNP023 2 times per day for about 5 months.
- **Higher dose**: For the 1st 4 weeks, participants took 25 or 50 mg of LNP023 2 times per day. Then, they took 200 mg of LNP023 2 times per day for about 5 months.

Rituximab: The participants received 1 gram (g) of rituximab through a needle in a vein called an intravenous (IV) infusion. Participants received 2 infusions over about 2 weeks during the trial.

Researchers randomly assigned participants to receive either dose level of LNP023 or rituximab using a computer.

In this trial, the participants, researchers and trial staff knew what treatment each participant received.

Participants could continue taking certain other medicines for MN during the trial.

What happened during this trial?

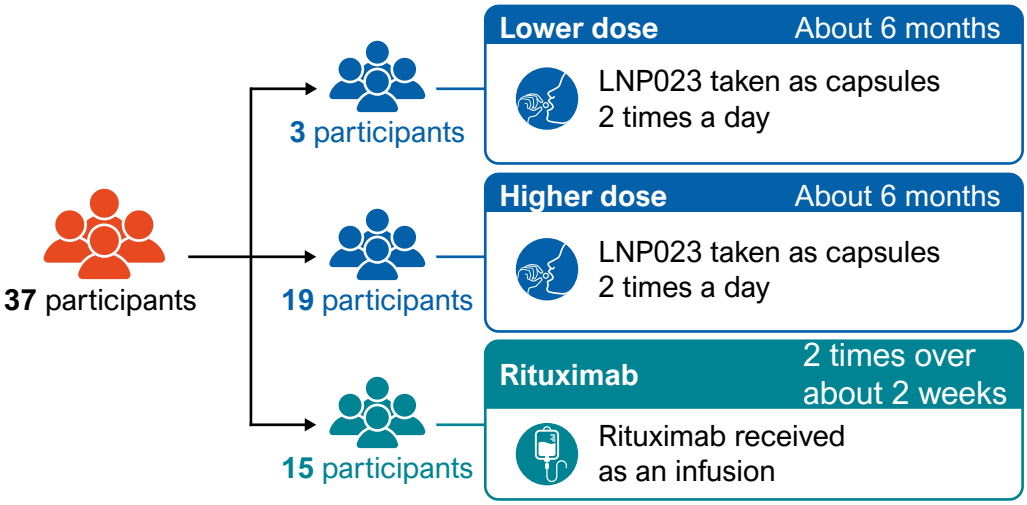
Before treatment — Up to 3 months

Trial staff checked the participants' health and MN to make sure the participants could be in this trial. They also measured the protein levels in participants' urine.

During treatment — Up to 6 months

Trial staff checked the participants' MN and general health throughout the trial. They also measured the protein levels in participants' urine.

Researchers assigned participants to receive 1 of the 3 planned treatments. The graphic below shows how many participants received each treatment.



During the trial, the researchers reviewed data from other LNP023 trials and decided not to continue the lower dose of LNP023. At that time, 2 participants already completed the 6 months of treatment with the lower dose of LNP023. One participant switched from the lower dose to the higher dose towards the end of the trial. The researchers also decided to change the starting dose for the higher dose of LNP023 from 25 to 50 mg.

After treatment — About 7 months

After the last dose of treatment, trial staff checked on the participants' general health in two ways:

- Trial staff called participants about 1 month after their last dose of treatment
- Participants returned to their trial site up to 2 times

What were the main results of this trial?

Did LNP023 lower protein levels in participants' urine more than rituximab?

After about 6 months, LNP023 did not lower protein levels in participants' urine more than rituximab. Participants who took the higher dose of LNP023 had protein levels in their urine go down. However, the levels did not go down more than in participants who received rituximab.

To learn this, researchers measured the participants **urine protein-creatinine ratio,** or **UPCR**. People with kidney damage have a higher UPCR, which means the kidneys are not working well and are letting too much protein into the urine. **If UPCR goes down, it may mean kidney damage is slowing down**.

What is UPCR?

UPCR is a test that compares the level of protein in urine to the level of creatinine in urine. **Creatinine** is a waste product that healthy kidneys filter from the blood into urine in small amounts.

For this test, trial staff collected and tested all of a participants' urine from a 24-hour time period. They did this before and after about 6 months of treatment. The researchers looked at the average change in protein levels in each participant's urine from before treatment to after treatment.

Because the researchers stopped the lower dose of LNP023, those participants were not included in the results.

Change in the level of protein in participants' urine

The results below show the average change in the level of protein in participants' urine after about 6 months of treatment.

