A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, SINGLE- AND MULTIPLE ASCENDING DOSE TRIAL TO EVALUATE THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF LEO 158968 IN HEALTHY SUBJECTS

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

Summary

ID

NL-OMON53439

Source
ToetsingOnline

Brief title
Investigating safety of LEO 158968 in healthy volunteers

Condition

- Autoimmune disorders

Synonym
inflammatory diseases

Research involving

Human

Sponsors and support

Primary sponsor: Leo Pharma
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: healthy volunteers, inflammatory diseases, LEO 158968

Outcome measures

Primary outcome

To evaluate the safety and tolerability of single and multiple ascending

intravenous (iv) and subcutaneous (sc) doses of LEO 158968 administrated to

healthy subjects

Secondary outcome

To evaluate the pharmacokinetics (PK) of LEO 158968, administered to healthy

subjects

To monitor potential development of antidrug antibodies (ADA) after LEO 158968

dosing in healthy subjects

Study description

Background summary

LEO 158968 is a new compound that may potentially be used for the treatment of several inflammatory diseases. LEO 158968 is a monoclonal antibody and is a *custom-made* protein that has been assembled in a laboratory. This can attach to proteins that are on the surface of body cells or that move in the blood.
LEO 158968 has been developed to block signaling pathways of three IL-1 family members that have important roles in several inflammatory diseases. IL-1 is a substance in the body which is involved in normal inflammatory and immune responses.

Study objective

In this study we will investigate how safe the new compound LEO 158968 is and how well it is tolerated when it is used by healthy subjects.

We also investigate how quickly and to what extent LEO 158968 is distributed and eliminated from the body. In addition, we look at the effect of LEO 158968 on your immune cells and specific markers in the blood.

We compare the effects of LEO 158968 with the effects of a placebo.

LEO 158968 has not been given to humans before. It has been extensively tested in the laboratory and on animals. LEO 158968 will be tested at various dose levels.

Study design

Part A:
The study lasts a maximum of 4 months from the screening to the follow-up check. For the research it is necessary to stay in the research center for 1 period of 6 days.

Day 1 is the day on which the study drug is received. We expect the volunteers to be in the research center one day before taking the research drug. In that case, you must report between 9:30 a.m. and 2:00 p.m. You will be informed about the exact time. The volunteers leave the study center on Day 5 (after 5 nights) of the study. After the stay in the research center there will be 5 short visits. These short visits take place on Days 8, 15, 29, 57 and 85.

LEO 158968 or placebo is given as an intravenous infusion or a subcutaneous injection.

Whether one receives LEO 158968 or placebo is determined by lottery. A maximum of 6 subjects per group receive LEO 158968 and 2 subjects receive placebo. Neither the volunteer nor the investigators know whether one is receiving LEO 158968 or placebo; We call this a double-blind study.

Part B:
The examination lasts a maximum of 5 months from the inspection to the follow-up check.

For the research it is necessary to stay in the research center for 4 periods. A 10-day period, 1 6-day period and 2 3-day periods.

Day 1 is the day on which the volunteer receives the research drug. We expect the volunteers at the research center one day before taking the research drug.

You must report between 9:30 a.m. and 2:00 p.m. You will be informed about the exact time. The entry time can be adjusted. If this happens, you will be informed in advance. The volunteer leaves the study center on Day 9 of the study. After the stay in the research center one will come back for 3 extra stays. These stays take place from Day 14 to Day 16 (2 nights), from Day 21 to Day 23 (2 nights) and from Day 28 to Day 33 (5 nights). After your stays at the research center there will be 7 short visits to the research center. These short visits take place on Days 36, 43, 57, 71, 85, 99 and 113.

LEO 158968 or placebo is given as a subcutaneous (subcutaneous) injection.

