A Safety, Tolerability and Pharmacokinetic Study of Single and Multiple Doses of LY3526318 in Healthy Participants

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The purpose of this study is to investigate how safe the compound LY3526318 is and how well it is tolerated when it is administered to healthy participants. It will also be investigated how quickly and to what extent LY3526318 is absorbed and…

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON50998

Source
ToetsingOnline

Brief title
A safety, PK and pilot FE study of LY3526318 in healthy participants

Condition

- Other condition

Synonym
Chronic Pain

Health condition

Chronische Pijn

Research involving

Human

Sponsors and support

Primary sponsor: Eli Lilly
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Food Effect, LY3526318, PK, Safety

Outcome measures

Primary outcome

Part A: To determine the pharmacokinetics of LY3526318 after a single oral dose administration

Part B: To determine the pharmacokinetics of LY3526318 after multiple oral dose administrations

Secondary outcome

Part A: To estimate the safety and tolerability of LY3526318 after single (Part A) oral administration to healthy participants

To evaluate the effect of a meal on the pharmacokinetics of LY3526318 in fed versus fasted conditions

Part B: To estimate the safety and tolerability of LY3526318 after multiple oral administrations to healthy participants

Study description

Background summary

In this study, LY3526318 is being researched as a potential treatment for chronic pain. The study compound is not registered in The Netherlands as a medication. This means that the study compound is still in development.

Current treatment options for chronic pain include so-called non steroidal-anti-inflammatory drugs (NSAIDs) and opioid-based therapeutics. Disadvantages of these treatment options are that NSAIDs are not completely effective as judged by many patients and that opioids are addictive and may have unwanted effects on brain functioning.

LY3526318 has a different working mechanism by inhibiting a protein called *transient receptor protein ankyrin 1* (TRPA1). This TRPA1-protein is present on nerve cells that transmit painful stimuli.

Study objective

The purpose of this study is to investigate how safe the compound LY3526318 is and how well it is tolerated when it is administered to healthy participants. It will also be investigated how quickly and to what extent LY3526318 is absorbed and eliminated form the body (this is called pharmacokinetics). LY3526318 has been administered to humans before and will be tested at various dose levels.

The effects of LY3526318 will be compared to the effects of a placebo. A placebo is a medicine without any active ingredient. Please note that when the term *study compound* is used in this document, this can refer to LY3526318, placebo, or both.

This study will be performed in 16 healthy male and female participants. The study consists of 2 parts (A and B) where the volunteer can only participate in 1 part. In Part A maximal 4 doses of LY3526318 will be administered, between each dose will be at least 14 days (2 weeks). In Part B multiple doses of LY3526318 will be administered once daily for up to 5 days.

Study design

Part A: LY3526318 or placebo is given as capsule (s) by mouth with 240 milliliters (ml) of water once per period. After taking the research drug, one of the researchers will inspect the hands and mouth.

A maximum of 4 doses of the study drug can be received. Depending on the results in the (previous) period (s), the next step will be determined. Up to 3 dose levels will be studied after fasting (fasting at least 8 hours prior to and at least 4 hours after dosing). Up to 2 of these dose levels that were studied after fasting may also be studied after food (a high-fat meal 30 minutes prior to dosing). The options are:
• 3 times without breakfast after an overnight fast and 1 time with a high-fat breakfast
• 2 times without breakfast after an overnight fast and 2 times after a high-fat breakfast

• 3 times without breakfast after an overnight fast
• 2 times without breakfast after an overnight fast and 1 time after a high-fat breakfast
• 2 times without breakfast after an overnight fast

The high-fat breakfast should be started right on time and eaten whole within 20 minutes.

Part A consists of 4 periods during which participants will stay in the research center for 4 days (3 nights) for each period. Each period is followed by 2 short visits, the time of arrival at the study center will be told during the stay in the clinic. Between 4 and 6 days after the last short visit there will also be a follow-up visit. Some participants will be scheduled for all 4 periods and some will be scheduled for only 1 or 2 periods. Between each period there will be at least 1 week. Day 1 is the day the study drug is administered. It is expected at the study center at 2:00 pm in the afternoon prior to study drug administration day. The entry time can be adjusted. If this happens, they will be informed in advance. The research center is left on Day 3 of the examination.

Part B: LY3526318 or placebo is given as capsule (s) by mouth with 240 milliliters (ml) of water once daily for 5 days. After taking the research drug, one of the researchers will inspect the hands and mouth.

