

CLINICAL STUDY RESULTS

A Study about Ravulizumab and Eculizumab in
Complement Inhibitor-naïve Patients
with Paroxysmal Nocturnal Hemoglobinuria (PNH)

THANK YOU!

Alexion would like to thank all of the patients, their families, and caregivers who took part in this clinical study. Taking part in studies like this one contributes directly to the discovery of new medicines for people with PNH.

STUDY IDENTIFICATION INFORMATION

TREATMENTS STUDIED: 1) ravulizumab, also known as ALXN1210 (trade name: Ultomiris®)
2) eculizumab (trade name: Soliris®)

STUDY TITLE: A Phase 3, Randomized, Open-label, Active-controlled Study of ALXN1210 Versus Eculizumab in Complement Inhibitor-naïve Adult Patients with Paroxysmal Nocturnal Hemoglobinuria.

STUDY NUMBERS: Europe, 2016-002025-11 | United States, NCT02946463 | Protocol, ALXN1210-PNH-301

BACKGROUND

What are clinical studies?

Clinical studies aim to answer specific questions about new or existing treatments, procedures, or vaccines and involve patients with health conditions or healthy volunteers. Clinical studies happen in several phases from phase 1 to 4.

This study is a phase 3. Phase 3 studies look at the overall risks and benefits of a new treatment compared to the routine treatment or care for the condition being studied. In this study, ravulizumab (new treatment) was compared with eculizumab (routine care) in adult patients with paroxysmal nocturnal hemoglobinuria.

What is paroxysmal nocturnal hemoglobinuria?

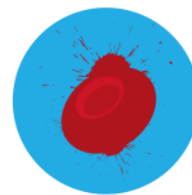
Paroxysmal nocturnal hemoglobinuria, also called PNH, is a very rare, lifelong blood disorder. In PNH, some or all of the red blood cells lack important protective proteins. Without these protective proteins, the body's natural defense system destroys the red blood cells. This process is known as hemolysis.



Red blood cell missing protective proteins



Red blood cell attacked



Red blood cell destroyed

In patients with PNH, hemolysis is always happening and can result in serious health problems.

What are the symptoms of PNH?



The most common symptoms of PNH include feeling tired, difficulty swallowing, trouble concentrating or thinking, shortness of breath, stomach pain, dark-colored urine, and erectile dysfunction in men. The lack of healthy red blood cells, known as anemia or being anemic, is a serious complication of PNH, which often results in patients needing blood transfusions.

Life-threatening complications from PNH can include blood clots, kidney failure, and other organ damage.

What treatments are available for PNH?

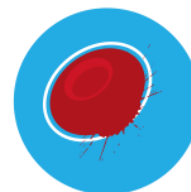
Ravulizumab and eculizumab, known as complement inhibitors, aim to block the destruction of the red blood cells, improve common symptoms of PNH, and prevent life-threatening complications. Complement inhibitors work by sticking to a protein in the blood called C5, which helps stop the red blood cells from breaking down.



Complement inhibitor treatment given directly into the bloodstream



Protective protein shields red blood cell from attack



Less destruction happening to red blood cell

What were the treatments used in this study?

There were 2 treatment groups in this study: ravulizumab and eculizumab. The treatments were given by an infusion, which means it was administered directly into the bloodstream using a drip. A computer selected at random who got ravulizumab and who got eculizumab.

RAVULIZUMAB



Up to 3000* mg infusion once each week for the first 2 weeks, then up to 3600* mg once every 8 weeks after that.

Each infusion was around 2 hours.

125 patients got ravulizumab infusions.

*Exact dose based on body weight.

ECULIZUMAB



600^ mg infusion once each week for the first 4 weeks, followed by 900^ mg once every 2 weeks after that.

Each infusion was around 35 minutes.

121 patients got eculizumab infusions.

^Dose not based on body weight.

PURPOSE OF THE STUDY

What were the researchers trying to find out in this study?

The researchers wanted to see if ravulizumab worked **as well as** eculizumab at treating patients with PNH who had never had treatment with a complement inhibitor. The side effects of both treatments, which is called the safety of the study, were also looked at. The study was not done to see if one treatment was better than the other.



