Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Two Year Study to Evaluate the Effect of Subcutaneous RO4909832 on Cognition and Function in Prodromal Alzheimer's Disease with Option for up to an Additional Two Years of Treatment and up to Three Years of an Open-Label Extension with Active Study Treatment

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To assess short-term and long-term safety and tolerability of gantenerumab (RO4909832) given at doses up to 1200mg subcutaneous (SC) every 4 weeks (Q4W).Secondary Objective of the Open-label extension:- To evaluate of the effect of 1200 mg...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cranial nerve disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON47181

Source
ToetsingOnline

Brief title
WN25203 part 3, Scarlet Road part 3

Condition

- Cranial nerve disorders (excl neoplasms)

Synonym
Alzheimer's disease, dementia

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: Alzheimer's disease, Gantenerumab, open label, Subcutaneous

Outcome measures

Primary outcome

Open-label extension: long-term and short-term safety and tolerability

Secondary outcome

- To evaluate of the effect of 1200 mg gantenerumab SC Q4W over time on

hippocampal volume, whole brain volume, ventricular enlargement,

and possibly other volumetric measures of the brain.

- To evaluate of the effect of 1200 mg gantenerumab SC Q4W on changes in

amyloid load over time by Positron Emission Tomography

(PET) Imaging using Florbetapir 18F , an amyloid PET ligand

- To evaluate the effect of 1200 mg gantenerumab SC Q4W over time on clinical

outcomes (cognition and function), as assessed with the CDRSOB, the ADAS-Cog,

the MMSE, the FCSRT-IR, the CDR global score, the FAQ, and to determine the

presence of and time to onset of dementia.

- To explore pharmacokinetics by determining the relationship of plasma

concentrations of gantenerumab on other responses

- To assess incidence of antigantenerumab antibodies, and if relevant, evaluate

its effect on the pharmacokinetic, pharmacodynamic, efficacy

and safety parameters

Study description

Background summary

RO4909832 (Mab31) is a human antibody directed against the amyloid plaques present in the brains of people with Alzheimer's disease. The deposition of amyloid in the brains plays an important role in the pathogenesis of this disease. Animal Models of passive immunization with anti-amyloid antibodies showed a decrease in amyloidosis and show improvement of cognitive functions. There is a great need to improve the treatment of Alzheimer's disease, especially for drugs that affect the course of the disease. Passive immunization with anti-amyloid antibodies, could improve the treatment of Alzheimer's disease. This study is an early stage of Alzheimer's disease (prodromal) investigating the effect of RO4909832. By decreasing amyloid amount in an early stage of the disease, it is assumed that less damage is done. PET scan data from the Phase 1 study (MAD study) raise the suggestion that an amyloid-reducing effect of gantenerumab occurs during the period of 6 months at doses of 60 and 200 mg IV.

Dosing in the double-blind placebo-controlled Parts 1 and 2 with the originally selected doses for Study WN25203 (105 and 225 mg) was suspended on 19 December 2014, following a planned interim futility analysis that estimated a low probability for meeting the prespecified primary outcome measure. Additional analyses indicated that higher doses of gantenerumab may potentially have clinically relevant effects on cognition and function.

Study objective

To assess short-term and long-term safety and tolerability of gantenerumab (RO4909832) given at doses up to 1200
mg subcutaneous (SC) every 4 weeks (Q4W).

Secondary Objective of the Open-label extension:
- To evaluate of the effect of 1200 mg gantenerumab SC Q4W over time on

hippocampal volume, whole brain volume, ventricular enlargement, and possibly other volumetric measures of the brain.
- To evaluate of the effect of 1200 mg gantenerumab SC Q4W on changes in amyloid load over time by Positron Emission Tomography (PET) Imaging using Florbetapir 18F , an amyloid PET ligand
- To evaluate the effect of 1200 mg gantenerumab SC Q4W over time on clinical outcomes (cognition and function), as assessed with the CDRSOB, the ADAS-Cog, the MMSE, the FCSRT-IR, the CDR global score, the FAQ, and to determine the presence of and time to onset of dementia. After 3 years in part 3, only MMSE will be administered.
- To explore pharmacokinetics by determining the relationship of plasma concentrations of gantenerumab on other responses
- To assess incidence of antigantenerumab antibodies, and if relevant, evaluate its effect on the pharmacokinetic, pharmacodynamic, efficacy and safety parameters

Study design

This is an multicenter open-label extension study (part 3 of study WN25203) with active study treatment.
During Part 3 study, subjects will receive gantenerumab Q4W that will be uptitrated starting from 105 or 225 mg based on the ApoE genotype to up to 1200 mg to reach the doses expected to give clinically meaningful effect in a less than 1 year.

Intervention

All subjects participating in the open-label extension (Part 3) will receive 1200 mg gantenerumab Q4W. Dosing will be started at 105 or 225 mg based on the ApoE genotype. Dose will be uptitrated up to 1200 mg.

Study burden and risks

For more information, please see the answer on question number E9.

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

- Adult patients, 50-85 years of age;- Patients with prodromal Alzheimer's Disease who are not receiving memantine or cholinesterase inhibitors;- Has a study partner who is able to provide accurate information as to the patient's cognitive and functional abilities, who agrees to provide information at clinic visits which require partner input for scale completion;- Has had sufficient education or work experience to exclude mental retardation;- Study partner has noticed a recent gradual decrease in patient's memory (e.g. over the last 12 months), which the patient may or may not be aware of;- Screening MMSE score of 24 or above;- Subjects who received double-blind treatment during either Part 1 or Part 2 prior to the futility analysis, and had at least one follow-up/drop-out visit will be eligible to enter Part 3.

Exclusion criteria

- Other prior or current neurologic or medical disorder which may currently or during the course of the study impair cognition or psychiatric functioning ;- A history of stroke ;- A documented history of transient ischemic attack within the last 12 months ;- History of schizophrenia, schizoaffective or bipolar disorder ;- Currently meets criteria for major depression ;- Within the last 2 years, unstable or clinical significant cardiovascular disease (e.g. myocardial infarction, angina pectoris)

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-04-2016
Enrollment:	11
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Gantenerumab
Generic name:	nvt

Ethics review

Approved WMO

Date:	11-04-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	04-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	04-01-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-09-2019
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	EUCTR2010-019895-66-NL
ClinicalTrials.gov	NCT01224106
CCMO	NL55627.056.15