NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects of LNP023 in people with paroxysmal nocturnal hemoglobinuria (PNH) who never received complement inhibitor therapy

Thank you!

Thank you to the participants who took part in the clinical trial for 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 summary helps the participants to understand their important role in medical research.

Trial information

Trial number: CLNP023C12301

Drug studied: LNP023, also known as iptacopan

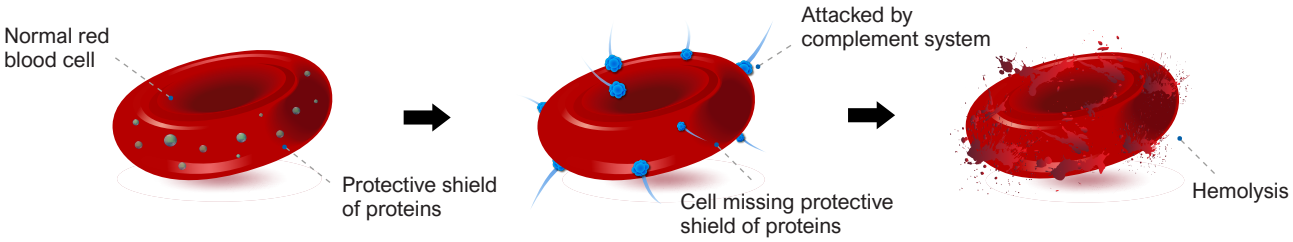
Sponsor: Novartis

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?

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare blood disorder in which the immune system destroys red blood cells. Red blood cells carry oxygen around the body using **hemoglobin (Hb)**. The immune system includes a group of proteins called the **complement system** whose role is to destroy abnormal cells**.** In healthy people, red blood cells have a shield of proteins that protect them from being attacked by the complement system. People with PNH are missing this shield. As a result, the complement system damages and breaks down red blood cells, a process which is called hemolysis.



Common symptoms of PNH are:

- Red or dark urine
- Shortness of breath
- Fatigue (tiredness)
- Low number of red blood cells (anemia)
- Blood clots in various parts of the body

PNH may vary from person to person. Some people require red blood cell transfusion to increase the number of red blood cells, while others require drugs to treat or prevent blood clots. A **red blood cell transfusion** is a medical procedure in which blood is transferred from a donor to a patient to treat a condition or replace lost blood. Transfusions may not be suitable for all patients and can cause unwanted side effects. Although the available treatments for PNH improve red blood cell count, usually they are not enough, and some patients may still need red blood cell transfusions. Therefore, there is a need to find better and more convenient treatments.

The trial drug, **LNP023**, blocks an important protein of the complement system which may help prevent the destruction of red blood cells and allow the body to restore its normal functions.

In this trial, researchers wanted to learn about the effects of LNP023 in participants with PNH who never received any medication that blocks the complement system.

The main questions that researchers wanted to answer were:

- How many participants responded to LNP023 treatment?
- What adverse events did 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 July 2021 and ended in April 2023. The trial was designed so that each participant would take part for up to 60 weeks.

When the trial ended, researchers created a report of the trial results. This summary is based on that report.

Who was in this trial?

40 participants with PNH received treatment in this trial.
Participants' ages ranged from 18 to 81 years. Their average age was 42 years.

The number of participants by gender and race are shown below.

Gender

- 23 Men
- 17 Women

Race

- 27 Asian
- 12 White
- 1 Black or African American

40 participants from **8 countries** took part in the trial. The map below shows the number of participants who took part in each country.

Participants **could take part** in this trial if they:

- Were at least 18 years old
- Had confirmed PNH
- Had an average hemoglobin (Hb) level of less than 10 grams per deciliter (g/dL)
- Had not received prior treatment with other medications that block the complement system

What treatments did the participants receive?

Researchers studied the following treatment:

LNP023: 200 milligrams (mg), provided as capsules, taken by mouth twice a day.

In this trial, all participants received the same treatment and the same dose, and they knew which drug they were taking.

