Open-label Extension of the ARGX-113-1802 Trial to Investigate the Long-term Safety, Tolerability, and Efficacy of Efgartigimod PH20 SC in Patients with Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

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This study has been transitioned to CTIS with ID 2023-507885-21-00 check the CTIS register for the current data. Primary objective:- To assess the long-term safety and tolerability of efgartigimod PH20 SC (efgartigimod co formulated with recombinant...

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

Summary

ID

NL-OMON52460

Source
ToetsingOnline

Brief title
ADHERE+

Condition

- Demyelinating disorders

Synonym
damaged myelin sheath of nerve fibers, inflammation of peripheral nervous system

Research involving

Human

Sponsors and support

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

Intervention

Keyword: CIDP, Efgartigimod, Extention, Phase 2

Outcome measures

Primary outcome

Primary endpoint:

• Safety and tolerability of the drug:

- Incidence of treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) by system organ class (SOC) and preferred term (PT);

- Incidence of clinically significant laboratory abnormalities.

Secondary outcome

Secondary endpoints:

• Change from baseline over time in the following scores and measurements:

- Adjusted INCAT score;

- Medical Research Council (MRC) Sum score;

- 24-item Inflammatory Rasch-built Overall Disability Scale (I-RODS) disability scores;

- Mean grip strength assessed by Martin vigorimeter;

- Timed Up-and-go (TUG) score.

• Percentage of patients without clinical deterioration over time, defined by adjusted INCAT deterioration >=1 point compared to baseline.

• Percentage of patients with and titers of binding antibodies (BAb) towards efgartigimod and the presence of neutralizing antibodies (NAb) against efgartigimod.

• Efgartigimod serum concentrations during the trial in the first 48-week treatment cycle.

• Changes from baseline over time of serum IgG levels (total and IgG subtypes).

• Change from baseline over time in:

- EuroQol 5 dimensions and 5 levels health-related quality-of-life questionnaire (EQ-5D-5L);

- Brief Pain Inventory - Short Form (BPI SF);

- 9 item Treatment Satisfaction Questionnaire for Medication (TSQM-9);

- Rasch-transformed Fatigue Severity Scale (RT-FSS);

- Hospital Anxiety and Depression Scale (HADS).

• Percentage of patients performing self-administration over time.

• Percentage of patients with treatment administered by caregiver over time.

Note that other endpoints for less frequent than weekly dosing with efgartigimod PH20 SC are defined in aseparate protocol appendix for a dosing frequency substudy.

Study description

Background summary

Efgartigimod (ARGX-113) is a human immunoglobulin (Ig) G1-derived Fc of the za allotype that binds with nanomolar affinity to human neonatal Fc receptor

