A comparative bioavailability study of a single dose of ziltivekimab formulation B in a manual syringe, formulation D in a manual syringe and formulation C in a pen-injector

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In this study we will look at the blood levels of the study compound ziltivekimab. We will investigate how quickly and to what extent different compositions of ziltivekimab are absorbed, transported, and eliminated from the body. Ziltivekimab is not...

Ethical review	Approved WMO
Status	Completed
Health condition type	Cardiac and vascular disorders congenital
Study type	Interventional

Summary

ID

NL-OMON53876

Source
ToetsingOnline

Brief title
Comparative bioavailability study of ziltivekimab formulation B, D and C

Condition

- Cardiac and vascular disorders congenital

Synonym
Atherosclerotic cardiovascular disease, Cardiovascular disease

Research involving
Human

Sponsors and support

Primary sponsor: Novo Nordisk A/S
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: Bioavailability, Healthy volunteers, Pharmacokinetic, Ziltivekimab

Outcome measures

Primary outcome

To compare the pharmacokinetic properties of a single s.c. administration of ziltivekimab in formulation B for the manual syringe, formulation D for the manual syringe, and formulation C for the pen-injector

Secondary outcome

To compare the pharmacokinetic properties of a single s.c. administration of ziltivekimab in formulation B for the manual syringe, formulation D for the manual syringe, and formulation C for the pen-injector, 50 days following dosing

Study description

Background summary

Ziltivekimab is a new compound that may potentially be used for the treatment of cardiovascular diseases. Ziltivekimab is an antibody that can bind a protein in the body called interleukin 6 (IL-6). IL-6 is a protein that plays an important role in inflammation processes and is involved in cardiovascular diseases such as arteriosclerosis and stroke. By binding to IL-6, ziltivekimab aims to reduce inflammation and thereby potentially reduce the risk for cardiovascular diseases.

The study compound remains in the body for a long time. The half-life, that is the time it takes for the amount of the study compound in the blood to be halved, is approximately 57 days for ziltivekimab. This is why you have to

return to the research center for visits over a long period.

Study objective

In this study we will look at the blood levels of the study compound ziltivekimab. We will investigate how quickly and to what extent different compositions of ziltivekimab are absorbed, transported, and eliminated from the body. Ziltivekimab is not yet approved for market. Ziltivekimab is hereinafter also referred to as *study compound*.

The study compound will be injected under the skin (this is called subcutaneous administration) of the abdomen. We will compare two different administration methods: a syringe and a pen-injector. A pen-injector is a device that is developed to make injections more easy and convenient. They are for example used by diabetes patients to inject insulin.

We will also investigate how safe ziltivekimab is and how well it is tolerated when it is used by healthy subjects.

Ziltivekimab has already been administered to patients with chronic kidney disease or rheumatoid arthritis. It has only been given to patients in a research setting. The current study will be the first study where ziltivekimab will be given to healthy subjects.

Study design

The study will take a total of about 31 weeks (about 7 months) from the screening until the follow-up visit.

In total the volunteer will come to the research center 16 times:
- once for the screening as described before, which will take place within 28 days before dosing.
- A visit to the research center on the day before dosing of the study compound (Day -1).
- A visit to the research center during which the study compound will be administered (Day 1). The volunteer will leave the research center approximately 2 to 4 hours after receiving the study compound.
- 12 visits after administration of the study compound. These visits will take place on Day 2, 3, 5, 8, 15, 22, 29, 36, 50, 71, 99, and 141.
- A follow-up visit on Day 183.

Intervention

The volunteer will be given ziltivekimab as an injection under the skin (subcutaneous) of the abdomen.

There are 3 different study treatments in this study. The volunteer will receive 1 of them. Which study treatment the volunteer will receive will be determined by drawing lots. the volunteer will have a 33.3% chance of receiving each study treatment . Both the volunteer and the study staff will know which study treatment the volunteer will receive.

Below you can see the 3 possible study treatments:
- Ziltivekimab B, injected with a manual syringe
- Ziltivekimab D, injected with a manual syringe
- Ziltivekimab C, injected with a pen-injector

The volunteer will receive a single dose of 15 milligram ziltivekimab on Day 1.

Study burden and risks

Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula (a tube in a vein in the arm) can sometimes lead to inflammation, swelling, hardening of the vein, blood clotting, and bleeding in the environment (bruising) of the puncture site. In some individuals, a blood draw can sometimes cause pallor, nausea, sweating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take about 168 milliliters (mL) of blood from the volunteer from screening to follow-up. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time at once. If the investigator thinks it is necessary for the safety of a subject, extra samples might be taken for possible additional testing. If this happens, the total amount of blood drawn may be more than the amount indicated above.

Heart tracing
To make a heart tracing, electrodes (small, plastic patches) will be placed on the volunteers arms, chest and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching). Any skin irritation usually disappears when the patches are removed.

Coronavirus test
Samples for the coronavirus test will be taken from the back of the volunteers 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 volunteers throat may cause the volunteer to gag. When the sample is taken from the back of the volunteers nose, the volunteer may experience a stinging sensation and the volunteers eyes may become watery.

If there is an outbreak of COVID-19 in your area, then the research center will take actions to minimize any risk of transmission and inform the volunteer about these changes.

Injections
When using a syringe or pen-injector to inject the study compound under the skin, this may cause a little discomfort, bruising, bleeding or swelling where the needle goes in. There is also a very small risk of infection where the needle goes in.

Contacts

Public
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Scientific
Novo Nordisk A/S

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Male or female
- Aged 18-64 years (both inclusive) at the time of signing informed consent.
- Body mass index (BMI) between 18.5 and 29.9 kg/m2 (both inclusive).
- Considered to be generally healthy based on the medical history, physical examination, and
the results of vital signs, electrocardiogram and clinical laboratory tests

performed during
the screening visit, as judged by the investigator.

Exclusion criteria

- Known or suspected hypersensitivity to study intervention(s) or related products.
- Female who is pregnant, breast-feeding or intends to become pregnant or is of childbearing
potential and not using adequate contraceptive method, as defined in section 10.4.
- Any disorder which in the investigator*s opinion might jeopardise participant*s safety or
compliance with the protocol.
- Use of prescription medicinal products or non-prescription drugs, except routine vitamins,
topical medication, highly effective contraceptives and occasional use of paracetamol,
acetylsalicylic acid within 14 days before trial product administration.
- Clinical evidence of, or suspicion of, active infection at the discretion of the investigator.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	03-02-2023
Enrollment:	200
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N/A
Generic name:	ziltivekimab

Ethics review

Approved WMO Date:	09-01-2023
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-01-2023
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	EUCTR2022-001862-37-NL
CCMO	NL83434.056.22

Study results

Date completed:	08-01-2024
Results posted:	21-06-2024

First publication
06-05-2024