What happened during this trial?

Before treatment

Up to 8 weeks

Trial doctors checked the participants to make sure they could be in this clinical trial.

During treatment

Up to 48 weeks

The treatment was done in **2 periods:**

Core Treatment Period (24 weeks)

All 40 participants received **LNP023** treatment for 24 weeks. They could also receive red blood cell transfusion during the study if they needed it. Participants' Hb levels were monitored throughout the study.

LNP023, 200 mg
40 participants

2 times a day for 24 weeks

Upon completion of the 24-week **Core Treatment Period**, participants could enter the **Extension Treatment Period**. Participants who completed 24 weeks of extension treatment were given the option to continue treatment in a separate trial, CLNP023C12001B, that studied the long-term effects of **LNP023**. This trial is currently ongoing.

Extension Treatment Period (24 weeks)

All the 40 participants entered the **Extension Treatment Period**.

LNP023, 200 mg
40 participants

2 times a day for 24 weeks

After treatment

Up to 30 days after the last dose

Participants had a final check-up within 30 days after their last dose of **LNP023** treatment.

What were the main results of this trial?

How many participants responded to LNP023 treatment?

- 92% of participants responded to LNP023 treatment by the end of the **Core Treatment Period.**
- 97% participants responded to LNP023 treatment by the end of the **Extension Treatment Period.**

After the 24-week **Core Treatment Period**, a participant was considered to have responded to LNP023 treatment if:

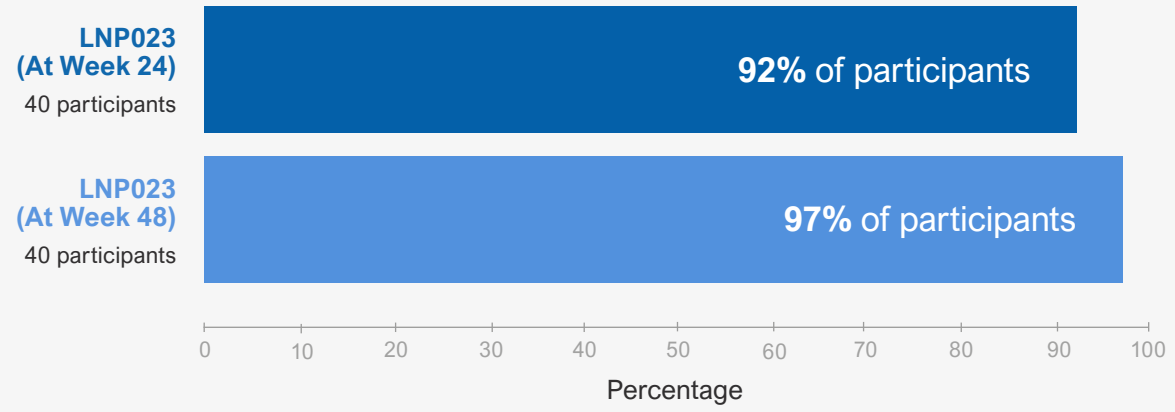
- Their Hb level increased by at least 2 g/dL from the start of the study when checked from Week 18 to Week 24.
- They did not require a red blood cell transfusion after Week 2 and up to Week 24.

For those participants who completed the **Extension Treatment Period** and received treatment for a total of 48 weeks, they were considered to have responded to treatment if:

- Their Hb level increased by at least 2 g/dL from the start of the study to Week 48.

The figure below shows the percentage of participants who responded to LNP023 treatment.

Percentage of participants that responded to LNP023 treatment



What were the other results of this trial?

How many participants responded to LNP023 treatment by having their Hb levels increase to at least 12 g/dL?

- 63% of participants had their Hb levels increase to at least 12 g/dL by the end of the **Core Treatment Period.**
- 80% of participants had their Hb levels increase to at least 12 g/dL by the end of the **Extension Treatment Period.**

In how many participants did LNP023 prevent the need for red blood cell transfusions?

