A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED, PHASE I STUDY TO ASSESS THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF SINGLE AND MULTIPLE ASCENDING DOSES OF THN391 IN HEALTHY SUBJECTS

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This study has been transitioned to CTIS with ID 2024-517955-10-00 check the CTIS register for the current data. In this study we will investigate how safe the new compound THN391 is and how well it is tolerated when it is used by healthy subjects....

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Dementia and amnestic conditions
Study type	Interventional

Summary

ID

NL-OMON53329

Source
ToetsingOnline

Brief title
THN391 first-in-human SAD and MAD study

Condition

- Dementia and amnestic conditions

Synonym
Dementia, Neurological diseases

Research involving

Human

Sponsors and support

Primary sponsor: Therini Bio
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: FIH, MAD, SAD, THN391

Outcome measures

Primary outcome

To assess the safety and tolerability of single ascending doses (SAD) of THN391

in healthy subjects (Part A).

To assess the safety and tolerability of multiple ascending doses (MAD) of

THN391 in healthy subjects (Part B)

Secondary outcome

To assess the pharmacokinetics (PK) of single and multiple doses of THN391 in

healthy subjects (Parts A/B).

To assess the potential immunogenicity of single and multiple doses of THN391

in healthy subjects (Parts A/B).

Study description

Background summary

THN391 is a new compound that may potentially be used for the treatment of neurological diseases, such as dementia. THN391 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. THN391 has been developed to block a specific part of the protein fibrin that has an important role in several neurological diseases. It is expected that THN391 does not reach the brain in healthy subjects, but it does in people

with neurologicaldisorders in which the so-called blood/brain barrier is affected.

Study objective

This study has been transitioned to CTIS with ID 2024-517955-10-00 check the CTIS register for the current data.

In this study we will investigate how safe the new compound THN391 is and how well it is tolerated when it is used by healthy subjects.

We also investigate how quickly and to what extent THN391 is distributed, and eliminated from the body. In addition, we look at the effect of THN391 on specific proteins and RNA expression changes.

We compare the effects of THN391 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 THN391, placebo, or both.

THN391 has not been administered to humans before. It has been extensively tested in the laboratory and on animals. THN391 will be tested at various dose levels.

Study design

The study will take a maximum of approximately Part A: 16 weeks (Groups 1 and 2) or 30 weeks (Group 3 and higher), Part B: 20 weeks (Groups 1 to 2) or 24 weeks (Groups 3 to 4) from the screening until the follow-up visit.

Part A:
In total the volunteer will visit the research center 8 times if the volunteer is in Groups 1 or 2 or 10 times if the volunteer is in Group 3 or higher:
- Once for the screening.
- Once for a stay in the research center. For the study it is necessary that the volunteer stays in the research center for 1 period of 6 days (5 nights). The volunteer will leave the research center on Day 4 of the study.
- After your stay in the research center there will be 6 short visits to the research center if the volunteer is in Group 1 or 2 or 8 short visits if the volunteer is in Group 3 or higher. For Groups 1 and 2, these short visits take place on Days 8, 15, 29, 43, 57 and 85. For Groups 3 and above, these short visits take place on Days 8, 15, 29, 43, 57, 85, 134 and 183.

Part B:
In total the volunteer will visit the research center 14 times if the volunteer is in Group 1 or 2 or 16 times if the volunteer is in Group 3 or 4:
- Once for the screening.

- Three times for a stay in the research center. For the study it is necessary that the volunteer stays in the research center for 1 period of 4 days (3 nights) and 32 periods of 3 days (2 nights). The volunteer will leave the research center on Day 2 of the study. After the volunteers stay in the research center, the volunteer will return to the research center for 2 additional stays. For Groups 1 to 2, these stays will take place from Day 14 to Day 16 (2 nights), and from Day 28 to Day 30 (2 nights). For Groups 3 to 4, these stays will take place from Day 28 to Day 30 (2 nights), and from Day 56 to Day 58 (2 nights).
- In between and after the volunteers stays in the research center there will be 10 short visits to the research center if the volunteer is in Groups 1 to 2, or 12 short visits to the research center if the volunteer is in Groups 3 to 4. For Groups 1 to 2, these short visits will take place on Days 4, 8, 18, 22, 32, 36, 43, 57, 85, and 113. For Groups 3 to 4, these short visits will take place on Days 4, 8, 15, 32, 36, 43, 60, 64, 71, 85, 113, and 141.

