A multi-centre, double-blind, parallel-group, randomized controlled study to investigate the efficacy, safety and tolerability of orally administred BI 409306 during a 12-week treatment period compared to placebo in patients with Alzheimer's disease.

Published: 17-12-2014
Last updated: 21-04-2024

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

Summary

ID

NL-OMON42045

Source
ToetsingOnline

Brief title
BI 409306 in patients with prodromal Alzheimer Disease

Condition

- Neurological disorders NEC

Synonym
prodromal Alzheimer Disease/Alzheimer Disease

Research involving
Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Boehringer Ingelheim

Intervention

Keyword: 12 weeks, Phase II, Placebo controlled, Prodromal AD

Outcome measures

Primary outcome

Change in cognition as measured by change from baseline in Neuropsychological

Test Battery (NTB - total score) after 12-week treatment.

Secondary outcome

Change from baseline in ADCS-MCI-ADL total score after 12-week treatment

Change from baseline in CDR-SB total score after 12-week treatment

Change from baseline in ADAS-cog11 (Alzheimer's Disease Assessment

Scale-cognitive subscale) total score after 12-week treatment

Study description

Background summary

Alzheimer*s disease (AD), a chronic progressive mental disorder, is the most common cause of dementia and accounts for 50 to 70 % of all cases. AD is mainly a disorder of the elderly; The age-specific prevalence of AD almost doubles every 5 years after age 65. Among developed nations,
approximately 1 in 10 elderly people (65+ years) is affected by dementia to some degree, In the prodromal stage of the disease, clinical symptoms may include impairment of episodic memory and/or other cognitive domains, like executive function, orientation and judgment.
Patients with these prodromal clinical symptoms showed an increased risk of developing Alzheimer*s dementia with progressive decline in the ability to

perform activities of daily living and the appearance of behavioral changes and/or psychiatric symptoms (mood
disturbances, hallucinations, personality changes). Subsequently and in accordance with the further progression of the disease there is an increasing utilization of resources and medical care finally leading to the need for full-time assisted living . The median time from onset of symptoms to death is estimated to be around 10 years.Currently approved AD treatment is purely symptomatic and only approved for Mild to Moderate AD This treatment isn*t approved for prodromal stages of the disease.
Patients with prodromal AD have an increased risk of eventually developing Alzheimer's dementia. Therefore, a symptomatic treatment that
delays the progress of these first symptoms cause by the underlying pathology might provide a substantial benefit to such patients.
A symptomatic treatment that proves to be more efficacious than the currently available compounds (AChEIs,
memantine) in improving both existing cognition deficits and the ability to better perform activities of daily living would provide a substantial benefit to patients.

Study objective

The primary objective of this study is to assess efficacy and safety of BI 409306 at doses of 10 mg, 25 mg and 50 mg once daily, 25 mg twice daily compared to placebo over a 12-week treatment period in male and female patients at least 55 years of age with prodromal AD.

Study design

This is a 12-week, multi-center, randomized, double-blind, double dummy placebo controlled, parallel group study in patients with AD.
In total, 288 patients with prodromal AD who meet the entry criteria are planned to be randomized in this trial.
After obtaining informed consent, patients will undergo a screening period of a maximum of 5 weeks. All patients who successfully complete the screening period and are eligible for the study, then enter a minimum of 2 weeks of single blinded placebo run-in before
randomization. Patients who successfully complete the single-blinded phase and who fulfil both the inclusion and exclusion criteria will be randomized to the 12-week double blind treatment period at visit3 and will be assigned to one of the 5 treatment groups namely: once daily (QD) 10 mg, 25 mg, or 50 mg BI 409306, or 25 mg BI 409306 twice daily (BID), or placebo.

Intervention

See table 4.1.1. of the clinical trial protocol

Study burden and risks

5 week screening period, 2 week run-in periode (v 1 and 2), 12 week treatment period with 5 visits and 2 phone calls, 1 follow up visit

Physical examination
Heart rate, breathing rate, and blood pressure
Questions for patient and study partner to complete
Blood taken for routine tests, PK, vitamin B12 and folate levels
Blood taken for testing of Syphilis and HIV
Urine taken for a pregnancy test and a drug screening test (if applicable).
Optional blood samples will be collected for additional biomarkers
Liver Function Tests (from safety lab sample)
Urine taken for routine tests
ECG (electrocardiogram)
1 x MRI (Magnetic Resonance Imaging)- if applicable
1 x CSF sampling. Not necessary if a useful past CSF sample or PET scan result are available

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

Written Informed Consent, 55 years or older, minimal 50 kg.
Patients with diagnosis of prodromal AD in accordance with the recommendation of the International Working Group (IWG), Dubois et al. 2007
Symptoms noticed by the patients
Cognitive testing confirming prodromal symptoms
Biomarker evidence of AD pathology
No evidence of other forms of dementia
No other concomitant illness or medication which could confound or prohibit completion in the trial by the patient

Exclusion criteria

Other forms of dementia, or a psychiatrical disorder or severe depression
Substantial concomitant cerebrovascular disease, Medical history of cancer, Significant ischemic heart disease, Significant gastrointestinal disorders, Uncontrolled endocrine disease, Significant pulmonary disease predisposing to hypoxia, Immunological disorders, Unstable/uncontrolled haematological disease, Any other systemic or multiple organ dysfunctions, Severe renal impairment, Any suicidal actions in the past 2 years, Previous participation in investigational drug studies of mild cognitive impairment within three months prior to screening, HIV or syphilis infection confirmed by a central lab test, intake of restricted medications as per protocol, pre-menopausal women not able or willing to take appropriate birth control, breast feeding women.

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):	27-01-2015
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	BI 409306
Generic name:	nvt

Ethics review

Approved WMO Date:	17-12-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-01-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-07-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-07-2015
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-09-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-09-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-04-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-06-2017
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	EUCTR2013-005031-24-NL
ClinicalTrials.gov	NCT02240693
CCMO	NL49930.056.14