After Week 2, LNP023 prevented the need for red blood transfusions in **39 out of 40 participants (98%).**

Researchers closely monitored the participants to see if they required red blood cell transfusion throughout the study.

How did participants' fatigue change after treatment?

- The average increase in the FACIT-Fatigue score was 10.8 by the end of the **Core Treatment Period.**
- The average increase in the FACIT-Fatigue score was 10.4 by the end of the **Extension Treatment Period.**

Researchers wanted to know if the treatment helped participants feel less tired and perform daily activities better. To learn this, researchers used the **FACIT-Fatigue questionnaire.**

The FACIT-Fatigue questionnaire is a 13-item questionnaire that was completed by the participants. Each item can be scored between 0-4, with the total score ranging between 0 and 52. Higher scores mean an improvement in fatigue symptoms.

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 during the treatment period up to 30 days after the last dose.

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 had adverse events.

- 8 participants had adverse events that were considered serious.
- None of the participants died due to any cause.
- None of the participants stopped the treatment due to an adverse event.

How many participants had adverse events?

The table below shows how many participants had adverse events.

Summary of adverse events

Participants who:	LNP023 40 participants
Had at least 1 serious adverse event	8 of 40 **(20%)**
Had at least 1 other adverse event	24 of 40 **(60%)**
Stopped the treatment due to an adverse event	0 of 40 **(0%)**
Died during the trial	0 of 40 **(0%)**

What serious adverse events did the participants have?

A total of 8 participants who received at least 1 dose of the trial drug had serious adverse events.

The table below shows the serious adverse events that happened in all participants. Some adverse events happened in the same participant.

Serious adverse events	LNP023 40 participants
COVID-19	2 of 40 **(5%)**
Relapse (return) of hemolysis Breakthrough hemolysis	1 of 40 **(3%)**
Clouding of the lens in the eyes Cataract	1 of 40 **(3%)**
Infection	1 of 40 **(3%)**
Lung infection Pneumonia	1 of 40 **(3%)**
Bacterial lung infection Pneumonia Bacterial	1 of 40 **(3%)**
Diabetes Type 2 diabetes mellitus	1 of 40 **(3%)**
Skin cancer Malignant melanoma	1 of 40 **(3%)**

What other adverse events did the participants have?

A total of 24 participants who received at least 1 dose of trial drug had other, non-serious adverse events.

The table below shows the other adverse events that happened in more than 3 participants.

Other adverse events	LNP023 40 participants
Headache	12 of 40 **(30%)**
COVID-19	7 of 40 **(18%)**
Infection of the nose and throat Upper respiratory tract infection	7 of 40 **(18%)**
Diarrhea	6 of 40 **(15%)**

What was learned from this trial?

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

The researchers concluded that:

- Nearly all participants responded to LNP023 treatment and had their Hb levels increased.
- All participants except one did not need a red blood cell transfusion.
- Participants' fatigue improved after LNP023 treatment.
- There were no new or unexpected safety concerns.

The 24-week results of this trial were submitted to health authorities in the United States. LNP023 received approval for the treatment of PNH in adults in the US.

At the time this summary was written, there are two ongoing studies of LNP023 in adult PNH patients. One among them is study CLNP023C12001B, and the other involves patients who have responded to other PNH treatments. Also, a study of LNP023 in children with PNH is planned.

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:

Go to **www.novctrd.com** → Click **Clinical Trial Results** → Agree to the terms **I agree** → Search for **CLNP023C12301**

For more information about this trial go to any of the following websites:

- clinicaltrials.gov – search using the number **NCT04820530**
- clinicaltrialsregister.eu/ctr-search/search – search using the number **2020-003172-41**

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

Full clinical trial title: A Multicenter, Single-arm, Open-label Trial to Evaluate Efficacy and Safety of Oral, Twice Daily Iptacopan in Adult PNH Patients Who Are Naive to Complement Inhibitor Therapy.

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