A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel, Multicenter Study to Evaluate the Safety and Efficacy of ALXN1720 in Adults with Generalized Myasthenia Gravis.

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This study has been transitioned to CTIS with ID 2023-508284-77-00 check the CTIS register for the current data. The purpose of this study is to evaluate the safety and efficacy of ALXN1720 for the treatment of gMG in adults with autoantibodies...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON56009

Source
ToetsingOnline

Brief title
ALXN1720-MG-301 (PREVAIL)

Condition

- Autoimmune disorders
- Muscle disorders
- Neuromuscular disorders

Synonym
Myasthenia Gravis; muscle weakness

Research involving

Human

Sponsors and support

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

Intervention

Keyword: ALXN1720, Complement C5 inhibitor, Generalized Myasthenia Gravis

Outcome measures

Primary outcome

Change From Baseline in Myasthenia Gravis-Activities of Daily Living (MG-ADL)

Total Score at Week 26

Secondary outcome

- Change From Baseline in Quantitative Myasthenia Gravis (QMG) Total Score at

Week 26

- Percentage of Responders Based on Reduction of the MG-ADL Total Score at Week

26

- Percentage of Responders based on Reduction of the QMG Total Score at Week 26

- Change From Baseline in Myasthenia Gravis Composite (MGC) Total Score at Week

26

Study description

Background summary

MG is a rare, debilitating disease characterized by the failure of neuromuscular signal transmission. The estimated prevalence of MG is between 145 to 361 per million persons. MG can present at any age. However, female incidence peaks in the third decade of life, whereas male incidence peaks in the sixth or seventh decade. Major advances in the therapy of MG have reduced

its mortality to 1.5%, a level comparable to the general population. Despite this improved overall prognosis, acute disease exacerbations with potentially life-threatening hypoventilation still occur and remain a serious concern.
Voluntary muscle contraction requires the release of acetylcholine from nerve endings at the NMJ. Patients with MG produce autoantibodies that target the AChR or proteins involved in the formation of AChR clusters on the surface of muscle fibers, eg, muscle-specific tyrosine kinase. Antibodies against AChR are detected in most patients with MG (> 80%). Activation of the terminal complement pathway contributes to the pathophysiology of MG in patients who express autoantibodies against the AChR. The receptor is located at the NMJ of muscle fibers. Its activation is essential for skeletal muscle movement. Complement recruitment in the presence of antibodies against the AChR is assumed to contribute to MG by damaging the NMJ through formation of the MAC.
Blocking terminal complement activity is an established treatment approach to MG. Its efficacy has been demonstrated in independent pivotal trials of eculizumab and ravulizumab, two monoclonal antibodies that inhibit the enzymatic cleavage of C5. Both eculizumab and ravulizumab are approved by the US Food and Drug Administration (FDA) for the treatment of gMG. C5 is a key component of the terminal complement pathway. Like eculizumab and ravulizumab, ALXN1720 inhibits C5 cleavage into the biologically active complement components C5a and C5b. Based on the shared mechanism of action, ALXN1720 may similarly show clinical efficacy in participants with gMG at doses that accomplish an equivalent level of C5 inhibition. The proposed ALXN1720 dosage regimen in this Phase 3 study is predicted to achieve complete terminal complement inhibition, defined as free C5 < 0.5 µg/mL in the serum over the entire treatment period in patients with gMG. Compared with conventional antibodies, ALXN1720 has a low molecular weight, allowing it to be concentrated in small volumes suitable for SC injection. Another benefit of ALXN1720 is its long half-life, allowing convenient once weekly dosing intervals.

Study objective

This study has been transitioned to CTIS with ID 2023-508284-77-00 check the CTIS register for the current data.

The purpose of this study is to evaluate the safety and efficacy of ALXN1720 for the treatment of gMG in adults with autoantibodies against AChR (AChR+). The study will also evaluate the safety and performance of the administration device (the PFS-SD).

Study design

ALXN1720-MG-301 is a Phase-3, randomized, double-blind, placebo-controlled, parallel, multicenter study to evaluate the safety and efficacy of ALXN1720 in adults with gMG.
The study comprises 3 periods: Screening (<= 4 weeks), randomized controlled

treatment (RCT; 26 weeks), and open label extension (96 weeks). Randomization takes place in the RCT period 1:1 to either ALXN1720 or placebo.

Intervention

Subjects will receive ALXN1720 or placebo, both administered through weekly subcutaneous injection by using a prefilled syringe with safety device (PFS-SD).

Study burden and risks

A weekly dose of study medication will be received via 1 or 2 subcutaneous injection(s). In the first 5 weeks, the subject will come to the hospital every week to receive the injection(s) and to be trained in self-administration of the injection(s). After that, the subject can administer the injection(s) at home (or have it administered by a caregiver). The subject should complete an electronic diary after each administration of study medication. Remote and hospital visits alternate, with the frequency of hospital visits decreasing over the course of the study. In total there are 39 visits in about 2.5 years, 24 of which were in hospital and 15 remotely. The subject is asked to complete several questionnaires one day before each hospital visit.
There is a small risk of serious meningococcal infection, therefore subjects receive a vaccination during screening if they have not had it in the past 3 years. If the subject cannot wait more than 2 weeks after the vaccination, to start the study medication, the subject will receive prophylactic antibiotics.

Acute disease exacerbations with potentially life-threatening hypoventilation still occur and remain a serious concern.
The potential risks identified for participants in association with the administration of ALXN1720 and the use of the PFS-SD are considered justified because of the measures taken to minimize these risks and the anticipated benefits that may be afforded to participants with gMG.

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

- Must be >= 18 years of age at the time of signing the informed consent
- Diagnosis of MG with generalized muscle weakness meeting the clinical criteria defined by Myasthenia Gravis Foundation of America (MGFA) Class II, III or IV
- Positive serological test for autoantibodies against AChR.

Exclusion criteria

- History of thymectomy or any other thymic surgery within 12 months prior to Screening
- Untreated thymic malignancy, carcinoma, or thymoma
- History of Neisseria meningitidis infection
- Pregnancy, breastfeeding, or intention to conceive during the course of the study.

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:	Recruiting
Start date (anticipated):	10-09-2024
Enrollment:	3
Type:	Actual

Medical products/devices used

Generic name:	Prefilled Syringe with Safety Device
Registration:	No
Product type:	Medicine
Brand name:	ALXN1720
Generic name:	gefurulimab

Ethics review

Approved WMO

Date:	18-01-2023
Application type:	First submission
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam

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Approved WMO Date:	06-04-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam)
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	Postbus 22660
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Approved WMO Date:	10-10-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-10-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-12-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-03-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EU-CTR	CTIS2023-508284-77-00
EudraCT	EUCTR2022-000460-21-NL
ClinicalTrials.gov	NCT05556096
CCMO	NL82162.018.22