NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects of LNP023 in people with paroxysmal nocturnal hemoglobinuria (PNH) who had anemia despite being treated with anti-C5 antibody

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: CLNP023C12302

Drug studied: LNP023, also known as iptacopan

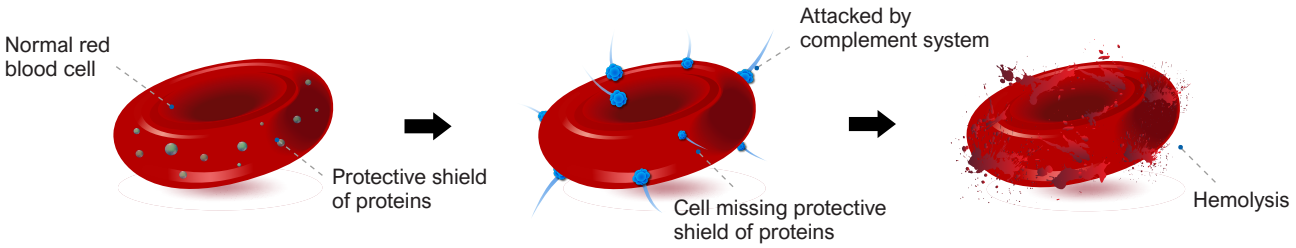
Sponsor: Novartis

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.

Anti-C5 antibodies are medicines that prevent the complement system from attacking the red blood cells and can therefore reduce hemolysis. **Eculizumab** and **ravulizumab** are **anti-C5 antibodies** that are approved for the treatment of PNH. Although these medicines improve red blood cell count, they may not be enough for some patients. 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 had anemia despite being treated with an **anti-C5 antibody**.

The main questions that researchers wanted to answer were:

- How many participants responded to **LNP023** treatment by having their Hb levels increase by 2 g/dL or more?
- How many participants responded to **LNP023** treatment by having their Hb levels increase to 12 g/dL or more?
- In how many participants did **LNP023** prevent the need for red blood cell transfusions?
- How did participants' fatigue change after 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 January 2021 and ended in March 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?

97 participants with PNH received treatment in this trial.
Participants' ages ranged from 20 to 84 years. Their average age was 51 years.

