A First-in-Human, Randomized, Double-Blinded, Placebo-Controlled Trial in Healthy Subjects to Investigate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Immunogenicity of Single and Multiple Ascending Intravenous Dose Levels of ARGX-117 and Subcutaneous Dose Levels of ARGX-117 Co-Mixed with Recombinant Human Hyaluronidase PH20

Published: 20-02-2020
Last updated: 17-01-2025

This is the first clinical study in which ARGX 117 is administered to humans. The purpose of this study is to investigate how safe the new compound ARGX-117 is and how well it is tolerated when it is administered to healthy volunteers. It will also...

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

Summary

ID

NL-OMON52853

Source
ToetsingOnline

Brief title
SAD and MAD study with IV and SC doses of ARGX-117

Condition

- Autoimmune disorders

Synonym
autoimmune diseases

Research involving
Human

Sponsors and support

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

Intervention

Keyword: ARGX-117, PD, PK, SAD/MAD

Outcome measures

Primary outcome

Part A (single ascending dose [SAD]): To evaluate the safety and tolerability of single ascending intravenous (IV) doses of ARGX-117 and subcutaneous (SC) doses of ARGX-117 co-mixed with recombinant human hyaluronidase PH20 (rHuPH20) in healthy adult subjects, compared to placebo.

Part B (multiple ascending dose [MAD]): To evaluate the safety and tolerability of multiple ascending IV doses of ARGX-117 and SC doses of ARGX-117 co-mixed with rHuPH20 in healthy adult subjects, compared to placebo.

Secondary outcome

Part A (SAD): To investigate the pharmacokinetics (PK), pharmacodynamic (PD), and immunogenicity effects of single ascending IV doses of ARGX-117 and SC doses of ARGX-117 co-mixed with rHuPH20 in healthy adult subjects.

Part B (MAD): To investigate the PK, PD, and immunogenicity effects of multiple

ascending IV doses of ARGX-117 and SC doses of ARGX-117 co-mixed with rHuPH20

in healthy adult subjects.

Study description

Background summary

ARGX-117 is a new compound that may be used for the treatment of diseases that are related to the so called complement system. The complement system is part of the immune system.

ARGX-117 is being developed to rapidly reduce tissue inflammation by inhibiting the complement system. The complement system is part of the innate immune system, which is not adaptable and does not change during an individual's lifetime. Overactivation of the complement system can lead to tissue destruction and organ damage. ARGX-117 inhibits a protein that plays an important role in the complement system.

This is the first clinical study in which ARGX-117 is administered to humans. It has been previously tested in the laboratory and on laboratory animals.

Study objective

This is the first clinical study in which ARGX 117 is administered to humans. The purpose of this study is to investigate how safe the new compound ARGX-117 is and how well it is tolerated when it is administered to healthy volunteers. It will also be investigated how quickly and to what extent ARGX 117 is absorbed and eliminated from the body (this is called pharmacokinetics). In addition, the effect of ARGX 117 on blocking of the complement system will be investigated (this is called pharmacodynamics).

Furthermore, the effect of the volunteers genetic information on their body*s response to ARGX-117 will be investigated. This part of the study is not mandatory.

This study will be performed in up to 112 healthy male or female volunteers. The study will be performed in 2 parts, Part A and Part B.

Part A of the study will consist of up to 9 groups of 8 volunteers each. Part B of the study will consist of up to 5 groups of 8 volunteers each.

ARGX-117 will be tested at various dose levels and via different routes of administration. The effects of ARGX 117 will be compared to the effects of a placebo. A placebo is a medicine without any active ingredient.

Study design

Part A:
The actual study will consist of 1 period during which the volunteer will stay in the research center for 10 days (9 nights). This will be followed by 10 short visits to the research center. These short visits will take place at 10:30 h in the morning on Days 15, 22, 29, 36, 50,64, 92, 120, 148 , and 204. Additionally, there is a follow-up visit on Day 260.

Day 1 is the day of administration of the study compound. The volunteer is expected at the research center at 14:00 pm 2 days prior to the day of administration of the study compound, so on Day -2. The volunteer will leave the research center on Day 8 of the study.

In Groups 1 to 8, the volunteer will receive ARGX-117 or placebo as a 2-hour intravenous infusion or the volunteer will receive ARGX-117 or placebo in combination with rHuPH20 as an injection under the skin (subcutaneous) or infusion under the skin over approximately1 hour. Group 9 is an optional group. Based on results in the preceding groups, it will be determined whether ARGX 117 or placebo isadministered intravenously or subcutaneously in Group 9.

For safety reasons in Groups 1 and 2, initially 3 volunteers will receive the study compound. Two of these volunteers will receive ARGX-117, and 1 volunteer will receive placebo. These 3 volunteers will be dosed one by one, with 24 hours between each dosing, to monitor the safety and tolerability of the study compound in each volunteer. If there are no concerns about the safety and tolerability at least 24hours after 3rd volunteer has been dosed, then the remaining 5 volunteers (4 will receive ARGX-117 and 1 will receive placebo) in thatgroup will receive the study compound.