Participants receive daily doses for up to 5 days, without breakfast after an overnight fast or after eating a high-fat, fixed-composition breakfast, or either option (fast or after a high-fat breakfast) on different days.

The high-fat breakfast should be started right on time and eaten whole within 20 minutes.

The actual research consists of 1 period during which one will stay in the research center for 9 days (8 nights). Day 1 through Day 5 are the days on which the study drug is administered. It is expected at 2:00 PM in the afternoon prior to the day of the first study drug administration at the study center. The entry time can be adjusted. If this happens, they will be informed in advance. The research center is left on Day 8 of the examination.

Intervention

Part A:

Period 1 Day 1 LY3526318 100 mg or placebo once Fasted
Period 2 Day 1 LY3526318 250 mg or placebo once Fasted
Period 3 Day 1 LY3526318 XX# mg or placebo once Fasted or after high fat breakfast
Period 4 Day 1 LY3526318 XX# mg or placebo once Fasted or after high-fat

breakfast

#: The dose will be based on the results of previous period(s).

Up to 2 of the doses will be administrated after a high-fat breakfast. This will be based on the results of previous period(s).

Part B:

Days 1 to 5 LY3526318 XX# mg or placebo once daily Fasted or after high-fat breakfast

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 about 170 milliliters (mL) of blood. This amount does not cause any problems in adults.

To make a heart tracing, electrodes (small, plastic patches) will be pasted at specific locations on the arms, chest and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).

The high-fat breakfast is a big breakfast consisting of 2 fried eggs, fried potatoes and bacon. The volunteers must consume the breakfast entirely within 20 minutes. Particularly for light eaters, it can be difficult to consume the entire breakfast, and it might cause some discomfort if they are not sed to a large breakfast.

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

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Aged 18 to 65 years, inclusive.
2. Healthy male participants, as determined through medical history and physical examination.
a. A nonvasectomized, male participant must agree to use a condom or abstain from
sexual intercourse from start of dosing until 105 days beyond the last dose of study
intervention.
b. No restrictions are required for a vasectomized male provided his vasectomy has been
performed at least 4 months or prior to screening. A male who has been vasectomized
*4 months prior to screening must follow the same restrictions as a nonvasectomized
male
c. Must agree not to donate sperm from start of dosing until 105 days beyond the last
dose of study intervention.
3. Healthy female participants of child-bearing potential who have a fertile male sexual

partner must be willing and able to practice effective contraception from admission to
105 days beyond the last dose of study intervention. Sexually active participants must use
a combination of 2 of the following methods of contraception, including at least 1 socalled
barrier method:
a. hormonal contraceptives (oral, transdermal patches, vaginal, or injectable)
b. intrauterine device with or without hormones
c. condom, diaphragm, or cervical cap (*barrier* method), and
d. sexual abstinence.
Contraceptive requirements do not apply for participants who are exclusively in a same-sex
relationship. Additional guidance is provided in Section 10.4, Appendix 4.
4. Have a body mass index of 18 to 32 kg/m2, inclusive.
5. Are reliable and willing to make themselves available for the duration of the study and
are willing to follow CRU-specific study procedures.
6. Have clinical laboratory test results within normal reference range for the population or
CRU, or results with acceptable deviations that are judged not clinically significant by the
investigator.
7. Capable of giving signed informed consent as described in Section 10.1.2, Appendix 1,
which includes compliance with the requirements and restrictions listed in the informed
consent form (ICF) and in this protocol.

Exclusion criteria

1. Have a history or presence of medical illness including, but not limited to, any
cardiovascular, hepatic, respiratory, hematological, endocrine, psychiatric or neurological
disease, convulsions, or any clinically significant laboratory abnormality that, in the
judgment of the investigator, indicate a medical problem that would preclude study
participation.
2. Any abnormalities identified following a physical examination of the participant that, in
the opinion of the investigator, would jeopardize the safety of the participant or interfere
with study conduct if they took part in the study.

3. Positive SARS-CoV-2 virus nasopharyngeal polymerase chain reaction test at Day -1.
4. Contact with SARS-CoV-2-positive or COVID-19 patient within the last 14 days prior to
admission to the CRU.

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):	29-12-2020
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO Date:	23-11-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-12-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	24-02-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-03-2021
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	EUCTR2020-004290-46-NL
CCMO	NL75806.056.20

Study results

Date completed:	21-04-2021
Results posted:	22-04-2022

First publication
15-09-2021