# A Long-Term, Single-Arm, Open-label, Multicenter Phase 3 Study to Evaluate the Safety and Tolerability of Multiple Subcutaneous Injections of Efgartigimod PH20 SC in Patients With Generalized Myasthenia Gravis

Published: 12-04-2021
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Primary:To evaluate the long-term safety and tolerability of efgartigimod PH20 SC in participants with Generalized Myasthenia Gravis (gMG).Secondary:• To evaluate the impact of efgartigimod PH20 SC on disease severity• To evaluate the effect of...

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

## Summary

### ID

NL-OMON54450

**Source**
ToetsingOnline

**Brief title**
ADAPT SC+

### Condition

- Autoimmune disorders
- Neuromuscular disorders

**Synonym**
Disease of the neuro muscular junction; Serious muscle weakness

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** PPD
**Source(s) of monetary or material Support:** Opdrachtgever

## Intervention

**Keyword:** Efgartigimod, Generalized Mysathenia Gravis, Phase 3, Subcutaneously

## Outcome measures

### Primary outcome

• Incidence and severity of adverse events (AEs), incidence of serious adverse events (SAEs), and changes in laboratory test results, physical examination results, vital signs, and electrocardiogram results

### Secondary outcome

• Myasthenia Gravis Activities of Daily Living (MG-ADL) total score changes from baseline and cycle baseline over time by cycle

• Percentage reduction in levels of total immunoglobulin G (IgG) from baseline and cycle baseline over time by cycle

• Percentage reduction of acetylcholine receptor binding autoantibodies (AChR-Ab) from baseline and cycle baseline over time by cycle in AChR-Ab seropositive participants

• Incidence and prevalence of anti-drug antibodies (ADAs) to efgartigimod over time

# Study description

**Background summary**

gMG is a rare, chronic, neuromuscular autoimmune disease caused by pathogenic IgGs targeting the neuromuscular junction (NMJ), producing reduced neuromuscular transmission and debilitating and potentially life-threatening muscle weakness and chronic fatigue. Generalized muscle weakness results in difficulties in mobility, speech, swallowing, vision, and respiration. Up to 20% of patients develop potentially life-threatening myasthenic crisis involving respiratory failure requiring mechanical ventilation.

ARGX 113 (efgartigimod) is an investigational antibody fragment and a first-in-class neonatal Fc receptor (FcRn) antagonist that is being evaluated for the treatment of patients with severe autoimmune diseases mediated by pathogenic IgG autoantibodies, including gMG. Approximately 90% of patients with gMG have detectable levels of IgG autoantibodies in the serum. Most commonly, these antibodies are against the acetylcholine receptor (AChR). Efgartigimod leads to degradation circulating disease-causing pathogenic antibodies by blocking FcRn.

FcRn is present throughout life and expressed predominantly in endothelial cells and cells of myeloid lineage. FcRn has a specific role in IgG homeostasis, recycling all IgG subtypes, which rescues them from lysosomal degradation. This FcRn-mediated recycling results in the longer half-life and higher concentrations of IgG, including pathogenic IgG autoantibodies, as compared to other Igs that are not recycled by FcRn. FcRn also promotes transcytosis of IgG into tissues. Additionally, FcRn recycles albumin using a site that is distinct from the IgG binding site.

Efgartigimod is a human IgG1 antibody Fc fragment, a natural ligand of FcRn, engineered for increased FcRn affinity at both physiological and acidic pH. Efgartigimod outcompetes endogenous IgG binding, preventing FcRn-mediated recycling of IgGs and increasing IgG degradation.

The efficacy of efgartigimod IV based on the percentage of MG-ADL responders was demonstrated against placebo in study ARGX-113-1704. Further, there was a strong association between total IgG and AChR-Ab reductions and clinical response, as measured by the percentage
of MG-ADL responders. This strong association was used to bridge from efgartigimod IV to efgartigimod PH20 SC in study ARGX-113-2001. This study showed noninferiority of the pharmacodynamic effect (as measured by IgG percent reduction at week 4) of efgartigimod
PH20 SC 1000 mg compared with efgartigimod IV 10 mg/kg in participants with gMG after 1 treatment cycle of 4 weekly administrations.

Given efgartigimod*s mechanism of action of reducing IgG levels, the strong association btween total IgG reduction and clinical response in patients with

gMG, the SC formulation of efgartigimod PH20 SC may provide an alternative to efgartigimod 10 mg/kg IV, giving patientswith gMG treatment optionality and flexibility.. A detailed description of the chemistry, pharmacology, efficacy, and safety of efgartigimod is provided in the Investigator*s Brochure (IB).

**Study objective**

Primary:
To evaluate the long-term safety and tolerability of efgartigimod PH20 SC in participants with Generalized Myasthenia Gravis (gMG).

Secondary:
• To evaluate the impact of efgartigimod PH20 SC on disease severity
• To evaluate the effect of efgartigimod PH20 SC on Pharmacodynamic (PD)
• To evaluate the immunogenicity of efgartigimod PH20 SC
• To evaluate the impact of efgartigimod PH20 SC on the quality of life (QoL) of the participants
• To evaluate feasibility of self administration of efgartigimod PH20 SC

Exploratory:
•To assess participant preference for and satisfaction with efgartigimod PH20 SC treatment

**Study design**

• This is a phase 3, multicenter, long-term, single-arm, open-label study to evaluate the long-term safety and tolerability of efgartigimod PH20 SC 1000 mg. The clinical efficacy, PD, PK, immunogenicity, impact on the QoL of the participants, treatment satisfaction, mode of administration participant preference and the feasibility of self administration will also be assessed.

