NOVARTIS

Clinical Trial Results Summary

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

Clinical trial protocol number: CLNP023X2203

Thank you!

Thank you to the participants who took part in the clinical trial for the drug **LNP023**, also known as **iptacopan**.

All of the participants helped the researchers learn more about how **LNP023** works in people with **IgA nephropathy**. Novartis sponsored this clinical 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.

Why was the research needed?

Researchers are looking for a better way to treat **IgA nephropathy**, also known as Berger's disease. IgA nephropathy is kidney disease that happens when immunoglobulin A (**IgA**) builds up in the kidneys. IgA is an antibody, which is a protein that the immune system makes to help fight infections. IgA usually attaches to infection in the body and signals the immune system to fight the infection.

In IgA nephropathy, the body makes an unusual type of IgA. The unusual IgA attaches to other IgA instead of an infection, builds up in the kidneys, and damages them. It also makes another part of the immune system called the “complement system”, more active in the kidneys. The **complement system** is made up of many different proteins that help the body fight off infections by attacking bacteria and viruses. An overactive complement system in the kidneys may damage the kidneys by attacking healthy kidney cells and tissues.

When IgA nephropathy damages the kidneys, they do not work well to filter waste from the blood. This lets protein and red blood cells leak into urine. Over time, the kidneys may stop working, which is called kidney failure.

Researchers think the trial drug **LNP023, also known as iptacopan,** may slow down kidney damage from IgA nephropathy.

Trial purpose

The main purpose of this trial was to learn more about the effects and safety of LNP023 for people with IgA nephropathy. It was also designed to help researchers choose which dose of LNP023 to use in later, larger trials for people with IgA nephropathy.

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

- How much did different doses of LNP023 lower protein levels in the urine?
- What medical problems did the participants have during the trial?

Trial drugs

The treatments in this trial were:

LNP023, which is designed to block steps in the complement system that may lead to IgA building up in the kidneys. The participants took it by mouth as capsules in either 10, 50, 100, or 200 milligram (mg) doses twice a day.

Placebo, which looks like LNP023, but does not have LNP023 in it. Using a placebo helps researchers better understand the effect of a trial drug.

How long was this trial?

This 2-part trial was designed so that each participant could take part for up to about 9 months. In Part 1, participants took their trial treatment for up to 3 months, and researchers used the results to design Part 2. In Part 2, participants took their trial treatment for up to 6 months. The trial started in February 2018 and ended in June 2021.

The researchers completed this trial as planned. When the trial ended, the researchers collected information on the trial treatments and created a report of the trial results. This summary is based on that report.

Who was in this trial?

112 participants with IgA nephropathy were in this trial. Participants' ages ranged from 18 to 70 years. They were 39 years old on average.

Participants reported their gender as:

Participants reported their race as:

The participants could take part in this trial if they had IgA nephropathy and:

- Were taking standard treatments for IgA nephropathy, such as an angiotensin converting enzyme inhibitor (ACEIs) or angiotensin receptor blocker (ARBs)
- Had not recently taken drugs that lower the activity of the immune system (immunosuppressants)
- Did not have a sign of severe kidney damage

Participants took part at 57 trial sites in Argentina, Australia, Belgium, Brazil, China, the Czech Republic, Colombia, Denmark, Finland, France, Germany, Hong Kong, India, Israel, Japan, Malaysia, the Netherlands, Norway, the Republic of Korea, Singapore, Sweden, Taiwan, Thailand, Turkey, and the United Kingdom.

What kind of trial was this?

This was a double-blind trial. This means that none of the participants, trial doctors, or trial staff knew what treatment the participants were taking. Some trials are done this way because knowing what treatment each participant is taking can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness towards all treatments.

What happened during this trial?

Up to **3 months** before treatment

During screening

Trial doctors checked participants' overall health and IgA nephropathy to make sure they could be in this clinical trial, including blood and urine tests.

112 participants took part in this trial.

Up to **6 months** of treatment

During treatment

The participants were randomly assigned to take LNP023 or a placebo:

- **LNP023:** 87 participants took 1 of these 4 doses by mouth as capsules:
  - **10 mg**, 2 times a day (20 participants)
  - **50 mg**, 2 times a day (19 participants)
  - **100 mg**, 2 times a day (22 participants, in Part 2 only)
  - **200 mg**, 2 times a day (26 participants)
- **Placebo:** 25 participants took the placebo by mouth as capsules 2 times a day

Part 1: participants took their trial treatment for up to **3 months**. Researchers looked at the results of this part to help design Part 2.

Part 2: participants took their trial treatment for up to **6 months**.