The study had 2 parts. Part 1 started in December 2016 and ended in January 2018. **This summary provides the results of Part 1, which is when all patients had received 26 weeks of treatment.** The plan is for Part 2 to finish in 2023, and the results be made available in 2024.

What were the main questions?

1. What percentage of patients who got ravulizumab did not need a blood transfusion compared to patients who got eculizumab?
2. How did hemolysis compare between the 2 treatments?

Were there any other important questions?

How did tiredness levels compare between the 2 treatments?

What percentage of patients in each treatment group had breakthrough hemolysis^?

What percentage of patients in each treatment group had stable hemoglobin levels?

How did the patients' overall quality of life compare between the 2 treatments?

^Breakthrough hemolysis means a patient experienced an increase in enzyme levels and a new or worsening symptom, or a serious complication, during treatment.

STUDY PARTICIPANTS

Who could take part?

To take part in the study, patients had to meet the following requirements:



Male or female, 18 years of age or older.



Confirmed diagnosis of PNH with 1 or more related sign or symptom.



Hemolysis confirmed by a blood test.

Any patient who had ever had eculizumab treatment or who was unwell due to a fever or infection could not take part.

All patients needed to have had a meningococcal vaccination no more than 3 years before taking part. If they had previously had a meningococcal infection, they could not take part.

How many patients took part?



134
men

+



112
women

=



246
patients

Patients were aged between 18 and 86 years.

Where was the study done?

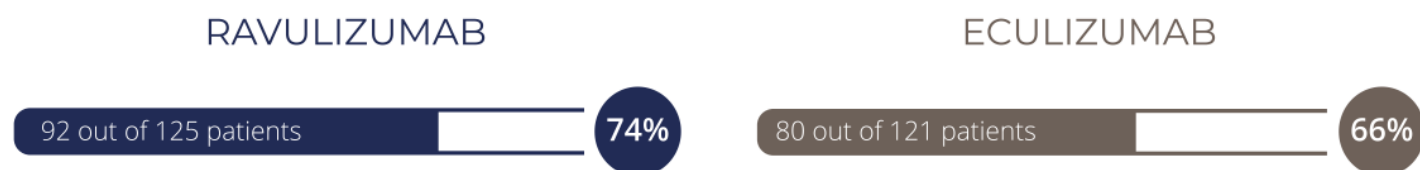
The study took place in 123 study centers in 25 countries across North America, South America, Europe, Asia, Africa, and Australia. The majority of patients (50%) were from Asia.

STUDY RESULTS

Answers to the main questions:

1. What percentage of patients who got ravulizumab did not need a blood transfusion compared to patients who got eculizumab?

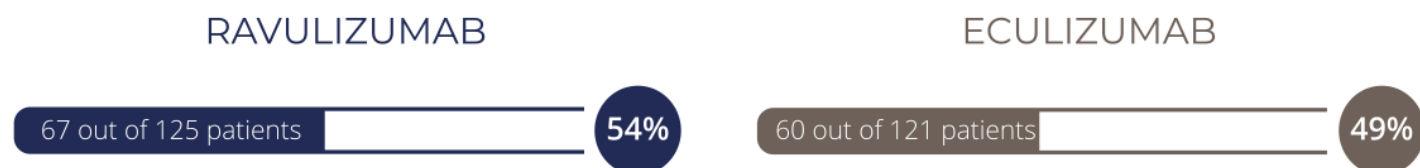
The researchers wanted to see if ravulizumab worked as well as eculizumab at reducing the need for a blood transfusion during the 26-week treatment period.



The results showed that 74% of patients who got ravulizumab did not need a blood transfusion compared to 66% of patients who got eculizumab.

2. How did hemolysis compare between the 2 treatments?

During hemolysis, the destruction of the red blood cells causes the release of an enzyme called lactate dehydrogenase (LDH) into the blood. LDH levels show how much hemolysis is happening in the body. Both ravulizumab and eculizumab aim to block hemolysis. If the treatment is working and blocking hemolysis, then the patients' LDH level should return within the normal range.



The results showed that 54% of patients who got ravulizumab had their LDH level return within the normal range during the treatment period compared to 49% of patients who got eculizumab. These levels remained stable during treatment for more than half of the patients in each group.

Answers to the other important questions:

How did tiredness levels compare between the 2 treatments?