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

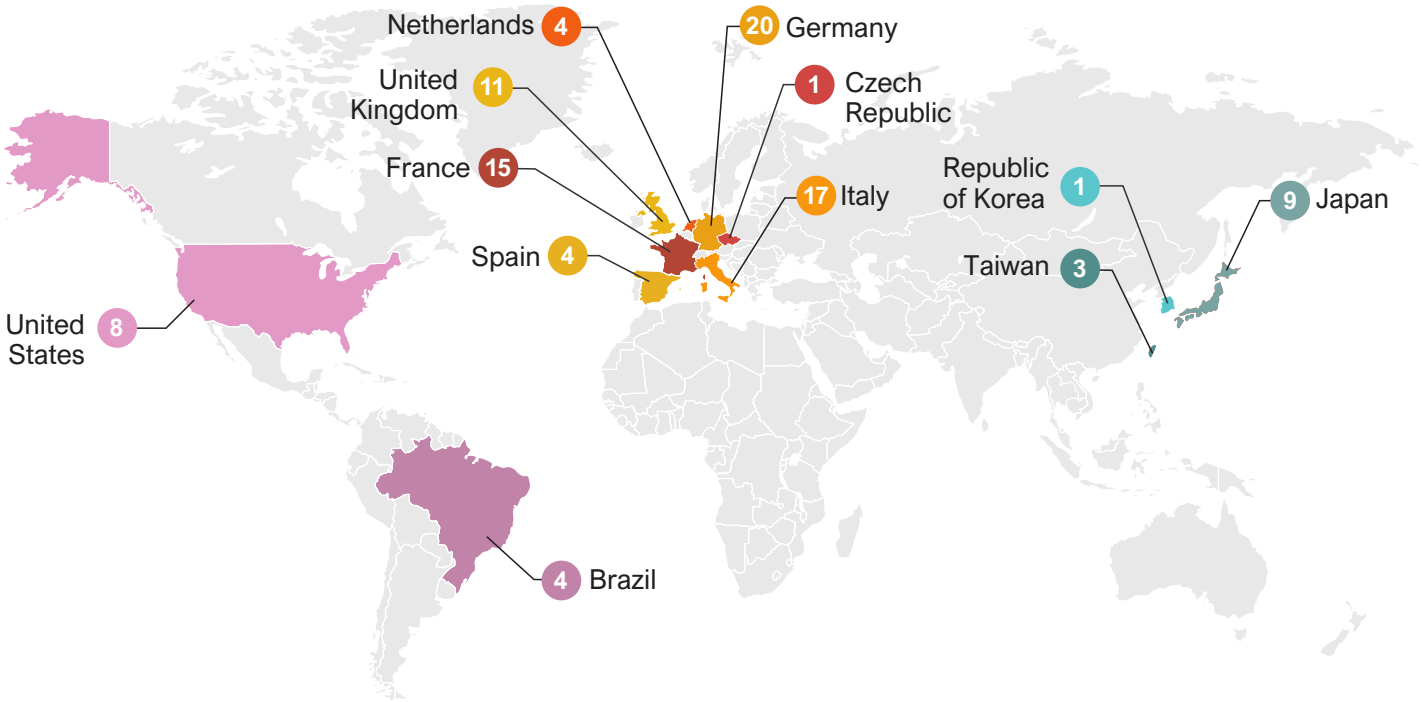
Gender

30 Men	67 Women

Race

74 White	19 Asian	4 Black or African American

97 participants from **12 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 taken **anti-C5 antibody** treatment regularly for at least 6 months before being assigned to treatment in this trial
- Had an average hemoglobin (Hb) level of less than 10 grams per deciliter (g/dL)

What treatments did the participants receive?

Researchers studied the following treatments:

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

Eculizumab or **ravulizumab:** Given as an injection into the vein.

Participants received **eculizumab** or **ravulizumab** as directed by their doctor.

In this trial, the participants, trial doctors, and trial staff knew which treatments and doses the participants received.

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.

All participants continued receiving their **anti-C5 antibody** treatment during these 8 weeks before receiving the study treatment.

During treatment

Up to 48 weeks

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

Core Treatment Period (24 weeks)

A total of 97 participants received either **LNP023** or continued taking **anti-C5 antibody** for 24 weeks. They were randomly assigned to 1 of 2 treatment groups. They could also receive red blood cell transfusion during the study if they needed it. Participants' Hb levels were monitored throughout the study.

LNP023 62 participants	**Anti-C5 antibody** 35 participants

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)

A total of 95 participants entered the **Extension Treatment period**.

LNP023 to LNP023 61 participants	**Anti-C5 antibody to LNP023** 34 participants

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 the treatment by having their Hb levels increase by 2 g/dL or more?

A higher percentage of participants who received **LNP023** responded to treatment and had a 2 g/dL or more increase in their Hb levels as compared to those who received **anti-C5 antibody**.

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 table below shows the percentage of participants who responded to the treatment.

Percentage of participants who responded to the treatment

	Core Treatment Period		Extension Treatment Period	
	LNP023 62 participants	**Anti-C5 Antibody** 35 participants	**LNP023 to LNP023** 62 participants	**Anti-C5 antibody to LNP023** 34 participants
At Week 24	82%	2%	--	--
At Week 48	--	--	82%	62%

Participants in the **LNP023 to LNP023** group received **LNP023** for 48 weeks.

Participants in the **Anti-C5 antibody to LNP023** group received **LNP023** for 24 weeks.

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

A higher percentage of participants who received **LNP023** responded to treatment and had their Hb levels increase to at least 12 g/dL as compared to those who received **anti-C5 antibody**.

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 12 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 to at least 12 g/dL from the start of the study to Week 48.

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

Percentage of participants who responded to the treatment

	Core Treatment Period		Extension Treatment Period	
	LNP023 62 participants	**Anti-C5 Antibody** 35 participants	**LNP023 to LNP023** 62 participants	**Anti-C5 antibody to LNP023** 34 participants
At Week 24	69%	2%	--	--
At Week 48	--	--	65%	50%

Participants in the **LNP023 to LNP023** group received **LNP023** for 48 weeks.

Participants in the **Anti-C5 antibody to LNP023** group received **LNP023** for 24 weeks.

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

After Week 2,

- A total of **57 out of 62 participants (92%)**, who took **LNP023** throughout the study did not require red blood cell transfusion.
- A total of **32 out of 34 participants (94%)**, who switched from **anti-C5 antibody** to **LNP023** in the Extension Treatment period did not require red blood cell transfusion.

Researchers closely monitored the participants to see if they required red blood cell transfusion throughout the study. They reported results for the 96 participants who received treatment for 48 weeks.

How did participants' fatigue change after treatment?