• Study duration and treatment duration: from the participant*s first visit in this study until, at the latest, 31 Dec 2024
- Year 1: 3-week TPs of once weekly injections, repeated as needed with at least 28 days between TPs
- Year 2 onward: 3-week TPs of once weekly injections. It is recommended to have IPs of at least 28 days, but a subsequent treatment period can be administered earlier based on clinical evaluation at the discretion of the investigator. A minimal interval of 7 days after the last investigational medicinal product (IMP) administration of the previous cycle must be maintained.

• At study entry, participants will be evaluated for the need of retreatment. Refer to the SoA in Section 1.3 of the protocol for timing of retreatment.

**Intervention**

• Efgartigimod PH20 SC 1000 mg will be administered by injection into the abdominal subcutaneous tissue or into the subcutaneous tissue of another appropriate injection site. Participants or their caregivers will be trained in self-administration. If the participant or caregiver completes the training to the satisfaction of the investigator, the participant or caregiver will be permitted to administer the investigational medicinal product (IMP).

• Participants and their caregivers must complete the training to the satisfaction of the site staff (a minimum of 1 site visit) before (self-)administering efgartigimod PH20 SC under the supervision of the site staff. Participants and caregivers who were in the SC arm in antecedent study ARGX-113-2001 and considered competent to (self-)administer may (self-)administer efgartigimod PH20 SC at home as of the second visit of the first TP. Participants and caregivers from the IV antecedent studies who are considered competent to (self-)administer may do so at home as of the second visit of the second TP onward. All participants must come to the site for the first administration of a TP, even if the participant or caregiver administers.

**Study burden and risks**

Overall, available data confirm that efgartigimod PH20 SC has been well tolerated across studies in different indications and has an acceptable safety profile. More detailed information about the known and expected benefits and risks and reasonably expected AEs of efgartigimod PH20 SC is provided in the current IB.

# Contacts

**Public**
PPD

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**Scientific**
PPD

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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. Must be capable of giving signed informed consent, which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol
2. Previously participated in antecedent studies ARGX-113-2001 or ARGX-113-1705 and are eligible for roll over
3. Contraceptive use by men and women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies and:
a. Male participants: No male contraception is required
b. Female participants:
* Women of Child bearing potential (WOCBP) must have a negative urine pregnancy test at baseline before IMP can be administered.

## Exclusion criteria

Participants are excluded from the study if any of the following criteria apply:
1. The participant was discontinued early from studies ARGX-113-2001 or ARGX-113-1705, unless the reason for discontinuation from study ARGX-113-1705 was to roll over into study ARGX-113-2002
a. Participants who, in the investigator*s judgment, are not benefiting from efgartigimod IV in study ARGX-113-1705 Part B are not eligible for roll over into ARGX-113-2002.
2. Are pregnant or lactating, or intend to become pregnant during the study or within 90 days after the last dose of IMP
3. Has any of the following medical conditions:

a. Clinically significant uncontrolled chronic bacterial, viral, or fungal infection at rollover
b. Any other known autoimmune disease that, in the opinion of the investigator, would interfere with accurate assessment of clinical symptoms of myasthenia gravis or put the participant at undue risk
c. History of malignancy unless deemed cured by adequate treatment with no evidence of reoccurrence for >=3 years before the first administration of IMP. Participants with the following cancers can be included at any time:
* adequately treated basal cell or squamous cell skin cancer
* carcinoma in situ of the cervix
* carcinoma in situ of the breast
* incidental histological findings of prostate cancer (TNM classification of malignant tumors stage T1a or T1b)
d. Clinical evidence of other significant serious diseases, or the participant has had a recent major surgery, or who have 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

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| Study phase: | 3 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

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| Recruitment status: | Completed |
| Start date (anticipated): | 10-08-2021 |
| Enrollment: | 2 |
| Type: | Actual |

## Medical products/devices used

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| Product type: | Medicine |
| Brand name: | Efgartigimod rHuPH20 SC |

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| Generic name: | Efgartigimod PH20 SC |

## Ethics review

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|---|---|
| Approved WMO Date: | 12-04-2021 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

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|---|---|
| Approved WMO Date: | 02-06-2021 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

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|---|---|
| Approved WMO Date: | 04-08-2021 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

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|---|---|
| Approved WMO Date: | 26-11-2021 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

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|---|---|
| Approved WMO Date: | 25-04-2022 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

Approved WMO

| | |
|---|---|
| Date: | 25-05-2022 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |

Approved WMO

| | |
|---|---|
| Date: | 25-10-2022 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |

Approved WMO

| | |
|---|---|
| Date: | 25-11-2022 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |

Approved WMO

| | |
|---|---|
| Date: | 15-04-2023 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |

Approved WMO

| | |
|---|---|
| Date: | 01-05-2023 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |

Approved WMO

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|---|---|
| Date: | 20-11-2023 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |

Approved WMO

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|---|---|
| Date: | 18-12-2023 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>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 | EUCTR2020-004086-38-NL |
| ClinicalTrials.gov | NCT04818671 |
| CCMO | NL77172.058.21 |