

The effects and safety of LNP023 for people with C3 glomerulopathy



Thank you!

Thank you to the participants who took part in the clinical trial for the trial drug **LNP023**, also called iptacopan. Every participant helped the researchers learn more about LNP023 for people with C3 glomerulopathy, formerly known as membranoproliferative glomerulonephritis (MPGN).

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: CLNP023X2202

Drug studied: LNP023

Sponsor: Novartis

What was the main purpose of this trial?

The main purpose of this trial was to learn if LNP023 lowered signs of kidney damage in people with C3 glomerulopathy, also called C3G. This trial also helped researchers to learn about the safety of LNP023.



C3G is a rare type of kidney disease that happens when part of the immune system called the **complement system** doesn't work the way it should. The complement system is made up of many different proteins that help the body fight off infections. One of these proteins is called **C3** or complement component 3.

In C3G, the complement system is overactive. This causes C3 proteins to build up in the kidneys and damage them. Damaged kidneys don't work as well to filter blood and allow too much protein into urine. Over time, the kidneys may stop working, which is called kidney failure.



LNP023 is a trial drug designed to block a protein in the complement system. Researchers think it may slow down or possibly reverse kidney damage from C3G.

This trial included 2 groups of participants with C3G:

- **Group A** – Participants who **did not** have a kidney transplant and had low levels of C3 in their blood
- **Group B** – Participants who **had** a kidney transplant and had C3G come back in the transplanted kidney

The main questions this trial was designed to answer:

- Did LNP023 lower protein levels in the urine of Group A participants?
- Did LNP023 lower the amount of C3 in the transplanted kidney of Group B participants?
- What medical problems did the participants have during this trial?

Keeping track of the medical problems helped to learn about the safety of LNP023.



Main results:

- For Group A: after 12 weeks of treatment, protein levels in the participants' urine went down to almost half of the amount from before treatment.
- For Group B: after 12 weeks, the amount of C3 was lower in the samples from their transplanted kidney compared to before treatment.

Most of the participants had medical problems during this trial. The researchers concluded there were no new safety concerns during the trial.

How long was this trial?



The trial began in February 2019 and ended in April 2021. All the participants in this trial took LNP023 for up to 24 weeks. It was planned for the participants to be in the trial for up to a year from the date they joined.

Who was in this trial?

27 participants with C3G were in this trial. They were divided into Group A and Group B:

Group A



16 participants – 10 men and 6 women. They were 18 to 59 years old.

All participants in Group A reported their race as White (Caucasian).

Group A included participants who:

- **Did not** have a kidney transplant
- Had low levels of C3 in their blood

Group B



11 participants – 8 men and 3 women. They were 18 to 70 years old.

9 participants in Group B reported their race as White (Caucasian),

1 participant reported their race as American Indian or Alaska Native, and

1 participant reported their race as Black or African American.

Group B included participants who:

- **Had** a kidney transplant
- Had C3G come back in the transplanted kidney



This trial took place in France, Germany, Italy, Spain, the United Kingdom, and the United States.

Visit novctrd.com for more information about:

- Who could and could not be in this trial
- Reasons why the participants did not complete the trial

Use trial number **CLNP023X2202** to find the scientific summary.

What trial treatment did the participants take?

All the participants in this trial took LNP023 as pills 2 times a day for up to 24 weeks. Everyone knew which treatment the participants took.

For the first 4 weeks of treatment, the participants started with a low dose of LNP023 and then took a higher dose each week. After the first 4 weeks, the participants took the highest dose for the next 8 weeks. After 12 weeks, the participants could choose to continue taking LNP023 for another 12 weeks or join another trial if the trial doctor thought it could help them. When the participants ended their treatment, their dose was slowly lowered over 2 weeks.

LNP023 is designed to block a protein in the complement system, which could weaken the immune system. Before starting treatment with LNP023, each participant received vaccines to protect them against certain infections like meningitis. Meningitis is swelling of the tissue and fluid that covers the brain and spinal cord, often caused by an infection.

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.

Did LNP023 lower protein levels in the urine of Group A participants?



Yes, after 12 weeks of treatment, protein levels in Group A participants' urine went down to almost half of the amount from before treatment.

To find this out, the trial doctors measured protein levels using the urine protein-creatinine ratio (UPCR) test. This test compares the levels of protein in urine to the level of creatinine. 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 the 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 this test, trial staff collected and tested all of a participant's urine over a 24-hour period before and after 12 weeks of treatment. The researchers looked at the average change in the level of protein in their urine after treatment.

Group A included participants who:

- **Did not** have a kidney transplant
- Had low levels of C3 in their blood

Did the level of protein in participants' urine go down?

The results below show the average change in the level of protein in participants' urine after 12 weeks of treatment.

UPCR test results

The level of protein in participants' urine **went down 45%**.