Trial doctors checked participants' overall health and IgA nephropathy, including blood and urine tests.

Up to **3 months** after treatment

During follow-up

Participants returned to their trial site about 3 months after their last dose of treatment for trial staff to check their overall health and IgA nephropathy, including blood and urine tests.

What were the main results of this trial?

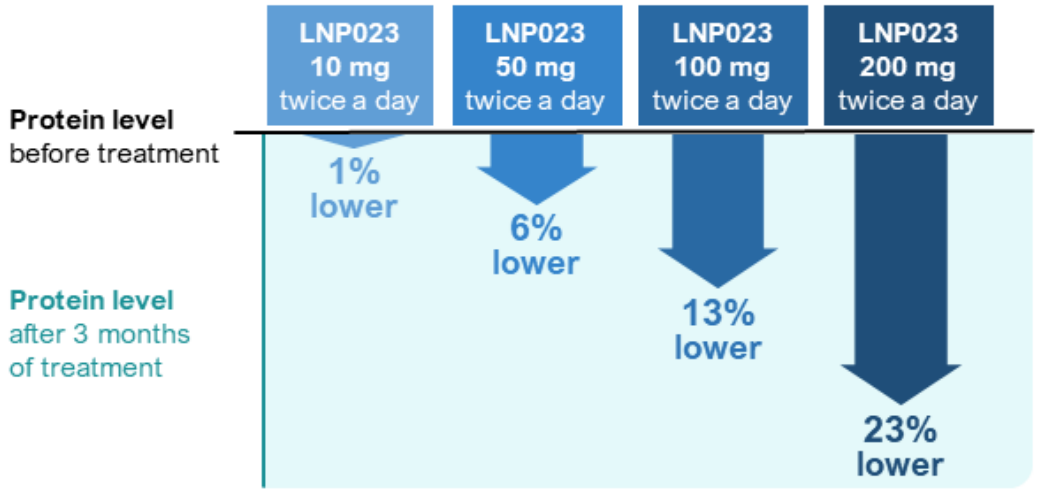
This is a summary of the overall results for all participants. It does not show the results of each individual participant. Results of individual participants could be different from the results of the total group of participants. More details on the results can be found on the websites listed at the end of this summary.

How much did different doses of LNP023 lower protein levels in the urine?

Researchers found that the 50, 100, and 200 mg doses of LNP023 given twice a day lowered the protein levels in the participant's urine after 3 months of treatment. The protein levels in the urine went down more as the dose of LNP023 went up. The 200 mg twice a day dose lowered the protein levels in the urine the most.

Change in protein level in participants' urine after 3 months of treatment

The graph below shows the average change in the protein level in participants' urine from before treatment to after 3 months of treatment. It adjusts for those who took the placebo.



To find this out, researchers measured the protein levels in participants' urine using a test called the **urine protein-creatinine ratio (UPCR)**. UPCR compares the level of protein in urine to the level of creatinine. A high level of protein in urine is a sign of kidney damage. Damaged kidneys leak protein from the blood into urine. Creatinine is a waste product that healthy kidneys filter from the blood into urine in small amounts.

People with kidney damage have a higher UPCR, which means their kidneys are not working well and are letting too much protein into urine. If their UPCR goes down, it means their kidney damage is slowing down.

For the UPCR test, participants collected all of their urine over a 24-hour period before, during, and after treatment. The researchers looked at how much UPCR changed from before treatment to after 3 months of treatment for the participants who took each dose of LNP023 compared to those who took the placebo.

What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called "**adverse events**".

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

This section is a summary of the adverse events that happened during treatment and during the 3-month follow-up after treatment. The websites listed at the end of this summary have more information about the adverse events that happened in this trial.

An **adverse event** is an 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 treatment.

What were the serious adverse events?

There were no deaths reported during this trial.

During trial treatment, 2 participants had serious adverse events and recovered:

- A participant who took the placebo was hospitalized after breathing in chlorine gas while cleaning a swimming pool (aspiration)
- A participant who took 50 mg LNP023 was hospitalized for severe COVID-19

During the 3-month follow-up after treatment, 6 participants had serious adverse events:

- 2 participants had kidney failure (renal impairment) - 1 participant who took 100 mg LNP023 and 1 who took 200 mg LNP023
- A participant who took 100 mg LNP023 had an infection in their appendix (appendicitis)
- A participant who took 50 mg LNP023 had severe COVID-19
- A participant who took 10 mg LNP023 had the flu (influenza)
- A participant who took placebo had a type of blood cancer (polycythemia vera)

What were the most common non-serious adverse events?

