A Phase 3b, Randomized, Open-label, Parallel-Group Study to Evaluate Different Dosing Regimens of Intravenous Efgartigimod to Maximize and Maintain Clinical Benefit in Patients With Generalized Myasthenia Gravis (gMG)

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Primary objective:- To assess the clinical efficacy of efgartigimod IV 10mg/kg administered in a q2w continuous regimen compared to that administered in a cyclic regimen.Secondary objectives:- To evaluate the safety and tolerability of both...

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

Summary

ID

NL-OMON54098

Source
ToetsingOnline

Brief title
ADAPT NXT

Condition

- Autoimmune disorders

Synonym
Generalized Muscle Weakness, Myasthenia Gravis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: ARGX-113, Different Dosing Regimens, Generalized Myasthenia Gravis, Open-label

Outcome measures

Primary outcome

Primary endpoint:

Mean of the average Myasthenia Gravis Activities of Daily Living (MG-ADL) total

score change from baseline during the visit of week (W)1 through W21 by regimen

arm.

Secondary outcome

Secondary endpoint:

1: Incidence and severity of adverse events (AEs), serious adverse events

(SAEs) and AEs of special interest (AESIs) Time point: 126 weeks

2: Incidence of serious adverse events (SAEs) and AEs of special interest

(AESIs) Time point: 126 weeks

3: Change from baseline in the Myasthenia Gravis - Activities of Daily Living

(MG-ADL) total score over time. A higher total score indicates

more impairment. Time point: 128 weeks

4: Normalized area under the effect curve (AUEC) of MG-ADL total score improvement from baseline during following intervals: Day 1 through Week7, Week 7 through Week 14, Week 14 trough Week 21 and Week 7 through Week 21. Time point: 21 weeks

5: Characterization of MG-ADL total score change from baseline during the following 5 intervals using mean and standard deviation: Week 1 through Week 7, Week 8 through Week 14, Week 15 through Week 21, Week 8 through Week 21 and Week 1 through Week 21. Time point: 21 weeks

6: Number of participants who have a >=2, 3, 4, or 5 points improvement in MG-ADL total score from baseline. during the following 5 intervals: Week 1 through Week 7, Week 8 through Week 14, Week 15 through Week 21, Week 8 through Week 21 and Week 1 through Week 21. Time point: 21 weeks

7: percentage of participants who have a >=2, 3, 4, or 5 points improvement in MG-ADL total score from baseline during the following 5 intervals: Week 1 through Week 7, Week 8 through Week 14, Week 15 through Week 21, Week 8 through Week 21 and Week 1 through Week 21. Time point: 21 weeks

8: Percentage of time, participants have a change in MG-ADL total score of at

least 2 points from baseline during Week 4 through Week 21. Time

point: 21 weeks

9: Number of participants who achieve minimal symptom expression (MSE), defined

as a MG-ADL total score of 0 or 1. Time point: 21 weeks

10: Percentage of participants who achieve minimal symptom expression (MSE),

defined as a MG-ADL total score of 0 or 1 in the following 5

intervals: Week 1 through Week 7, Week 8 through Week 14, Week 15 through Week

21, Week 8 through Week 21 and Week 1 through Week

21. Time point: 21 weeks

Study description

Background summary

Generalized myasthenia gravis (gMG) is a disorder where your immune system attacks your muscles. This leads to muscle weakness in different places in your body. 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. 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. The study drug wants to be an alternative or addition to the existing therapies offering more specific modulation of the immune system with less side-effects.

The study drug is a fragment of a human antibody that has been modified to better bind to a specific protein, called FcRn. Antibodies are proteins that our body uses to fight and prevent infections. In some diseases, antibodies can attack your own body. The FcRn protein keeps the antibody level up. The study drug is a compound that is similar to these antibodies that are naturally present in the human body. The levels of antibodies are reduced after the study drug binds to FcRn. This means that the levels of antibodies attacking your own

body are also reduced.

Study objective

Primary objective:
- To assess the clinical efficacy of efgartigimod IV 10mg/kg administered in a q2w continuous regimen compared to that administered in a cyclic regimen.

