NOVARTIS

# Clinical Trial Results Summary

# A clinical trial to learn about the effects of iptacopan in people with paroxysmal nocturnal hemoglobinuria who switched from anti-C5 antibody treatment

## Thank you!

Thank you to the participants who took part in the clinical trial for **paroxysmal nocturnal hemoglobinuria (PNH)**. Every participant helped the researchers learn more about the trial drug **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:** CLNP023C12303

**Drug studied:** **Iptacopan**, also known as **LNP023**

**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.

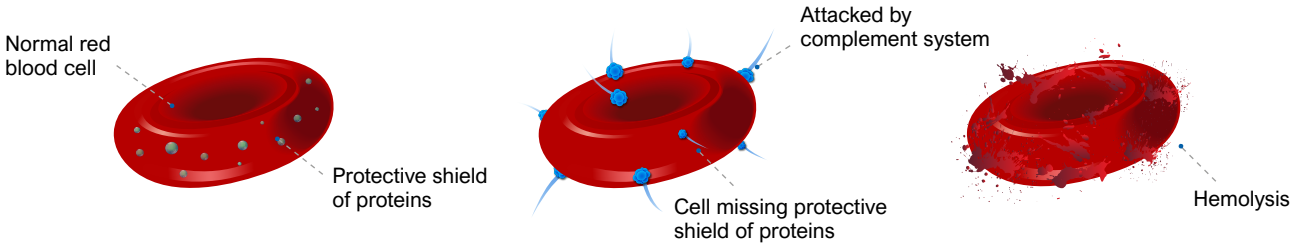
This summary only shows the results of a single clinical trial. Other clinical trials may have different results.

# What was the main purpose of this trial?

The main purpose of this trial was to learn about the effects of **iptacopan** in adults with **paroxysmal nocturnal hemoglobinuria (PNH)** who switched from their current **anti-C5 antibody** treatment to **iptacopan**.

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

**Antibodies** are made by our immune system (the body's natural defense) to fight off infection or anything that is harmful to the body.

**Anti-C5 antibodies** are a type of treatment that prevents the complement system from attacking the red blood cells, which can reduce hemolysis.

**Eculizumab** and **ravulizumab** are **anti-C5 antibodies** that are approved for the treatment of **PNH**. Although these medicines can increase the levels of red blood cells, they may not be enough for some patients.

The trial drug, **iptacopan**, is already approved for adults with **PNH**. **Iptacopan** works by blocking an important protein of the complement system. This helps prevent the destruction of red blood cells and improve symptoms.

**Drug**
iptacopan

**Pronounced as**
ip-tah-KOH-pan

In this trial, researchers wanted to find out if switching to **iptacopan** after receiving **anti-C5 antibodies** would keep hemoglobin levels from dropping in adults with **PNH**. The trial focused on people who were responding to their treatment with either **eculizumab** or **ravulizumab**. Their hemoglobin levels were steady for at least 6 months before switching to **iptacopan**.

**The main questions that researchers wanted to answer were:**

- Did **iptacopan** keep hemoglobin levels as steady as **anti-C5 antibodies** after 24 weeks of treatment?
- Did **iptacopan** raise hemoglobin levels after switching from **anti-C5 antibodies**?
- How many participants achieved hemoglobin levels of 12 g/dL or more during the trial?
- Did participants feel less tired after 12 and 24 weeks of **iptacopan** treatment?
- What medical problems, also called adverse events, happened during this trial?
  - An **adverse event** is any sign or symptom that participants have during a trial. Adverse events **may** or **may not** be caused by treatments in the trial.

# How long was this trial?

The trial began in April 2023 and ended in October 2024.

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

# Who was in this trial?

**52 participants** with **PNH** received **iptacopan** treatment in this trial.
Participants' ages ranged from 20 to 76 years. Their average age was 46 years.

