# A randomized, double-blind, placebo-controlled, parallel-group, phase 2 study to evaluate the safety and efficacy of CT1812 in subjects with mild to moderate Alzheimer's disease

Published: 12-07-2022
Last updated: 14-03-2025

The purpose of this study is to evaluate the safety and efficacy of two doses of the study drug CT1812 per day for six months in subjects with mild to moderate Alzheimer's disease. CT1812 will be compared with a placebo. A placebo is a product...

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Structural brain disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON53705

**Source**
ToetsingOnline

**Brief title**
Clinical Trial of CT1812 in Mild to Moderate Alzheimer*s Disease

### Condition

- Structural brain disorders
- Dementia and amnestic conditions

**Synonym**
Alzheimer's Disease; Dementia

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Cognition Therapeutics, Inc.
**Source(s) of monetary or material Support:** Cognition therapeutics;inc. en NIH

## Intervention

**Keyword:** Alzheimer's disease, CT1812, Dementia, Phase 2

## Outcome measures

**Primary outcome**

Safety will be assessed via the monitoring of:

- The incidence and severity of adverse events.

- Changes in vital signs.

- Changes in physical exam findings.

- Changes in electrocardiogram findings.

- Changes in clinical laboratory testing (serum chemistry, hematology,

urinalysis).

- Changes in the Columbia Suicide Severity Rating Scale (C-SSRS).

Affective and cognitive measurements:

Mini Mental State Exam (MMSE), ADAS-Cog 11 and ADAS-Cog 13 (Delayed Recall and

digit cancellation added to ADAS-Cog 11 in the ADAS-Cog 13), Neuropsychological

Test Battery (NTB) (NTB includes Trails A & B, Digit Span, Letter & Category

Fluency (COWAT and CFT)), ADCS-Clinical Global Impression of Change

(ADCS-CGIC), en ADCS-Activities of Daily Living (ADCS-ADL).

Pharmacokinetic assessments include:

- CT1812 CSF/plasma concentration ratio (end of study only).

- Changes in pre-dose CT1812 plasma concentrations.

- Plasma CT1812 metabolites.

Pharmacodynamics assessments include:

CSF- abeta, tau, phospho-tau, neurogranin, synaptotagmin, SNAP25 (synaptosomal-associated protein 25), Neuro Filament Light Chain (NFL) and Aβ oligomers. Other exploratory target engagement biomarkers may also be evaluated.

**Secondary outcome**

NA

# Study description

**Background summary**

Alzheimer's disease is a progressive, incurable illness. It is characterised by degeneration of large parts of the brain resulting in a gradual decline of cognitive functions and behaviour with typical symptoms of memory loss in patients. Therapeutic options for Alzheimer's disease are limited and only alleviate the symptoms. There is a need for treatments that address the underlying pathological process of the disease.

The human body is made up of small functional units called 'cells'. The human brain contains specialised cells called neurons. These neurons are connected and communicate with each other using so-called 'synapses'. This results in the formation of networks that are essential for memory and other cognitive functions (which require conscious intellectual activity such as thinking, reasoning, or remembering). Alzheimer's disease disrupts these networks, resulting in loss of function of the neurons and synapses. Subsequently, Alzheimer's disease leads to the death of neurons. This causes deterioration of memory and other cognitive functions.

CT1812 has been studied in both animals and humans. These studies indicate that CT1812 could restore and enhance the functioning of neurons and synapses. It could therefore be a valuable therapeutic option in Alzheimer's disease. To further explore whether CT1812 could be a valuable treatment option and is safe, this additional study is being conducted.

## Study objective

The purpose of this study is to evaluate the safety and efficacy of two doses of the study drug CT1812 per day for six months in subjects with mild to moderate Alzheimer's disease. CT1812 will be compared with a placebo. A placebo is a product without any active ingredients.