(FcRn). Efgartigimod encompasses IgG1 residues D221-K447 (European Union [EU] numbering scheme) and has been modified with the so-called ABDEG* technology (ABDEG* = antibody that enhances IgG degradation) to increase its affinity for FcRn at both physiological and acidic pH. The increased affinity for FcRn of efgartigimod at both acidic and physiological pH results in a blockage of FcRn mediated recycling of IgGs.
Given the essential role of the FcRn receptor in IgG homeostasis, inhibiting this FcRn function, as is achieved by efgartigimod, leads to rapid degradation of all IgGs, including disease associated autoantibodies of the IgG isotype. This approach is thought to result in alleviation of signs and symptoms in IgG-driven autoimmune diseases.
The safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of intravenous (IV) administrations of efgartigimod have been investigated in the first-in-human trial ARGX 113 1501 in healthy adult subjects. A second trial ARGX-113-1702 in healthy adult subjects investigated the bioavailability, safety, tolerability, immunogenicity, PK, and PD following SC administration of efgartigimod and evaluated the reduction of the IV infusion time from 2 hours to 1 hour.
Phase 2 trials in immune thrombocytopenia (ITP; ARGX 113 1603) and myasthenia gravis (MG; ARGX 113 1602) have indicated that efgartigimod administered by IV infusion is well tolerated, induces a specific, rapid PD effect (ie, reduction in IgG levels, including autoantibody levels), and is associated with improvement in clinical signs and symptoms in patients with ITP and MG, separately.) Additionally, the safety and tolerability of efgartigimod is being evaluated for the treatment of patients with pemphigus in the Phase 2 trial ARGX 113 1701 and for the treatment of patients with MG in the Phase 3 trial ARGX 113 1704.
For the Phase 2 trials in patients with CIDP, a fixed dose of 1,000 mg of efgartigimod PH20 SC was selected based on the results of the Phase 1 trial ARGX 113 1901 in healthy subjects that achieved a similar PD effect as that observed in generalized myasthenia gravis (gMG) and ITP, ie, IgG reduction, at steady state as achieved by weekly 10 mg/kg IV infusions. Doses of 10 mg/kg efgartigimod IV have demonstrated a favorable safety and efficacy profile across Phase 2 trials in MG and ITP patients. To select the fixed SC dose, an open label, parallel group trial in healthy male subjects (ARGX-113-1901) has been performed to investigate the PK, PD, safety, and tolerability of different single fixed SC dose levels of efgartigimod co administered with rHuPH20.
In the current OLE trial, as well as in the main trial, efgartigimod is co formulated with the permeation enhancer rHuPH20 (efgartigimod PH20 SC). rHuPH20 acts as a spreading factor that increases the dispersion and absorption of other co administered drugs and allows SC dosing of greater volumes than without rHuPH20. SC injections of rHuPH20 with fluids, small molecules, peptides, and proteins (eg, IgG) were well-tolerated in all clinical trial populations studied to date.

Study objective

This study has been transitioned to CTIS with ID 2023-507885-21-00 check the CTIS register for the current data.

Primary objective:
- To assess the long-term safety and tolerability of efgartigimod PH20 SC (efgartigimod co formulated with recombinant human hyaluronidase PH20 [rHuPH20] for subcutaneous [SC] administration).

Secondary objectives:
- To determine the long-term efficacy.
- To evaluate the immunogenicity (anti-drug antibodies [ADA]) against efgartigimod during the first 48-week treatment cycle [followed by a safety follow-up period, if applicable]).
- To evaluate the pharmacokinetics (PK) of efgartigimod PH20 SC (during the first 48-week treatment cycle
[followed by a safety follow-up period, if applicable]).
- To evaluate the pharmacodynamic (PD) effect of efgartigimod PH20 SC (ie, total immunoglobulin G [IgG]
- To evaluate additional patient-reported outcomes (PROs) (including patient-reported quality of life and
satisfaction with treatment).
- To explore self-administration of the treatment.
- To explore administration of the treatment by caregivers.
Note that there are other objectives for patients with less frequent than weekly dosing of efgartigimod PH20 SC
which are described in a separate protocol appendix for a dosing frequency substudy.

Study design

This is an open-label extension of the ARGX-113-1802 trial to investigate the long-term safety, tolerability, and efficacy of efgartigimod PH20 SC in patients aged 18 years and older with CIDP.
Patients will be given the opportunity to continue efgartigimod PH20 SC treatment in this OLE trial in the event any of the following four conditions are occurring, provided the patient has not permanently discontinued IMP:
• The patient experiences a clinical deterioration, (i.e., increase [worsening] in adjusted Inflammatory Neuropathy Cause and Treatment [INCAT] disability score in Stage B of ARGX-113-1802 as described in the ARGX-113-1802 protocol.
• The patient completes the Week 48 visit of Stage B of the ARGX-113-1802 trial without any clinical deterioration.
• The patient is in Stage A or Stage B of the ARGX-113-1802 trial at the time sufficient events for the primary endpoint analysis of that trial have been reached and it is stopped.
• The patient completes the Week 48 visit of this OLE trial (Patients will be offered the opportunity to continue in this trial until 2 years after marketing authorization in apatient*s local country or until efgartigimod PH20 SC becomes

commercially available for patients with CIDP or
becomes available via continued access program, whichever comes first.).
The OLE trial is planned in treatment cycles, each with a duration of 48 weeks.
In the OLE trial, 1,000 mg efgartigimod PH20 SC will be administered SC weekly,
ie, at the same dose and frequency as in the main ARGX 113 1802 trial.
The investigational medicinal product (IMP, ie, efgartigimod PH20 SC) will be
administered at the site at the scheduled visits. Other IMP administrations
will be administered by the patient (self-administration) or via a home nurse
or concierge service for visit at the trial site.

