A Randomized, Open-label, Parallel Group Study to Compare the Pharmacokinetics, Pharmacodynamics and Safety and Tolerability of a Subcutaneous Formulation with an Intravenous Formulation of ARGX-113 in Healthy Male Subjects.

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To compare the pharmacokinetics, pharmacodynamics, safety and tolerability of a subcutaneous formulation with an intravenous formulation of ARGX-113 in healthy male subjects

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

Summary

ID

NL-OMON46383

Source
ToetsingOnline

Brief title
ARGX-113-1702 (CS0287)

Condition

- Autoimmune disorders

Synonym
myasthenia gravis, primairy immunne thrombocytopeny

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Pharmacodynamics, Pharmacokinetics, Phase 1, Safety

Outcome measures

Primary outcome

Primary endpoint:

Primary pharmacokinetic parameter is AUC0-inf.

Secondary outcome

Secondary endpoints:

* Safety parameters include vital signs, ECG and (S)AEs, hematology, blood chemistry and urinalysis.

* Pharmacodynamic parameters are Total Immunoglobulin G (IgG) and IgG subtype (IgG 1, IgG 2, IgG 3, and IgG 4) levels and IgA and IgM levels.

* Secondary pharmacokinetic parameters are Cmax, Tmax, AUC0-t, AUC0-72, AUC0-96, AUC0-336, t1/2, CL, Vz, Vz/F and CL/F.

* Immunogenicity parameter is the individual serum titer of ADA directed against ARGX- 113.

Study description

Background summary

ARGX-113 is being developed as a treatment for so-called autoimmune diseases, diseases where the immune system of the patient does not recognize cells or molecules of its own body and attacks them with antibodies. This response can damage different parts of the body, including skin and muscles. ARGX-113 should enhance the removal of the antibodies, thus preventing these antibodies from damaging the bodies of patients with autoimmune diseases.

The current study is aimed at evaluating a new way of administering ARGX-113, i.e. injection under the skin. To this end, one group of volunteers will receive the study drug directly into the blood by infusion. In a second group of volunteers, ARGX-113 will be injected under the skin. A third group of volunteers will first receive two doses of the study drug into the blood stream and will then receive weekly injections under the skin for several weeks. A fourth group of volunteers will receive 4 doses of study drug directy into the blood by infusion.

Study objective

To compare the pharmacokinetics, pharmacodynamics, safety and tolerability of a subcutaneous formulation with an intravenous formulation of ARGX-113 in healthy male subjects

Study design

A Randomized, Open-label, Parallel Group Study

Intervention

After assessing eligibility during a 3*week screening period, approximately 32 subjects will participate in the study. Subjects will come to the study center on the day before first administration (Day -1) of the study drug to (re)confirm eligibility.
For Treatment A and B, subjects will receive ARGX-113 on Day 1 either as a single dose via an i.v. infusion over 2 hours (Treatment A) or as a single dose consisting of multiple subcutaneous injections (Treatment B). Blood samples for determination of ARGX-113 will be collected pre-dose and at selected time points up to Day 43 (± 2 days) post-dose. Blood samples to determine total IgG, IgG subtypes (IgG 1, IgG 2, IgG 3, and IgG 4), IgA and IgM will be collected pre-dose and at selected time-points up to EOS on Day 57 (±2 days). Blood samples to determine the individual plasma titer of anti-drug antibodies (ADA) directed against ARGX-113 will be collected pre-dose and at selected time points up to EOS. Subjects will be admitted to the clinic on Day -1 and will stay until Day 3. Subjects will return to the clinic for at least 10 more ambulant visits up to Day 43 (± 2 days) and an EOS visit on Day 57 (± 2 days).

For Treatment C, subjects will receive ARGX-113 as an i.v. infusion over 2 hours on Day 1 and Day 4 and as two subcutaneous injections per day on Days 8, 15, 22, 29, 36, 43, 50, and 57. Blood samples for determination of ARGX-113 will be collected pre*dose and at selected time points up to Day 99 (±2) post* dose. Blood samples to determine total IgG, IgG subtypes (IgG 1, IgG 2, IgG 3, and IgG 4), IgA and IgM will be collected pre-dose and at selected time-points up to EOS on Day 113 (±2 days). Blood samples to determine the individual plasma titer of ADA directed against ARGX-113 will be collected pre-dose and at selected time points up to EOS. Subjects will be admitted to the clinic 3 times (from Day -1 to Day 1, from Day 7 to Day 8, and from Day 56 to Day 58). Subjects will return to the clinic for at least 18 ambulant visits up to Day 99 (± 2 days) and an EOS visit on Day 113 (± 2 days).
Adverse events (AEs) will be recorded throughout the study for all treatment groups.
For Treatment D, subjects will receive ARGX-113 as an i.v. infusion over 1 hour on Day 1, 8, 15 and 22. Blood samples for determination of ARGX-113 will be collected pre*dose and at selected time points up to Day 64 (±2 days) post* dose. Blood samples to determine total IgG, IgG subtypes (IgG 1, IgG 2, IgG 3, and IgG 4), IgA and IgM will be collected pre-dose and at selected time-points up to EOS on Day 78 (±2 days). Blood samples to determine the individual serum titer of ADA directed against ARGX-113 will be collected pre-dose and at selected time points up to EOS. Subjects will be admitted to the clinic 2 times (from Day -1 to Day 2 and from Day 21 to Day 23). Subjects will return to the clinic for at least 13 ambulant visits up to Day 64 (± 2 days) and an EOS visit on Day 78 (± 2 days).