## Study design

This is a multi-center, randomized, double-blind, placebo-controlled, parallel group 36 week multicenter Phase 2 study of two doses of CT1812 in adults with mild to moderate Alzheimer*s Disease (AD). Participants will be screened for eligibility by physical, laboratory, psychometric and neurologic examinations, and neuroimaging. Pre-drug CSF and blood samples will be obtained < 42 days prior to randomization at Baseline/Day 1. After having met all inclusion criteria, and none of the exclusion criteria, participants will be randomized to one of three treatment arms (CT1812 at doses of 100 or 300 mg/d or placebo, up to n=48 group). Participants will take study treatment daily for 182 days. On day 210 a follow-up visit takes place. The total duration of participation in the study, including the screening period, is approximately 254 days.

## Intervention

Each patient will receive active druk (CT1812 for 100mg/day or 300 mg/day) or a placebo during the study. CT1812 or the placebo will be provided to patients as capsules. Capsules will be administered orally.

## Study burden and risks

Risks associated with study participation are the potential for adverse reaction to the study medicatie, concomitant medication, invasive study assessments like blood draws, ECG test, MRI scan, PET scan, X-ray and Lumbar Puncture.
The most common adverse events associated with CT1812 that were reported in previous clinical trials are: headache, nausea, vomiting, diarrhea, constipation, abdominal pain, dyspepsia, upper respiratory tract infection, lightheadedness, fainting, muscle pain, dizziness, rash, increased level of liver enzymes in blood, decrease in lymphocyte count.

# Contacts

**Public**
Cognition Therapeutics, Inc.

Sidney St., 2403
Pittsburgh 15203PA
US
**Scientific**
Cognition Therapeutics, Inc.

Sidney St., 2403
Pittsburgh 15203PA
US

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

1. Men, and women of non-childbearing potential, 50-85 years of age inclusively, with a
diagnosis of mild to moderate Alzheimer*s disease according to the 2011 NIA-AA criteria
and at least a 6 month decline in cognitive function documented in the medical record.
i) Non-childbearing potential for women is defined as postmenopausal (last natural
menses greater than 24 months) or undergone a documented bilateral tubal ligation
or hysterectomy. If last natural menses less than 24 months, a serum FSH value confirming post-menopausal status can be employed.

ii) Male subjects who are sexually active with a woman of child-bearing potential
must agree to use condoms during the trial and for 3 months after last dose unless
the woman is using an acceptable means of birth control. Acceptable forms of birth
control include, birth control pills, or any double combination of:
intrauterine device (IUD), diaphragm, sponge, and cervical cap. Periodic
abstinence, coitus interruptus, exclusive use of spermicides and lactational
amenorrhea method (LAM) are not acceptable contraceptive methods.
2) Diagnostic confirmation by amyloid PET with florbetaben or another approved amyloid PET
ligand. Previous amyloid imaging study with a positive result will be accepted. If none is
available, then amyloid PET will be conducted during screening. Diagnostic confirmation by
a CSF sample collected at the optional screening visit lumbar puncture in place of amyloid PET will
also be acceptable. Inclusion via CSF samples requires: low Aβ 42
OR low Aβ 42/40 ratio AND either increased total-tau OR increased phospho-tau
based on the ranges established by the central lab.
3) Neuroimaging (MRI, or CT scan due to contraindication of MRI is approved by Medical Monitor) obtained during screening consistent with the clinical diagnosis of
Alzheimer*s disease and without findings of significant exclusionary abnormalities (see
exclusion criteria, number 4). An historical MRI, (or CT scan),up to 1 year prior to screening, may be
used if there is no history of intervening neurologic disease or clinical events
(such as a stroke, head trauma etc.) and the subject is without clinical symptoms or signs
suggestive of such intervening events.
4) MMSE 18-26 inclusive.
5) No active depression and a GDS <=6 (see exclusion criteria number 6). Subjects with a GDS >6 may be allowed to enroll if the investigator does not believe the subject is clinically depressed. Investigators must contact the Medical Monitor to discuss eligibility.
6) Modified Hachinski <=4.
7) Formal education of eight or more years.
8) Participants must have a caregiver/ study partner who in the opinion of the site principal
investigator, has contact with the study subject for a sufficient number of hours per week
to provide informative responses on the protocol assessments, oversee the administration
of study drug, and is willing and able to participate in all clinic visits and

