A clinical trial to evaluate the safety, tolerability, and pharmacokinetics of single and multiple ascending oral doses of LEO 153339 in healthy subjects

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In this study we will investigate how safe the new compound LEO 153339 is and how well it is tolerated when it is used by healthy participants. We also investigate how quickly and to what extent LEO 153339 (and the breakdown product) is absorbed,...

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

Summary

ID

NL-OMON51974

Source
ToetsingOnline

Brief title
A single and multiple ascending dose trial of LEO 153339 in healthy adults

Condition

- Other condition

Synonym
Psoriasis

Health condition

Psoriasis

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Healthy adults, LEO 153339, MAD, SAD

Outcome measures

Primary outcome

To evaluate the safety and tolerability of LEO 153339 in healthy subjects.

Secondary outcome

To evaluate the pharmacokinetics (PK) of LEO 153339 and LEO 159074

(N-glucuronide metabolite) in healthy subjects.

Study description

Background summary

LEO 153339 has not been given to humans before. As LEO 153339 will be given to humans for the first time in this study, side effects of LEO 153339 in humans are not known yet. LEO 153339 has been studied extensively in the laboratory and in animals.

Secukinumab is a compound that has a similar mode of action as LEO 153339. The most common side effects reported in patients that took secukinumab over 12 and 52 weeks were upper respiratory infections, headache, and diarrhea.

Animal experiments have been done with doses much higher than those planned in the current study. In an experiment where animals received 600 mg/kg and 400 mg/kg LEO 153339, 3 out of 10 animals showed convulsions. Subjects are also under strict medical supervision and additional measures are taken, such as neurological examinations, EEGs, and cognitive tests (Cogstate Safety Battery test) to make sure that they remain safe from serious effects.

Study objective

In this study we will investigate how safe the new compound LEO 153339 is and how well it is tolerated when it is used by healthy participants.

We also investigate how quickly and to what extent LEO 153339 (and the breakdown product) is absorbed, transported, and eliminated from the body. In addition, in Part 2 we look at the effect of LEO 153339 on immune cells in the blood.

We also look at the effect of your genetic information on your body*s response to LEO 153339. We compare the effects of LEO 153339 with the effects of a placebo.

LEO 153339 has not been given to humans before. It has been extensively tested in the laboratory and on animals. LEO 153339 will be tested at various dose levels.

Study design

Part 1

The study will take a maximum of 5 weeks from the screening until the follow-up.

It is necessary that subjects stay in the research center for one period of 6 days (5 nights).

Screening > Day *30 up to Day *3
Arrival > Day *2
In-house stay > Day *2 up to Day 4
Departure > Day 4
Follow-up > Day 4

Subjects will be given LEO 153339 or placebo as oral capsules with 240 milliliters (mL) of (tap) water. One of the investigators will inspect the hands and mouth after the study compound intake. This it to check if they have taken the study compound. In one group (Group B1), LEO 153339 can be given as a cloudy drink (suspension).

Based on emerging data from the study, it may also be decided that the dose will be given in the form of a cloudy drink (suspension), for example when it appears that the capsule is not sufficiently absorbed by the body.

Part 2

The study will take a maximum of 6 weeks from the screening until the follow-up.

It is necessary that subjects stay in the research center for one period of 12 days (11 nights).

Screening > Day *30 up to Day *3
Arrival > Day *2
In-house stay > Day *2 up to Day 10
Departure > Day 10
Follow-up > Day 10

Subjects will be given LEO 153339 or placebo as oral capsules with 240 milliliters (mL) of (tap) water. One of the investigators will inspect the hands and mouth after the study compound intake. This it to check if they have taken the study compound.

Based on emerging data from the study, it may also be decided that the dose will be given in the form of a cloudy drink (suspension), for example when it appears that the capsule is not sufficiently absorbed by the body.

On Day 5, subjects will receive the morning dose of the study compound after eating a high-fat breakfast with a standard composition. This breakfast must be started exactly on time and must be finished within 20 minutes. The entire breakfast must be consumed.

Intervention

Part 1

The study compound will be given once on Day 1.
The table below shows the planned dose levels for each group. The doses of later groups can be adjusted. For example because the study compound had more or less effect than was expected. The dose for the next group will only be increased if the lower dose of the previous group was found to be well tolerated and in case of no objection by the Medical Research Ethics Committee. The study will be discontinued or the dose will be decreased if, in the opinion of the investigators, unacceptable side effects appear.

Group | Treatment* | How often | How
A1 | LEO 153339 10 mg or placebo | Once | Capsule
A2 | LEO 153339 40 mg or placebo | Once | Capsule
A3 | LEO 153339 100 mg or placebo | Once | Capsule
A4 | LEO 153339 200 mg or placebo | Once | Capsule
A5 | LEO 153339 375 mg or placebo | Once | Capsule
A6 | LEO 153339 375 mg or placebo | Once | Cloudy drink
A7 | LEO 153339 750 mg or placebo | Once | Cloudy drink
B1** | LEO 153339 X mg | Once | Cloudy drink

* In case the dose level will be lower or higher than planned, subjects will be informed verbally.
** Group B1 is only done if needed. All participants will receive LEO 153339 and no participant will receive placebo. The dose that will be used will be

based on the results of the previous groups.