Intervention

The volunteer will be given THN391 or placebo as an intravenous infusion (solution of the compound that will be administered directly in a blood vessel).

Part A:
Group Day Treatment How often How
1 1 THN391 0.3 mg/kg# or placebo once intravenous infusion
2 1 THN391 1 mg/kg* or placebo once intravenous infusion
3 1 THN391 3 mg/kg* or placebo once intravenous infusion
4 1 THN391 10 mg/kg* or placebo once intravenous infusion
5 1 THN391 20 mg/kg* or placebo once intravenous infusion
* In case the dose level will be lower or higher than planned, the volunteer will be informed verbally.
# This means that 0.3 mg of THN391 will be administered per 1 kg of body weight.

Part B:
Group Days Treatment How often How
1 1, 15, 29 THN391 3 mg/kg# or placebo once every 2 weeks intravenous infusion
2 1, 15, 29 THN391 10 mg/kg* or placebo once every 2 weeks intravenous infusion
3 1, 29, 57 THN391 20 mg/kg* or placebo once every 4 weeks intravenous infusion
4 1, 29, 57 THN391 40 mg/kg* or placebo once every 4 weeks intravenous infusion
* In case the dose level will be lower or higher than planned, the volunteer will be informed verbally.
# This means that 3 mg of THN391 will be administered per 1 kg of body weight.

Study burden and risks

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 Part A: 338.4 milliliters (mL) (Groups 1 and 2) or 396.4 mL (Groups 3 and higher) Part B: 364.4 milliliters (ml) (Groups 1 to 2) or 400.2 milliliters (Groups 3 to 4) 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. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Coronavirus test (if applicable)
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
Therini Bio

2108 N St. Suite 4963
Sacramento CA 95816
US
Scientific
Therini Bio

2108 N St. Suite 4963
Sacramento CA 95816
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Willing and able to sign the ICF.
2. Male or female subjects aged 18 to 55 years old, inclusive, at screening.
3. Subjects of good physical and mental health on the basis of medical history, physical examination, clinical laboratory, ECG, and vital signs, as judged by the Investigator.
4. Subjects with a weight between 50.0 kg and 110.0 kg (inclusive) and a body mass index (BMI) between 18.0 kg/m2 and 32.0 kg/m2, inclusive, at screening.
5. At screening, female subjects must not be pregnant or lactating, or of nonchildbearing potential (either surgically sterilized or physiologically incapable of becoming pregnant, or at least 1 year postmenopausal [amenorrhea duration of 12 consecutive months]); nonpregnancy will be confirmed for all females by a negative serum pregnancy test at screening, at each admission, and follow-up.

Further criteria apply

Exclusion criteria

1. Subjects who, in the opinion of the Investigator, are or have experienced significant and/or acute illness within 5 days prior to screening or (first) admission to the clinical research center.
2. Subjects who, in the opinion of the Investigator, are experiencing clinical signs and/or symptoms of an infection, including sinusitis, cellulitis, bronchitis, or urinary tract infections, within 5 days prior to screening or (first) admission to the clinical research center.
3. Subjects with a history of coagulation or clotting disorders, either genetic or acquired, including but not limited to: deep vein thromboses (with or without pulmonary embolism), Protein C, S, or antithrombin deficiencies, Factor

V or prothrombin mutations, von Willebrand disease, hemophilia, antiphospholipid syndrome, or disseminated intravascular coagulation.
4. Subjects with a positive screen for hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV) antibodies, or human immunodeficiency virus (HIV) 1 and 2 antibodies.
5. Subject who are current smoker or use nicotine products within 3 months prior to screening.

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):	14-04-2023
Enrollment:	96
Type:	Actual

Ethics review

Approved WMO

Date:	21-02-2023
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	03-04-2023
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-10-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-10-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-05-2024
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
EU-CTR	CTIS2024-517955-10-00
EudraCT	EUCTR2022-003831-24-NL
CCMO	NL83710.056.23