A Phase 1, Randomized, Placebo-Controlled, Double-Blind, Single Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of DNL919 in Healthy Participants

Published: 08-06-2022
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To investigate the safety and tolerability of DNL919To characterize the serum PK of DNL919

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

Summary

ID

NL-OMON51440

Source
ToetsingOnline

Brief title
FIH of DNL919 in healthy volunteers

Condition

- Demyelinating disorders

Synonym
Alzheimers, Alzheimer's Disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Alzheimer's Disease, Antibody, Transferrin, TREM2

Outcome measures

Primary outcome

Incidence, severity, and seriousness of treatment-emergent adverse event

(TEAEs)

Secondary outcome

• DNL919 serum PK parameters following single IV doses of DNL919, including but

not limited to:

o maximum concentration (Cmax)

o area under the concentration-time curve from time zero to infinity (AUCinf)

Study description

Background summary

This Phase 1 study will evaluate the safety, tolerability, PK, and PD of DNL919 for the first time in healthy participants to assess the appropriateness of further development of DNL919 for the treatment of AD, a disease in which TREM2 activation-mediated microglial cell modulation may provide therapeutic benefit. The principal aim of this study is to obtain safety and tolerability data when DNL919 is administered through IV as a first dose to healthy participants. This information, together with the PK and PD data, will inform the design of future studies.

Study objective

To investigate the safety and tolerability of DNL919

To characterize the serum PK of DNL919

Study design

This is a Phase 1, randomized, double-blind, placebo-controlled single ascending dose study to evaluate the safety, tolerability, PK, and PD of DNL919 administered via IV infusion.

Intervention

DNL919 or placebo

Study burden and risks

Infusion of the study drug (TREM2 antibody) might result in infusion-related reactions. In addition, DNL919 is an investigational drug and has not been given to human subjects before, therefore, unexpected side effects might occur such as hypersensitivity reactions. In animals, reductions in reticulocyte and red blood cell count (anemia) have been reported, as well as immune cell infiltration into nerves upon repeated dosing, and myocardial degeneration and brain necrosis upon Q1W dosing at high dose levels.
Subjects in cohort A3 and beyond might have discomfort during or after the lumbar punctures. Moreover, subjects in cohort A6-A8 are exposed to radiation due to the FDG-PET. Lastly, subjects in cohort A6-A8 will get an MRI scan, which uses strong magnets that could affect metal objects inside the body.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Healthy male participants and healthy female participants of non childbearing potential aged between 18 and 55 years, inclusive, with a body mass index (BMI) between 18.5 and 32 kg/m2, inclusive

Exclusion criteria

Women of childbearing potential will be excluded in this study because reproductive toxicity studies have not yet been performed. Also, participants with any history of clinically significant neurological, psychiatric, endocrine (including diabetes mellitus), pulmonary, cardiovascular, gastrointestinal, hepatic, pancreatic, renal, metabolic, hematologic, immunologic, or allergic disease, or other major disorders.

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):	24-07-2022
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	08-06-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-06-2022
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:	24-11-2022
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	EUCTR2022-000756-10-NL
CCMO	NL80808.056.22