Secondary objectives:
- To evaluate the safety and tolerability of both treatment regimens used throughout the study.
- To assess the clinical efficacy of efgartigimod IV in both treatment regimens over time.
- To compare the number of participants who achieve maximal clinical effect during different treatment regimens.

Study design

This is a phase 3b, multicenter, randomized, open-label, parallel-group study to evaluate alternative dosing regimens for the IMP in patients with gMG. The clinical efficacy, maximum clinical effect, safety, and tolerability will be assessed for 2 treatment regimens: cyclic and continuous.

The target population in adult patients with gMG who have an MG-ADL total scole of more than 5 points and more than 50% of the total score attributed to nonocular symptoms at screening and baseline.

All participants will be confirmed to be seropositive for AChR-Abs.

Participants must be receiving concomitant gMG treatment from screening through the end of Part A.

All participants will start Part A by receiving the cyclic regimen, receiving efgartigimod infusions q7d during a 3-week induction period for a total of 4 infusions.

After the fourth infusion at W3, the 2 regimens will be compared in a regimen comparison period. On the day 1 visit, participants will be randomized 3:1 to either the continuous or cyclic regimen. Part A ends after all predose assessments are performed at the W21 visit.

The cyclic regimen comprises IMP administered q7d in 3-week TPs for 4 infusions, separated by 4-week IPs. The continuous regimen comprises infusions q2w.

Part B begins with the infusion at the W21 visit, with the assessments at this

visit acting as the baseline for Part B. Participants in the cyclic regimen arm will receive 1 additional TP of 4 weekly infusions during W21 through W24 as bridging doses before switching to a continuous regimen at AV26. Participants in the continuous regimen arm will continue with the continuous regimen in Part B.

If efgartigimod becomes commercially available for patients with gMG or available through another patient program for gMG, participants will have the choice to switch to one of these options after completing Part A of the study.

After W21 for participants in the continuous regimen arm or during W28 for participants in the cyclic regimen arm, participants who have maintained clinical improvement, based on clinical judgment and guided by the MG-ADL scale, will have the option to transition to receiving the IMP q3w. All other participants will continue to receive IMP infusions q2w.

Participants who are unable to maintain clinical improvement based on clinical judgment after transitioning to the q3w infusion regimen will return to the q2w infusion regimen. The decision to switch between the q2w and q3w dosing regimens must be made on the last dosing day of the current dosing regimen (ie, at least 2 weeks before the next dose).

Participants who resume the q2w regimen and maintain clinical improvement for 1 year while receiving the q2w regimen will have another opportunity to transition to the q3w regimen.

The total study duration is up to 128 weeks. The study consists of:
* Approximately 2 weeks of screening, with an additional 7 days allowed as needed to ensure all lab tests results have been received
* Part A (regimen comparison period) - 21 weeks
* Part B (extension period) - up to 105 weeks

Intervention

The study duration is a maximum of 128 weeks, comprising the following study periods:
• Screening period - approximately 2 weeks, with an optional additional 7 days allowed to ensure all test results have been received
• Part A (regimen comparison period) - 21 weeks
• Part B (extension period) - up to 105 weeks

Participants will receive efgartigimod throughout the study. Starting after the W3 visit through the W21 visit, participants will be on either a cyclic regimen or a continuous regimen based on the randomization performed on day 1. In Part B, all participants will transition to a continuous regimen.

Part A

All participants will receive 4 weekly IMP infusions at day 1 (W0), W1, W2, and W3. Participants randomized to the cyclic regimen arm will receive an additional 2 cycles of efgartigimod (each including TP infusions q7d for a total of 4 infusions in 3 weeks followed by a fixed 4-weeks IP), starting at W7. Participants randomized to the continuous regimen arm will receive efgartigimod q2w, starting at W5. Part A ends after all predose assessments have been performed at the W21 visit.