In all other groups, initially 2 volunteers will receive the study compound in each group. One volunteer will receive ARGX-117, and 1 volunteer will receive placebo. After administration, the safety and tolerability of the study compound in these 2 volunteers will be closelymonitored. If there are no concerns about the safety and tolerability 24 hours after administration, then the remaining 6 volunteers (5 willreceive ARGX-117 and 1 will receive placebo) in that group will receive the study compound.

Volunteer will be tested for the presence of coronavirus upon admission to the research center. Until the test results are available, volunteer will be separated from other participants and only have very limited contact with study staff. This is to avoid virus spread from potentially infected participants to other participants or to the study staff because, until the results are

available, it is not certain whether volunteer is infected or not and can thus potentially infect others. The test results will be available within one hour. If the volunteer test positive for coronavirus, he/she cannot participate in the study.

The coronavirus test will be done at the following timepoints:
•Day -2 (admission to the research center)
•Day -1
•Day 2
•Day 260 (follow-up visit)

Part B:
For Group 1, 4 and 5 the actual study will consist of 3 periods during which the volunteer will stay in the research center first for 11 days (10nights), then for 4 days (3 nights), and then for 10 days (9 nights). This will be followed by 11 short visits to the research center. These short visits will take place at 10:30 h in the morning on Days 36, 43, 50, 57, 64, 78, 92, 120, 148, 176, and 232. Additionally, there is a follow-up visit on Day 288.

Day 1 is the first day of administration of the study compound. The volunteer is expected at the research center at 14:00 h in the afternoon two days prior to the first day of administration of the study compound, so on Day -2. After the second administration of the study compound on Day 8, the volunteer will leave the research center on Day 9 of the study. Then the volunteer will return in the afternoon of Day 13 for the third administration of the study compound on Day 15 and the volunteer will leave on Day 16. The third period will be from Day 20 to Day 29, with the fourth administration of the study compound on Day 22.

For Group 2 and 3, the actual study will consist of 2 periods during which the volunteer will stay in the research center first for 17 days(16 nights) and then for 10 days (9 nights). This will be followed by 11 short visits to the research center. These short visits will take place at 10:30 h in the morning on Days 36, 43, 50, 57, 64, 78, 92, 120, 148, 176, and 232. Additionally, there is a follow-up visit on Day288.

Day 1 is the first day of administration of the study compound. The volunteer is expected at the research center at 14:00 pm 2 days prior to the first day of administration of the study compound, so on Day -2. After the second administration of the study compound on Day 8,the volunteer will leave the research center on Day 15 of the study. Then the volunteer will return in the afternoon of Day 20 for the third administration of the study compound on Day 22, after which the volunteer will leave again on Day 29.

In Group 1: the volunteer will receive ARGX-117 or placebo 4 times, with at least 1 week between each administration.
In Group 2 and 3: the volunteer will receive ARGX-117 or placebo 3 times, with

at least 1 week between each administration.
In Group 4 and 5: the volunteer will receive ARGX 117 or placebo 4 times in combination with rHuPH20 as an injection under the skin

The starting dose and the time between each administration will be confirmed after evaluation of the results in Part A.
Volunteer will be tested for the presence of coronavirus upon admission to the research center. Until the test results are available, volunteer will be separated from other participants and only have very limited contact with study staff. This is to avoid virus spread from potentially infected participants to other participants or to the study staff because, until the results are available, it is not certain whether volunteer is infected or not and can thus potentially infect others. The test results will be available within one hour.
If volunteer test positive for coronavirus, he/she cannot participate in the study.

The coronavirus test will be done at the following timepoints:
Group 1, 4 and 5: the coronavirus test is performed upon entry to the research center on Day -2, 13, 20, and 288 (follow-up visit), and also during the volunteers stay in the research center on Day -1, 2, 14, 16, 21 and 23.

Group 2, and 3:
Day -2, -1, 2, 20, 21, 23, and 288

Intervention

Part A:
In Groups 1 to 8, ARGX-117 or placebo will be given as a 2-hour intravenous infusion or ARGX-117 or placebo will be given in combination with rHuPH20 will as an injection under the skin (subcutaneous) or infusion under the skin over approximately 1 hour. Group 9 is an optional group. Based on results in the preceding groups, it will be determined whether ARGX-117 or placebo is administered intravenously or subcutaneously in Group 9.

