A randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer*s Disease (AD)

Published: 10-10-2017
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The purpose of this study is to determine the effect of treatment on cognition, overall clinical status and underlying pathology in subjects with a risk of occurrence of the first clinical symptoms of Alzheimer's disease.People without...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Structural brain disorders
Study type	Interventional

Summary

ID

NL-OMON50603

Source
ToetsingOnline

Brief title
CCNP520A2202J (Generation II)

Condition

- Structural brain disorders

Synonym
Alzheimer's Disease, Dementia

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V (sponsor/verrichter van dit onderzoek)

Intervention

Keyword: Alzheimer's Disease, APOE4 hetrozygote, CNP520

Outcome measures

Primary outcome

- Time to dignosis of MCI due to AD or dementia due to AD

- APCC (API Preclinical Cognitive Battery test score)

Secondary outcome

- Global clinical status

- RBANS

- MRI, cerebral amyloid angiopathy

- Atophy

- AD related biomarkers

Study description

Background summary

Alzheimer's disease (AD) is one of the most common neurological disorders worldwide, the most common and invalidating age-related disorder. AD causes progressive amnesia, dementia, and eventually erratic problems and death. Currently, the only pharmacological therapy is symptomatic drugs such as cholinesterase inhibitors (Cheis) or other drugs against AD's secondary behavioral symptoms.

Study objective

The purpose of this study is to determine the effect of treatment on cognition, overall clinical status and underlying pathology in subjects with a risk of occurrence of the first clinical symptoms of Alzheimer's disease.
People without cognitive problems with genotype APOE4 HT and age 60 to 75 years are selected because they represent a population with a particularly high risk of progression to MCI (mild cognitive impairment) due to the disease of Alzheimer's disease and / or dementia due to Alzheimer's disease.

Study design

In the pre-screening phase, participants will receive disclosure of their individual test results for APOE genotyping. In the follow-up after release of the genetic information, telephone appraisal talks are conducted with participants to whom their genotype is released.
In the treatment phase, a randomized, double-blind, placebo-controlled, two-cohort, two-cohort study carried out in parallel with subjects receiving at least 60 months of treatment or associated placebo treatment. The duration of treatment given to each subject depends on the timing of the randomization within the study, i.e. subjects will be treated until the last subject has been treated for approximately 60 months. As recruitment is expected to take up to 3 years, subjects who have been randomized early in the investigation may be treated to 96 months.

The randomization ratio is 2: 1: 2 (CNP520 50 mg, CNP520 15 mg, Placebo)

Intervention

Buccal swab; 1x if not done before
Blood pressure, Pulse: During screening 1x, then every visit.
ECG: During screening 1x, at month 3, then every six months
Physical research including neurological and dermatological research: During screening 1x, at strat treatment, at month 3, then every 6 months
Pictures of the skin: During screening 1x, then if necessary
Blood collection: During screening 2x, at month 3, then every six months
Urine collection: During screening 1x, at start treatment, at month 3, then every six months
MRI: During screening 1x, at month 6 and 12, thereafter annually
CSF or PET scan: screening (CSF prefered): During screening 1x. Optional: At year 2, year 5 and at EOS.
Completion of Questionnaires: During screening 3x, at start treatment, at month 3, then every six months

Study burden and risks

The benefits of CNP520 have not yet been established and may not directly benefit from participation in this research. The information provided by this

research may be useful to the subject and / or other people at risk of occurrence of the first clinical signs of Alzheimer's disease. The burden and risk are therefore high, the subjects are not ill at the time of participation. However, there is no other way to investigate this product.

Contacts

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Novartis

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Screening part I: Participants eligible for inclusion must fulfill all of the following criteria prior to scheduling the genetic disclosure.
- Written informed consent must be obtained before any assessment is performed as part of the study, including consent to receive disclosure of their risk estimates to develop clinical symptoms of AD based on their APOE genotype and, if HTs, with evidence of elevated brain amyloid.

