A Phase 2/3, Randomized, Double-Blinded, Placebo-Controlled, Parallel-Group, 2-Arm, Multicenter, Operationally Seamless Study to Evaluate the Efficacy, Safety, Tolerability, Pharmacodynamics, Pharmacokinetics, and Immunogenicity of Efgartigimod PH20 SC in Participants Aged 18 Years and Older With Active Idiopathic Inflammatory Myopathy

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This study has been transitioned to CTIS with ID 2024-512785-33-00 check the CTIS register for the current data. Primary objective: To evaluate the clinical improvement of efgartigimod PH20 SC treatment compared with placebo, in addition to standard...

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

Summary

ID

NL-OMON55955

Source
ToetsingOnline

Brief title
alkivia (ARGX-113-2007)

Condition

- Autoimmune disorders

Synonym
idiopathic inflammatory myopathy; myositis

Research involving
Human

Sponsors and support

Primary sponsor: argenx BV
Source(s) of monetary or material Support: By the study sponsor (refer to B7)

Intervention

Keyword: Efgartigimod, Idiopathic Inflammatory Myopathy, Phase 2/3

Outcome measures

Primary outcome

The primary study endpoint is the total improvement score (TIS).

Secondary outcome

Key secondary endpoints:

• Time to reach TIS >=20 (first *minimal clinical improvement*)

• Percentage of participants with TIS >=20

• Time to reach TIS >=40 (first *moderate clinical improvement*)

• Percentage of participants with TIS >=40

• Change in manual muscle testing-8 (MMT8) score

• Change in Patient Global Assessment of Disease Activity (PGA)

• Change in Physician Global Assessment of Disease Activity (MDGA)

• Proportion of participants achieving target oral prednisone dosage of <=5 mg

(or equivalent)

For other secondary endpoints and exploratory endpoints please refer to the

study protocol

Study description

Background summary

IIM, also referred to as myositis, are inflammatory disorders of the skeletal muscle. This heterogeneous group of diseases includes many subtypes with varying pathologies. There is evidence that some IIM subtypes*specifically DM, IMNM, and certain other subtypes of PM (ASyS)*are likely driven by IgG autoantibodies (including myositis-specific antibodies [MSAs] and myositis-associated antibodies [MAAs]).

Many patients with IIM have persistent impairment of muscle function, which leads to difficulties in daily life activities and a low health-related quality of life. The typical treatment for IIM is high-dose glucocorticoids combined with immunosuppressive drugs. The deleterious long-term effects of corticosteroids have been well established and include osteoporosis, cataracts, and weight gain. There are no therapies approved by the United States Food and Drug Administration (FDA) or the European regulatory authorities based on results of randomized controlled trials for IMNM and PM. Only 1 licensed treatment (10% intravenous immunoglobulin [IVIg]) is available for adults with DM that was approved based on results of randomized controlled clinical trials.Given efgartigimod*s mechanism of action of reducing IgG levels, efgartigimod PH20 SC may benefit patients with these specific IIM subtypes.

Study objective

This study has been transitioned to CTIS with ID 2024-512785-33-00 check the CTIS register for the current data.

Primary objective: To evaluate the clinical improvement of efgartigimod PH20 SC treatment compared with placebo, in addition to standard of care immunomodulatory therapy.

Key secondary objectives:
• To evaluate additional measures of the efficacy of efgartigimod PH20 SC in achieving clinical response
• To evaluate the effect of efgartigimod PH20 SC on muscle strength
• To evaluate the effect of efgartigimod PH20 SC on patient and physician global assessments of disease activity
• To evaluate the steroid-sparing effect of efgartigimod PH20 SC (phase 3 stage

only)

For other secondary objectives and exploratory objectives please refer to the study protocol.

Study design

This is a randomized, double-blinded, placebo-controlled, parallel group, multicenter, operationally seamless phase 2/3 study to evaluate the efficacy, safety, tolerability, PK, PD, and immunogenicity of efgartigimod PH20 SC in adult participants with active IIM. This study consists of 2 distinct stages (a phase 2 stage and a phase 3 stage) with separate cohorts of participants.

After screening, a 24-week (phase 2) or 52-week (phase 3) treatment period follows, during which participants will be randomized to receive either efgartigimod PH20 SC 1000 mg or matching placebo (with the same concentration of rHuPH20) weekly in addition to their background treatment for IIM.
In both stages, during the treatment period, participants will receive weekly SC fixed doses of IMP (either efgartigimod PH20 SC or matching placebo) except in the last week (week 24 [phase 2] or week 52 [phase 3]) in which participants will attend the final treatment period visit. At the end of the treatment period (ie, week 24 [visit 7, phase 2] or week 52 [visit 14, phase 3]), eligible participants may enroll in the open-label extension (OLE) study ARGX-113-2011, in which all participants will be treated with efgartigimod PH20 SC. Otherwise, participants will continue a 56-day safety follow-up period.

