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: CLNP023X2204
Drug studied: LNP023
Sponsor: Novartis

What was the main purpose of this trial?

The purpose of this trial was to learn if LNP023 reduced damage to red blood cells in people with PNH. This trial also helped researchers to 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 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. It also can cause 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.

The main questions this trial was designed to answer:

- How many participants had a sign of hemolysis go down after receiving LNP023 for 12 weeks?
- 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: All 12 participants who took LNP023 for 12 weeks had a sign of hemolysis go down. This means fewer red blood cells were being broken down. The researchers concluded there were no new safety concerns for LNP023 in this trial.

How long was this trial?

The trial began in April 2019 and ended in February 2022. It was planned for the participants to be in the trial for a little more than 2 years.

Who was in this trial?

13 participants were in this trial – 7 women and 6 men. The participants were 20 to 62 years old. Their average age was 38.

All participants reported their race as Asian.

Every participant in this trial had PNH and:

- Signs of hemolysis
- Were not treated with other medicines that block or reduce the complement system
- Did not have certain health conditions that could affect the complement system

This trial took place in Malaysia, the Republic of Korea, Singapore, and Taiwan.

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 participants did not complete the trial

Use trial number **CLNP023X2204** to find the scientific summary.

What trial treatments did the participants take?

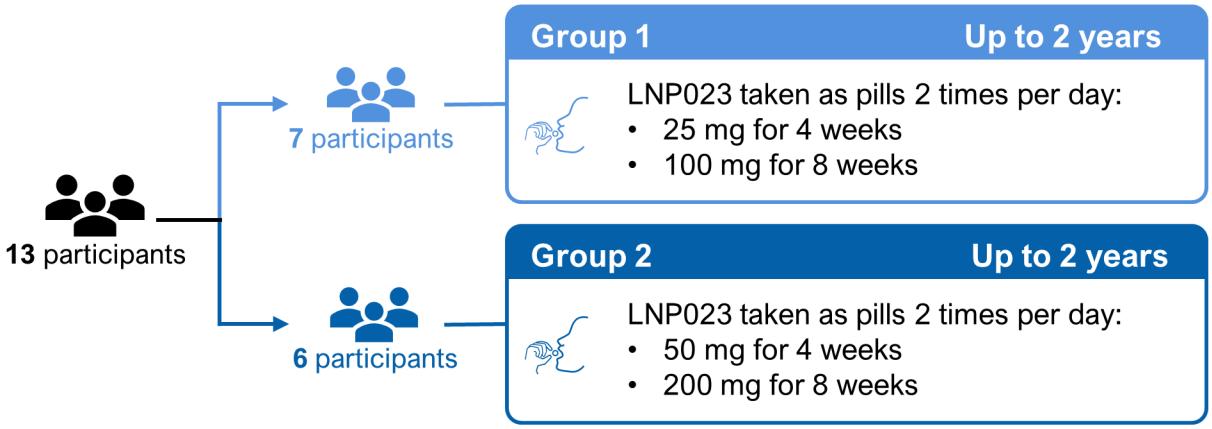
The participants were randomly assigned to one of these treatment groups:

- **Group 1**: took 25 milligrams (mg) of LNP023 2 times per day for 4 weeks and then 100 mg 2 times per day for 8 weeks.
- **Group 2**: took 50 mg of LNP023 2 times per day for 4 weeks and then 200 mg 2 times per day for 8 weeks.

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

The participants took LNP023 by mouth as pills 2 times a day for up to about 2 years. The participant, trial staff, and researchers knew which treatment the participant took.

The graphic below shows how many participants were assigned to each treatment group.
1 participant in **Group 2** left the trial early and only received 2 days of treatment.



The participants started by taking the lower dose of their assigned dose for 4 weeks and moved to the higher dose for 8 weeks. The participants could take the higher dose earlier if their signs of hemolysis didn't go down enough. If their signs of hemolysis went down after the 12 weeks, the participants could continue taking LNP023 up to 2 years. After that, they could join another trial to continue taking LNP023.

If a participant's signs of hemolysis didn't go down, or they didn't join the follow-up trial, they could take smaller doses of LNP023 for 2 weeks before stopping LNP023 completely.

Before starting treatment with LNP023, each participant 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 had any signs of infections, 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.

How many participants had a sign of hemolysis go down after receiving LNP023 for 12 weeks?

All 12 participants who took LNP023 for 12 weeks had a sign of hemolysis go down. This means fewer red blood cells were being broken down.

The participants gave many blood samples during the first 12 weeks of treatment. The trial staff tested their blood samples for a protein called **lactate dehydrogenase (LDH)**.