- Male or female, age 60-75 years inclusive, at the time of signing the informed consent.
- Females must be considered post-menopausal and not of child bearing potential i.e. they have had 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (e.g. history of vasomotor symptoms), or have had surgical bilateral oophorectomy (with or without hysterectomy), total hysterectomy, or tubal ligation.
- Intellectually, visually and auditorily capable, fluent in, and able to read, the language in which study assessments are administered (e.g. completion of at least 6 years of regular schooling or sustained employment or equivalent local level of knowledge).
- Mini-Mental State Examination total score *24.
- Willing to have a study partner throughout the study.Screening part II: Participants eligible for inclusion must fulfill all of the following criteria prior to randomization based on the results from the screening test procedures.
- Carrier of at least one *4 allele of the APOE gene: HMs with elevated or not elevated brain amyloid OR HTs with elevated brain amyloid (as measured in CSF collected via lumbar puncture or by amyloid PET imaging).
Note: In cases where both lumbar puncture (CSF) amyloid and amyloid PET imaging tests are performed, at least one should be indicative of elevated brain amyloid.
- Cognitively unimpaired at screening visit as defined by: Score of 85 or greater on the RBANS delayed memory index score AND CDR global score of 0
- Having a study partner who agrees to participate in the study and who is intellectually, visually, and auditorily capable, and fluent in, and able to read, the language in which study assessments are administered.

Exclusion criteria

Screening part I: Participants will be excluded if they fulfill any of the following criteria prior to scheduling the genetic disclosure.
- Current medical or neurological condition that might impact cognition or performance on cognitive assessments e.g. MCI, dementia, Huntington*s or Parkinson*s disease etc.
- Advanced, severe progressive or unstable disease that may interfere with the safety, tolerability and study assessments, or put the participant at special risk e.g. active hepatitis, HIV infection, severe renal impairment, severe hepatic impairment etc.
- History of malignancy of any organ system, treated or untreated, within the past 60 months, regardless of whether there is evidence of local recurrence or metastases. However, localized nonmalignant tumors not requiring systemic chemo- or radio-therapy, localized basal or squamous cell carcinoma of the skin, or in-situ cervical cancer are permitted.
- Current treatment with Cholinesterase Inhibitors and/or another AD treatment.
- Clinically relevant depigmenting or hypopigmenting conditions or

active/history of chronic urticaria in the past year.
- Score *yes* on item 4 or 5 of the Suicidal Ideation section of the C-SSRS PRO, if this ideation occurred in the past 6 months, or *yes* on any item of the Suicidal Behavior section, except for the *Non-Suicidal Self-Injurious Behavior*, if this behavior occurred in the past 2 years prior to screening.
- Lacking psychological readiness to receive APOE genotype/amyloid status results, as assessed based on investigator*s judgement supported by the pre-disclosure rating scales: Geriatric Depression Scale total score >6; Six Item Subset Inventory of the modified State Trait Anxiety Inventory total score >17.
- Contraindication or intolerance to MRI investigations.Screening part II: Participants fulfilling any of the following criteria based on results from the screening test procedures will be excluded.
- A positive drug screen, if, in the investigator*s opinion, this is due to drug abuse. Participants with a positive drug screen not believed to be related to drug abuse can be re-screened.
- Significantly abnormal laboratory results at screening, meeting the exclusionary alert values specified in the Laboratory Manual. If, in the opinion of the investigator, an abnormal finding is the result of a temporary condition, the laboratory test can be repeated.
- Current significant ECG findings from central reader that are assessed as clinically significant by the investigator. QTc interval >500 ms is exclusionary.
- Brain MRI results from the central reading showing findings unrelated to AD that, in the opinion of the investigator might be a leading cause of future cognitive decline, might pose a risk to the participant, or might confound MRI assessment for safety monitoring (e.g. extensive white matter lesions, stroke, cerebrovascular disease as evidenced by multiple lacunar infarcts *20 mm or single infarct >20 mm, evidence of cerebral contusion etc.).
- If PET scans are scheduled for this participant: Total dosimetry above the acceptable exposure in the country when combining the previous or planned Nuclear Medicine Radiology exposure and the scheduled study PET scan(s).
- If CSF sampling is scheduled for this participant: Contraindication to lumbar puncture e.g. low platelet count, abnormal prothrombin time international normalized ratio, history of back surgery (except microdiscectomy or laminectomy over one level), signs or symptoms of intracranial pressure etc.

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:	Recruitment stopped
Start date (anticipated):	17-07-2018
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	CNP520
Generic name:	CNP520

Ethics review

Approved WMO Date:	10-10-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-06-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-07-2018
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-07-2019
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-03-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2016-002976-28-NL
ClinicalTrials.gov	NCT03131453
CCMO	NL61015.029.17