Intervention

efgartigimod PH20 SC 1000 mg or matching placebo (with the same concentration of rHuPH20)

Study burden and risks

The potential risks associated with efgartigimod PH20 SC are justified by the anticipated benefits that may be afforded to participants with IIM in this study and considering measures implemented to minimize risks. The favorable balance between risks and anticipated efficacy/benefits supports the use of efgartigimod PH20 SC in clinical development in IIM.

Please refer to protocol section 2.3 for the full risk/benefit assessment.

Contacts

Public

argenx BV

Industriepark Zwijnaarde 7
Zwijnaarde (Ghent) B-9052
BE
Scientific
argenx BV

Industriepark Zwijnaarde 7
Zwijnaarde (Ghent) B-9052
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Ability to consent in the jurisdiction in which the study is taking place and capable of giving signed informed consent.
• A definite or probable clinical diagnosis of idiopathic inflammatory myopathy (IIM)
• One of the following medical histories:
a. Diagnosis of dermatomyositis (DM) or juvenile dermatomyositis (JDM), (age of disease onset <18 years of age). The diagnosis date for juvenile dermatomyositis should not be >5 years from the screening date.
b. Diagnosis of polymyositis (PM) (including antisynthetase syndrome (ASyS))
c. Diagnosis of immune-mediated necrotizing myopathy (IMNM)
• Diagnosed with active disease as defined by the presence of at least 1 of the following criteria:
a. Abnormal levels of at least 1 of the following enzymes: creatine kinase (CK), aldolase, LDH. aspartate aminotransaminase (AST), alanine aminotransferase (ALT), based on central laboratory results
b. Electromyography demonstrating active disease within the past 3 months

c. Active dermatomyositis (DM) skin rash
d. Muscle biopsy indicative of active idiopathic inflammatory myopathy (IIM) in the past 3 months
e. Magnetic resonance imaging within the past 3 months indicative of active inflammation
• Muscle weakness
• Receiving a permitted background treatment for idiopathic inflammatory myopathy.
• Contraceptive use consistent with local regulations, where available, for individuals participating in clinical studies. Women of childbearing potential must have a negative serum pregnancy test during screening and a negative urine pregnancy test at baseline before receiving investigational medicinal product (IMP).

The full list of inclusion criteria can be found in the protocol.

Exclusion criteria

• A clinically significant active infection at screening
• A COVID-19 polymerase chain reaction (PCR)-positive test before enrollment
• Any other known autoimmune disease that, in the investigator*s opinion, would interfere with an accurate assessment of clinical symptoms of idiopathic inflammatory myopathy (IIM) or put the patient at undue risk
• A history of malignancy unless considered cured by adequate treatment, with no evidence of recurrence for >= 3 years before the first administration of the investigational medicinal product (IMP). Adequately treated participants with the following cancers can be included at any time:
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
• Severe muscle damage
• Glucocorticoid-induced myopathy that the investigator considers the primary cause of muscle weakness or permanent weakness linked to a non-idiopathic inflammatory myopathy (IIM) cause
• Juvenile myositis (JDM) diagnosed >5 years from screening or juvenile myositis with extensive calcinosis or severe calcinosis.
• Uncontrolled interstitial lung disease or any other uncontrolled idiopathic inflammatory myopathy (IIM) manifestation that, in the opinion of the investigator, would be likely to require treatment with prohibited medication during the study
• Other inflammatory and noninflammatory myopathies: inclusion body myositis, infectious myopathy, overlap myositis, metabolic myopathies, muscle dystrophies or a family history of muscle dystrophy, drug-induced or endocrine induced myositis, and juvenile myositis (other than juvenile dermatomyositis (JDM))

• Clinically significant disease, recent major surgery or intends to have surgery during the study, or has any other condition in the opinion of the investigator that could confound the results of the study or put the patient at undue risk
• Known hypersensitivity reaction to investigational medicinal product (IMP) or 1 of its excipients
• Received a live or live-attenuated vaccine less than 4 weeks before screening.
• Positive serum test at screening for active viral infection with any of the following conditions:
a. Hepatitis B virus (HBV)
b. Hepatitis C virus (HCV)
c. HIV
• Participant has previously participated in an efgartigimod clinical trial and received at least 1 dose of investigational medicinal product (IMP).
• Participant is concurrently participating in any other clinical study, including a noninterventional study.
• Participant has a current or history (ie, within 12 months of screening) of alcohol, drug, or medication abuse.
• Participant is pregnant or lactating or intends to become pregnant during the study.
• Participant has severe renal impairment .
• Participant is institutionalized by a court or other governmental order or is in a dependent relationship with the sponsor or investigator.

The full list of exclusion criteria can be found 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:	Recruiting
Start date (anticipated):	05-03-2024
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Efgartigimod PH20
Generic name:	n/a

Ethics review

Approved WMO Date:	28-09-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-12-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-04-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-09-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	06-12-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-01-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-02-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-04-2024
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
EU-CTR	CTIS2024-512785-33-00
EudraCT	EUCTR2021-001277-23-NL
CCMO	NL80454.018.22