A randomised double-blind placebo-controlled clinical trial investigating the effect and safety of oral semaglutide in subjects with early Alzheimer*s disease (EVOKE plus)

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This study has been transitioned to CTIS with ID 2023-506918-45-00 check the CTIS register for the current data. Primary objectiveTo confirm the superiority of oral semaglutide versus placebo on the change in cognition and function in subjects with...

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

Summary

ID

NL-OMON51141

Source
ToetsingOnline

Brief title
EVOKE plus

Condition

- Dementia and amnestic conditions

Synonym
Alzheimer, Dementia

Research involving

Human

Sponsors and support

Primary sponsor: Novo Nordisk
Source(s) of monetary or material Support: Novo Nordisk

Intervention

Keyword: Alzheimer□s disease, Oral semaglutide

Outcome measures

Primary outcome

Change in the Clinical Dementia Rating - Sum of Boxes (CDR-SB) score from

baseline (week 0) to week 104

Secondary outcome

Secondary confirmatory endpoints

-Change in the Alzheimer*s Disease Cooperative Study Activities of Daily Living

Scale for MCI (ADCS-ADLMCI) score from baseline (week 0) to week 104

-Time to progression to dementia (CDR global >=1.0) among subjects with MCI (CDR

global = 0.5) at baseline From baseline (week 0) to week 104

Supportive secondary endpoints

-Change in the 13-item Alzheimer*s Disease Assessment Scale - Cognitive

Subscale (ADAS-Cog-13) score From baseline (week 0) to week 104

-Change in the Montreal Cognitive Assessment (MoCA) score from baseline (week

0) to week 104

-Change in the Alzheimer*s Disease Composite Score (ADCOMS) From baseline (week

0) to week 104

-Change in the Mini-Mental State Examination (MMSE) score from baseline (week 0) to week 104

-Change in the 10-item Neuropsychiatric Inventory (NPI) score from baseline (week 0) to week 104

-Time to progression in disease stage based on global CDR score from baseline (week 0) to week 104

-Number of treatment emergent adverse events (TEAEs) From baseline (week 0) to week 104

-Change in high sensitivity C-reactive protein level from baseline (week 0) to week 104

-Time to first occurrence of major adverse cardiovascular event (MACE) comprising non-fatal myocardial infarction, non-fatal stroke and allcause death from baseline (week 0) to week 104

-Time to first occurrence of stroke from baseline (week 0) to week 104

-Change in the EQ-5D-5L proxy score from baseline (week 0) to week 104

Extension phase

-Change in the CDR-SB score from baseline (week 0) to week 156

-Change in the ADCS-ADL-MCI score from baseline (week 0) to week 156

-Time to progression to dementia (CDR global >=1.0) among subjects with MCI (CDR global = 0.5) at baseline From baseline (week 0) to week 156

Study description

Background summary

Dementia is a rapidly growing public health concern causing a significant global socioeconomic impact. Clinically, the continuum of disease progression from mild cognitive impairment (MCI) to mild, moderate and severe dementia is accompanied by gradual loss of cognitive function and increasing difficulties in performing activities of daily living. Therefore, therapeutic interventions targeting the early stages of cognitive impairment could have substantial clinical and economic consequences for patients, their caregivers and society. Currently there are no treatments available
for the treatment of MCI and only symptomatic treatments are available for dementia of the Alzheimer*s type. Semaglutide and liraglutide are structurally similar glucagon-like peptide-1 receptor agonists (GLP-1 RAs) modified via fatty acid acylation, while semaglutide was further optimised to provide the convenience of oral administration. The potential effects of semaglutide and liraglutide on cognition and related mechanisms have been investigated in relevant preclinical models of Alzheimer*s disease, atherosclerosis and inflammation.

Study objective

This study has been transitioned to CTIS with ID 2023-506918-45-00 check the CTIS register for the current data.

Primary objective
To confirm the superiority of oral semaglutide versus placebo on the change in cognition and function in subjects with MCI or mild dementia, both of the Alzheimer*s type.

