CLINICAL STUDY RESULTS

A Study about Ravulizumab in Patients with Atypical Hemolytic Uremic Syndrome (aHUS) Who Have Not Previously Been Treated with a Complement Inhibitor

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 atypical hemolytic uremic syndrome.

STUDY IDENTIFICATION INFORMATION

TREATMENT STUDIED:	Ravulizumab, also known as ALXN1210 (trade name: Ultomiris®)
STUDY TITLE:	Single Arm Study of ALXN1210 in Complement Inhibitor Treatment-Naïve Adult and Adolescent Patients with Atypical Hemolytic Uremic Syndrome (aHUS)
STUDY NUMBERS:	Europe, 2016-002027-29 | United States, NCT02949128 | Protocol, ALXN1210-aHUS-311

ALEXION

BACKGROUND

What are clinical studies?

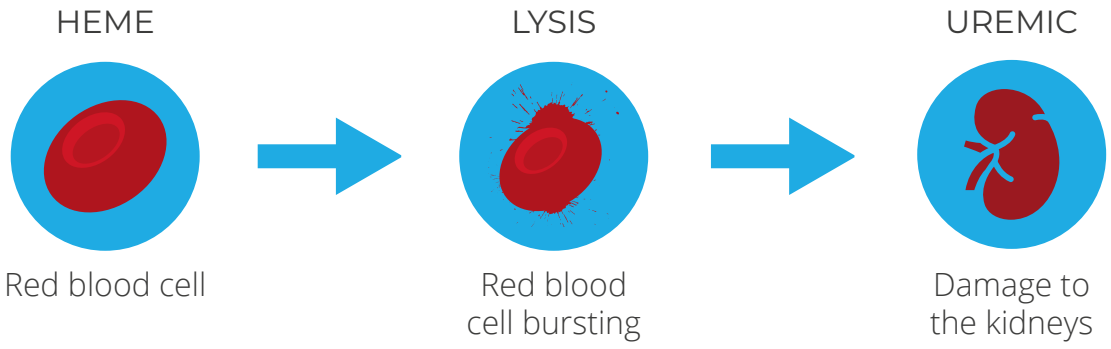
Clinical studies aim to answer specific questions about new or existing treatments, procedures, or vaccines and involve patients with health conditions or healthy volunteers. Clinical studies are done in several phases, from phase 1 to phase 4.

This is a phase 3 study. Phase 3 studies look at the overall risks and benefits of a treatment. In this study, the risks and benefits of ravulizumab as a treatment for atypical hemolytic uremic syndrome are being investigated.

What is atypical hemolytic uremic syndrome (aHUS)?

Atypical hemolytic uremic syndrome, also called aHUS, is a rare disease that causes the body's natural defense system, called the immune system, to destroy red blood cells, causing damage to organs.

The word hemolytic comes from "heme" meaning red blood cells and "lytic" from the word "lysis" meaning to break up or burst. The word "uremic" refers to symptoms of kidney damage and the word "syndrome" is used because multiple organs in the body are affected.



aHUS causes microscopic blood clots to form in the body, which block or slow the blood flow to the body's cells, tissues, and organs. The kidneys are the most common organ affected and often suffer the most severe damage.

What causes aHUS?

aHUS occurs when part of the immune system called the "complement pathway" does not work properly. This causes unstable movement of blood through the small blood vessels, which results in microscopic blood clots.

What are the symptoms of aHUS?

aHUS has different causes and can be unpredictable, making it difficult to diagnose. The most common symptoms include a lack of energy and feeling tired. Life-threatening complications can include kidney failure, high blood pressure, and heart disease. Some patients with kidney failure need dialysis or a kidney transplant.

What treatments are available for aHUS?

When the study first started, eculizumab (Soliris®) was a commonly used treatment for aHUS. Eculizumab is a complement inhibitor. Complement inhibitors aim to stop microscopic blood clots forming, and improve the symptoms and life-threatening complications of aHUS. Eculizumab is given by infusion every 2 weeks. An infusion means the medicine is given directly into the bloodstream, through a vein, via a drip.

What were the treatments used in this study?

Ravulizumab is also a complement inhibitor, like eculizumab. Ravulizumab is given by infusion, but it lasts longer in the bloodstream so it is given every 8 weeks for most patients.

PURPOSE OF THE STUDY

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

The researchers wanted to see if ravulizumab could safely and effectively treat adults with aHUS who had not previously been treated with a complement inhibitor. They looked at how each patient responded to the treatment.

