A Phase 3 Study of Danicopan (ALXN2040) as Add-on Therapy to a C5 Inhibitor (Eculizumab or Ravulizumab) in Patients with Paroxysmal Nocturnal Hemoglobinuria Who Have Clinically Evident Extravascular Hemolysis (EVH)

Published: 07-10-2020
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To evaluate the efficacy of danicopan as compared to placebo as add-on therapy to a C5 inhibitor at 12 weeks.

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

Summary

ID

NL-OMON55171

Source
ToetsingOnline

Brief title
ALXN2040-PNH-301

Condition

- Red blood cell disorders

Synonym
Paroxysmal Nocturnal Hemoglobinuria, PNH

Research involving
Human

Sponsors and support

Primary sponsor: Alexion Pharmaceuticals
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Add-on Therapy, Danicopan, Evident Extravascular Hemolysis (EVH), Paroxysmal Nocturnal Hemoglobinuria

Outcome measures

Primary outcome

Change From Baseline In Hemoglobin (Hgb)

Secondary outcome

* Percentage Of Participants With Transfusion Avoidance

* Change From Baseline In Functional Assessment Of Chronic Illness Therapy

(FACIT) Fatigue Scores; Scoring 0-52

* Change From Baseline In Absolute Reticulocyte Count

Study description

Background summary

PNH is a rare blood disease in which red blood cells are attacked by a part of the body*s immune system known as the complement system. People with PNH produce red blood cells without key immune proteins attached. Without these immune proteins, the complement system recognizes the red blood cells as a threat and destroys them throughout the body. The destruction of red blood cells is largely responsible for many of the symptoms of PNH and causes anemia. Currently, C5 inhibitors are the only approved treatment for PNH. C5 inhibitors work by suppressing the activity of a specific portion of the complement system. Some patients on approved C5 inhibitor therapies may continue to have anemia.
This study looks at an investigational drug called ALXN2040. This drug is being developed to treat PNH by blocking a protein called factor D in the complement system. By blocking factor D, ALXN2040 may help further treat PNH in patients currently receiving a C5 inhibitor but this is not yet proved. This study will

determine if ALXN2040 (danicopan), when used with a C5 inhibitor, improves anemia in patients with PNH.

Study objective

To evaluate the efficacy of danicopan as compared to placebo as add-on therapy to a C5 inhibitor at 12 weeks.

Study design

This is a multiple-region, randomized, double-blind, placebo-controlled, multiple-dose, Phase 3 study in patients with PNH who have clinically evident EVH on a C5 inhibitor (eculizumab or ravulizumab).

Intervention

Treatment Period 1 * The patient will receive either placebo or ALXN2040 (1:2 chance) orally three times a day for 12 weeks.
Treatment Period 2 * The patient will receive ALXN2040 orally three times a day for 12 weeks.
Long Term Extension * The patient will receive ALXN2040 orally three times a day for 52 weeks.

Study burden and risks

Subject*s participation in this study will last up to 18 months and consists of a 24-week study period and the 52-week long-term extension. This includes up to 35 visits (20 to the study center, 15 have the potential to be completed at home using a visiting healthcare service). Aside from the intervention described above, participation in this study involves blood draws at multiple visits. Participants will be subjected to questions regarding medical history, concomitant medications, vaccination history and adverse events; urine sampling; pregnancy tests; measurement of vital signs; physical examination; ECGs and patient reported outcomes and quality of life questionnaires. Subjects will be expected to take the IP as explained, not take part in other medical studies, keep their appointments for visits, monitor their temperature daily at home and seek emergency medical attention if needed, not discuss information about the study in public places while the study is in progress, keep a patient card with them at all times, not donate blood/sperm/ova and use appropriate forms of contraception.
In 266 healthy volunteers, the most commonly experienced side effects (experienced by 5 or more subjects) included: headache, nausea (a feeling of wanting to vomit), throat irritation, nasal congestion, upper respiratory tract infection, feeling hot, indigestion, bruising, diarrhea, stomach inflammation, abdominal discomfort or pain, muscle pain, increase in blood creatine phosphokinase (a marker of muscle injury), throat discomfort, and dizziness or

feeling faint. The majority of events were mild.
However, PNH is a serious, life-threatening disease, and there are unmet needs in this population that are not addressed by an approved C5 inhibitor that could potentially be addressed by an effective oral FD inhibitor.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Diagnosis of PNH
* Clinically Evident EVH defined by:
- Anemia (Hgb *9.5 gram/deciliter) with absolute reticulocyte count * 120 x 10^9/liter.
- At least 1 packed red blood cell or whole blood transfusion within 6 months prior to the start of the study.

* Receiving a C5 inhibitor for at least 6 months prior to Day 1
* Platelet count *30,000/microliters (*L)
* Absolute neutrophil counts *750/*L.
* Documentation of/or willingness to receive vaccinations and prophylactic antibiotics as required.

Exclusion criteria

* History of a major organ transplant or hematopoietic stem cell transplantation (HSCT).
* Known aplastic anemia or other bone marrow failure that requires HSCT or other therapies including anti-thymocyte globulin and/or immunosuppressants.
* Known or suspected complement deficiency.
* Laboratory abnormalities at screening, including:
- Alanine aminotransferase >2 x ULN.
- Direct bilirubin >2 x ULN (unless due to EVH or documented Gilbert's Syndrome.
* Current evidence of biliary cholestasis.
* Estimated glomerular filtration rate <30 milliliters/minute/1.73 meter squared and/or are on dialysis.
* Evidence of human immunodeficiency virus, hepatitis B, or active hepatitis C infection at screening.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-05-2021

Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N/A
Generic name:	Danicopan

Ethics review

Approved WMO Date:	07-10-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-05-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2019-003829-18-NL
ClinicalTrials.gov	NCT04469465
CCMO	NL74809.056.20