Secondary objectives
To compare the effects of oral semaglutide versus placebo in subjects with MCI or mild dementia, both of the Alzheimer*s type, on:
• progression to dementia among subjects with MCI at baseline
• neuropsychiatric symptoms
• safety and tolerability
• quality of life

Study design

This is a randomised (1:1), double-blind, placebo-controlled, multicentre, multinational trial comparing oral semaglutide 14 mg OD versus placebo, both added to standard of care in subjects with MCI or mild dementia of the Alzheimer*s type.

Intervention

Oral semaglutide 3mg, 7mg, 14mg tablets or placebo tablets.

Study burden and risks

The safety and tolerability of oral semaglutide is well established in a comprehensive clinical development programme for T2DM. Based on this extensive clinical experience, all necessary precautions are implemented in the trial design and planned conduct of the trial to minimise risks associated with the treatment as well as participation in the trial. Taking into account the measures taken to minimise risk to subjects participating in this trial, the potential risks identified in association with oral semaglutide are justified by the anticipated benefits that may be afforded to subjects with MCI or mild dementia of the Alzheimer*s type.

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 or female, aged 55-85 years (both inclusive) at the time of signing informed consent.
- MCI or mild dementia of the Alzheimer's type according to the National Institute of Aging-Alzheimer's Association (NIA-AA) 2018 criteria
- Clinical Dementia Rating (CDR) global score of 0.5 and CDR of 0.5 or more in at least one of the three instrumental activities of daily living categories (personal care, home & hobbies, community affairs) Or CDR global score of 1.0
- Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) delayed memory index score of less than or equal to 85
- Mini-Mental State Examination (MMSE) greater than or equal to 22
- Amyloid positivity established with either amyloid positron emission tomography (PET) or cerebrospinal fluid (CSF) Aβ1-42
- If receiving an approved Alzheimer's disease treatment (such as acetylcholinesterase inhibitors or memantine) the dose must have been stable for at least 3 months prior to screening and should not be changed during the trial unless medically necessary

Exclusion criteria

-Brain magnetic resonance imaging (MRI) (or computerised tomography (CT)) scan suggestive of clinically significant structural central nervous system (CNS) disease confirmed by central read (e.g. cerebral large- vessel disease [large vessel (cortical) infarcts greater than 10 mm in diameter], prior macro-haemorrhage [greater than 1 cm^3], cerebral vascular malformations, cortical hemosiderosis, intracranial aneurism(s), intracranial tumours, changes suggestive of normal pressure hydrocephalus)
-Brain MRI (or CT) scan suggestive of strategic infarcts defined as bilateral thalamic lacunar infarcts and singular paramedian thalamic infarcts confirmed by central read
-Evidence of a relevant neurological disorder other than mild cognitive impairment (MCI) or mild dementia of the Alzheimer's type at screening, including but not limited to Parkinson's disease, Lewy body disease, frontotemporal dementia of any type, Huntington's disease, amyotrophic lateral sclerosis, multiple sclerosis, systemic lupus erythematosus, progressive supranuclear palsy, neurosyphilis, human immunodeficiency virus (HIV), learning disability, intellectual disability, hypoxic cerebral damage, or significant head trauma with loss of consciousness that led to persistent cognitive deficits
-Evidence of a clinically relevant or unstable psychiatric disorder, based on Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria, including schizophrenia or other psychotic disorder, or bipolar disorder. A subject with a history of major depression who has not had an episode in the last 24 months before the day of screening and is considered in remission or

whose depression is controlled with treatment can be included in the trial per investigator's judgement

Study design

Design

Study phase:	3
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):	01-07-2021
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet bekend
Generic name:	oral semaglutide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	18-03-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	25-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-06-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-07-2023

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	CTIS2023-506918-45-00
EudraCT	EUCTR2020-004864-25-NL
CCMO	NL76794.056.21
Other	UTN:U1111-1259-2920