A phase 1, randomized, open-label, parallel group trial to investigate the pharmacodynamics, pharmacokinetics, safety, and tolerability of different single subcutaneous dose levels of Efgartigimod co administered with rHuPH20 in healthy adult male subjects

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

Summary

ID

NL-OMON48123

Source
ToetsingOnline

Brief title
Efgartigimod co-administered with rHuPH20 in healthy subjects

Condition

- Autoimmune disorders

Synonym
immune thrombocytopenia, myasthenia gravis

Research involving
Human

Sponsors and support

Primary sponsor: argenx BVBA
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Efgartigimod, PD, PK, rHuPH20

Outcome measures

Primary outcome

- To investigate the pharmacodynamics (PD) of four different subcutaneous dose levels of efgartigimod co-administered with rHuPH20 at 2,000 U/mL.

Secondary outcome

- To investigate the single-dose pharmacokinetics (PK) of four different subcutaneous dose levels of efgartigimod co-administered with rHuPH20 at 2,000 U/mL.

- To investigate the safety, tolerability, and immunogenicity of four different subcutaneous dose levels of efgartigimod co-administered with rHuPH20 at 2,000 U/mL.

- To assess the time required to administer the different volumes of efgartigimod co-administered with rHuPH20 SC.

Study description

Background summary

Efgartigimod is a new compound that may eventually be used for the treatment of autoimmune diseases such as myasthenia gravis and immune thrombocytopenia.

Autoimmune diseases are diseases where antibodies produced by the body*s immune system, attack cells of their own body.

In the autoimmune diseases myasthenia gravis, pemphigus and immune thrombocytopenia the immune system specifically produces so called IgG antibodies. In myasthenia gravis these IgG antibodies affect muscle cells so that these cannot contract anymore. This causes muscle weakness in the arms and legs, or in extreme cases it may affect. the muscles involved in breathing. In immune thrombocytopenia these antibodies attack blood platelets, which results in an increased tendency to bleed, bruise or cause a rash.
Efgartigimod promotes the break-down of these IgG antibodies so they cannot attack the body*s own cells, and is expected to improve the symptoms of these autoimmune diseases.

Study objective

The purpose of this study is to investigate the effects of the new compound efgartigimod on IgG antibodies. It will also be investigated how quickly and to what extent efgartigimod given together with rHuPH20, is absorbed and eliminated from the body and how fast it can be injected. In addition, the effect of efgartigimod on the body will be investigated.

It will also be investigated how safe efgartigimod in combination with rHuPH20 is, and how well it is tolerated when it is administered to healthy volunteers.

rHuPH20 is an enzyme that is used to temporarily improve the spreading of fluids that are injected under the skin, so it causes less swelling. It is thought to improve absorption of the study drug into the body. rHuPH20 has been co-administered with other approved drugs for this purpose.

Efgartigimod has been administered to humans before. It also has been previously tested in the laboratory and on animals. Efgartigimod will be tested at various dose levels in this study.

Study design

The study will consist of 1 period during which you will stay in the research center for 8 days (7 nights). This will be followed by 7 days during which the volunteer will visit the research center for a short visit. These short visits will take place on Day 9, 11, 15, 22, 29, 43 and 57 (the follow-up).

Efgartigimod (1 of 4 doses) together with rHuPH20 will be given as a single injection under the skin in a total volume of approximately 4.7 mL to 10.8 mL. It is anticipated that the dose can be administered in approximately 5 minutes or less.

The planned dose levels and volumes for the study are as follows:

Group Efgartigimod (+ rHuPH20*) Administered volume
1 750 mg 4.7 mL
2 1250 mg 7.7 mL
3 1750 mg 10.8 mL
4 10 mg/kg# XX mL

* The concentration of rHuPH20 (0.018 mg/ml for the administered volume) will be the same for all doses of efgartigimod.
# This means that 10 mg of efgartigimod will be administered per 1 kg of body weight, so the actual dose and volume will depend on the body weight.

Intervention

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Study burden and risks

Efgartigimod has been investigated in 4 clinical trials up to date, and was found to be well-tolerated. Efgartigimod has been administered to healthy volunteers intravenously in doses up to 50 mg/kg. A few subjects treated with doses of 25 mg/kg or 50 mg/kg showed abnormalities in white blood cell counts, but all subjects recovered within 2 to 4 days after stopping with the treatment. Also, some subjects showed increased C-reactive protein levels, but these levels went back to normal within 3 to 6 days after stopping with the treatment, and there were no signs of possible infections.

Patients with myasthenia gravis who received 10 mg/kg efgartigimod intravenously for 4 weeks, showed a decrease in IgG antibodies and improvement

of symptoms, and treatment with efgartigimod was well tolerated. The most common side effect was headache, reported in some patients treated with efgartigimod but also common in patients who received placebo.

In patients with immune thrombocytopenia, treatment with 5 or 10 mg/kg intravenous efgartigimod for 4 weeks resulted in a decrease in IgG antibodies and an increase in blood platelets (the blood cells that are destroyed by the disease). Treatment with efgartigimod was well tolerated. The few observed side effects were petechiae (tiny red patches on the skin or inside the mouth or eyelids), high blood pressure, and vomiting.

The study compound may also have side effects that are still unknown. If during the study more information becomes available regarding adverse events that may be related to the study compound, the responsible doctor will inform the volunteer about this.

rHuPH20 is a permeation (diffusion) enhancer with a well-characterized nonclinical and clinical safety profile that allows the rapid delivery of large volumes of fluid and/or co-administered drugs under the skin (subcutaneously). In clinical studies, the subcutaneous administration of rHuPH20 in combination with other substances was well-tolerated. Adverse effects may include mild and short-lived injection site reactions, such as redness, swelling, pain and itching. Adverse events in these trials were related to the co-administered drug or have been associated with the rapid introduction of a relatively large volume of fluid in the subcutaneous space. rHuPH20 is co-formulated or co-administered with several products in the US and EU (e.g., Herceptin® SC, MabThera® SC, HyQvia®).

Possible discomforts due to procedures

Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.

A subcutaneous injection may be painful and may cause mild swelling

In total, we will take up to 180 milliliters of blood from the volunteer. This amount does not cause any problems in adults.

To make a heart tracing, electrodes will be pasted at specific locations on your arms, chest and legs. Prolonged use of these electrodes can cause skin irritation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- healthy male subjects
- 18-70 yrs, inclusive
- BMI: 18.0-30.0 kg/m2, inclusive and with a body weight of at least 50 kg and no more than 100 kg prior to dosing.

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. Previous participation in clinical trials with efgartigimod (ARGX-113) and/or any products co-formulated with rHuPH20. Significant blood loss (including blood donation >500 mL) or transfusion of any blood product within 12 weeks prior to the IMP administration or scheduled transfusion within 4 weeks after the end of the trial.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-07-2019
Enrollment:	32
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Efgartigimod
Generic name:	ARGX-113

Ethics review

Approved WMO Date:	17-06-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-06-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2019-002102-40-NL
CCMO	NL70427.056.19