A randomized, placebo-controlled, double-blind, parallel-group Phase 2a exploratory study with placebo run-in to investigate PK/PD effects, safety, tolerability and pharmacokinetics of REM0046127 oral suspension compared with placebo in subjects with mild to moderate Alzheimer's disease

Published: 01-06-2022
Last updated: 14-03-2025

• To assess the tolerability and safety of the investigational medicinal product

Ethical review	Approved WMO
Status	Completed
Health condition type	Mental impairment disorders
Study type	Interventional

Summary

ID

NL-OMON53612

Source
ToetsingOnline

Brief title
REMAD-02

Condition

- Mental impairment disorders

Synonym
Alzheimer disease, dementia

Research involving
Human

Sponsors and support

Primary sponsor: ReMYND
Source(s) of monetary or material Support: ReMynd

Intervention

Keyword: Alzheimer, Phase 2 studie

Outcome measures

Primary outcome

• Incidence of treatment-emergent adverse events

Secondary outcome

NA

Exploratory endpoints are listed in protocol in section 3.0

Study description

Background summary

Alzheimer*s disease is the most common form of dementia in the elderly, affecting up to 30% of the population at the age of 85. This disease leads to a loss of nerve cells and impairs the function of your brain. It can also lead to behavioural abnormalities and a decreasing ability to perform basic activities of daily living.

At the moment, there are two kinds of treatment available for Alzheimer patients. But these treatments are only capable of acquiring a short-term improvement of the symptoms and cannot cure or stop the disease.

REM0046127 is a new investigational medicinal product developed for the treatment of patients suffering from Alzheimer*s Disease. In the diseased nerve cells of patients with Alzheimer disease, the levels of Ca2+ (an ion in the body fluids) are elevated, this results in nerve cells not working well anymore. REM0046127 could lower these increased levels of Ca2+ to normal levels in laboratory experiments with cells mimicking Alzheimer disease. This

medication has been tested in 66 young and 7 elderly healthy volunteers but has not yet been tested in Alzheimer patients. Therefore, the aim of this study is to be observe if and how the medication works and if it can stop the decay of the nerve cells and maybe even reverse cognitive impairments caused by their loss. The study in healthy volunteers showed that REM0046127 was well tolerated and safe.

Study objective

• To assess the tolerability and safety of the investigational medicinal product

Study design

A phase 2, randomized, placebo-controlled, double-blind multicenter study

Intervention

If the screening has been successfully passed, the subject will be randomized after the placebo run-in phase on Day 1 to one of the possible treatment arms.
- Group 1: Active dose oral suspension twice a day. The maximal dose is 87,5 mg twice a day (175 mg a day) but dose can also be lower.
- Group 2: Placebo suspension (twice a day).

Study burden and risks

This is the second study in which REM0046127 is administered in humans. Given that REM0046127 was safe and well tolerated at all dose levels tested in the Phase 1 study, it is currently not possible to classify any AE as expected.

REM0046127 may improve cognitive decline which may improve daily living for patients with mild to moderate AD. The results of the study might help people with a similar condition in the future.
A direct benefit from the study medication cannot be guaranteed.

There is a chance that you will be assigned to the placebo treatment group and will not get the study medication

There may be some discomfort from the measurements during the study

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

1. Mild to moderate AD as characterized by the following clinical, cognitive, and functional criteria.
a. Biomarker profile reflecting AD, according to The National Institute on Aging*Alzheimer's Association (NIA-AA) Research Framework based on Screening CSF Aβ1-42 and p-tau concentrations
b. Clear EEG deficit as assessed by the EEG reader
c. MMSE score above 12 (preferably above 16) and a maximum of 24
2. A brain imaging study, such as magnetic resonance imaging (MRI) and/or computed tomography (CT) scan having been performed within last 6 months from day of the Screening visit or during the Screening phase of this study consistent with the clinical diagnosis of AD and excluding other potential causes of dementia. If there has been a significant change in clinical status suggestive of stroke or other possible central neurological disease with onset between the time of the last MRI or CT and the Screening evaluation, an MRI scan should be repeated during Screening procedures if considered appropriate by the Investigator
3. Age 50 to 85
4. BMI above 18 and below 30 kg/m2