To do this, they tested the patients' blood to see if they had:

- a decrease in the levels of lactate dehydrogenase, or LDH
- an improvement in their platelet count
- a decrease in creatinine levels

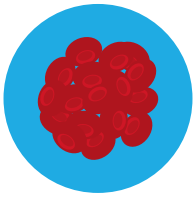
These are called blood parameters. They are described in more detail on the next page.

LDH LEVELS

LDH levels show how many red blood cells are bursting. In aHUS, LDH levels are high.

If ravulizumab works, the patient's LDH level will decrease.

PLATELET COUNT



In aHUS, platelets decrease rapidly because they are "consumed" by microscopic blood clots.

If ravulizumab works, the patient's platelet count will increase.

CREATININE LEVELS

Creatinine levels show how well the kidneys are functioning. In aHUS, creatinine levels are high.

If ravulizumab works, the patient's creatinine level will decrease.

This summary shows the results for both 26 weeks and 52 weeks of ravulizumab treatment for 56 patients. It also shows information about the safety of ravulizumab for 58 patients.

What was the main question?

How many patients responded to ravulizumab during 26 weeks of treatment?

Were there any other important questions?

How long did it take for the patients to respond to 26 weeks of treatment with ravulizumab?

Did ravulizumab improve the patients' stage of kidney disease?

Did ravulizumab reduce the need for dialysis?

Did ravulizumab improve the patients' quality of life?

How many patients responded to ravulizumab during 52 weeks of treatment?

Was ravulizumab safe during 52 weeks of treatment?

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STUDY PARTICIPANTS

Who could take part in the study?

To be able to take part in the study, each patient had to meet the following requirements:

Male or female, 18 years of age or older

Abnormal LDH levels, platelet count, and creatinine levels

No previous treatment with eculizumab or ravulizumab

Complement inhibitors increase the risk of potentially life-threatening meningococcal infection, which is caused by a germ called *Neisseria meningitidis*. To help prevent meningococcal disease, all patients had to be adequately vaccinated before receiving ravulizumab.

Where was the study done?

The study is being done in 41 study centers in 14 countries across North America, Asia, Europe, and Australia. It started in March 2017 and is still ongoing.

How many patients took part in the study?

19
men

+

39
women

=

58
patients

Patients were between 19 and 77 years of age and from diverse ethnic backgrounds.

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How unwell were the patients at the start of the study?

Nearly all of the patients who took part in the study were very unwell. Half of the patients had needed treatment in an intensive care unit for an average of 10 days. At the start of the study, 48 out of 56 patients (86%) were in hospital because of aHUS, and 8 out of 58 patients (14%) previously had a kidney transplant.

The researchers looked at the blood parameters of each patient to see how severe their illness was. They also looked at the stage of each patient's kidney disease. At the start of the study, 39 out of 54* patients (72%) had the most severe stage of chronic kidney disease (stage 5), and 29 out of 56 patients (52%) had recently received dialysis.

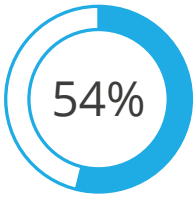
*Data available for 54 of the 56 patients who took part in this study.

TREATMENT RESULTS

Answer to the main question:

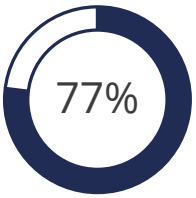
How many patients responded to ravulizumab during 26 weeks of treatment?

To answer this question, the researchers compared the patients' blood parameters from the start of the study to the end of 26 weeks of treatment.



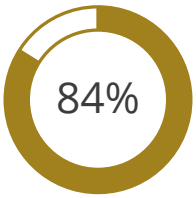
30 out of 56 patients (54%) had a complete response to treatment. This means that, for these patients, all of their blood parameters returned within a normal range during 26 weeks of treatment.

LDH LEVELS



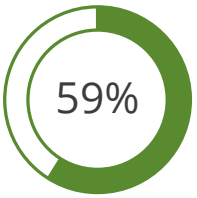
LDH levels for 43 out of 56 patients (77%) decreased to a normal range.

PLATELET COUNT



The platelet count for 47 out of 56 patients (84%) increased to a normal range.

CREATININE LEVELS



Creatinine levels for 33 out of 56 patients (59%) decreased by at least 25%.

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Answers to the other important questions:

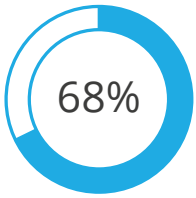
How long did it take for the patients to respond to 26 weeks of treatment with ravulizumab?