Intervention

SAD part:
Group A1, Day 1, LEO 158968 5 mg or placebo, once, Intravenous infusion
Group A2, Day 1, LEO 158968 10 mg or less, or placebo, once, Intravenous infusion
Group A3, Day 1, LEO 158968 15 mg or less, or placebo, once, Intravenous infusion
Group A4, Day 1, LEO 158968 45 mg or less, or placebo, once, Intravenous infusion
Group A5, Day 1, LEO 158968 85 mg or less, or placebo, once, Intravenous infusion
Group A6, Day 1, LEO 158968 85 mg or less, or placebo, once, Subcutaneous injection
Group A7, Day 1, LEO 158968 225 mg or less, or placebo, once, Intravenous infusion
Group A8, Day 1, LEO 158968 450 mg or less, or placebo, once, Subcutaneous injection
Group A9, Day 1, LEO 158968 900 mg or less, or placebo, once, Subcutaneous injection
Group A10, Day 1, LEO 158968 1350 mg or less, or placebo, once, Subcutaneous injection
Group A11, Day 1, LEO 158968 250mg or less, or placebo, once, Intravenous infusion
Group A12, Day 1, LEO 158968 500mg or less, or placebo, once, Intravenous infusion

MAD part:
Group B1, Day 1, 8, 15, 22 and 29, LEO 158968 150 mg or less, or placebo, once weekly, Subcutaneous injection
Group B2, Days 1, 8, 15, 22 and 29, LEO 158968 300 mg or less, or placebo, once weekly, Subcutaneous injection
Group B3, Day 1, 8, 15, 22 and 29, LEO 158968 600 mg or less, or placebo, once weekly, Subcutaneous injection

Study burden and risks

Blood draw
Blood draws may hurt or cause bruising. Using an indwelling cannula can sometimes cause inflammation, swelling, hardening of the artery, or blood clotting and bleeding around the puncture site. In some individuals, a blood draw can sometimes cause paleness, nausea, sweating, slow heart rate, or drop in blood pressure with dizziness or fainting.

All in all, we take approximately 364 milliliters (ml) with an intravenous infusion or 314 milliliters (ml) with an injection under the skin from the volunteer from the examination to the follow-up check for the SAD part or 566 milliliters for the MAD part . This amount does not cause any problems in adults. If the researcher considers this necessary to ensure the safety of the subject, additional samples can be taken for any additional testing. If this happens, the total amount of blood drawn may be more than the amount indicated above.

ECG
To make a heart film, electrodes are placed on the arms, chest and legs. Prolonged use of these electrodes may cause skin irritation.

Coronavirus test
Samples for the coronavirus test will be taken with cotton swabs at the back of the nose and throat. Taking the samples only takes a few seconds, but can cause discomfort and discomfort. Taking a sample from the back of the throat may result in gagging. When the sample is taken at the back of the nose, one may experience a stinging sensation and the eyes may water.

Contacts

Public
Leo Pharma

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Scientific
Leo Pharma

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DK

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Age: 18 to 60 years, inclusive, at screening
Sex: Male or female
Body mass index: 18.0 kg/m2 to 32.0 kg/m2, inclusive, at screening
Health status: In good health as judged by the Investigator based on medical history, physical examination, electrocardiogram (ECG), hematology, biochemistry, and urinalysis.

Exclusion criteria

1. Male subjects sexually active with a woman of childbearing potential who are not willing to use a barrier method of contraception (eg, condom) from the time of first dose of investigational medicinal product (IMP) until 16 weeks after the last dose, in conjunction with this female partner using a highly effective form of contraception.
2. Female subjects who are pregnant, lactating, or planning to become pregnant during the time of the trial.
3. Subjects with any surgical or medical condition which might significantly alter the absorption, distribution, metabolism, or excretion of any drug.
4. Positive polymerase chain reaction (PCR) test for COVID-19 at Day -1, or contact with COVID-19 positive (or suspected) persons within 14 days prior to first dose.
5. ECG with QT-interval corrected for heart rate (QTc) using Fridericia*s formula (QTcF) >450 msec for men, >460 msec for women, confirmed by repeat measurement at screening.
6. Treatment with any prescribed or nonprescribed systemic or topical medication within 7 days prior to the first dose of IMP (excluding paracetamol; including herbal remedies), unless, in the opinion of the Investigator and the Sponsor, the medication will not interfere with the trial procedures or

compromise safety.

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	10-01-2023
Enrollment:	120
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	24-10-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-12-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	14-06-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-06-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-10-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-01-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-01-2024
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	EUCTR2022-002768-65-NL
CCMO	NL82783.056.22