The table below shows the **non-serious adverse events** that happened during treatment and the 3-month follow-up in at least 6 out of 112 participants (5%) during either period.

	Treatment period (treatments taken twice a day)					3-month follow-up period				
	LNP023 10 mg	LNP023 50 mg	LNP023 100 mg	LNP023 200 mg	Placebo	LNP023 10 mg	LNP023 50 mg	LNP023 100 mg	LNP023 200 mg	Placebo
Number of participants:	**20**	**19**	**22**	**26**	**25**	**20**	**19**	**22**	**26**	**25**
Headache	**2** (10%)	**2** (11%)	**2** (9%)	**2** (8%)	**6** (24%)	**0** (0%)	**0** (0%)	**1** (5%)	**0** (0%)	**0** (0%)
Back pain	**1** (5%)	**0** (0%)	**3** (14%)	**1** (4%)	**3** (12%)	**1** (5%)	**0** (0%)	**0** (0%)	**1** (4%)	**0** (0%)
Diarrhea	**0** (0%)	**2** (11%)	**1** (5%)	**1** (4%)	**3** (12%)	**1** (5%)	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)
The common cold Nasopharyngitis	**2** (10%)	**2** (11%)	**0** (0%)	**1** (4%)	**2** (8%)	**0** (0%)	**2** (11%)	**0** (0%)	**1** (4%)	**0** (0%)
Throwing up Vomiting	**3** (15%)	**2** (11%)	**0** (0%)	**1** (4%)	**1** (4%)	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)
Feeling dizzy Dizziness	**2** (10%)	**3** (16%)	**1** (5%)	**0** (0%)	**0** (0%)	**1** (5%)	**0** (0%)	**1** (5%)	**0** (0%)	**1** (4%)
Feeling weak and tired Fatigue	**0** (0%)	**2** (11%)	**1** (5%)	**0** (0%)	**3** (12%)	**0** (0%)	**0** (0%)	**0** (0%)	**1** (4%)	**0** (0%)

The adverse events for participants who took the trial treatments for 6 months were similar to those of participants who took them for 3 months.

How has this trial helped?

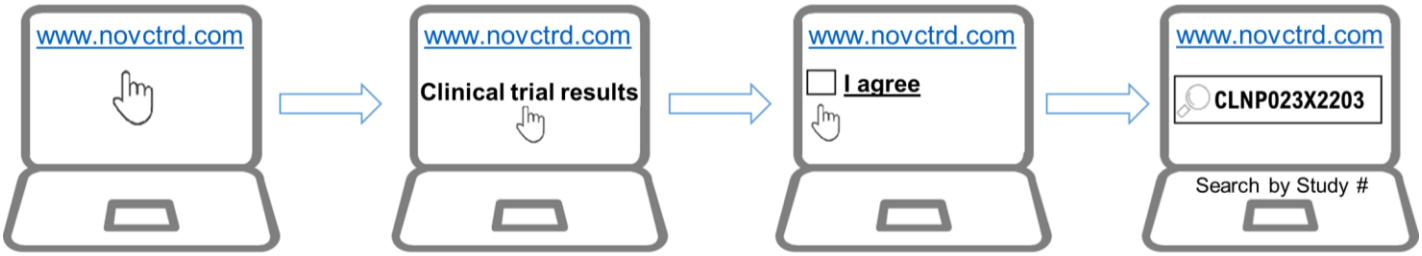
This trial helped researchers learn how well LNP023 works at different doses and if it is safe to use in people with IgA nephropathy. They learned that protein levels in urine went down more in participants who took the 200 mg dose of LNP023 twice a day than those who took the placebo and other doses of LNP023 twice a day. The researchers found no new safety concerns for LNP023 in people with IgA nephropathy.

This was the first trial of LNP023 in people with IgA nephropathy. More research is needed to confirm its results. Another trial, CLNP023A2301 (NCT04578834), is a larger trial to learn more about the safety and effects of the 200 mg dose of LNP023 for people with IgA nephropathy.

Please remember, this summary only shows the results of one clinical trial. Other clinical trials may have different results. Researchers and health authorities look at the results of many clinical trials to understand which drugs work and if they are safe. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

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).



You can find more information about this trial on these websites:

- www.clinicaltrials.gov. Use the NCT identifier NCT03373461 in the search field.
- www.clinicaltrialsregister.eu. Use the EudraCT identifier 2017-000891-27 in the search field.

Full clinical trial title: An adaptive seamless randomized, double-blind, placebo-controlled, dose ranging study to investigate the efficacy and safety of LNP023 in primary IgA nephropathy patients

Thank you

Thank you for taking part in this trial. 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.

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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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