A phase 1, randomized, open-label, parallel-group study to compare the pharmacodynamics, pharmacokinetics, safety, and tolerability of multiple intravenous infusions of efgartigimod with multiple subcutaneous injections of efgartigimod PH20 SC in healthy subjects.

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

Summary

ID

NL-OMON49985

Source
ToetsingOnline

Brief title
Comparing PK, PD, safety of efgartigimod SC and IV.

Condition

- Autoimmune disorders

Synonym
Auto immune diseases

Research involving
Human

Sponsors and support

Primary sponsor: argenx BV
Source(s) of monetary or material Support: Pharmaceutical/Biotechnological Industry

Intervention

Keyword: autoimmune diseases, efgartigimod, PD, PK

Outcome measures

Primary outcome

To demonstrate that the pharmacodynamic (PD) effect of 4 once weekly subcutaneous (SC) injections of 1000 mg efgartigimod PH20 SC is noninferior to that of 4 once weekly intravenous infusions (IV) of efgartigimod at a dose of 10 mg/kg by comparing the percentage reduction in total IgG levels after 4 weeks (day 29), ie, one week after the 4th administration, using a noninferiority margin of 10%.

Secondary outcome

To further compare the PD effect of efgartigimod IV and efgartigimod PH20 SC over time

- To evaluate the pharmacokinetics (PK) of efgartigimod IV and efgartigimod PH20 SC

- To evaluate the safety, tolerability, and immunogenicity of efgartigimod IV and of efgartigimod PH20 SC

Study description

Background summary

The actual study will consist of 4 periods during which the volunteer will stay in the research center for 2, 2, 2, and 7 days (1, 1, 1, and 6 nights) respectively. This will be followed by 4 days during which you will visit the research center for a short visit. These short visits will take place on Day 29, 36, 50, 64 and 78.

Efgartigimod is a new compound that may potentially be used for the treatment of autoimmune diseases such as myasthenia gravis, pemphigus, and immune thrombocytopenia. Autoimmune diseases are diseases where antibodies produced by the body*s immune system attack the body*s own cells. The immune system is the body*s defense system that protects against invading pathogens.
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 (the cells in the blood that are involved in blood clotting), which results in an increased tendency to bleed and bruise. In pemphigus the IgG antibodies attack the *glue* (desmoglein) that holds the skin cells together, causing blisters. Efgartigimod promotes the break-down of these IgG antibodies so they can no longer 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 compare administration of efgartigimod under the skin (subcutaneously/SC) to administration directly into a blood vessel (intravenously/IV). This is being studied to compare if subcutaneous injection is equally safe and effective as an intravenous injection.

The effect of the different types of administration of efgartigimod on the presence of immunoglobulins IgG in your blood will be investigated (this is called pharmacodynamics). It will also be investigated how quickly and to what extend efgartigimod is absorbed and eliminated from the body.

We will also investigate how safe the compound efgartigimod is and how well it is tolerated when it is administered to healthy volunteers.

Efgartigimod has been administered to humans before. It has also been previously tested in the laboratory and on animals. Efgartigimod PH20 SC will

be tested at a fixed dose, whereas efgartigimod IV will be dosed proportionally to your weight.

When efgartigimod PH20 is given as a subcutaneous injection, it is administered in combination with rHuPH20. rHuPH20 is a substance 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 the uptake of the study compound in the body. rHuPH20 has been given with other approved drugs for this purpose before.

This study will be performed in up to 54 healthy male and female volunteers.

Study design

Efgartigimod will be given as either an intravenous infusion (solution of the compound that will be administered directly in a blood vessel) or as an injection under the skin (subcutaneous).

Over the course of the study, the volunteer will receive 4 doses. The volunteer will receive 1 dose every 7 days.

There are 2 possible treatments:
• 10 mg/kg* efgartigimod directly into a blood vessel (intravenously) as a 1-hour infusion
• 1000 mg efgartigimod combined with 2000 U/mL rHuPH20 as a single injection under the skin (subcutaneously)
* This means that 10 mg of efgartigimod will be administered per 1 kg of body weight, so the actual dose will depend on the volunteers body weight

The volunteer will receive either 4 doses intravenously or 4 doses subcutaneously. the volunteer will be randomly assigned to one of the treatments. Neither you nor the responsible study doctor decide which treatment you receive.

Intervention

Efgartigimod will be given as either an intravenous infusion (solution of the compound that will be administered directly in a blood vessel) or as an injection under the skin (subcutaneous).

Study burden and risks

The study compound may cause side effects.

Taking part in a clinical study involves some risks and possible discomfort.
All medications can cause side effects (unwanted or unpleasant effects) in some people. Not all of the side effects that the study compound can cause may be

known at this time.

Efgartigimod has been investigated in 3 healthy volunteer clinical trials and was found to be well-tolerated. Efgartigimod has been administered to healthy volunteers intravenously (directly into a blood vessel) 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 they went back to normal within 2 to 4 days after stopping with the treatment. Also, some subjects showed increased C-reactive protein levels (which is a marker of inflammation/infection), but these levels went back to normal within 3 to 6 days after stopping with the treatment, and there were no signs of infection or inflammation. Efgartigimod has been administered to healthy volunteers subcutaneous (directly into skin) in doses up to 10 mg/kg and was found to be well-tolerated.

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 and safe. The most common side effects were headache, decreases in white blood cell counts, increases in levels of a blood test marker for inflammation (C-reactive protein levels), injection site bruise, fatigue, runny nose/common cold, and mouth/throat discomfort. Some of the observed side effects were observed in the placebo group (a dummy medicine that mimics the study compound, but with no active ingredient), as well as in doses higher than the dose that will be used in this study.

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 found to be safe and 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 can also cause an immune reaction. This can be fever, itching, rashes and, in severe cases, an allergic/anaphylactic reaction.

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 (subcutaneous). 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®). The study compound may also have side effects that are

still unknown.

Contacts

Public
argenx BV

Industriepark Zwijnaarde 7
Zwijnaarde 9052
BE
Scientific
argenx BV

Industriepark Zwijnaarde 7
Zwijnaarde 9052
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy, adult males and females of non-childbearing potential between 18-65 years of age, inclusively, with a BMI between 18-30 kg/m2, and body weight between 50-100 kg.

Exclusion criteria

1. The subject has previously participated in clinical studies with

efgartigimod (ARGX-113).
2. The subject has a known hypersensitivity to one of the components in the IMP, or a history of severe allergic or anaphylactic reactions, in the opinion of the investigator.
3. The subject tests positively at screening for any of the following conditions:
a. an active hepatitis B infection (acute or chronic) at screening as determined by HepB serology
b. Hepatitis C Virus (HCV): serology positive for HCV-Ab
c. HIV positive serology
4. Subjects with clinically significant active or chronic uncontrolled bacterial, viral, or fungal infection at screening.
5. Subjects with clinical evidence of other significant serious diseases, subjects who underwent a recent major surgery, or any other reason which could confound the results of the trial or put the subject at undue risk.
For more exclusion criteria see Protocol.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	18-08-2020
Enrollment:	54
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	efgartigimod
Generic name:	n.a.

Ethics review

Approved WMO Date:	09-03-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-03-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-08-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-10-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-01-2021
Application type:	Amendment
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	EUCTR2019-004985-17-NL
CCMO	NL72946.056.20

Study results

Date completed: 11-02-2021

Results posted: 30-12-2021

First publication
14-09-2021