A **lower** level of protein in the urine is a sign that kidney damage is **slowing down**.

Did LNP023 lower the amount of C3 in the transplanted kidney of Group B participants?



Yes, the amount of C3 was lower in samples from the participants' transplanted kidney after 12 weeks of treatment.

To find this out, the Group B participants had a biopsy of their transplanted kidney. This means a sample of kidney tissue was taken. They had a biopsy before they began taking LNP023 and after 12 weeks of treatment.

To make sure results were looked at fairly, kidney experts who weren't connected to the trial looked at the participants' kidney tissue samples. They looked to see the amount of C3 that built up and scored the participants' samples from 0 (no buildup) to 12 (most buildup). The researchers looked at the change in the participants' scores after 12 weeks of treatment.

Group B included participants who:

- **Had** a kidney transplant
- Had C3G come back in the transplanted kidney

Did the amount of C3 in participants' kidneys go down?

The results below show the change in the median C3 score for samples from the participants' transplanted kidney after 12 weeks of treatment. The **median** is the middle number when a list of numbers is ordered from smallest to largest.

C3 score results

The C3 scores in participants' kidneys **went down 2.5**



A **lower** C3 score means their kidney had **less** C3 buildup.

What other results were learned?

Did LNP023 lower other signs of kidney damage?

After 12 weeks of treatment, the researchers looked for changes to other signs of kidney damage in the participants' blood and urine samples. These included:

- Other urine tests that measure protein levels, similar to the UPCR test
- **eGFR** (estimated glomerular filtration rate): A blood test that shows how well the kidneys work to filter waste from the blood
- **Creatinine clearance**: A blood test that shows how much creatinine the kidneys remove from the blood
- Testing for blood in the participants' urine

Based on these results, the researchers concluded there were no signs the participants' kidney damage was getting worse 12 weeks after treatment.

Did LNP023 affect the level of C3 proteins in the complement system?

The researchers looked at the effect of LNP023 on the complement system by measuring the blood levels of C3. After 12 weeks of treatment, they found that C3 levels returned to normal levels in both groups of participants.

What medical problems did the participants have during this trial?

Medical problems that happen during trials are called "adverse events". Trial doctors looked for any adverse events during the visits to the trial site. The participants also reported adverse events.

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

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.

This section includes adverse events that happened during treatment and up to 1 month after treatment.



Most of the participants (22 of 27 participants) reported adverse events. 2 participants had adverse events that were considered serious: potassium level in blood was too high and an overdose. The researchers concluded there were no new safety concerns during the trial.

What serious adverse events did participants in Groups A and B have?

None of the participants in Group A reported serious adverse events.

2 of the 11 participants (18%) in Group B reported a total of 2 serious adverse events:

- **Potassium level in blood was too high** | hyperkalemia
- **Overdose**

No participants died during the trial.

What other adverse events did the participants in Groups A and B have?

- **Group A:** 14 of the 16 participants (88%) reported adverse events.
- **Group B:** 8 of the 11 participants (73%) reported adverse events.

The table below shows the adverse events that happened in **2 or more participants** in either group. Other adverse events were reported by fewer participants.

	LNP023 – Group A 16 participants		LNP023 – Group B 11 participants	
Possible sign of damage to the muscles, heart, or brain Blood creatinine phosphokinase increased	13% 2 of 16		9% 1 of 11	
Headache	0% 0 of 16		18% 2 of 11	
High blood levels of potassium Hyperkalemia	0% 0 of 16		18% 2 of 11	
High blood pressure Hypertension	6% 1 of 16		9% 1 of 11	
Pain in the upper belly Abdominal pain upper	13% 2 of 16		0% 0 of 11	
Throwing up Vomiting	6% 1 of 16		9% 1 of 11	

What was learned from this trial?

This was the first trial to learn about the safety and effects of LNP023 in people with C3G. The researchers learned there were no new safety concerns for LNP023 in people with C3G. They also learned that LNP023 could:

- Lower signs of kidney damage from C3G
- Change levels of C3 protein in the complement system

The results of this trial will help researchers design future trials.

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 the following websites:

- [novctrd.com](https://www.clinicaltrials.gov) – search using the study number **CLNP023X2202**
- [clinicaltrials.gov](https://www.clinicaltrials.gov) – search using the number **NCT03832114**
- clinicaltrialsregister.eu/ctr-search – search using the number **2017-000889-29** If more trials are planned, they will appear on the public websites above. When there, search for **LNP023, iptacopan, or C3G**.



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

Full trial title:

An open-label, non-randomized study on efficacy, pharmacokinetics, pharmacodynamics, safety and tolerability of LNP023 in two patient populations with C3 glomerulopathy



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

1-888-669-6682 (USA)

+41-61-324 1111 (EU)