Higher dose LNP023

The level of protein in participants' urine **went down 12%**

Rituximab

The level of protein in participants' urine **went down 36%**

These results only include participants who completed the higher dose of LNP023 or rituximab trial treatments.

What were the other results of this trial?

Did LNP023 affect other measures of MN and kidney damage more than rituximab?

The researchers found:

- The LNP023 higher dose group had lower levels of certain complement proteins compared to the rituximab group
- About the same number of participants in the LNP023 higher dose group and rituximab group had their MN get less severe
- The early morning urine protein levels went down in the LNP023 higher dose group. But, not as much as the rituximab group.
- The rituximab group showed higher kidney function after about 1 year. There was no meaningful change in kidney function for the LNP023 higher dose group.
- None of the participants' MN went away completely

What adverse events did the participants have?

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.

This section is a summary of the adverse events that happened from a participant's first dose of trial treatment until 30 days after their last dose or their last study visit.

An **adverse event** is:

- Any **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.

Most participants (22 of 37) had adverse events. More participants who took either dose level of LNP023 had adverse events than those who received rituximab. 7 participants had adverse events that were considered serious. 1 participant left the trial due to an adverse event. The researchers concluded there were no new safety concerns for LNP023 in this trial.

How many participants had adverse events?

Participants who:	Lower dose LNP023 3 participants	Higher dose LNP023 19 participants	Rituximab 15 participants
Had at least 1 **serious adverse event**	0 of 3 0%	3 of 19 16%	4 of 15 27%
Had at least 1 **other adverse event**	2 of 3 67%	13 of 19 68%	7 of 15 47%
Left the trial due to an adverse event	0 of 3 0%	1 of 19 5%	0 of 15 0%
Died during the trial	0 of 3 0%	0 of 19 0%	0 of 15 0%

What serious adverse events did the participants have?

7 participants had serious adverse events. No participants died.

The table below shows the most common serious adverse events that happened in **3 or more** participants. Additional serious adverse events happened in fewer participants.

	Lower dose LNP023 3 participants	Higher dose LNP023 19 participants	Rituximab 15 participants
A blood clot in the lungs Pulmonary embolism	0 of 3 0%	1 of 19 5%	2 of 15 13%

What other adverse events did the participants have?

22 participants had other adverse events.

The table below shows the other adverse events that happened in **3 or more** participants. Additional adverse events happened in fewer participants.

	Lower dose LNP023 3 participants	Higher dose LNP023 19 participants	Rituximab 15 participants
COVID-19	**0 of 3** 0%	**3 of 19** 16%	**1 of 15** 7%
Headache	**0 of 3** 0%	**3 of 19** 16%	**0 of 15** 0%
Low potassium levels in the blood Hypokalemia	**0 of 3** 0%	**2 of 19** 11%	**1 of 15** 7%
Muscle cramps Muscle spasms	**1 of 3** 33%	**1 of 19** 5%	**1 of 15** 7%
The common cold Nasopharyngitis	**0 of 3** 0%	**1 of 19** 5%	**2 of 15** 13%

What was learned from this trial?

Researchers learned about the effects and safety of LNP023 compared to rituximab in people with MN. The trial ended early because there was enough data to know that LNP023 did not increase kidney function more than rituximab.

The researchers concluded that LNP023 did not lower protein levels in participants' urine more than rituximab.

They also found that:

- The LNP023 higher dose group had lower levels of certain complement proteins compared to the rituximab group
- About the same number of participants in the LNP023 higher dose group and rituximab group had their MN get less severe
- The early morning urine protein levels went down in the LNP023 higher dose group. But not as much as the rituximab group.
- The rituximab group showed higher kidney function after about 1 year. There was no meaningful change in kidney function for the LNP023 higher dose group.
- None of the participants' MN went away completely

Researchers look at the results of many trials to learn about the safety and effects of new treatments. Other trials may be planned for LNP023 in people with MN.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website **www.novctrd.com**

Follow these steps to find the scientific summary:

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

- clinicaltrials.gov – search using the number **NCT04154787**
- clinicaltrialsregister.eu/ctr-search/search – search using the number **2019-001734-34**

If more trials are planned, they will appear on the websites above. When there, search for **LNP023**, **iptacopan** or **membranous nephropathy**.

Full clinical trial title: A randomized, open-label, two arm, parallel group, proof-of-concept clinical trial to investigate the efficacy and safety of LNP023 compared with rituximab in the treatment of subjects with idiopathic membranous nephropathy

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1-888-669-6682 (US) | +41-61-324 1111 (EU)

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