A Randomized, Open-label, Placebo-Controlled, Parallel-Group Study to Evaluate the Immune System's Response to the Polyvalent Pneumococcal Vaccine (PNEUMOVAX 23) in Healthy Participants Receiving Intravenous Efgartigimod or Placebo.

Published: 21-10-2021
Last updated: 05-04-2024

The purpose of this study is to investigate the effect of the study compound efgartigimod on the immune system's response to vaccination with Pneumovax 23. We also investigate how safe efgartigimod is and how well it is tolerated when it is...

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

Summary

ID

NL-OMON50337

Source
ToetsingOnline

Brief title
Immune system response to PNEUMOVAX 23 with efgartigimod IV

Condition

- Autoimmune disorders

Synonym
auto immune diseases, disease in which the immune system attacks its own body

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Autoimmune diseases, Efgartigimod, Pneumococcal Vaccine

Outcome measures

Primary outcome

To evaluate the humoral immune response to the PNEUMOVAX 23 vaccine in healthy

participants receiving efgartigimod intravenously (IV)

Secondary outcome

- To evaluate the safety and tolerability of efgartigimod IV in healthy

participants vaccinated with PNEUMOVAX 23

Study description

Background summary

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. It is expected to improve the symptoms of these autoimmune diseases

In this study we will investigate to what extent the study compound affects the immune system*s response (eg, IgG levels to a vaccine. This will be tested with the pneumococcal vaccine Pneumovax 23. It protects against pneumococci infection. The pneumococcus is a bacterium that can for example cause pneumonia. If this bacterium enters the bloodstream or nervous system, people can contract meningitis from it. Vaccination is the best protection against pneumococcal disease. Vaccination with Pneumovax 23 normally will result in an increase of IgG antibodies against pneumococci and this response could be impacted by Efgartigimod as it promotes the breakdown of all IgG antibodies.

Study objective

The purpose of this study is to investigate the effect of the study compound efgartigimod on the immune system's response to vaccination with Pneumovax 23.

We also investigate how safe efgartigimod is and how well it is tolerated when it is used by healthy participants. In addition, we look at the presence of immunoglobulins IgG (antibodies) in your blood (this is called pharmacodynamics). Please see Section 3.0 for more information on IgG.

We compare the effects of efgartigimod with the effects of a placebo. A placebo is a compound without any active ingredient. Please note that when the term *study compound* is used in this document, we mean efgartigimod, placebo, or both.

Efgartigimod has been administered to humans before (see Section 6.0 for an overview). It has also been previously tested in the laboratory and on animals

Pneumovax 23 is the latest vaccine against pneumococci infection and is already approved for use in humans.

Study design

The examination lasts a maximum of 12 weeks from the inspection to the follow-up check.

We first want to know if the volunteer is suitable to participate. The researcher will first discuss the ICF document with the volunteer. When the volunteer decides to participate in the study, the researcher will sign this document together with the volunteer.

The researcher then performs the examination.

We test female participants for pregnancy. Female participants cannot participate in the study if they are pregnant or breastfeeding.

It is also possible that a volunteer is healthy, but is not suitable to participate. For example, because the volunteer is too heavy or too light according to the requirements of the study.

For the research it is necessary that the volunteer stays in the research center for 4 periods of 2 days (1 night). After this there are 4 more visits to the research center. These visits are on Day 36, 50 and 64, with an additional visit on either Day 29 or Day 43 (depending on which group the volunteer is in).

The study drug is given on Days 1, 8, 15, and 22. The volunteer is expected at the study center the day before each dose, i.e. on Days -1, 7, 14, and 21. The volunteer should then be at approximately 11:00 a.m. o'clock in the morning report. The entry time can be adjusted. If this happens, the volunteer will be informed in advance. After each administration, the volunteer should remain in the study center for observation for at least 30 minutes and then go home.

For the visits during the follow-up period, the volunteer is expected at the research center between 1:00 PM and 3:30 PM. We make an appointment for a specific time within this time frame.

The volunteer will receive efgartigimod or placebo as an intravenous infusion. The infusion lasts 1 hour.
The Pneumovax 23 vaccine is given as an injection with a needle into the muscle of the volunteer's upper arm.

Whether the volunteer receives efgartigimod or placebo is determined by lottery. Out of a total of approximately 36 participants, 24 participants will receive efgartigimod and 12 participants will receive placebo. Both the volunteer and the investigators know whether the volunteer is receiving efgartigimod or the placebo; open label research.

The study drug is given 4 times: on Days 1, 8, 15 and 22. Depending on which group the volunteer is in, the Pneumovax 23 vaccine is given either before the last study drug administration on Day 22, or at the visit on Day 36 (two weeks after the last dose of study drug).

There are 3 possible treatments in this study. The treatment the volunteer receives is determined by drawing lots.

Intervention

the volunteer will be given efgartigimod or placebo as an intravenous infusion (solution of the compound that will be administered directly in a blood vessel). The infusion takes 1 hour.

The Pneumovax 23 vaccine will be given as an injection with a syringe in the muscle of the upper arm of the volunteer.

