NOVARTIS

The effects and safety of LFG316 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 **LFG316**, also called tesidolumab and **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

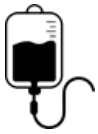
Trial number: CLFG316X2201
Drugs studied: LFG316 and LNP023
Sponsor: Novartis

What was the main purpose of this trial?

The main purpose of this trial was to learn if LFG316 reduced the damage to red blood cells in people with PNH. This trial also helped researchers learn about the safety of LFG316 and 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 a 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.



LFG316 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 trial's sponsor decided to stop studying LFG316. Because of this, participants could switch from receiving LFG316 to another trial drug for PNH called LNP023.

LNP023 is a trial drug designed to block a different 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:

- Did a sign of hemolysis go down?
- What medical problems did the participants have during this trial?
  Keeping track of the medical problems helped to learn about the safety of LFG316 and LNP023.

Main results: After receiving LFG316 for the first 4 weeks, all participants had a sign of hemolysis go down. This means fewer red blood cells were broken down when LFG316 was taken. A sign of hemolysis continued to stay down when participants continued to take LFG316 during the trial.

The researchers concluded there were no new safety concerns for LFG316 or LNP023 in this trial.

How long was this trial?

The trial began in September 2015 and ended in May 2022. It was planned for the participants to be in the trial for up to and about 6 and half years.

Who was in this trial?

10 participants were in this trial – 6 men and 4 women. The participants were 27 to 66 years old. Their average age was 43.

7 participants reported their race as Asian and 3 participants reported their race as White (Caucasian).

Every participant in this trial had PNH and:

- signs of hemolysis
- were vaccinated against meningitis
- were not receiving treatment 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 the Czech Republic, Japan, and Lithuania.

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 **CLFG316X2201** to find the scientific summary.

What trial treatments did the participants receive?

Every participant received:

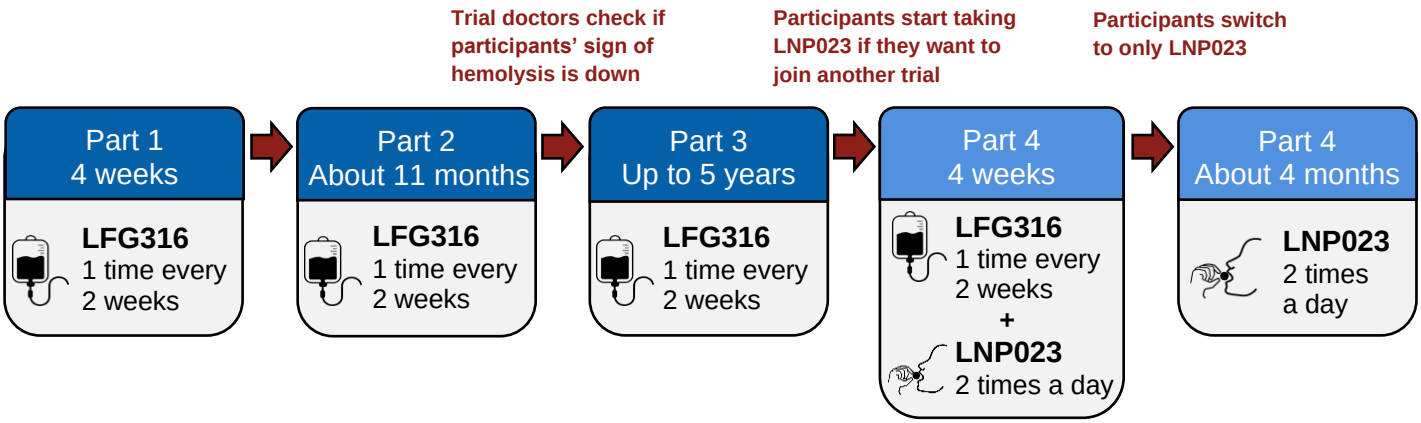
- **LFG316** – 20 milligrams for every kilogram of their weight (mg/kg) as an infusion into a vein once every 2 weeks.
- **LNP023** – 200 milligrams (mg) as capsules taken 2 times a day.