Group Study compound Dose# Route of administration
1 ARGX-117 or placebo 0.1 mg/kg Intravenous
2 ARGX-117 or placebo 0.5 mg/kg Intravenous
3 ARGX-117 or placebo 2.5 mg/kg Intravenous
4 ARGX-117 or placebo 10 mg/kg Intravenous
5 ARGX-117 or placebo 30 mg/kg Intravenous
6 ARGX-117 or placebo 60 mg/kg Intravenous
7 ARGX-117 or placebo 60 mg/kg Subcutaneous
8 ARGX-117 + rHuPH20 or
Placebo + rHuPH20 80 mg/kg Intravenous
9 ARGX-117 (+ rHuPH20) or
Placebo (+ rHuPH20) 15mg/kg subcutaneous

Part B:
In Group 1: the volunteer will receive ARGX-117 or placebo 4 times, with at least 1 week between each administration.
In Group 2 and 3: the volunteer will receive ARGX-117 or placebo 3 times, with at least 1 week between each administration.
In Group 4 and 5: the volunteer will receive ARGX 117 or placebo 4 times in combination with rHuPH20 as an injection under the skin

Group Day Study compound Dose# Route of administration
1 1 ARGX-117 or placebo 10 mg/kg Intravenous
8 10 mg/kg
15 10 mg/kg
22 10 mg/kg.

2 1 ARGX-117 or placebo 60 mg/kg Intravenous
8 10 mg/kg
22 10 mg/kg.

3 1 ARGX-117 or placebo 10 mg/kg Intravenous.
8 ARGX-117 or placebo 50 mg/kg Intravenous.
22 ARGX-117 or Placebo 20 mg/kg Intravenous.

4 1 ARGX-117 + rHuPH20 15mg/kg Subcutaneous.
or Placebo + rHuPH20
8 ARGX-117 + rHuPH20 15mg/kg
Subcutaneous.
or Placebo + rHuPH20
15 ARGX-117 + rHuPH20
or Placebo + rHuPH20 15 mg/kg Subcutaneous.
29 ARGX-117 + rHuPH20
or Placebo + rHuPH20 15 mg/kg
Subcutaneous.

5 1 ARGX-117 PH20 or 1200mg
Subcutaneous.
Placebo PH20
8 ARGX-117 PH20 or 1200mg
Subcutaneous.
Placebo PH20
15 ARGX-117 PH20 or 1200mg
Subcutaneous.
Placebo PH20
22 ARGX-117 PH20 or 1200mg
Subcutaneous.
Placebo PH20

Study burden and risks

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

In total, we will take approximately 677 milliliters (mL) of blood from you.

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

Samples for the coronavirus test will be taken from the back of the nose and throat using swabs. Taking the samples only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the throat may cause the volunteer to gag. When the sample is taken from the back of the nose, the volunteer may experience a stinging sensation and the eyes may become watery.

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)

Inclusion criteria

1. The subject is between 18-65 years of age, inclusive, at the time the informed consent form is signed.
2. The subject is either male or female of non-childbearing potential. Females in the following categories are considered a woman of non-childbearing potential:
a. Postmenopausal female: A postmenopausal state is defined as continuous amenorrhea for at least 1 year without an alternative medical cause and a follicle-stimulating hormone (FSH) measurement of >40 IU/L. A historical pretreatment FSH measurement of >40 IU/L is accepted as proof of a postmenopausal state for subjects on hormone replacement therapy.
b. Surgically sterile female: women who have had a documented permanent sterilization procedure (ie, hysterectomy, bilateral salpingectomy, or bilateral oophorectomy).
3. Female subjects must have a negative serum pregnancy test on day -1 before IMP can be administered.
4. The subject has a body mass index (BMI) within the range 18-30 kg/m2 and body weight 50-100 kg (inclusive) before IMP administration.
5. The subject is able to understand the requirements of the trial and provide written informed consent (including consent for the use and disclosure of research-related health information) and is willing and able to comply with the trial protocol procedures (including the required trial visits).
Further criteria apply.

Exclusion criteria

1. The subject has a known hypersensitivity to one of the components of the IMP, or, in the opinion of the investigator, a history of a significant allergic reaction to any drug.
2. The subject has previously participated in a clinical trial with efgartigimod and was administered an IMP.
3. The subject has a positive serum test at screening for an active viral infection with any of the following conditions:
a. Hepatitis B virus (HBV) that is indicative of an acute or chronic infection
b. Hepatitis C virus (HCV) based on HCV antibody assay
c. Human immunodeficiency virus (HIV)
4. The subject tests positively at screening for SLE as determined by the SLE test panel.

5. The subject has a known family history of SLE.
Further criteria apply.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	10-03-2020
Enrollment:	112
Type:	Actual

Ethics review

Approved WMO Date:	20-02-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-03-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-06-2020

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-08-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-08-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-01-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-01-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	12-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-12-2022
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	EUCTR2019-004986-42-NL
ClinicalTrials.gov	NCT04532125
CCMO	NL72813.056.20

Study results

Date completed:	26-08-2022
Results posted:	08-06-2023

First publication
11-05-2023