A phase 1, randomized, double-blind, placebo-controlled, single ascending dose, multiple ascending dose and food effect study to evaluate the safety, tolerability, and pharmacokinetics of LMT503 in healthy subjects.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON51292

Source
ToetsingOnline

Brief title
LMT503 First-in-human SAD, MAD, and FE study

Condition

- Gastrointestinal inflammatory conditions

Synonym
Inflammatory bowel disease, long lasting inflammation of the digestive tract

Research involving

Human

Sponsors and support

Primary sponsor: Lmito Therapeutics Inc.
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Bowel disease, Inflammatory, LMT503

Outcome measures

Primary outcome

- To assess the safety and tolerability of single and multiple ascending oral

doses of LMT503 in healthy subjects

Secondary outcome

- To assess the pharmacokinetic (PK) profile of single and multiple ascending

oral doses of LMT503 in healthy subjects.

- To evaluate the effect of food on the safety and tolerability of LMT503

following a single oral dose of LMT503 in healthy subjects.

- To assess the effect of food on the absorption and the PK profile of LMT503

following a single oral dose of LMT503 in healthy subjects.

Study description

Background summary

LMT503 is a new compound that may potentially be used for the treatment of inflammatory bowel disease. Inflammatory bowel disease is a term used to describe disorders that involve long lasting inflammation of the digestive tract. Inflammatory bowel disease is a name for 2 conditions, Crohn*s disease and ulcerative colitis. The long lasting inflammation of the digestive tract can lead to damage to the digestive tract. Both Crohn*s disease and ulcerative colitis usually are characterized by diarrhea, rectal bleeding, abdominal pain,

fatigue and weight loss.

The exact cause of inflammatory bowel disease is unknown, but inflammatory bowel disease is the result of a defective immune system. A good functioning immune system attacks foreign organisms, such as viruses and bacteria, to protect the body. In inflammatory bowel disease the immune system responds incorrectly. This incorrect response causes long-lasting inflammation of the digestive tract. LMT503 influences the response of the immune system by changing the overactivated macrophages, a type of blood cells that normally defend the body against infection and injury. LMT503 changes the macrophages from a type that causes inflammation to a type that reduces inflammation, and induces with this a possible resolution. This change might be a promising therapy for inflammatory bowel disease.

Study objective

This study has been transitioned to CTIS with ID 2024-519180-17-00 check the CTIS register for the current data.

In this study we will investigate how safe the new compound LMT503 is and how well it is tolerated when it is used by healthy participants.

We also investigate how quickly and to what extent LMT503 is absorbed, transported, and eliminated from the body (this is called pharmacokinetics). In addition, the effect of food on the absorption of LMT503 in the body will be investigated (Part A, Group 3 only).

We compare the effects of LMT503 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 LMT503, placebo, or both.

LMT503 has not been used by humans before. It has been extensively tested in the laboratory and on animals. LMT503 will be tested at various dose levels.

Study design

Part A:

For the research it is necessary that the volunteer stays in the research center for 1 period of 5 days (4 nights). For Group 3 it will be 2 periods of 5 days (4 nights) and there will be at least 2 weeks between both administrations of the study drug. The in-house stay(s) will be followed by 1 short visit to the research center. This short visit will take place 5 to 7 days after the (for group 3, last) stay in the research center.

Day 1 is the (for Group 3, first) day on which the volunteer receives the study

compound. We expect the volunteer 1 day before Day 1 in the research center. The volunteer leaves the study center on Day 4 (3 days after taking the study drug) of the study.

Below is an overview of the days on which the volunteer stays in the research center or on which a visit is made to the research center:

- Screening
Day -28 to Day 1 prior to the treatment period

- In-house stay
Day -1 (arrival) to Day 4 (departure)
(for Group 3, at least 2 weeks after Day 1 there will be another in-house stay of 5 days.

- Follow-up
5 to 7 days after the (last for Group 3) stay in the research center.

Part B:

For the research it is necessary that the volunteer stays 1 period of 11 days (10 nights) in the research center. The in-house stay will be followed by 1 short visit to the research center. This short visit will take place 5 to 7 days after your stay in the research center.

Day 1 is the first day on which the volunteer receives the study compound. We expect the volunteer 1 day before Day 1 in the research center. The volunteer leaves the study center on Day 10 of the study.

Below is an overview of the days on which the volunteer stays in the research center or on which a visit is made to the research center.

- Screening
Day -28 to Day 1 prior to the treatment period

- In-house stay
Day -1 (arrival) to Day 10 (departure)

- Follow-up
5 to 7 days after the stay in the research center.