Whether the volunteer will receive efgartigimod or placebo will be determined by chance. Of the total of approximately 36 participants, 24 participants will receive efgartigimod and 12 participants will receive placebo. Both the volunteer and the investigators know if efgartigimod or placebo will be administered; open-label study.

The study compound will be given 4 times: on Day 1, 8, 15, and 22. Depending on what group the volunteer is in, the Pneumovax 23 vaccine will be given either prior to the last administration of the study compound on Day 22, or on the visit on Day 36 (two weeks after the last study compound dose).

There are three possible treatments in this study. Which treatment the volunteer will receive will be determined by drawing lots.

Study burden and risks

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. It is very important that the volunteer reports anything they feel to their responsible doctor. The volunteer should not wait until the next scheduled visit.

Efgartigimod has been investigated in 3 other clinical trials with healthy volunteers 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 volunteers 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.

The most commonly reported side effects in healthy subject studies with

efgartigimod were:
• headache
• decreases in white blood cell counts
• increase in level of a blood test marker for inflammation (C-reactive protein)
• injection site bruise
• Injection site redness
• fatigue
• common cold
• mouth/throat discomfort
• back pain

Some of these side effects were observed in the placebo group, and some were observed in doses higher than the dose that will be used in this study.

The most commonly reported side effects in other studies in subjects with Thrombocytopenia and Myasthenia Gravis included:
• headache
• common cold
• diarrhea
• upper respiratory tract infection
• nausea
• urinary tract infection
• muscle pain
• mouth/throat discomfort

Most of these side effects were mild to moderate in intensity, resolved quickly and were assessed as not related to the study compound. Most common side effects that were considered related to the study compound included inflammation of airway passages, upper respiratory tract infection, urinary tract infection, headache, and muscle pain.

The study compound can also cause an immune reaction. This can be fever, itching, rashes and, in severe cases, an allergic/anaphylactic reaction. Your responsible doctor will ask you if you have ever had any allergic reactions.

It is possible that the body of the volunteer produces antibodies against the study compound. These antibodies can make them less sensitive to the study compound in the future. It is not expected that the presence of these antibodies will have consequences for their health.

The study compound may also have (serious) side effects that are still unknown. In addition to unknown side effects, there is a (small) chance that an allergic reaction will occur. This can be caused by the study compound or other ingredients that are used to prepare the formulation.

If during the study more information becomes available regarding side effects

that may be related to the study compound, the responsible doctor will inform the volunteer about this.

The Pneumovax 23 vaccine may also cause side effects.

The most frequent ones (reported in more than 10% of participants vaccinated with Pneumovax 23 for the first time in a drug study) are:
• Injection-site pain/soreness/tenderness
• Injection-site swelling/induration
• Headache
• Reddening of the skin at injection-site
• Lack of energy / fatigue
• Myalgia

Contacts

Public
Argenx BV

Industriepark Zwijnaarde 7
Ghent 9052
BE
Scientific
Argenx BV

Industriepark Zwijnaarde 7
Ghent 9052
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. At least18 years of age at the time of signing the informed consent form (ICF)
2. Healthy as determined by medical evaluation including medical history, physical examination, laboratory tests, and cardiac monitoring
3. Body mass index (BMI) between 18 kg/m2 to 30 kg/m2 (inclusive)
4. Contraceptive use by men and women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies.
5. Capable of giving signed informed consent as described in Appendix 1, Section 10.1.3, which includes compliance with the requirements and restrictions listed in the ICF and in this protocol
6. Abstains from smoking for at least 3 months prior to screening
7. Negative urine drug screen (amphetamines, barbiturates, benzodiazepines, cannabis, cocaine, opiates, methadone, and tricyclic antidepressants) at screening and on day -1
8. Negative alcohol urine test at screening and on day -1
9. Agrees to restrict excessive strenuous physical activities 96 hours prior to screening, 96 hours prior to the visits in the treatment period (D-1, D7, D14, and D21), and 96 hours prior to the visits in follow-up period

Exclusion criteria

1. Clinically significant active or chronic bacterial, viral, including or fungal infection at day -1
2. History of malignancy unless deemed cured by adequate treatment with no evidence of recurrence for >=3 years before the first administration of study intervention. Participants with the following cancers can be included at any time:
a. Adequately treated 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 (TNM stage T1a or T1b)
3. Clinical evidence of other significant serious diseases, a recent major surgery, or any other condition that, in the opinion of the investigator, could confound the results of the study or put the participant at undue risk
4. Use of an investigational product within 2 months or 5 half-lives (whichever is longer) before the first dose of study intervention
5. Use of any monoclonal antibody within 3 months prior to the initial study intervention administration

For more exclusion criteria see the protocol.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-11-2021
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	efgartigimod
Generic name:	n.a.
Product type:	Medicine
Brand name:	PNEUMOVAX 23

Ethics review

Approved WMO Date:	21-10-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-11-2021
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-01-2022
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	EUCTR2021-004878-53-NL
CCMO	NL79381.056.21

Study results