A phase 1, randomised, double-blind, placebo-controlled, single ascending dose study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and immunogenicity of Ent001 in healthy subjects

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

Summary

ID

NL-OMON51546

Source
ToetsingOnline

Brief title
Ent001 IV First in Human SAD Study in adult healthy subjects

Condition

- Gastrointestinal inflammatory conditions
- Diabetic complications

Synonym
type 1 diabetes and inflammatory bowel disease (ulcerative colitis)

Research involving
Human

Sponsors and support

Primary sponsor: Enthera S.r.l.
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Ent001, Healty subjects, SAD = Single-ascending dose, Safety

Outcome measures

Primary outcome

To evaluate the safety and tolerability of single ascending doses (SAD) of

Ent001 in adult healthy male and female subjects

Secondary outcome

To evaluate the pharmacokinetics (PK) of SAD of Ent001 in adult healthy male

and female subjects

To assess the presence of antidrug antibodies (ADAs) against Ent001 following

SAD of Ent001 in adult healthy male and female subjects

Study description

Background summary

Ent001 is a new compound that may potentially be used for the treatment of type 1 diabetes and inflammatory bowel disease (ulcerative colitis). Ent001 works by inhibiting the TMEM219 receptor which is present on certain cells of the pancreas, colon and other organs. The inhibition of this receptor has a protective effect on these cells. In the case of type 1 diabetes this could result in more cells that produce insulin and therefor reduce the effects of the diabetes. In the case of inflammatory bowel disease more colon cells can be

preserved which could reduce the burden of disease.

Study objective

In this study we will investigate how safe the new compound Ent001 is and how well it is tolerated when it is used by healthy subjects.

We also investigate how quickly and to what extent Ent001 is absorbed, transported, and eliminated from the body (this is called pharmacokinetics). In addition, we look at the effect of Ent001 on some substances and cells in the blood (this is called pharmacodynamics).

We compare the effects of Ent001 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 Ent001, placebo, or both.

Ent001 has not been administered to humans before. It has been extensively tested in the laboratory and on animals.

Study design

The study will take a maximum of 18 weeks from the screening until the follow-up visit.

In total the volunteer will visit the research center 14 times:
- once for the screening.
- once for the volunteers stay in the research center. For the study it is necessary that the volunteer stay in the research center for 1 period of 5 days (4 nights). The volunteers are expected at the research center the day before the day of administration of the study compound. The volunteer has to be at the research center between 9:30 hrs and 14:00 hrs. Prior to entry into the research center the volunteer will be notified of the exact time. Day 1 is the day when the volunteer receive the study compound. The volunteer will leave the research center on Day 4 of the study.
- 11 times for short visits and one time for the follow-up visit. After the volunteers stay in the research center there will be 11 short visits to the research center. These short visits will take place on Days 5, 8, 10, 14, 21, 28, 35, 42, 56, 70 and 84. The follow-up visit will take place on Day 98.

The volunteer will be given Ent001 or placebo as an intravenous infusion (solution of the compound that will be administered directly in a blood vessel).

Whether the volunteer will receive Ent001 or placebo will be determined by chance. Per group, 4 subjects will receive Ent001 and 2 subjects will receive placebo.

Intervention

Group Day Treatment How often Dosing form
1 1 Ent001 0.15 mg/kg or placebo Once Infusion into the bloodstream (intravenous infusion)
2 Ent001 0.5 mg/kg or placebo
3 Ent001 1.7 mg/kg or placebo
4 Ent001 5 mg/kg or placebo
5 Ent001 10 mg/kg or placebo

Study burden and risks

possible discomforts:
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 345 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. To monitor the electrical activity of your heart over a longer period, electrodes (small, plastic patches) will be placed on the chest and abdomen. Prolonged use of these electrodes can cause skin irritation (rash and itching).

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.

Contacts

Public
Enthera S.r.l.

Via V. Gioberti 8
Milano 20122
IT
Scientific
Enthera S.r.l.

Via V. Gioberti 8
Milano 20122
IT

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Sex: male or female; females must be of nonchildbearing potential or postmenopausal.
2. Age: 18 to 65 years, inclusive, at screening.
3. Body mass index: 18.0 kg/m2 to 30.0 kg/m2, inclusive, at screening. Calculated as body weight (kg) divided by height (m)2.
4. Weight: >=50 kg at screening.
5. Status: healthy subjects.

Further criteria apply

Exclusion criteria

1. Previous participation in the current study.
2. Employee of ICON or the Sponsor.
3. History of sensitivity to any of the study treatments, or components thereof, or any clinically significant history of allergic conditions as judged by the Investigator (including drug allergies, asthma, eczema, or anaphylactic reactions, but excluding untreated, asymptomatic, seasonal allergies at the time of dosing).
4. The subjects who have had a prior allergic reaction, including anaphylaxis, to any other human, humanized, chimeric, or rodent antibodies.
5. Using tobacco products within 3 months prior to dosing.

Further criteria apply

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:	Recruiting
Start date (anticipated):	09-01-2023
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	05-08-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-08-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-09-2023
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	EUCTR2022-002176-37-NL
CCMO	NL82057.056.22

Study results

Results posted: 20-06-2024

First publication
13-05-2024