NOVARTIS

The effects and safety of LNP023 for people with paroxysmal nocturnal hemoglobinuria

Thank you!

Thank you to the participants who took part in the clinical trial for paroxysmal nocturnal hemoglobinuria, also called PNH. Every participant helped the researchers learn more about **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: CLNP023X2201
Drug studied: LNP023
Sponsor: Novartis

What was the purpose of this trial?

The purpose of this trial was to learn if LNP023 with standard of care reduced damage to red blood cells in people with PNH. This trial also helped researchers learn about the safety of LNP023.

Paroxysmal nocturnal hemoglobinuria, also called **PNH,** is a rare type of blood disease in which the immune system attacks red blood cells. This happens because the red blood cells are missing a certain protein that protects them from attacks by part of the immune system. This part of the immune system is called the **complement system.** It is made up of many different proteins that also help the body fight off infections.

In people with PNH, the complement system damages and breaks down red blood cells, which is called **hemolysis**. Without treatment, PNH can cause bone marrow failure, where the body does not make enough healthy blood cells. PNH can also cause severe tiredness, pain, and sometimes life-threatening blood clots.

LNP023 is a trial drug designed to block a protein in the complement system. Researchers think it may prevent or reduce hemolysis caused by PNH.

Standard of care is the typical treatment doctors use for patients with PNH.

The main questions this trial was designed to answer:

- Did a sign of hemolysis go down in the participants who took LNP023?
- 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: After receiving LNP023 with standard of care for 13 weeks, a sign of hemolysis did go down. This means fewer red blood cells were broken down when LNP023 was taken with standard of care.

The researchers concluded there were no new safety concerns for LNP023 in this trial.

How long was this trial?

The trial began in April 2018 and ended in February 2022. It was planned for the participants to be in the trial for up to 3 and a half years.

Who was in this trial?

16 participants were in this trial – 10 men and 6 women. The participants were 24 to 78 years old. Their average age was 47.

15 participants reported their race as White, and 1 participant reported their race as unknown.

Every participant in this trial had PNH and:

- signs of hemolysis
- were receiving the standard of care for PNH at least 3 months before starting the trial.

This trial took place in France, Germany and Italy.

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 **CLNP023X2201** to find the scientific summary.

What trial treatments did the participants take?

Participants were assigned to one of these treatment groups:

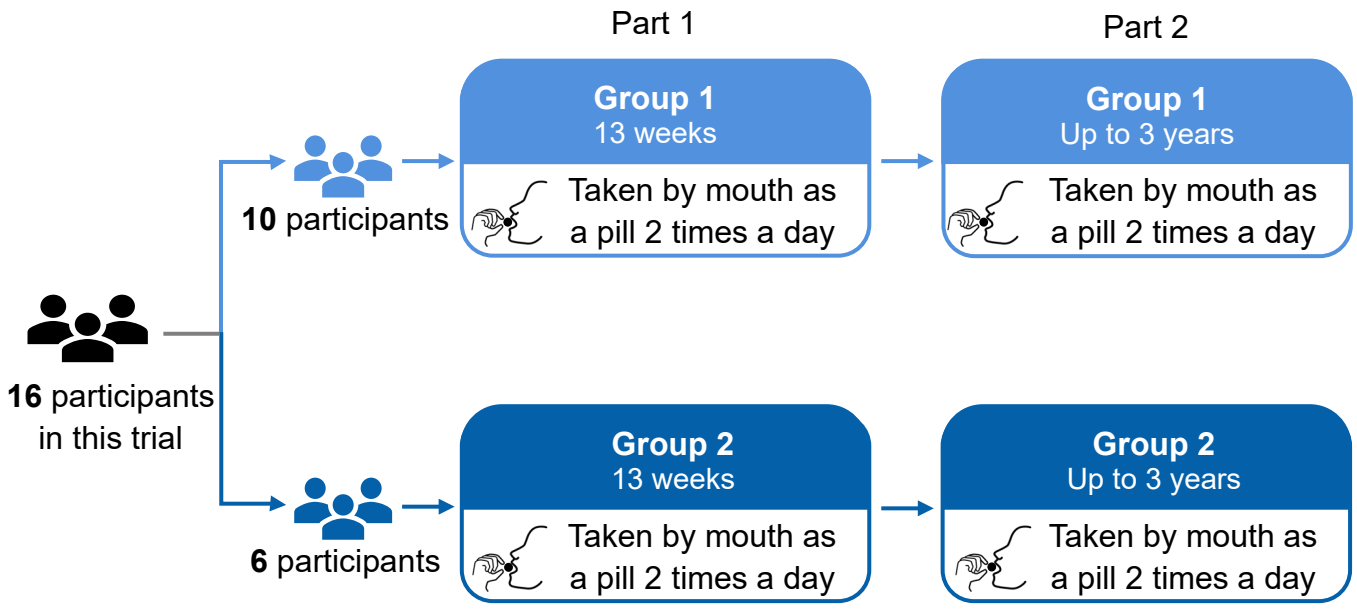
- **Group 1:** 200 milligrams (mg) of LNP023 2 times a day
- **Group 2:** 50 mg or 200 mg of LNP023 2 times a day

All participants took LNP023 by mouth as pills 2 times a day. In Group 2, participants started with 50 mg of LNP023. After 14 days, participants could start taking 200 mg of LNP023 if their signs of hemolysis did not go down enough.