The trial staff, researchers, and participants knew which treatment they took.

The trial was split into four parts:

- Part 1: First, all participants took LFG316 for 4 weeks.
- Part 2: Then, all participants continued taking LFG316 for about 11 months.
- Part 3: If participants' signs of hemolysis went down in part 1 and 2, they could continue receiving LFG316 for up to 5 years.
- Part 4: Last, participants switched from receiving LFG316 to LNP023. Participants could only do this if they wanted to join another trial with LNP023 and were vaccinated against flu and pneumonia.

The graphic below shows how long and how often participants received each treatment:



Only 9 participants started Part 4. One participant left the trial before joining Part 4.

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?

To find this out, the trial staff took many blood samples from participants during the treatment periods. The trial staff tested participant's blood samples for a protein called **LDH**.

In this study, the researchers determined the effect of LFG316 on a sign of hemolysis by looking at:

- The number of participants who had their LDH levels go down
- Whether LDH levels went down and stayed down during the trial's 3 parts

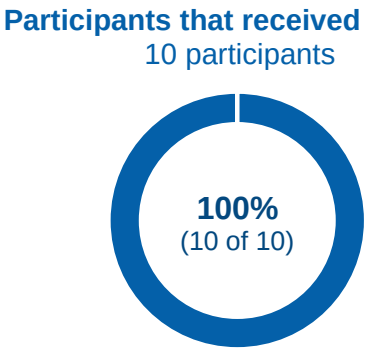
What is LDH?
LDH is a protein that cells release when they break down. If a person's LDH level goes down, it's a sign of less hemolysis.

How many participants had LDH levels go down during the first 4 weeks of treatment?

All 10 participants had their LDH levels go down during the first 4 weeks of receiving LFG316.

During the first 4 weeks of treatment, the researchers determined the number of participants who had a meaningful change in LDH levels. Researchers considered a participant's LDH level to have a meaningful change if their levels went down to at least 60% of the level before trial treatment.

Number of participants who had their LDH levels go down during the first 4 weeks



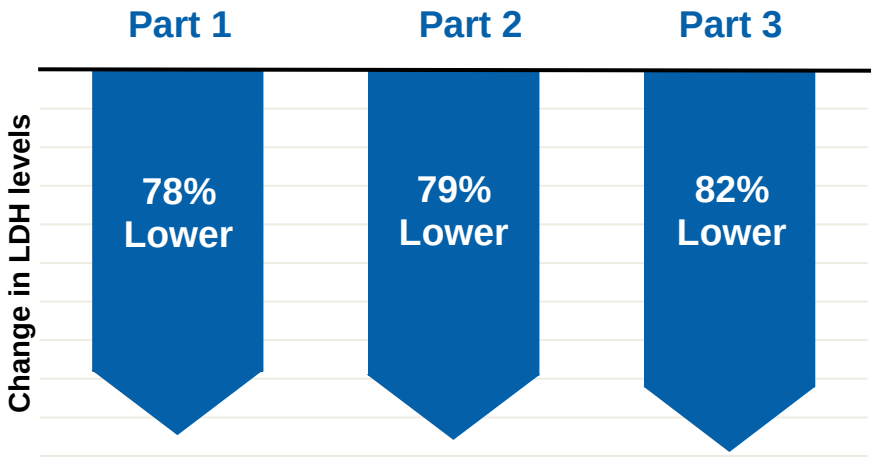
Did LDH levels go down and stay down while taking LFG316?

Yes, average LDH levels went down and stayed down while taking LFG316.

To find this out, trial staff measured participants' average LDH levels at different time points during the trial's parts. The researchers determined that LDH levels went down in Part 1 of the trial and stayed down during Part 2 and 3.

Percentage change in LDH levels

The graph below shows the average change in LDH levels when taking LFG316 over Parts 1 to 3.



Lower LDH levels mean **less** hemolysis

LDH levels continued to stay down when participants switched from LFG316 to LNP023 in Part 4.

What other results were learned?

How much and how fast did LFG316 get into the blood?