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

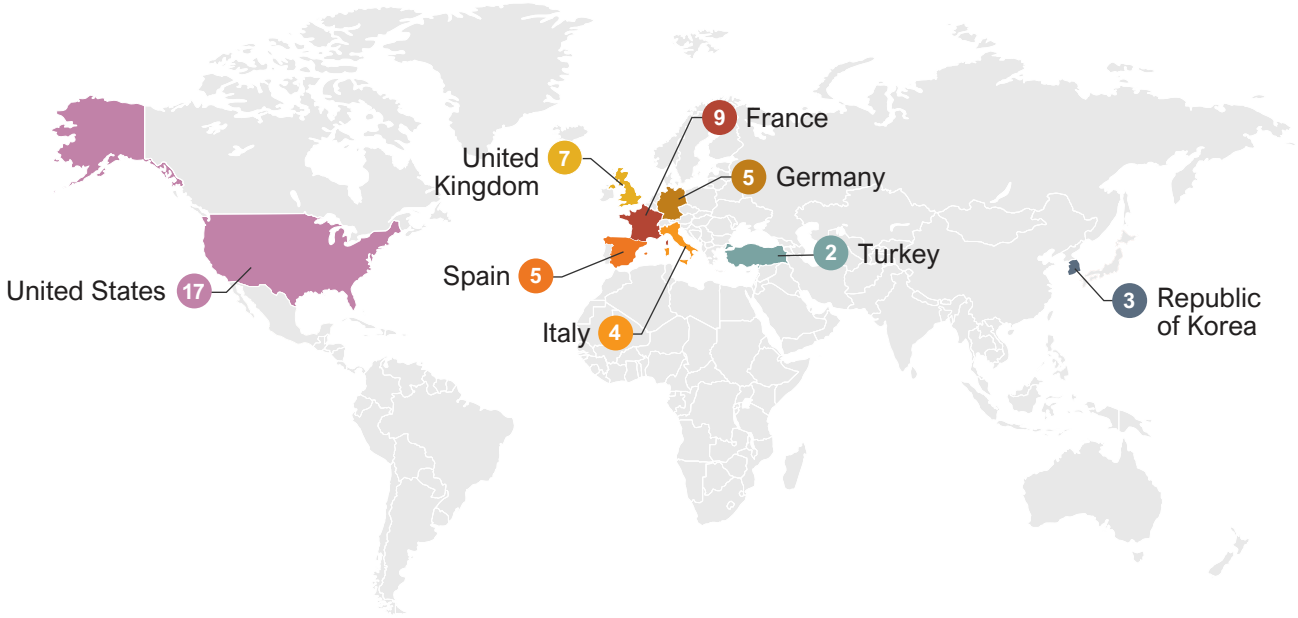
**Sex**

| | |
|---|---|
| 32 Male | 20 Female |

**Race**

| | | | |
|---|---|---|---|
| 35 White | 9 Not reported | 4 Asian | 4 Unknown |

**52 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**
- Were on stable **anti-C5 antibody** treatment of either **eculizumab** or **ravulizumab** for at least 6 months before this trial
- Had an average hemoglobin level of 10 grams per deciliter (g/dL) or higher
- Did not need a red blood cell transfusion for at least 6 months before this trial

A **red blood cell transfusion** is a medical procedure where blood from a donor is given to a patient to replace lost red blood cells and help restore hemoglobin levels.

# What treatments did the participants receive?

Researchers studied the following treatment:

**Iptacopan: 200 milligrams (mg),** provided as capsules, taken by mouth, 2 times a day.

The participants, researchers, and trial staff knew that all participants were receiving **iptacopan**.

# What happened during this trial?

## Before treatment

Up to 8 weeks

The trial staff checked to make sure the participants could be in this trial.

## During treatment

Up to 24 weeks

A total of 52 participants received **iptacopan**. Participants' hemoglobin levels were monitored throughout the trial.

**Iptacopan**, 200 mg
Taken by mouth, 2 times a day

52 participants

## After treatment

Up to 30 days after the last dose

- Participants who completed 24 weeks of treatment were given the option to continue treatment in a separate trial, **CLNP023C12001B**, which is studying the long-term effects of **iptacopan**. Their final visit in this trial was at Week 24.
- Participants who stopped treatment early had to visit the clinic for an end-of-treatment visit.
- Participants who completed the treatment and did not continue in the **CLNP023C12001B** trial were checked for adverse events for up to 30 days after the last dose.

# What were the main results of this trial?

## Did iptacopan keep hemoglobin levels as steady as anti-C5 antibodies after 24 weeks of treatment?

Researchers found that people who switched to **iptacopan** were able to keep their hemoglobin levels steady, and also had an increase, after 24 weeks.

Participants provided regular blood samples so researchers could track their hemoglobin levels throughout the trial.

**Iptacopan** met the trial goal by keeping hemoglobin levels steady. This means that, the average hemoglobin level did not drop by more than 1 g/dL between the start of the trial and Weeks 18 to 24.