Part 2

The study compound will be given once, twice (12 hours apart), or 4 times daily (6 hours apart) for 7 days. On the last dosing day (Day 7), only one dose will be given. The table below shows the planned dose levels for each group. The doses of later groups can be adjusted. For example because the study compound had more or less effect than was expected. The dose for the next group will only be increased if the lower dose of the previous group was found to be well tolerated and in case of no objection by the Medical Research Ethics Committee. The study will be discontinued or the dose will be decreased if, in the opinion of the investigators, unacceptable side effects appear.

Group | Treatment* | How often | How
C1 | LEO 153339 40 mg or placebo | Once, twice or four times daily** | Capsule
C2 | LEO 153339 100 mg or placebo | Once, twice or four times daily** | Capsule
C3 | LEO 153339 250 mg or placebo | Once, twice or four times daily** | Capsule or cloudy drink
C4 | LEO 153339 500 mg or placebo | Once, twice or four times daily** | Capsule or cloudy drink
C5 | LEO 153339 800 mg or placebo | Once, twice or four times daily** | Capsule or cloudy drink
C6 | LEO 153339 1000 mg or placebo | Once, twice or four times daily** | Capsule or cloudy drink

* In case the dose level will be lower or higher than planned, subjects will be informed verbally.
** Only 1 dose will be given on the last dosing day (Day 7)

Study burden and risks

Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula 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 140 (Part 1) or 290 (Part 2) milliliters (mL) of blood. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time. If the investigator thinks it is necessary for the safety of a participant, extra samples might be taken for possible additional testing. If this happens, the total amount of blood drawn will be more than the amount indicated above.

Heart tracing
To make a heart tracing, electrodes will be placed on arms, chest and legs. To monitor heart rate, electrodes will be placed on chest and abdomen. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Brain activity (EEG)
We will measure the electrical activity in the brain by making an EEG. For this, we will place 19 electrodes on different locations on the head (we will use a cap for this). The electrodes are connected to a machine that determines the electrical activity. During the EEG subjects should be resting comfortably.

Meals/Fasting
If you have to fast for a prolonged time during the study, this may lead to symptoms such as dizziness, headache, stomach upset, or fainting.

Coronavirus test
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 subjects to gag. When the sample is taken from the back of the nose, subjects may experience a stinging sensation and the eyes may become watery.

Part 2 only

Meals/Fasting
The high-fat breakfast is a big breakfast containing 2 fried eggs, fried potatoes, bacon and more. Subjects must consume the whole breakfast. It can be difficult to consume the entire breakfast, particularly for light eaters.

Contacts

Public
Leo Pharma A/S

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Healthy adult males and females.
Age between 18 and 65 years (both inclusive) at screening.
A body mass index (BMI) between 18.0 and 32.0 kg/m2 (both inclusive).
In good health at screening and/or check-in (Day -2 and Day -1) as judged by the investigator based on medical history, physical examination, vital signs, 12 lead ECG, and clinical laboratory evaluations.

Exclusion criteria

Male subjects sexually active with a woman of childbearing potential who are not willing to use a barrier method of contraception (e.g. condom) from the time of first dose of IMP until 3 months after the last dose, in conjunction with this female partner using a highly effective form of contraception. For vasectomised male subjects, male subjects with a female partner with bilateral tubal occlusion or ligation, and heterosexually abstinent male subjects (when this is in line with the
preferred and usual life style of the subject and not just being without a current partner), no additional contraception is required.
Female subjects who are pregnant, lactating, or of childbearing potential
Any surgical or medical condition or cholecystectomy which might significantly alter the absorption, distribution, metabolism, or excretion of any drug.
Positive polymerase chain reaction (PCR) test for coronavirus disease 2019 (COVID-19) at Day -2 or Day -1 or within 8 weeks prior to screening or check-in, or contact with COVID-19 positive (or suspected) persons within 14 days prior to first dose.
Treatment with any prescribed or non-prescribed 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.
Treatment with any non-marketed drug substance (that is, an agent which has not yet been made available for clinical use following registration) within 3 months prior to the first dose of IMP.
ECG with QT interval corrected for heart rate using Fridericia's formula (QTcF) >450 msec confirmed by repeat measurement at screening.

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:	Recruitment stopped
Start date (anticipated):	17-05-2021
Enrollment:	134
Type:	Actual

Ethics review

Approved WMO

Date:	20-04-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	07-05-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-02-2022
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	EUCTR2020-005748-51-NL
CCMO	NL77226.056.21