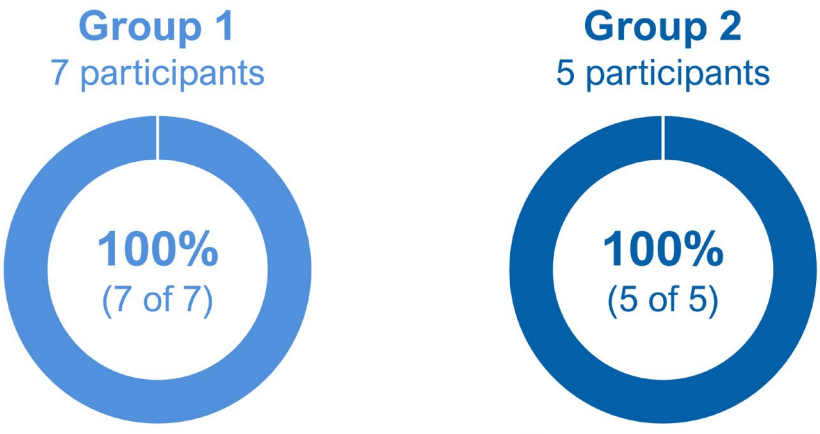
The researchers considered a participant's LDH level to have a meaningful change if their LDH levels went down to either:

- At least 60% of the level before trial treatment
- A healthy level

All participants who took LNP023 for 12 weeks had their LDH levels go down. This means that all participants had less hemolysis.

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.

The number of participants who had their LDH levels go down by week 12



The charts above do not include 1 participant from **Group 2** who left the trial early and only received 2 days of treatment.

What other results were learned?

Did different doses of LNP023 lower signs of hemolysis more after 4 weeks?

The trial staff measured other signs of hemolysis in the participants' blood samples after 4 weeks of treatment. Signs of hemolysis included LDH, ferritin, and bilirubin levels. The researchers then compared the signs in participants in Group 1 to participants in Group 2.

Overall, the researchers found that the participants in Group 2 had their LDH levels go down more after 4 weeks compared to participants in Group 1. For the other signs, the researchers found no difference between Group 1 and Group 2 after 4 weeks.

What are ferritin and bilirubin?

Ferritin is a protein that stores iron in blood cells.

Bilirubin is a product made when red blood cells break down.
If a person's ferritin and bilirubin levels go down, it's a sign of less hemolysis.

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

During the 12 weeks of treatment, the trial staff measured the participants' blood samples for:

- Other signs of hemolysis, including bilirubin and ferritin levels
- Signs of healthy red blood cells, including hemoglobin levels and number of red blood cells

Overall, the researchers found that while taking LNP023 for 12 weeks, the participants' other signs of hemolysis went down, and the signs of healthy red blood cells went up.

Did LNP023 affect signs of blood clots?

The trial staff also measured signs of blood clots in the participants' blood samples. The researchers found that these signs stayed about the same during treatment.

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 7 days after completing treatment, if the participant didn't join the follow-up trial.

Most of the participants (9 of 13) had adverse events. The most common adverse event was headache. None of the participants had adverse events that were considered serious. The researchers concluded there were no new safety concerns for LNP023 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?

Group 1: 4 of 7 participants or 57% had an adverse event.

Group 2: 5 of 6 participants or 83% had an adverse event.

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

	Group 1 7 participants		Group 2 5-6 participants	
	25 mg	100 mg	50 mg	200 mg
Headache	0% 0 of 7	14% 1 of 7	50% 3 of 6	20% 1 of 5
Fever Pyrexia	14% 1 of 7	29% 2 of 7	0% 0 of 6	20% 1 of 5

1 participant in Group 2 left the trial due to an adverse event.

What was learned from this trial?

This trial helped researchers learn about the effects and safety of LNP023 in people with PNH.

The researchers concluded that all 12 participants who took LNP023 for 12 weeks had a sign of hemolysis go down. This means less red blood cells were being broken down. The researchers found no new safety concerns for LNP023 in this trial.

The researchers also learned that after 4 weeks, participants who took the higher dose of LNP023 had their LDH levels go down more. The other signs of hemolysis were about the same.

In addition, during 12 weeks of treatment, the participants who took either dose of LNP023 had:

- Other signs of hemolysis go down
- Signs of healthy red blood cells go up
- Signs of blood clots stay about the same

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 learns about how well a trial drug works and if there are any new safety concerns 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 **CLNP023X2204**
- **clinicaltrials.gov** – search using the number **NCT03896152**

For more information about the follow-up trial that participants could join after this trial, search the websites above using the study number **CLNP023C12001B**.

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:
A multi-center, randomized, open-label, efficacy, safety, pharmacokinetics and pharmacodynamics study, assessing multiple LNP023 doses in adult patients with paroxysmal nocturnal hemoglobinuria and 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