All participants took LNP023 in addition to the standard of care for PNH which was eculizumab. If the trial doctors determined it was appropriate, participants could also stop taking the standard of care after 6 months of taking LNP023. The participants, trial staff, and researchers knew which treatment the participants took.

The trial was split into two parts. In the **first part**, all participants took LNP023 for 13 weeks. Then, in the **second part,** participants continued taking LNP023 for up to about 3 years. If participants' signs of hemolysis went down after being in this trial, the participants could join another trial to continue taking LNP023.

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



Each participant also received vaccines to protect them against certain infections like pneumonia, flu, and meningitis. The participants also took antibiotics if:

- they started taking LNP023 less than 4 weeks after they received their vaccines
- they started taking LNP023 before getting their vaccines
- they had any signs of infection, such as a fever

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 a sign of hemolysis go down in the participants who took LNP023?

Yes, a sign of hemolysis went down after taking LNP023 with standard of care for 13 weeks. This means fewer red blood cells were broken down when LNP023 was taken with the standard of care treatment.

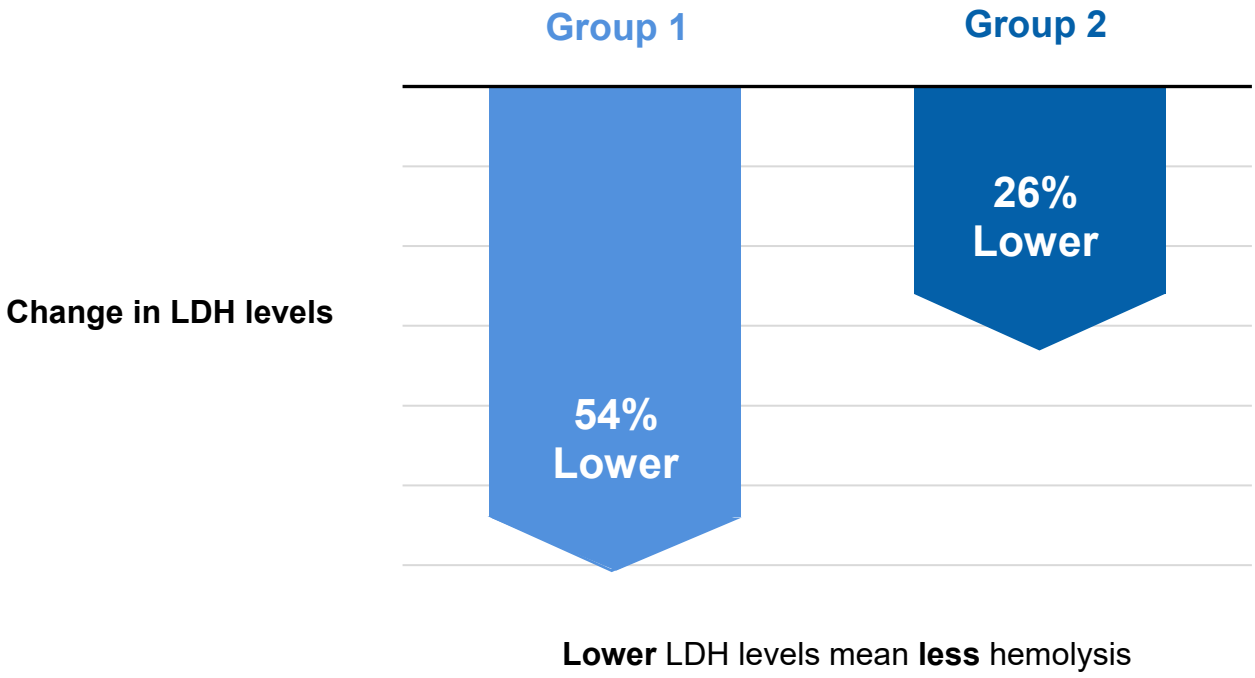
To find this out, the trial staff took many blood samples from participants during the first 13 weeks of treatment. The trial staff tested their blood samples for a protein called **lactate dehydrogenase (LDH).**

After receiving LNP023 for 13 weeks, LDH levels went down in both treatment groups. This means fewer red blood cells were broken down when LNP023 was taken with standard of care treatment.

What is LDH?
LDH is a protein that cells release when they break down. If a person's LDH level goes down, it's a sign of less hemolysis.

Percent change in LDH levels

The graph below shows the average percent change in LDH levels from before treatment with LNP023 to after 13 weeks of treatment with LNP023.



What other results were learned?

Did LNP023 affect other signs of hemolysis and signs of new red blood cells?

The trial staff measured the participants' blood samples for:

- Other signs of hemolysis, which included bilirubin levels
- Signs of new red blood cells, which included hemoglobin levels and number of red blood cells

Researchers also counted how many transfusions participants needed during the trial. If less transfusions are needed, this is a sign of less hemolysis.