Patients in both treatment groups reported feeling less tired. The improvement in tiredness levels was similar between the 2 treatments.

What percentage of patients in each treatment group had breakthrough hemolysis*?

RAVULIZUMAB



5 out of 125 patients (4%) had breakthrough hemolysis. The earliest it happened was around 10 weeks into treatment.

ECULIZUMAB



13 out of 121 patients (11%) had breakthrough hemolysis. The earliest it happened was around 6 weeks into treatment.

*Breakthrough hemolysis means an increase in LDH levels and a new or worsening symptom or a serious complication.

What percentage of patients in each treatment group had stable hemoglobin levels?

During hemolysis, the destruction of the red blood cells causes the release of hemoglobin, which is then free to enter the bloodstream. Free hemoglobin can lead to serious health problems, such as blood clots and damage to organs. The researchers checked each patient’s hemoglobin level during the study to see if it remained stable on treatment.

RAVULIZUMAB



ECULIZUMAB



The results were similar between treatment groups. 68% of patients who got ravulizumab had stable hemoglobin levels compared to 65% of patients who got eculizumab.

How did the patients' overall quality of life compare between the 2 treatments?

Each patient rated their health, ability to function, and symptoms of PNH on a questionnaire. An improvement in their questionnaire score of 10 or more indicated a meaningful change in quality of life.



More patients who got ravulizumab had a meaningful change in their quality of life at the end of the treatment period compared with patients who got eculizumab.

Summary of answers:

Ravulizumab worked as well as eculizumab during 26 weeks of treatment at:

- Reducing the need for a blood transfusion
- Blocking the destruction of the red blood cells
- Lowering LDH enzyme levels
- Reducing tiredness
- Reducing breakthrough hemolysis
- Stabilizing hemoglobin levels
- Improving quality of life

SIDE EFFECTS

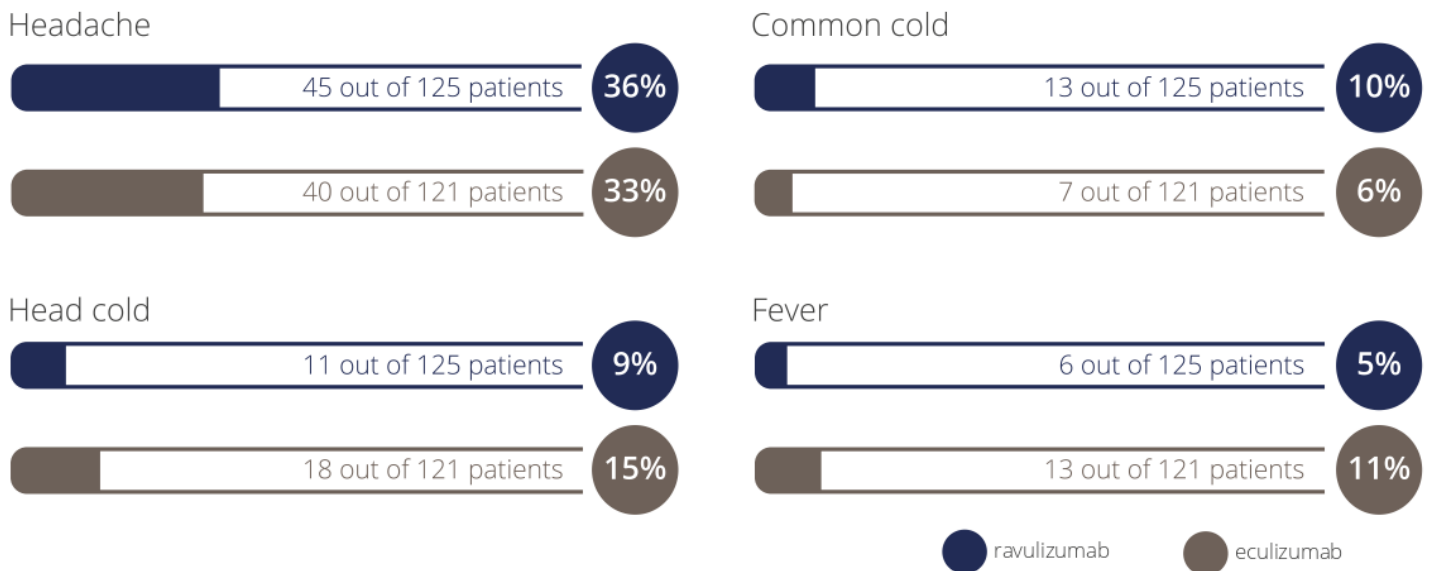
How is the safety of participants in clinical studies monitored?

