Open-label Uncontrolled Trial to Evaluate Pharmacokinetics, Pharmacodynamics, Safety, and Activity of Efgartigimod in Children From 2 to Less Than 18 Years of Age With Generalized Myasthenia Gravis

Published: 19-07-2021
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This study has been transitioned to CTIS with ID 2024-513854-31-00 check the CTIS register for the current data. To confirm an age-adjusted optimum dose of efgartigimod IV and provide (model-predicted) evidence for a treatment response.

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

Summary

ID

NL-OMON54483

Source
ToetsingOnline

Brief title
ARGX-113-2006

Condition

- Autoimmune disorders
- Central nervous system infections and inflammations

Synonym
Generalized Myasthenia Gravis, gMG

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Efgartigimod, Generalized Myasthenia Gravis, gMG, Myasthenia Gravis

Outcome measures

Primary outcome

Efgartigimod concentrations as input for compartmental, model-driven analysis to determine (age and size dependency of) clearance (CL) and volume of distribution (Vd)

PD parameters: total IgG levels and anti-acetylcholine receptor antibodies (AChR-Ab) as input for PK/PD modeling analysis

Secondary outcome

• Incidence and severity of adverse events (AEs), incidence of serious AEs (SAEs), incidence of AEs of special interest (AESIs), and changes in laboratory test results, physical examination results, vital sign measurements, and electrocardiogram (ECG) (Part B only for ECGs)

• Efgartigimod serum concentrations

• Levels of total IgG and AChR-Ab absolute values, change from baseline, and percent (%) reduction from baseline

• Incidence and prevalence of antidrug antibodies (ADA) against efgartigimod

• MG-ADL total score: absolute value and change from baseline

• Total Quantitative Myasthenia Gravis (QMG) score: absolute value and change

from baseline

• Total score EQ-5D-Y: absolute value and change from baseline

• Quality of Life in Neurological Disorders (Neuro-QoL) Pediatric Fatigue

Score: values and change from baseline

• Change in protective antibody titers to vaccines received before or received

during the trial

Study description

Background summary

gMG is a rare, chronic, neuromuscular autoimmune disease caused by pathogenic IgGs targeting the neuromuscular junction, 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.

Efgartigimod is a human immunoglobulin (Ig) G1 (IgG1)-derived Fc fragment that binds with nanomolar affinity to human neonatal Fc receptor (FcRn) that is being developed for the treatment of generalized myasthenia gravis. Overall, efgartigimod IV has been well tolerated in healthy adult participants and in participants with gMG. No major safety findings have arisen in ongoing and completed studies with efgartigimod. Further information can be found in the IB. Trial ARGX-113-2006 is the first clinical trial administering efgartigimod intravenously in a pediatric population. There is no scientific rationale that suggests that the mechanism of action of efgartigimod differs between the adult and pediatric populations, as such, a similar safety profile is anticipated between the 2 populations.

Study objective

This study has been transitioned to CTIS with ID 2024-513854-31-00 check the CTIS register for the current data.

To confirm an age-adjusted optimum dose of efgartigimod IV and provide (model-predicted) evidence for a treatment response.

Study design

ARGX-113-2006 is an open-label, multicenter, uncontrolled trial in pediatric participants with gMG. Before starting the trial, the appropriate dose for the adolescent group (12 to less than 18 years) was predicted based on adult-exposure modeling. The trial is composed of a dose-confirmatory part (Part A), followed by a treatment response-confirmatory part (Part B). For the analysis of the primary objective, at least 12 evaluable participants will be enrolled in the trial with at least 6 evaluable participants per age group (at least 6 adolescents aged 12 to less than 18 years and at least 6 children aged 2 to less than 12 years).

Intervention

Efgartigimod infusion IV. This concerns one infusion in part A, and 4 infusions in 3 weeks in part B.

Study burden and risks

In previous clinical studies with efgartigimod in adults, some people experienced side effects. Some side effects could be related to efgartigimod. Many of these side effects were mild or moderated, lasted a short time, and required little or no treatment.

Among all reported side effects, those that were considered related to efgartigimod were inflammation of the airway passages, upper respiratory tract infection, urinary tract infection, headache, and muscle pain. Treatment with efgartigimod could increase the chance of infections.