For the 30 patients who had a complete response to treatment, on average, their blood parameters returned to a normal range approximately 12 weeks after the first infusion of ravulizumab.

For some patients, a complete response to treatment was seen as early as 7 days after the first infusion of ravulizumab.

Did ravulizumab improve the patients' stage of kidney disease?

The researchers looked at the number of patients with available data who had an improvement in the stage of their chronic kidney disease during 26 weeks of treatment.



The stage of chronic kidney disease improved in 32 out of 47 patients (68%).

Did ravulizumab reduce the need for dialysis?

DIALYSIS DISCONTINUED

Of the 29 patients on dialysis before receiving ravulizumab, 17 patients (59%) discontinued dialysis during treatment.

DIALYSIS STARTED

Of the 27 patients not on dialysis before receiving ravulizumab, 7 patients (26%) started dialysis during treatment. 1 patient stopped dialysis before the end of the study.

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Did ravulizumab improve the patients' quality of life?

Two questionnaires were used in the study to measure how patients rated their quality of life. One questionnaire focused on tiredness, and the other questionnaire focused on overall health.

The researchers compared the answers to the questionnaires at the start of the study and after 26 weeks of treatment with ravulizumab.

TIREDNESS

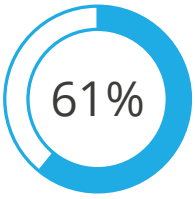
The majority of patients reported feeling less tired during 26 weeks of treatment with ravulizumab.

OVERALL HEALTH

The majority of patients reported an improvement in their overall health during 26 weeks of treatment with ravulizumab.

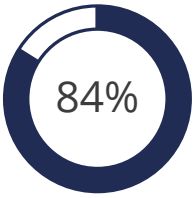
How many patients responded to ravulizumab during 52 weeks of treatment?

The researchers compared the patients' blood parameters from the start of the study to the end of 52 weeks of treatment. Blood parameters returned to a normal range for most of the patients.



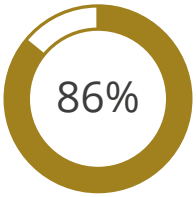
During 52 weeks of treatment, 34 out of 56 patients (61%) had a complete response to ravulizumab.

LDH LEVELS



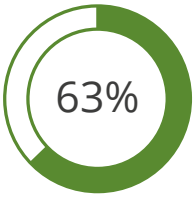
LDH levels for 47 out of 56 patients (84%) decreased to a normal range.

PLATELET COUNT



The platelet count for 48 out of 56 patients (86%) increased to a normal range.

CREATININE LEVELS



Creatinine levels for 35 out of 56 patients (63%) decreased by at least 25%.

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SAFETY RESULTS

How is the safety of participants in clinical studies monitored?

The safety of every participant is essential throughout the development and testing of treatments. The study doctors keep a record of all symptoms or abnormal findings the participants have during treatment. These symptoms and abnormal findings are called "adverse events." Adverse events may or may not be caused by treatments in the study.