The average change in the FACIT-Fatigue score was higher for participants who received **LNP023** as compared to those who received **anti-C5 antibody**.

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.

The table below shows the results for participants who received at least one dose of treatment and had scores before and after treatment at Week 24 and 48.

Average Increase in FACIT-Fatigue score at Week 24 and 48

	Core Treatment Period		Extension Treatment Period	
	LNP023 62 participants	**Anti-C5 Antibody** 31 participants	**LNP023 to LNP023** 55 participants	**Anti-C5 antibody to LNP023** 26 participants
At Week 24	**8.6**	**0.3**	**--**	**--**
At Week 48	**--**	**--**	**9.8**	**11.0**

Participants in the **LNP023 to LNP023** group received **LNP023** for 48 weeks.

Participants in the **Anti-C5 antibody to LNP023** group received **LNP023** for 24 weeks

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 from the start of treatment 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.

85 participants had adverse events.

- 13 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:	Anti-C5 Antibody 35 participants	Any LNP023 96 participants
Had at least 1 serious adverse event	5 of 35 **(14%)**	13 of 96 **(14%)**
Had at least 1 other adverse event	21 of 35 **(60%)**	62 of 96 **(65%)**
Stopped the treatment due to an adverse event	0 of 35 **(0%)**	0 of 96 **(0%)**
Died during the trial	0 of 35 **(0%)**	0 of 96 **(0%)**

Anti-C5 antibody group includes participants who received **anti-C5 antibody** during the Core Treatment Period.

Any LNP023 group includes participants who received **LNP023** at any time during the study.

What serious adverse events did the participants have?

A total of 13 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 at least 3 participants.

Serious adverse events	Anti-C5 Antibody 35 participants	Any LNP023 96 participants
COVID-19	2 of 35 **(6%)**	1 of 96 **(1%)**

What other adverse events did the participants have?

A total of 62 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 at least 10% of participants.

Other adverse events	Anti-C5 Antibody 35 participants	Any LNP023 96 participants
COVID-19	7 of 35 **(20%)**	25 of 96 **(26%)**
Headache	1 of 35 **(3%)**	14 of 96 **(15%)**
Relapse (return) of hemolysis Breakthrough hemolysis	6 of 35 **(17%)**	7 of 96 **(7%)**
Inflammation of the nose and throat Nasopharyngitis	3 of 35 **(9%)**	12 of 96 **(13%)**
Diarrhea	2 of 35 **(6%)**	12 of 96 **(13%)**
Nausea	1 of 35 **(3%)**	11 of 96 **(11%)**

What was learned from this trial?

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

The researchers concluded that:

- More participants responded to the **LNP023** treatment and had their Hb levels increased as compared to those who took **anti-C5 antibody**.
- Most participants who received **LNP023** did not require red blood cell transfusion as compared to those who took **anti-C5 antibody**.
- Participants who received **LNP023** had a larger improvement in fatigue as compared to those who took **anti-C5 antibody**.
- No new or unexpected safety concerns were found.

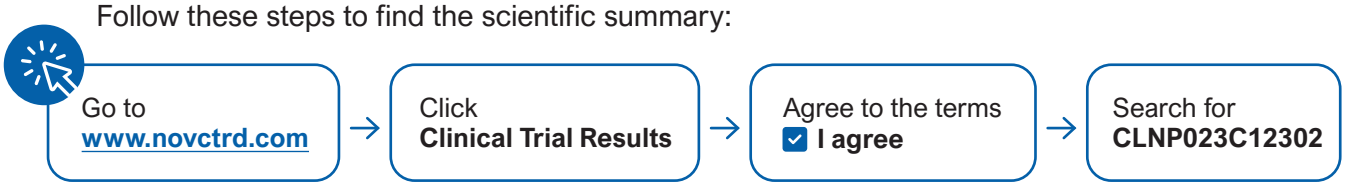
The 24-week results of this trial were submitted to health authorities in the United States. **LNP023** received approval for the treatment of PNH in adults in the US.

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:



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

- **clinicaltrials.gov** – search using the number **NCT04558918**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2019-004665-40**

Other trials with LNP023 will appear on the public websites above. When there, search for **LNP023** or **iptacopan**.

Full clinical trial title: A Randomized, Multicenter, Active-comparator Controlled, Open-label Trial to Evaluate Efficacy and Safety of Oral, Twice Daily LNP023 in Adult Patients With PNH and Residual Anemia, Despite Treatment With an Intravenous Anti-C5 Antibody

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