Study burden and risks

The dosage levels of the study drug are based on a previous clinical trial conducted by the sponsor and on ongoing studies in patients with the study medication. The risk to health at the chosen dose is limited, but the patients may experience any of the side effects in the ICF or symptoms that have not been reported before.

Volunteers health is closely monitored during the study to minimize these risks. If the volunteers experience side effects, the investigator will treat them where necessary. If new information is available on the safety of the study medication, the volunteers are informed as soon as possible.

The blood collection procedure is not dangerous.

Contacts

Public

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Male, between 18-55 years of age, inclusive, on the day of signing the Informed Consent Form (ICF).
2. Body mass index (BMI) between 18-30 kg/m2, inclusive with a weight of at least 50 kg and no more than 100 kg, inclusive (only for subjects receiving Treatment A, B and D) at Screening and prior to first dosing. For subjects in Treatment subset C1 a body weight between 50 and 70 kg (inclusive) and for subjects in Treatment subset C2 a body weight between 80 and 100 kg (inclusive) at Screening and prior to first dosing.
3. Willingness and ability to understand the purpose and risks of the study and provide signed and dated informed consent prior to any procedures and be available for all study visits.
4. Non-vasectomized male subjects having a female partner of childbearing potential must agree to the use of an effective method of contraception until 90 days after the last administration of study drug.
5. Subjects have to agree not to donate sperm until 90 days after the last administration of study drug.
6. Judged by the investigator to be in good health based upon the results of a medical

history, physical examination, vital signs, 12-lead electrocardiogram (ECG), and laboratory findings.
7. Agree to discontinue and refrain from intake of all medications (including over-the-counter and/or prescription medication, dietary supplements, nutraceuticals, vitamins and/or herbal supplements such as Ginkgo biloba or St John*s wort), except occasional paracetamol use (maximum dose of 2 g/day and maximum of 10 g/2 weeks), at least 2 weeks prior to the first study drug administration. In addition, subjects must agree to the prohibitions and restrictions for this study.
8. Subject is a non-smoker, and not using any nicotine-containing products. A non-smoker is defined as an individual who has abstained from smoking for at least 1 year prior to Screening.
9. Negative urine drug screen (amphetamines, barbiturates, benzodiazepines, cannabis, cocaine, opiates, methadone, and tricyclic antidepressants) at Screening and Day -1.
10. Negative alcohol breath test at Screening and Day-1.
11. Oral body temperature < 38.0°C at Screening and prior to dosing on Day 1.

Exclusion criteria

1. Known hypersensitivity to study drug ingredients or a significant allergic reaction to any drug as determined by the investigator, such as anaphylaxis requiring hospitalization.
2. Active infection; a recent serious infection (i.e., requiring injectable antimicrobial therapy or hospitalization) within the 8 weeks prior to screening.
History or active infection with viral infection with human immunodeficiency virus (seropositivity to HIV-1 or -2 antibodies).
Active or chronic viral infection with hepatitis B virus (HBV) serologically defined as: HBsAg positive or (Anti-HBs negative and anti-HBc positive.
Active infection with hepatitis C virus (HCV) or known seropositivity.
Subjects must have a negative TB Quantiferon test at screening.
Subjects with an undetermined Quantiferon TB result will be allowed one retest, if not negative on retesting, the subject will be excluded
3. Subjects with known clinically relevant immunological disorders.
4. History of severe allergic or anaphylactic reactions.
5. Known history or any symptom of clinically significant illness in the 6 months before the first study drug administration.
6. Presence or having sequelae of gastrointestinal, liver, kidney or other conditions known to interfere with the absorption, distribution, metabolism, or excretion of drugs.
7. History of malignancy within the past 5 years (except for basal cell carcinoma of the skin that has been treated with no evidence of recurrence).
8. Clinically relevant abnormalities detected on ECG regarding either rhythm or conduction (e.g., QTcF > 450 ms [millisecond], or a known long QT syndrome). A first degree heart block or sinus arrhythmia will not be considered as a significant abnormality.
9. Clinically relevant abnormalities detected on vital signs prior to first dosing.
10. Significant blood loss (including blood donation [> 500 mL]), or had a transfusion of any blood product within 12 weeks prior to the initial study drug administration or plan one within 4 weeks after the end of the study.

11. Treatment with any drug known to have a well-defined potential for toxicity to a major organ in the last 3 months preceding the initial study drug administration.
12. The subject has a history of consuming more than 21 units of alcoholic beverages per week or has a history of alcoholism or drug/chemical/substance abuse within past 2 years prior to screening (Note: one unit = 330 mL of beer, 110 mL of wine or 28 mL of spirits).
13. Consumption of a large quantity of coffee, tea (> 6 cups per day) or equivalent.
14. Concurrent participation or participation within 90 days prior to the initial study drug administration in a drug/device or biologic investigational research study.
15. Administration of a vaccine within 60 days prior to initial study drug administration.
16. Administration of any systemic immunosuppressant agent within 6 months prior to initial study drug administration.
17. Administration of any systemic steroid within 2 months prior to initial study drug administration.
18. Administration of an injectable drug within 30 days prior to the initial study drug administration.
19. Investigator or any sub-investigator, research assistant, pharmacist, study coordinator, or other staff or relative thereof who is directly involved in the conduct of the study.
20. Any condition or circumstances that in the opinion of the investigator may make a subject unlikely or unable to complete the study or comply with study procedures and requirements.
21. Unsuitable vein for infusion and/or blood sampling.

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):	03-10-2017
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	03-10-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-10-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-05-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-06-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-07-2018
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	EUCTR2017-003335-11-NL
CCMO	NL63279.056.17