Part B
Part B begins with the infusion at the W21 visit. The assessments taken at W21 will also serve as the baseline assessments for Part B. Participants in the cyclic regimen arm will receive 1 additional TP of 4 weekly infusions during W21 through week 24 as bridging doses before switching to a continuous regimen during week 26. Participants in the continuous regimen arm will continue with the continuous regimen in Part B.

Study burden and risks

The participant's participation in this study will last up to 128 weeks and consists of:
* Approximately 2 weeks of screening, with an additional 7 days allowed as needed to ensure all lab tests results have been received
* Part A (regimen comparison period) - 21 weeks
* Part B (extension period) - up to 105 weeks

The participant will visit the hospital approximately 65 times during this period. Each visit will take among 4 hours to complete.

The study will consist of a screening, treatment and a follow-up period.

The following tests and procedures will take place during the hospital visits:
• Physical exam (including body weight and hight), vital signs.
• ECG
• Blood and urine samples
• Pregnancy tests in women of childbearing potential
• Covid-19 test using a swab
• Questionnaires
• Ask about their ethnicity

Please refer to page 20-26 of the protocol (schedule of events) for more information.

Possible side effects that are already known are described in the Investigator's Brochure and in paragraph 6 of the subject informed consent form.

Contacts

Public
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Scientific
argenx BV

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Participants are eligible to be included in the study only if all of the following criteria apply:
1. Capable of giving signed informed consent as described in Section 10.1.3 of the protocol, which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol.

2. At least 18 years of age, at the time of signing the informed consent.

3. Diagnosed with gMG with confirmed documentation and supported by a physical exam and confirmed seropositivity for AChR-Abs by the central laboratory. During the screening or rescreening period, any historical results for AChR-Ab can be used, as long as the results are <=1 year old.

4. Meets the clinical criteria as defined by the Myasthenia Gravis Foundation of America (MFGA) class II, III, or IV

5. Has an MG-ADL total score >=5 at screening and the day 1 visit, with more than 50% of the score due to nonocular symptoms.

6. Concomitant gMG treatment is permitted. Permitted concomitant gMG treatment includes nonsteroidal immunosuppressive drugs (NSIDs), steroids, and/or (AChE) inhibitors. If receiving corticosteroids and/or NSIDs, must be on a stable dose for at least 1 month before screening.

7. Agrees to use contraceptive measures consistent with local regulations and the following:
a. Male participants: (contraceptive measures provided in Section 10.4.2.2 of the protocol, refer to Section 10.7 of the protocol for country specific requirements)
b. WOCBP (defined in Section 10.4.1 of the protocol) must have a negative serum pregnancy test at screening and a negative urine pregnancy test at baseline before receiving IMP (Section 10.4.2.1. of the protocol, see Section 10.7 of the protocol for country-specific requirements).

Exclusion criteria

Participants are excluded from the study if any of the following criteria apply:
1. Clinically significant uncontrolled active or chronic bacterial, viral, or fungal infection at screening that is not sufficiently resolved in the investigator's opinion.

2. A positive test for SARS-CoV-2 at screening

3. Any other known autoimmune disease that, in the opinion of the investigator, would interfere with an accurate assessment of the clinical symptoms of gMG and/or put the participant at undue risk.

4. History of malignancy unless deemed cured by adequate treatment with no evidence of reoccurrence for >=3 years before the first administration of the IMP. Participants with the following cancers can be included at any time, provided they are adequately treated at screening: a. Basal cell or squamous cell skin cancer b. Carcinoma in situ of the cervix c. Carcinoma in situ of the breast d. Incidental histological finding of prostate cancer (TNM stage T1a or T1b)

5. Clinical evidence of other significant serious diseases, a recent (<3 months) major surgery, or any other condition that, in the opinion of the

investigator, could confound the results of the study or put the participant at undue risk

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:	Recruiting
Start date (anticipated):	19-10-2022
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Efgartigimod
Generic name:	Efgartigimod

Ethics review

Approved WMO

Date:	01-03-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	26-07-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-10-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-01-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-04-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-07-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-08-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-10-2023
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
EudraCT	EUCTR2021-002504-12-NL
ClinicalTrials.gov	NCT04980495
CCMO	NL79087.018.22