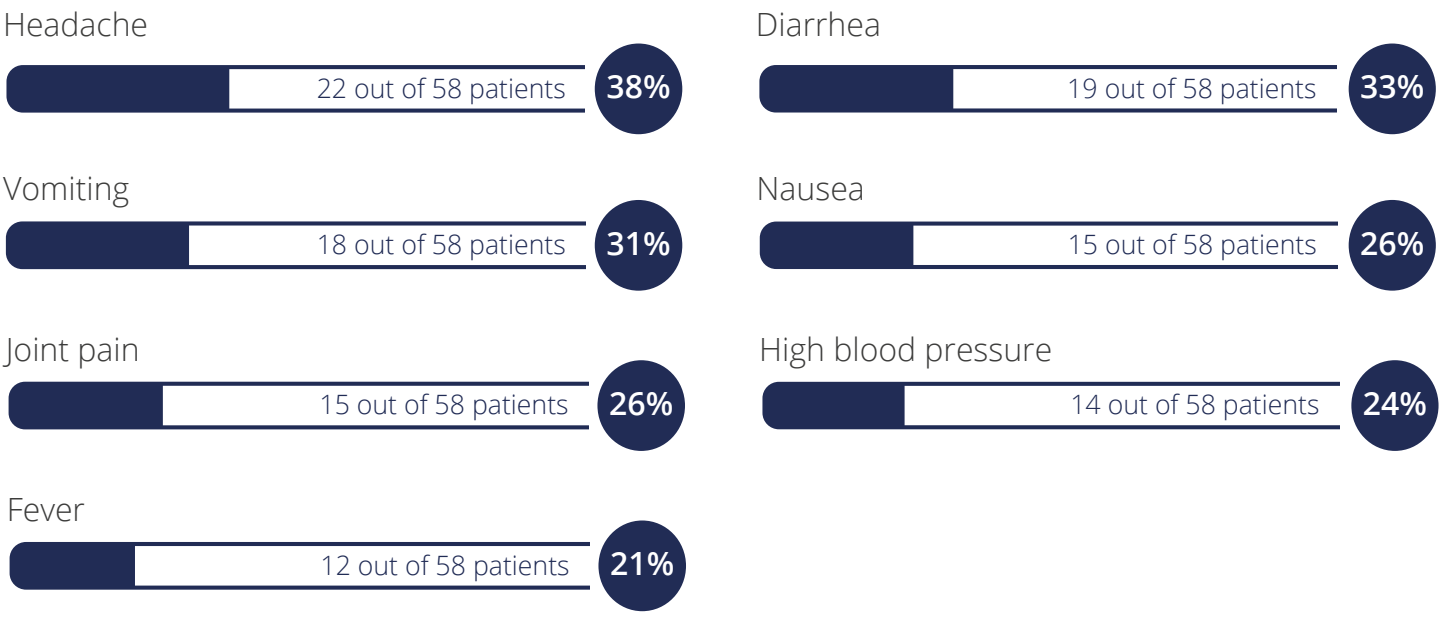
Adverse events vary from person to person. For example, one participant might get a headache or have unusual blood results, while another might get a rash.

An adverse event that is life-threatening or causes a participant to be hospitalized is called *serious.*

An independent committee of experts met regularly throughout the study to review all of the safety information.

Was ravulizumab safe during 52 weeks of treatment?

All patients had at least 1 adverse event during the study. The most common adverse events, experienced by more than 20% of patients, are shown below:



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Did any of the patients in this study have a serious adverse event?

Overall, 33 out of 58 patients (57%) had a serious adverse event. The most common serious adverse event was a lung infection, called pneumonia, and high blood pressure. 3 patients (5%) had pneumonia, and 3 patients (5%) had high blood pressure.

2 serious adverse events may have been related to ravulizumab.

Were there any other important safety findings in this study?

No meningococcal infections were reported during 26 weeks or 52 weeks of treatment with ravulizumab.

3 out of 58 patients (5%) stopped taking part in the study because of the adverse events they had. 4 patients died while they were taking part in the study. The deaths were due to other ongoing severe illnesses and were not thought to be caused by ravulizumab.

OUTCOME OF THE STUDY

During 26 weeks of treatment with ravulizumab:

- 30 out of 56 patients (54%) had a complete response.
- Blood parameters returned within a normal range approximately 12 weeks after the first infusion.
- 32 out of 47 patients (68%) had less severe chronic kidney disease.
- The majority of patients experienced an improvement in their quality of life.

During 52 weeks of treatment with ravulizumab:

- 34 out of 56 patients (61%) had a complete response.
- No meningococcal infections were reported.

The results showed that patients with aHUS who had never had treatment with a complement inhibitor responded well to treatment with ravulizumab. Overall, the researchers found no safety concerns about ravulizumab as a treatment for patients with aHUS.

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How has this study helped patients and researchers?

More than half of the patients who took part in the study had a complete response to treatment with ravulizumab. Patients also reported an improvement in their quality of life, including a reduction in fatigue, which is a disabling symptom of aHUS.

Ravulizumab is an approved treatment for aHUS in some countries. If you have any questions about ravulizumab for the treatment of aHUS, 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 answers to the questions the researchers had and information about the adverse events experienced by patients when treated with ravulizumab.

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

www.clinicaltrials.gov
Use the study number NCT02949128 to search for more information on this website.

www.clinicaltrialsregister.eu
Use the study number 2016-002027-29 to search for more information on this website.

Further studies

For more information about other studies investigating ravulizumab for the treatment of diseases where the immune system attacks healthy parts of the body, please follow the links below.

ALXN1210-TMA-313, Ravulizumab in Thrombotic Microangiopathy After Hematopoietic Stem Cell Transplant

ALXN1210-TMA-314, Ravulizumab in Children with Thrombotic Microangiopathy After Hematopoietic Stem Cell Transplantation

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