A Phase 3, Randomized, Open-Label, Active-Controlled Study of ALXN1210 Versus Eculizumab in Adult Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) currently treated with Eculizumab

Published: 27-03-2017
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Efficacy of ALXN1210Sub-study: to Evaluate Patient Preference for the Treatment of Paroxysmal Nocturnal Hemoglobinuria (PNH)

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Red blood cell disorders
Study type	Interventional

Summary

ID

NL-OMON50494

Source
ToetsingOnline

Brief title
ALXN1210-PNH-302

Condition

- Red blood cell disorders

Synonym
bleeding disorder

Research involving
Human

Sponsors and support

Primary sponsor: Alexion Pharmaceuticals
Source(s) of monetary or material Support: pharmaceutical company

Intervention

Keyword: ALXN1210, Eculizumab, lactate dehydrogenase normalization, PNH

Outcome measures

Primary outcome

Hemolysis as directly measured by lactate dehydrogenase percent change

(LDH-PCHG)

Secondary outcome

- Change from baseline in quality of life (QoL) as assessed by the Functional

Assessment of Chronic Illness Therapy (FACIT)-Fatigue

- Percentage of patients who achieve transfusion avoidance (TA)

- Proportion of patients with stabilized hemoglobin

Study description

Background summary

Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired hemolytic disorder that occurs most frequently in adults. The pathology and clinical presentations in patients with PNH are driven by uncontrolled terminal complement activation on red blood cells (RBCs).
The only approved treatment for PNH is eculizumab (Soliris®). Eculizumab is a humanized monoclonal antibody that specifically binds to the complement protein C5 with high affinity. ALXN1210 was engineered from eculizumab to preserve immediate and complete C5 inhibition while providing sustained complement inhibition throughout a prolonged dosing interval (1 month or longer). ALXN1210 and eculizumab share > 99% amino-acid sequence homology.
The main objective of effective PNH treatment with targeted therapy is to provide immediate, complete, and sustained inhibition of terminal complement activity to block hemolysis and prevent thrombosis. More specifically,

incomplete C5 blockade may increase risk of potentially life-threatening breakthrough hemolysis (Hill 2012a, Lee 2013). Any loss of efficacy at the end of a dosing interval or missed doses due to inconvenience of dosing intervals may put patients at substantial medical risk. Patients treated with eculizumab are required to receive maintenance infusions every 2 weeks. Given that PNH is a chronic disease, this regimen may have a significant impact on patients in terms of individual patient concerns associated with missed work and more importantly may impact treatment compliance.
ALXN1210 has been designed to have the same rapid onset of action and effective blockade of complement, with an increased serum half-life to yield an increased duration of pharmacologic activity relative to eculizumab. The substantially longer half-life of
ALXN1210 is expected to produce sustained terminal complement inhibition during a longer dosing interval and thus reduce the potential risk of breakthrough complement-mediated hemolysis during the treatment period, thus improving the overall health of patients.

Study objective

Efficacy of ALXN1210

Sub-study: to Evaluate Patient Preference for the Treatment of Paroxysmal Nocturnal Hemoglobinuria (PNH)

Study design

This is a Phase 3, open-label, randomized, active-controlled, multicenter study.

Intervention

26-week randomized treatment period followed by an extension period in which all patients will receive ALXN1210.

Study burden and risks

Potential risks associated with ALXN1210 include infections (N. meningitidis and other encapsulated organisms), immunogenicity, and hypersensitivity. Please refer to the IB, section 2.2 for a detailed description of Potential Risks Associated with ALXN1210, Summary of Data, and Monitoring Guidance for the Investigator.

Contacts

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Alexion Pharmaceuticals

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Male or female * 18 years of age
2. Treated with eculizumab for PNH for at least 6 months prior to Day 1
3. Lactate dehydrogenase (LDH) * 1.5 x upper limit of normal (ULN) at Screening
4. PNH diagnosis confirmed by documented by high-sensitivity flow cytometry
5. Documented meningococcal vaccination not more than 3 years prior to, or at the time of, initiating study treatment.
6. Female patients of childbearing potential must use highly effective contraception starting at screening and continuing until at least 8 months after the last dose of ALXN1210
7. Willing and able to give written informed consent and comply with study visit schedule

Exclusion criteria

1. History of bone marrow transplantation
2. Body weight < 40 kilograms
3. History of or ongoing major cardiac, pulmonary, renal, endocrine, or hepatic disease that, in the opinion of the investigator or sponsor, would preclude participation.
4. Unstable medical conditions (eg, myocardial ischemia, active gastrointestinal bleed, severe congestive heart failure, anticipated need for major surgery within 6 months of randomization, coexisting chronic anemia unrelated to PNH)
5. Females who are pregnant, breastfeeding or who have a positive pregnancy test at screening or Day 1
6. Participation in another interventional clinical study or use of any experimental therapy within 30 days before initiation of study drug on Day 1 in this study or within 5 half-lives of that investigational product, whichever is greater.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-08-2017
Enrollment:	13
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ALXN1210
Generic name:	-
Product type:	Medicine
Brand name:	Soliris
Generic name:	Eculizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-03-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-07-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-08-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-08-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-10-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-11-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	18-01-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-03-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-03-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-05-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-08-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-08-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-10-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-02-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-05-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	31-07-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-08-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-10-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-09-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-09-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-01-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-03-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-03-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-06-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-002026-36-NL
CCMO	NL60929.091.17