Optional Dosing Frequency Substudy: Note that after a minimum period of weekly
dosing in this OLE trial, as specified in Section 11.9 (Dosing Frequency
Substudy), patients who have a stable clinical condition for at least 12 weeks
will be offered to receive less frequent dosing to evaluate
the maintenance of the clinical condition by administration of efgartigimod
PH20 SC 1000 mg at 2 lower dosing frequencies.

Intervention

Patients eligible for the extention study will receive open-label IMP as weekly
SC administrations of efgartigimod PH20 SC

Study burden and risks

Risks
No major safety findings have arisen in the ongoing and completed trials, nor
any pattern of adverse events (AEs)
which would raise concerns or alter the potential benefit-risk profile of
efgartigimod.
In clinical trials to date, efgartigimod has been well-tolerated in healthy
adult subjects and patients with gMG and ITP,
separately: the majority of treatment-emergent adverse events (TEAEs) were
considered to be mild (grade 1) in
severity. No TEAEs of grade >=3 have been reported. The most common TEAE
suspected to be related to efgartigimod
is headache; however, there is no evidence that headache occurs more frequently
in patients administered
efgartigimod than in patients administered placebo.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Ability to understand the requirements of the trial, provide written informed consent (including consent for the use and disclosure of research-related health information), willingness and ability to comply with the trial protocol procedures (including required trial visits) of this trial.

2.a. Male or female patient with one of the following options:
- Have completed the Week-48 visit of Stage B of the ARGX-113-1802 trial and are considered to be eligible for treatment with efgartigimod PH20 SC; or
- Have deteriorated during Stage B of the ARGX-113-1802 trial and are considered to be eligible for treatment with efgartigimod PH20 SC, or
- Have been offered the participation in the OLE trial due to early termination of the ARGX-113-1802 trial (because sufficient events for the primary endpoint analysis of the that trial have been reached and it is stopped) and are considered to be eligible for treatment with efgartigimod PH20 SC treatment; or
- Have completed the Week-48 visit of the previous cycle of the OLE trial and are considered to be eligible to continue with efgartigimod PH20 SC treatment.

Optional Dosing Frequency Substudy: Note that after a minimum period of weekly dosing in this OLE trial, as specified in a separate protocol appendix for a

dosing frequency substudy, patients who have a stable clinical condition for at least 12 weeks will be offered the option to receive less frequent dosing to evaluate the maintenance of the clinical condition by administration of efgartigimod PH20 SC 1000 mg at 2 lower dosing frequencies.

3. Women of childbearing potential who have a negative urine pregnancy test at baseline before IMP administration.

4.a. Women of childbearing potential must use an acceptable method of contraception from signing the ICF untul the date of the last dose of IMP.

5. Inclusion criterion removed via protocol amendment #4.

Exclusion criteria

1. Week-48/ED visit in the ARGX-113-1802 trial or the Week-48 visit of the previous OLE participation occurred more than 14 days prior to SD1 of the OLE trial or the start of a new treatment cycle in the OLE trial and more than 21 days since the last dose of IMP.

2. Pregnant and lactating women and those intending to become pregnant during the trial.

3. a. Patients with clinical evidence of other significant serious disease or patients who underwent a recent or have a planned major surgery, or patients who (intend to) use prohibited medications and therapies during the trial, or any other reason which could confound the results of the trial or put the patient at undue risk.

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):	19-01-2022
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	efgartigimod PH20 SC
Generic name:	efgartigimod PH20 SC

Ethics review

Approved WMO Date:	01-05-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-09-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-11-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-12-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-12-2020

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-10-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-02-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-04-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-06-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-01-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-02-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-04-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	23-05-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	CTIS2023-507885-21-00
EudraCT	EUCTR2019-003107-35-NL
CCMO	NL73190.078.20