Hemoglobin levels **increased by an average of 2 g/dL** over that time.

# What were the other results of this trial?

## Did iptacopan raise hemoglobin levels after switching from anti-C5 antibodies?

Researchers found that participants' hemoglobin levels increased by an average of 2 g/dL after 24 weeks of treatment with **iptacopan**. This meant that switching from **anti-C5 antibody** treatment to **iptacopan** led to higher levels of hemoglobin in adults with **PNH**.

## How many participants achieved hemoglobin levels of 12 g/dL or more during the trial?

Researchers found that **93% of participants** had a hemoglobin level of 12 g/dL or more between Weeks 18 and 24.

## Did participants feel less tired after 12 and 24 weeks of iptacopan treatment?

After 12 weeks of treatment with iptacopan, participants' average **FACIT-Fatigue** scores went up by around 5 points. After 24 weeks, scores were on average 4 points higher than at the start of the trial. This means participants felt less tired and had more energy to perform daily activities.

Researchers wanted to know if **iptacopan** helped participants feel less tired and perform daily activities better. To learn this, researchers used the **FACIT-Fatigue** questionnaire. They compared scores from before **iptacopan** treatment with scores after 12 and 24 weeks of treatment.

The **FACIT-Fatigue questionnaire** includes 13 questions that participants answer. Each question is scored from 0 to 4, with the total score ranging from 0 to 52. Higher scores mean participants felt less tired and had more energy.

# What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all medical problems, also called adverse events, that happen in trials. They track adverse events 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 the 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.

A total of **44 out of 52 participants (85%)** had adverse events, including serious and other adverse events.

- **2 out of 52 participants (4%)** had adverse events that were considered serious.
- **1 out of 52 participants (2%)** left the trial due to an adverse event.
- **None** of the participants died.

The safety results from this trial are similar to those seen in previous trials with **iptacopan**.

## How many participants had adverse events?

| Participants who: | **Iptacopan** 52 participants |
|---|---|
| Had any adverse event, **including serious and other** | 44 of 52 **(85%)** |
| Had at least **1 serious adverse event** | 2 of 52 **(4%)** |
| Left the trial due **to an adverse event** | 1 of 52 **(2%)** |

## What serious adverse events did the participants have?

Overall, 2 participants had 1 or more serious adverse events. These included:

- **Fever** (pyrexia)
- **Bleeding on the surface of the brain** (subdural hematoma)
- **Bacterial lung infection** (pneumonia bacterial)

## What other (not including serious) adverse events did the participants have?

The table below shows the other adverse events that happened during the trial.

| | **Iptacopan**<br>52 participants |
|---|---|
| **Headache** | 9 of 52 **(17%)** |
| **Diarrhea** | 6 of 52 **(12%)** |
| **Common cold**<br>Nasopharyngitis | 6 of 52 **(12%)** |
| **Nausea** | 6 of 52 **(12%)** |
| **Tiredness**<br>Fatigue | 4 of 52 **(8%)** |
| **Infection of the nose, sinuses, and the upper throat**<br>Upper respiratory tract infection | 3 of 52 **(6%)** |
| **Mouth and throat pain**<br>Oropharyngeal pain | 3 of 52 **(6%)** |

# What was learned from this trial?

This trial helped researchers learn about the effects of **iptacopan** in people with **paroxysmal nocturnal hemoglobinuria (PNH)** who switched from their current **anti-C5 antibody** treatment.

The researchers concluded that:

- Hemoglobin levels stayed steady and even increased over 24 weeks in participants who switched to **iptacopan**. Most participants had a hemoglobin level of 12 g/dL or more.
- Participants felt less tired and were overall satisfied with **iptacopan** treatment.
- The safety results from this trial were similar to those seen in previous trials with **iptacopan**.

At the time this summary was written, there was one ongoing trial (CLNP023C12001B) of **iptacopan** in people with **PNH**. Future trials of **iptacopan** in people with **PNH** are also 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** → Accept the terms ☑ **I accept** → Search for **CLNP023C12303**

For more information about this trial go to this website:

clinicaltrials.gov – search using the number **NCT05630001**

euclinicaltrials.eu/ – search using the number **2022-502148-10-00**

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

**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 Have Hb≥10 g/dL in Response to Anti-C5 Antibody and Switch to Iptacopan

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