A side effect is any symptom a participant has during the study. Side effects can vary from person to person. A lot of research is needed to see which side effects the study treatment causes and which side effects happen by chance. So, researchers keep a record of all the side effects participants have when new treatments are studied.

Any side effect thought to be an important medical event, requires a person to go to the hospital, could be life-threatening, or causes death, is called a serious side effect. A serious side effect may or may not be related to the treatment the participant was taking.

What side effects did patients have in this study?

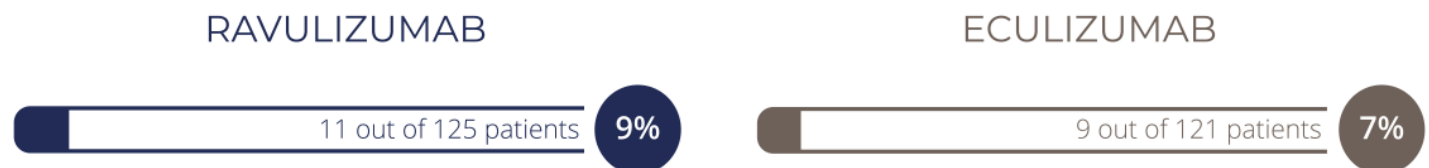
The most common side effects, which happened in more than 10 out of 100 patients (10%) in either treatment group, are shown below:



41% of patients in both treatment groups had a side effect that was thought by the study doctor to be related to the treatment they had.

What serious side effects did patients have in this study?

Overall, 20 out of 246 patients (8%) had a serious side effect.



11 patients (9%) got ravulizumab and 9 patients (7%) got eculizumab. The most commonly reported serious side effect was a fever. 3 patients experienced this: 1 on ravulizumab and 2 on eculizumab.

Were there any other important safety findings in this study?



Complement inhibitors increase a patient's risk of meningococcal infection. An independent group was in place to monitor all patients for any cases of meningococcal infection. There were no meningococcal infections reported in either treatment group.

None of the patients who got either treatment stopped taking part because of the side effects they had. 1 patient who got eculizumab chose not to carry on in the study. Another patient who got eculizumab stopped taking part on the advice of the study doctor. No patients died during their participation in Part 1 of this study.

OUTCOME OF THE STUDY

The results showed that ravulizumab worked **as well as** eculizumab at treating patients with PNH who had not previously had treatment with a complement inhibitor. The side effects experienced were similar in both treatment groups. Ravulizumab was considered safe and was well tolerated.

How has this study helped patients and researchers?

The information collected in this study was from one of the largest clinical studies in patients who had never had treatment with eculizumab. From a patient and health care perspective, being able to take ravulizumab once every 8 weeks, compared to eculizumab once every 2 weeks, may reduce the burden of treatment.



Before a treatment can be approved for patients to use, researchers look at the results of many studies to decide which treatments work best and are safe. If you have any questions about ravulizumab or eculizumab for the treatment of PNH, please talk to your doctor. You should not change your treatment based on the results of this study without talking to a doctor first.

MORE INFORMATION

Useful clinical study websites

This document provides a summary of the main results of the study. It includes information about the side effects that happened in the study and the results of the questions the researchers wanted to answer.

A full report may be available to read at one of the following clinical trial registers:



www.clinicaltrials.gov

Use the study number NCT02946463 to search for more information on this website.



www.clinicaltrialsregister.eu

Use the study number 2016-002025-11 to search for more information on this website.

Further studies

Several studies are either currently running or completed. Please follow the links below to find out more information.

[PNH Registry](#)

[ALXN1210-PNH-302 Adults with PNH currently treated with eculizumab](#)

[ALXN1210-PNH-303 Ravulizumab administered subcutaneously vs. intravenously](#)

[ALXN1210-PNH-304 Children and adolescents with PNH](#)