A 90-week, multi-center, randomized, double-blind, placebo-controlled study in patients with mild Alzheimer*s Disease (AD) to investigate the safety, tolerability and Abeta-specific antibody response following repeated i.m. injections of adjuvanted CAD106

Published: 25-02-2010
Last updated: 04-05-2024

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

Summary

ID

NL-OMON36379

Source
ToetsingOnline

Brief title
CAD106A2203

Condition

- Other condition
- Neurological disorders NEC

Synonym

Alzheimer Disease, Dementia

Health condition

Dementie van het Alzheimer type

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Bedrijf: Novartis

Intervention

Keyword: active immunization, AD, adjuvant, CAD106

Outcome measures

Primary outcome

Frequency of adverse events, cerebral MRI scan, injection-related reactions collected in a patient diary, vital signs, neurological and physical examination, ECG, blood sedimentation rate, hematology, blood chemistry, urinalysis, specific immunological safety tests in blood and CSF

Secondary outcome

Ab-specific antibody levels in serum and CSF, Ab- and Qb-specific T-cells, MMSE, CDR, ADCS - ADL, NPI-Q, ADAS - Cog, CogState Tests, COWAT, CFT; Volumetric MRI. Additionally, PET imaging with florbetapir F18 if participating in PET substudy.

Study description

Background summary

Alzheimer*s disease (AD) is one of the most prevalent neurological disorders

among the elderly worldwide. Currently, the only pharmacological therapies available are symptomatic drugs, such as cholinesterase inhibitors, and other drugs to control the secondary behavioral symptoms of AD. Accumulating evidence strongly suggests that the *-amyloid peptide plays a causal role in AD and that successful strategies for a disease-modifying therapy are likely to include products that directly or indirectly affect the deposition of *-amyloid in the brain. Immunotherapy has emerged as a promising approach to achieve this goal. CAD106 is such immunotherapy and the safety and immunogenicity of CAD106 need to be further evaluated in AD patients. The current study focuses on the assessment of the safety and tolerability of the theraphy, in combination with an adjuvant.

Study objective

The purpose of this study is to evaluate the benefit of adding an adjuvant to CAD106 and to select the dose of CAD106 and adjuvant to be used in further development. Additionally, clinical and biomarker measures (CSF, plasma biomarkers, volumetric MRI) will be assessed to generate hypotheses to be further studied in Phase IIb/III. PET imaging with florbetapir F18 (at participating centers) will also support this additional objective.

Study design

This is a multi-center, randomized, double-blind, placebo-controlled study in patients with mild AD. After a screening period of max. 5 weeks, eligible patients will be allocated to the active drug (CAD106 +/- adjuvant) or placebo in a 7:1 randomization ratio under double-blind conditions. Study medication will be injected intramuscular at weeks 0, 6, 12, 24, 36, 48 and 60. Thereafter patients will continue in the study for a total duration of 90 weeks. Frequent safety evaluations will be performed to allow close monitoring of patients, in particular 2 lumbar punctures, and 6 MRIs to monitor any unwanted immune response. An independent, unblinded Data Safety Monitoring Board will review the data from the study on an ongoing basis and will be involved in all the major decisions during the study.

Intervention

In cohort I all patients receive 7 injections of CAD106 or placebo. There are 6 arms:
- Arm 1: Injection 1-7: CAD106 150 ug + Alum 150 ug
- Arm 2: Injection 1-3: CAD106 150 ug + Alum 50 ug, injection 4-7: CAD106 150 ug + Alum 450 ug
- Arm 3: Injection 1-7: Placebo + Alum 150 ug
- Arm 4: Injection 1-3: CAD106 150 ug + MF59 250 uL, injection 4-7: CAD106 450 ug without adjuvant
- Arm 5: Injection 1-3: CAD106 150 ug + MF59 150 uL, injection 4-7: CAD106 450

ug without adjuvant
- Arm 6: Injection 1-3: Placebo + MF59 250 uL, injection 4-7: Placebo without adjuvant

In cohort II all patients receive 7 injections of CAD106 (with or without adjuvant) or placebo. There are 3 arms:
- CAD106 450 ug + Alum 450 ug
- CAD106 450 ug without adjuvant
- Placebo + Alum 450 ug

Study burden and risks

The patient will visit the hospital 22 times during 90 weeks. During these visits, the following assessments will take place: 22 x lab assessment 2 x lumbar punction 22 x blood pressure, pulse, body temperature and weight 11 x physical examination and neurological examination 6 x ECG 6 x cerebral MRI, 6 x completion of different tests/scales. In case patient participates in the PET substudy: additionally 3 x PET imaging with Florbetapir F18. The patient needs to complete a diary for 7weeks. The blood draws, the lumbar punctions and the intravenous injections with Florbetapir (latter is performed only in the patients participating in the PET substudy) may cause some discomfort. These assessments will be performed by well trained personnel with experience. For some people MRI scan and PET imaging (latter is performed only in the patients participating in the PET substudy) may cause some discomfort. To be able to take part in the study, there should be a care giver/partner with the patient that will join the patient to all study visits.

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

- Male and female patients below the age of 85 years. For PET Substudy (amendment 3): Male and female patients equal to or above the age of 50 years and below the age of 85 years
- Female patients must be without childbearing potential (post-menopausal or surgically sterilized).
- Diagnosis of dementia of the Alzheimer*s type according to the DSM-IV criteria
- Patients who satisfy the criteria for a clinical diagnosis of probable AD established by NINCDS-ADRDA
- Mild AD as confirmed by a MMSE score of 20 to 26 (both inclusive)
- Primary caregiver is present and willing to assent in writing to taking the responsibility for assessing the condition of the patient throughout the study, and for providing input to safety and tolerability assessments in accordance with all protocol requirements.

Exclusion criteria

- Any medical or neurological condition, other than AD, that contributes significantly to the patient*s dementia
- History in the past two years or current diagnosis of CNS inflammation
- Evidence of vascular dementia or other cerebrovascular disease
- Current DSM-IV diagnosis of major depression and/or any other DSM-IV Axis 1 diagnosis that may interfere with the evaluation of the patient*s response to study medication
- Current diagnosis of an active, uncontrolled seizure disorder.
- History or current diagnosis of an active autoimmune disease
- Coronary heart disease
- Symptomatic heart failure
- Initiation or change in dose of current treatment with cholinesterase-inhibitors (ChEIs) and/or other AD treatment in the 4 weeks prior to clinical assessments

- History of alcohol or drug abuse within the last 2 years and/or current alcohol/drug abuse
- Patients who have been declared mentally incompetent

Study design

Design

Study phase:	2
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):	03-06-2010
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	25-02-2010
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	24-03-2010
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO

Date:	06-07-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-07-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-11-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-12-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-12-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-01-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-03-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-06-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	25-07-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-08-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-09-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-10-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-02-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-03-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-04-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-06-2012

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-07-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-10-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-11-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-01-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2009-012394-35-NL
ClinicalTrials.gov	NCT01097096
CCMO	NL30823.000.09