Overall, the researchers found that while taking LNP023 with standard of care for 13 weeks:

- the other signs of hemolysis went down
- the signs of new red blood cells went up
- less participants needed transfusions

What is bilirubin?
Bilirubin is a product made when red blood cells break down. If a person's bilirubin level goes down, it's a sign of less hemolysis.

What is hemoglobin?
Hemoglobin is a protein in your red blood cells. If a person's hemoglobin level is low, it means they have less new red blood cells being made.

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.

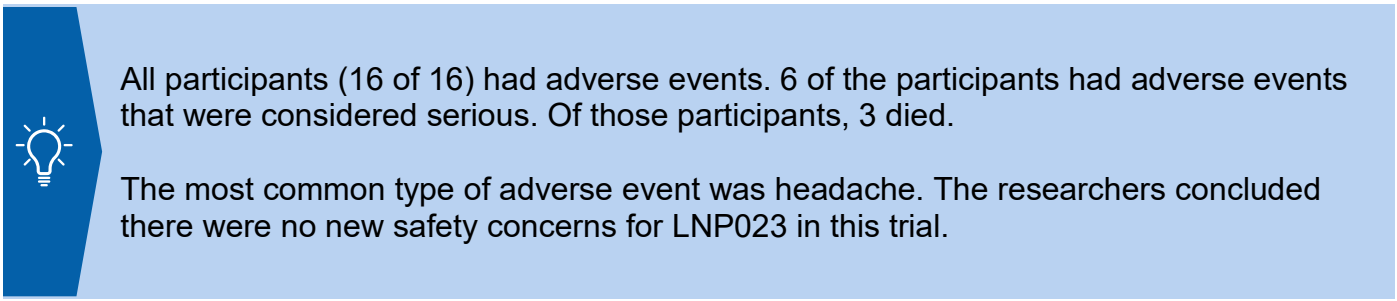
Many trials are needed to know if a drug or treatment causes an adverse event.

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 30 days after completing treatment.



All participants (16 of 16) had adverse events. 6 of the participants had adverse events that were considered serious. Of those participants, 3 died.

The most common type of adverse event was headache. The researchers concluded there were no new safety concerns for LNP023 in this trial.

What serious adverse events did the participants have?

4 of 10 or 40% of participants in Group 1 had a total of 7 serious adverse events:

- **Bleeding inside the skull** | Hemorrhage intracranial
- **Cancer of the tongue** | Squamous cell carcinoma of the tongue
- **A sore in a blood vessel** | Penetrating aortic ulcer
- **Mouth cancer** | Squamous cell carcinoma of the oral cavity
- **Over production of white blood cells** | Lymphoproliferative disorder
- **Skin cancer** | Basal cell carcinoma
- **Infection in the stomach** | Escherichia bacteremia

3 participants in Group 1 died from serious adverse events.

2 of 6 or 33% of participants in Group 2 had a total of 3 serious adverse events:

- **Bladder cancer** | Bladder transitional cell carcinoma
- **Infection in any part of the urinary system** | Urinary tract infection
- **Small tissue growth in the bladder** | Urinary bladder polyp

No participants in Group 2 died from serious adverse events.

What other adverse events did the participants have?

All participants (16 of 16) in both groups had adverse events.

The table below shows the adverse events that happened in a total of **4 or more participants**. Additional adverse events happened to fewer participants.

	Group 1 10 participants	Group 2 6 participants
Headache	20% 2 of 10	50% 3 of 6
Fever Pyrexia	30% 3 of 10	33% 2 of 6
Weakness Asthenia	20% 2 of 10	33% 2 of 6
High level of a type of fat, triglycerides, in blood Hypertriglyceridemia	20% 2 of 10	33% 2 of 6

What was learned from this trial?

This trial learned about the effects and safety of LNP023 in people with PNH.

The researchers concluded that all participants who took LNP023 with standard of care for 13 weeks had a sign of hemolysis go down. This means fewer red blood cells were broken down. The researchers found no new safety concerns for LNP023 in this trial.

In addition, participants who took either dose of LNP023 had other signs of hemolysis go down, signs of new red blood cells go up, and less participants needed blood transfusions.

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 how well a trial drug works and if there are any new safety concerns in a small number of participants. If more trials are planned for LNP023 or PNH, they will appear on the public websites below.

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** – search using the study number **CLNP023X2201**
- **clinicaltrials.gov** – search using the number **NCT03439839**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2017-000888-33**

If more trials are planned, they will appear on the public websites above. When there, search for **LNP023**, **iptacopan, paroxysmal nocturnal hemoglobinuria, or PNH.**

Full trial title: An open label, single arm, multiple dose study to assess efficacy, safety, pharmacokinetics and pharmacodynamics of LNP023 when administered in addition to Standard of Care (SoC) in patients with paroxysmal nocturnal hemoglobinuria (PNH) with signs of active hemolysis

? 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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1-888-669-6682 (USA)

+41-61-324 1111 (EU)

www.novartisclinicaltrials.com