The study will be executed in line with the Code of conduct for resisting minors.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Participants are eligible to be included in the trial only if all of the following criteria apply: 1. Ability of the participant and/or his/her legally authorized representative to understand the requirements of the trial and provide written informed consent/assent, if applicable (including consent/assent for the use and disclosure of research-related health information), willingness and ability to comply with the trial protocol procedures (including attending the required trial visits). 2. Male or female participants between 2 to less than 18 years of age at the time of providing informed consent/assent. Age groups are enrolled in a staggered fashion respectively: 6 participants in the 12 to less than 18 years of age group followed by 6 participants in the 2 to less than 12 years of age group at the time of providing informed consent/assent. 3. Diagnosed with gMG with confirmed documentation 4. Meeting the clinical criteria as defined by the Myasthenia Gravis Foundation of America (MGFA) class II, III, and IVa. 5. Eligible participants should have an unsatisfactory response (efficacy and/or safety) to immunosuppressants, steroids or AChE inhibitors and should be on stable concomitant gMG therapy of adequate duration before screening. 6. Positive serologic test for anti-AChR antibodies at screening (for younger participants (<15kg) historical values can be used). 7. Contraceptive use for sexually active participants of childbearing potential should be consistent with local regulations regarding the methods of contraception for those participating in clinical trials. A participant is of childbearing potential if, in the opinion of the investigator, he/she is biologically capable of having children (for example, female participants have started their menses, and male participants have reached the middle of puberty). a. Male participants: Male participants must agree to not donate sperm from the time of providing informed consent/assent until they have completed the trial. b. Female adolescents of childbearing potential: Female adolescents of childbearing potential must have a negative serum pregnancy test at screening and a negative urine pregnancy test at baseline before IMP can be administered.

Exclusion criteria

Participants are excluded from the trial if any of the following criteria apply: 1. Participants with MGFA class I, IVb, and V. 2. Female adolescents of childbearing potential: Pregnancy or lactation, or the participant intends to become pregnant during the trial or within 90 days after the last dose of IMP. 3. Has any of the following medical conditions: a) Clinically significant uncontrolled active or chronic bacterial, viral, or fungal infection at screening. b) Any other known autoimmune disease that, in the opinion of the investigator, would interfere with an 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 recurrence for >=3 years before the first administration of the 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 have had a recent major surgery, or who have any other condition that, in the opinion of the investigator, could confound the results of the trial or put the participant at undue risk. 4. Estimated glomerular filtration rate (eGFR) less than 30 mL/min/1.73m2 at screening. 5. Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) greater than 2 times the upper limit of normal (ULN) and bilirubin greater than 1.5 × ULN, or any other clinically meaningful abnormalities. 6. Worsening muscle weakness secondary to concurrent infections or medications (aminoglycosides, fluoro-quinolones, beta-blockers, etc). 7. A documented lack of clinical response to plasma exchange (PLEX). 8. Received a live or live-attenuated vaccine fewer than 28 days before screening. (Receiving an inactivated, subunit, polysaccharide, or conjugate vaccine any time before screening is not exclusionary.) 9. Received a thymectomy <3 months before screening or 1 is planned to be performed during the trial period. 10. The following results from these diagnostic assessments will be considered exclusionary: a) Positive serum test at screening for an active viral infection with any of the following conditions: • Hepatitis B virus (HBV) that is indicative of an acute or chronic infection (https://www.cdc.gov/hepatitis/HBV/PDFs/SerologicChartv8.pdf) • Hepatitis C virus (HCV) based on HCV antibody assay b) Positive HIV serology at screening. c) Positive nasopharyngeal swab PCR test for SARS-CoV-2 at screening. 11. Using the following prior or concomitant therapies: a) Use of an investigational product within 3 months or 5 half-lives (whichever is longer) before the first dose of the IMP. b) Use of any monoclonal antibody within the 6 months before the first dose of the IMP. c) Use of intravenous immunoglobulin (IVIg), immunoglobulins administered subcutaneously (SC) or intramuscularly, or PLEX within 4 weeks before screening. 12. Total IgG levels below the lower limit of normal (LLN) according to the reference ranges of the central laboratory for participant by sex and age at screening. 13. A known hypersensitivity reaction to efgartigimod or any of its excipients. 14. Current participation in another interventional clinical trial. 15. History (within 12 months of screening) of current alcohol, drug, or medication abuse as assessed by the investigator. 16. Previous participation in an efgartigimod trial with at least 1 dose of IMP received.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-07-2022
Enrollment:	2
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	19-07-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	15-04-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	19-05-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	17-06-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	26-03-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	14-04-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	23-06-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	03-07-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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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	CTIS2024-513854-31-00
EudraCT	EUCTR2020-005841-18-NL
CCMO	NL78028.058.21