The volunteer will receive LMT503 or placebo as tablets by mouth with 240 milliliters (ml) of water.

Only for Part A, Group 3: The volunteer may not lie down during the first 4 hours after taking the study drug (unless instructed to do so by one of the investigators), as this may affect the absorption of the study drug.

Only for Part A, Group 3: All participants will receive the study drug once with and once without breakfast. In the 2nd period, they receive a high-fat breakfast with a fixed composition that must be started right on time and eaten completely within 20 minutes.

Whether the volunteer receives LMT503 or placebo is determined by lottery. In each group, 6 participants receive LMT503 and 2 participants receive placebo. Neither the volunteer nor the researchers know whether the volunteer is receiving LMT503 or placebo. If it is important for health, for example in the case of a serious side effect, this can be looked up.

For safety reasons, we will first give 2 participants the study drug in Part A, Group 1. One participant receives LMT503 and 1 participant receives placebo. The safety and tolerability of the study drug in these 2 participants is being carefully examined. If there are no problems within 24 hours of dosing, the remaining 6 participants in Group 1 will also receive the study drug (5 will receive LMT503 and 1 will receive placebo). If the results of the previous groups show that extra caution is needed, the other groups can also follow this dosing schedule. If this is the case, the volunteer will be informed about this before the start of the group.

After taking the study drug, one of the researchers will inspect the volunteer's hands and mouth. This is to check whether the study drug has been taken.

Intervention

In the table below shows the planned dose levels for each group. The doses after the first group can be adjusted based on the results of the previous group(s). For example because the study compound had more or less effect than was expected. However, the dose will not be lower than 50 mg and not higher than 900 mg. 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.

Part A:
Group 1 will receive LMT503 50 mg or placebo on day 1, once daily after fasting.
Group 2 will receive LMT503 150 mg or placebo on day 1, once daily after fasting.
Group 3 will receive LMT503 300 mg or placebo on day 1, once daily after

fasting.
will receive LMT503 300 mg or placebo on day 1#, once daily after being fed (high fat breakfast).
Group 4 will receive LMT503 600 mg or placebo on day 1, once daily after fasting.
Group 5 will receive LMT503 XXX mg$ or placebo on day 1, once daily after fasting.
Group 6 will receive LMT503 XXX mg$ or placebo on day 1, once daily after fasting.

* If the amount will be higher or lower than planned, we will inform the volunteers.
# Day 1 of the second period of stay.
$ The dose is determined during the study and based on the results of the previous groups.

Part B:
Group 1 will receive LMT503 150 mg or placebo on days 1 to 7, once daily after fasting or being fed.
Group 2 will receive 300 mg of LMT503 or placebo on days 1 to 7, once daily after fasting or being fed.
Group 3 will receive LMT503 600 mg or placebo on days 1 to 7, once daily after fasted or being fed.

* If the amount will be higher or lower than planned, we will tell the volunteers.
# Food status is determined based on the results of Group 3 of Part A.

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 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 115 mL (Part A group 1,2,4,5 and 6) ; 203 mL (Part A group 3) ; 178 mL (Part B) of blood from screening to follow-up. These amounts do not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken at once 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 may be more than the amount indicated above.

Heart tracing:

To make a heart tracing, electrodes will be placed on arms, chest and legs. Prolonged use of these electrodes can cause skin irritation.

Fasting:
If someone has 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 gagging. When the sample is taken from the back of the nose, The volunteer may experience a stinging sensation and eyes may become watery.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Sex : male or female.
2. Age : 18 to 65 years, inclusive, at screening.
3. Body mass index : 18.0 to 30.0 kg/m2, inclusive, at screening.
4. Weight : 50 to 110 kg, inclusive, at screening.
5. Status : healthy subjects.

Further criteria apply, see protocol.

Exclusion criteria

1. Previous participation in the current study.
2. Employee of PRA or the Sponsor.
3. History of relevant drug and/or food allergies.
4. Using tobacco products within 2 months prior to (first) admission.
5. History of alcohol abuse or drug addiction (including soft drugs like cannabis products).

Further criteria apply, see protocol.

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:	Pending
Start date (anticipated):	11-04-2022
Enrollment:	72

Type:	Anticipated

Ethics review

Approved WMO Date:	09-02-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-04-2022
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
EU-CTR	CTIS2024-519180-17-00
EudraCT	EUCTR2022-000044-29-NL
CCMO	NL80502.056.22