5. If taking concomitant medications, treated with stable doses of drugs essentially required for chronic medical conditions which do not lead to exclusion, during a period of at least 3 months prior to screening, and dose regimen is expected to remain stable during the conduct of the study
6. If taking an approved cholinesterase inhibitor or NMDA antagonist for treatment of Alzheimer*s disease, treated with a stable dose for at least 6 months prior to the screening visit and the dose is not expected to change during the study as per investigators judgement, or must be off such Alzheimer medication for a period of 8 weeks prior to screening
7. Willing and able to give informed consent.
8. Have a caregiver who assists the participant every day and has intimate knowledge of the participant*s cognitive, functional, and emotional states and of the participant*s personal care. The caregiver must be willing to accompany the participant to all study visits and to supervise IMP administration as well as report adverse events. The caregiver must be willing and able to give informed consent for their own participation and be able to read and write
9. Be able to read, write, speak clearly for the cognitive tests, with eyesight and hearing sufficient to enable completion of the cognitive tests

Exclusion criteria

Subjects are excluded from the study if any of the following criteria apply:
1. COVID-19 positive test at the screening visit
2. Clinical, laboratory or neuro-imaging findings consistent with:
i. Other primary degenerative dementia, (dementia with Lewy bodies, fronto-temporal dementia, Huntington*s disease, Creutzfeldt-Jakob Disease, Down*s syndrome, etc.)
ii. Other neurodegenerative condition (Parkinson*s disease, amyotrophic lateral sclerosis, etc.)
iii. Cerebrovascular disease (major infarct, one strategic or multiple lacunar infarcts, extensive white matter lesions > one quarter of the total white matter)
iv. Other central nervous system diseases (severe head trauma, tumors, subdural hematoma or other space occupying processes, etc.)
v. Seizure disorder
vi. Other infectious, metabolic or systemic diseases affecting central nervous system (syphilis, present hypothyroidism, present vitamin B12 or folate deficiency, serum electrolytes out of normal range, juvenile onset diabetes mellitus, etc.)
3. Current presence of a clinically significant major psychiatric disorder according to the criteria of the DSM-IV, or symptom that could affect the subject's ability to complete the study
4. Current clinically significant systemic illness, e.g., neoplasia, that is likely to result in deterioration of the subject's condition or affect the subject's safety during the study

5. History of liver disease, including Gilbert*s disease or alcohol abuse
6. Active liver disease or jaundice, or out-of-range values of alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, gamma-glutamyl transferase (GGT), Alkaline Phosphatase (ALP) and/or lactate dehydrogenase (LDH)
7. History of severe post-lumbar puncture syndrome
8. Abnormalities in the blood clotting system or abnormal coagulation status
9. Women of childbearing potential.
Refer to Appendix X for the definitions of woman of nonchildbearing potential.
10. Male subjects with female partners of child-bearing potential who are unwilling or unable to adhere to contraception requirements
11. Participation in another clinical study during the last 3 months
12. Wheelchair-bound or bed-ridden
13. Hypersensitivity to the IMP, or components thereof, or significant drug or other allergies
that, in the opinion of the investigator, contraindicates participation in the study
14. Any other criteria which in the opinion of the Investigator causes the subject not to qualify for the study

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:	Completed
Start date (anticipated):	14-09-2022
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	REM0046127
Generic name:	REM0046127

Ethics review

Approved WMO Date:	01-06-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-04-2023
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
EudraCT	EUCTR2022-000080-43-NL
ClinicalTrials.gov	NCT05478031
CCMO	NL80568.056.22

Study results

Date completed: 05-04-2024

Summary results
Trial ended prematurely