The trial staff took blood samples from each participant during the trial. This allowed researchers to learn how much and how fast LFG316 got into the participants' blood over time. This information helps researchers confirm the dose amount for LFG316.

The researchers found that after receiving one dose of LFG316:

- the levels of LFG316 in the participants' blood reached expected levels
- the amount of LFG316 in the participants' blood was highest after about 2 and a half hours

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.

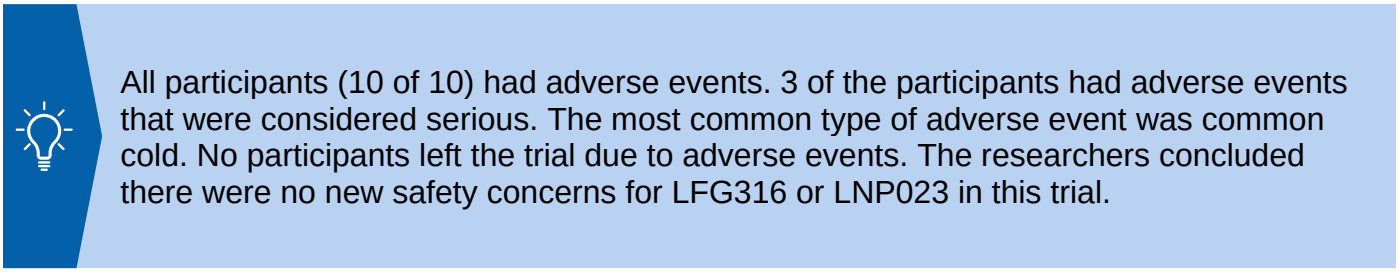
Many trials are needed to know if a drug or treatment causes an adverse event.

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 8 weeks after completing treatment.



All participants (10 of 10) had adverse events. 3 of the participants had adverse events that were considered serious. The most common type of adverse event was common cold. No participants left the trial due to adverse events. The researchers concluded there were no new safety concerns for LFG316 or LNP023 in this trial.

What serious adverse events did the participants have?

3 of 10 participants, or 30%, had a total of 6 serious adverse events:

- **Bacteria in the blood** | Bacteraemia
- **Common Cold** | Nasopharyngitis
- **Flu** | Influenza
- **Infection**
- **Kidney problems** | Renal impairment

- **Stomach flu** | Enterocolitis Viral

All serious adverse events happened in parts 1 to 3 of the trial.

There were no deaths during the trial.

What other adverse events did the participants have?

Part 1 to 3: 10 of 10 participants, or 100%, had an adverse event.

Part 4: 6 of 9 participants, or 67%, had an adverse event.

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

	LFG316 Part 1 to Part 3 10 Participants	LFG316 and LNP023 Part 4 9 participants
Common cold Nasopharyngitis	**80%** 8 of 10	**0%** 0 of 9
Headache	**50%** 5 of 10	**11%** 1 of 9
Infection of the urinary bladder Cystitis	**40%** 4 of 10	**0%** 0 of 9

What was learned from this trial?

This trial helped researchers learn about the effects of LGF316 as well as the safety of LFG316 and LNP023 in people with PNH**.**

The researchers concluded that all participants who took LFG316 had a sign of hemolysis go down and stay down in the trial. This means fewer red blood cells were being broken down. The researchers found no new safety concerns for LFG316 or LNP023 in this trial.

The researchers also learned that after receiving a dose of LFG316, the amount of LFG316 in the blood was highest after about 2 and a half hours.

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 helps researchers learn 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 the following websites:

- **novctrd.com** – search using the study number **CLFG316X2201**
- **clinicaltrials.gov** – search using the number **NCT02534909**
- **clinicaltrialsregister.eu/ctr-search** – search using the number **2014-005338-74**

If more trials are planned, they will appear on the public websites above. When there, search for **LFG316**, **tesidolumab**, **LNP023, iptacopan, paroxysmal nocturnal hemoglobinuria, or PNH.**

Full trial title: An open-label proof of concept study to assess the efficacy, safety and pharmacokinetics of LFG316, an anti-C5 monoclonal antibody in patients with paroxysmal nocturnal hemoglobinuria (PNH).

? 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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