A Randomized, Double-Blind, Placebo-Controlled, Multicenter Phase 3 Trial to Evaluate the Efficacy, Safety and Tolerability of ARGX-113 in Patients with Myasthenia Gravis Having Generalized Muscle Weakness.

Published: 26-09-2018
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Primary Objective:- Efficacy of ARGX-113 as assessed by the percentage of "Myasthenia Gravis Activities of Daily Living (MG-ADL) responders" in the acetylcholine receptor (AChR)-antibody (Ab) seropositive population.Secondary Objectives:1...

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

Summary

ID

NL-OMON47956

Source
ToetsingOnline

Brief title
ARGX-113-1704 (ADAPT)

Condition

- Autoimmune disorders

Synonym
Myasthenia Gravis (MG)

Research involving
Human

Sponsors and support

Primary sponsor: argenx BVBA
Source(s) of monetary or material Support: argenx BVBA

Intervention

Keyword: ARGX-113, Generalized Muscle Weakness, Myasthenia Gravis

Outcome measures

Primary outcome

Efficacy of ARGX-113 as assessed by the percentage of "Myasthenia Gravis Activities of Daily Living (MG-ADL) responders" (acetylcholine receptor (AChR)-antibody (Ab) seropositive population)

Secondary outcome

1. Efficacy of ARGX-113 as assessed by the percentage of "QMG responders" in the AChR-Ab seropositive population.

2. Efficacy of ARGX-113 as assessed by the percentage of "MG-ADL responders" in the overall population (AChR-Ab seropositive and AChRAb seronegative patients).

3. Efficacy of ARGX-113 as assessed by the percentage of time that patients show a "clinically meaningful improvement" in total MG-ADL score during the trial in the AChR-Ab seropositive population.

4. Duration of response

5. Onset of efficacy of ARGX-113 as assessed by the percentage of "early MG-ADL responders" in the AChR-Ab seropositive population.

Study description

Background summary

Generalized myasthenia gravis (gMG) is an autoimmune disorder. It is caused by an error in the transmission of nerve impulses to muscles. It occurs when normal communication between the nerve and muscle is interrupted at the neuromuscular junction (the place where nerve cells connect with the muscles they control). The treatment of gMG is based on a variety of medications and medical procedures used either alone or in combination. Since the majority of already existing treatment options can give side-effects in patients while not always giving the symptom control needed there is room for improvement. ARGX-113 wants to be an alternative or addition to the existing therapies offering more specific modulation of the immune system with less side-effects.

A previous study with ARGX-113 involving 24 patients diagnosed with gMG, has shown that 75% of the patients treated with ARGX-113 experienced relief in their symptoms for at least 6 weeks compared with only 25% of patients who received a placebo.

Study objective

Primary Objective:
- Efficacy of ARGX-113 as assessed by the percentage of "Myasthenia Gravis Activities of Daily Living (MG-ADL) responders" in the acetylcholine receptor (AChR)- antibody (Ab) seropositive population.

Secondary Objectives:
1. Efficacy of ARGX-113 as assessed by the percentage of "QMG responders" in the AChR-Ab seropositive population.
2. Efficacy of ARGX-113 as assessed by the percentage of "MG-ADL responders" in the overall population (AChR-Ab seropositive and AChRAb seronegative patients).
3. Efficacy of ARGX-113 as assessed by the percentage of time that patients show a "clinically meaningful improvement" in total MG-ADL score during the trial in the AChR-Ab seropositive population.
4. Duration of response
5. Onset of efficacy of ARGX-113 as assessed by the percentage of "early MG-ADL responders" in the AChR-Ab seropositive population.
6. Safety and tolerability of ARGX-113 in the overall population and in subgroups.

Study design

This is a randomized, double-blind, placebo-controlled, multicenter Phase 3

trial to evaluate the efficacy, safety, tolerability, quality of life and impact on normal daily activities of ARGX-113 in patients with gMG.

Intervention

The patient will be randomly assigned to 1 of the following treatment groups:
* The study drug ARGX-113 (10 milligrams per kilogram of body weight [10 mg/kg], with a maximum of 1200 mg)
* Placebo

Study burden and risks

For full details see table 1 in the protocol (schedule of assessments) page 13-16

The patient participation in this study will last approximately 28 weeks. During this time the patient will visit the hospital approximately 19 times. The screening visit and the treatment visits will take about 3-4 hours. The other hospital visits will take about 2 hours.

During these visits the following tests and procedures will take place:
- physical examinations will be done and questions will be asked about medical history.
- ECGs will be done
- weight, height, blood pressure, temperature, heartbeat will be measured
- blood and urine sampling will be taken.
- The research physician will also test female pa rticipants of childbearing potential for pregnancy.
- Subjects need to complete several questionnaires that will evaluate the Efficacy and quality of life and for an Suicidality assessment

Possible side effects that are already known are described in the IB and patient information letter.

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

1. Patients with the ability to understand the requirements of the trial, provide written informed consent, and comply with the trial protocol procedures.
2. Male or female patients aged * 18 years.
3. Diagnosis of MG with generalized muscle weakness meeting the clinical criteria for diagnosis of MG as defined by the Myasthenia Gravis Foundation of America (MGFA) class II, III, IVa and IVb., Other more specific inclusion criteria are further defined in the protocol.

Exclusion criteria

1.Pregnant and lactating women, and those intending to become pregnant during the trial or within 90 days after the last dosing.
2. Male patients who are sexually active and do not intend to use effective methods of contraception during the trial or within 90 days after the last dosing or male patients who plan to donate sperm during the trial or within 90 days after the last dosing.
3. MGFA Class I and V patients
4. Patients with worsening muscle weakness secondary to concurrent infections or medications.
5.Patients with known seropositivity or who test positive for an active viral infection at Screening with:
- Hepatitis B Virus (HBV) (except patients who are seropositive because of HBV vaccination)

- Hepatitis C Virus (HCV)
- Human Immunodeficiency Virus (HIV), Other more specific exclusion criteria are further defined in the protocol.

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:	Completed
Start date (anticipated):	09-07-2019
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Not available
Generic name:	efgartigimod

Ethics review

Approved WMO

Date:	26-09-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	30-04-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	04-10-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	11-11-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2018-002132-25-NL

Register	ID
ClinicalTrials.gov	NCT03669588
CCMO	NL67217.058.18

Study results

Date completed: 06-04-2020

Results posted: 23-11-2020

First publication
18-08-2020