some study
assessments. The caregiver/ study partner must provide written informed consent to
participate in the study.
9) Participants living at home or in the community (assisted living
acceptable).
10) Ability to swallow CT1812 capsules.
11) Stable pharmacological treatment of any other chronic conditions for at least 30 days prior
to screening.
12) Participants must be capable of providing written informed consent to the study procedures
and for use of protected health information [Health Insurance Portability and Accountability
Act (HIPAA) and European General Data Protection Regulation (GDPR) if
applicable]. Written informed consent also shall be obtained from the
responsible caregiver. All consent processes must be undertaken in the presence of a
witness and prior to any study procedures.
13) Must consent to apolipoprotein E (ApoE) genotyping for data analysis stratification.
14) Participants shall be generally healthy with mobility (ambulatory or ambulatory-aided, i.e.,
walker or cane), vision and hearing (hearing aid permissible) sufficient for compliance with
testing procedures.
15) Must be able to complete all screening evaluations.

## Exclusion criteria

1) Hospitalization (except for planned procedures) or change of chronic concomitant
medication within one month prior to screening.
2) Participants living in a continuous care nursing facility.
3) Contraindications to the MRI examination for any reason. CT scan may be substituted for an MRI if a subject is unable to tolerate an MRI or an MRI is contraindicated for medical reasons. The proposed CT scan will be approved by the Medical Monitor on a case-by-case basis.
4) Screening MRI (or historical MRI, or CT scan due to contraindication of MRI if approved by medical monitor)) of the brain indicative of significant abnormality, including, but not limited to, prior hemorrhage or infarct >1 cm3, >3 lacunar infarcts, cerebral contusion, encephalomalacia, aneurysm, vascular malformation, subdural hematoma, hydrocephalus, space-occupying lesion (e.g. abscess or brain tumor such as meningioma). If a small incidental meningioma is observed, the Medical Monitor may be contacted to discuss eligibility.

5) Clinical or laboratory findings consistent with:
a) Other primary degenerative, (dementias such as dementia with Lewy bodies, frontotemporal
dementia, Huntington*s disease, Creutzfeldt-Jakob Disease, Down syndrome, etc.).
b) Other neurodegenerative condition (Parkinson*s disease, amyotrophic lateral sclerosis,
etc.).
c) Seizure disorder.
d) Other infectious, metabolic or systemic diseases affecting the central nervous system
(syphilis, present hypothyroidism, present vitamin B12 or folate deficiency, other
laboratory values etc.).
6) A current DSM-V diagnosis of active major depression, schizophrenia or bipolar disorder.
Subjects with depressive symptoms successfully managed by a stable dose of an antidepressant or antipsychotic would be allowed to enroll
7) Clinically significant, advanced or unstable disease that may interfere with outcome
evaluations, such as:
a) Chronic liver disease, liver function test abnormalities or other signs of hepatic
insufficiency (ALT, AST, alkaline phosphatase > 1.5 ULN, lactate dehydrogenase (LDH)
> 1.5 x ULN).
b) Respiratory insufficiency.
c) Renal insufficiency eGFR < 50 mL/min based on the CKD*EPI formula, as calculated by
the central laboratory.
d) Heart disease (myocardial infarction, unstable angina, heart failure, cardiomyopathy
within six months before screening).
e) Bradycardia (<50 beats/min.) or tachycardia (>100 beats/min.). If the heart rate is below 50 beats/min the subject may be eligible to enroll if the Investigator has determined that the heart rate < 50 beats/min is stable and not clinically significant. If the heart rate is above 100 beats/min, the heart rate assessment may be repeated to assess eligibility.
f) Poorly managed hypertension (systolic >160 mm Hg and/or diastolic >95 mm Hg) or
hypotension (systolic <90 mm Hg and/or diastolic <60 mm Hg).
g) Uncontrolled diabetes defined by HbA1c >7.5% in participants with diabetes, Only those
subjects with known diabetes are required to get a HbA1c at screen.
8) History of cancer within 3 years of screening with the exception of fully excised non-melanoma skin cancers or non-metastatic prostate cancer that has been stable for at least 6

months.
9) Seropositive for human immunodeficiency virus (HIV).
10) History of acute/chronic hepatitis B or C and/or carriers of hepatitis B (seropositive for
hepatitis B surface antigen [HbsAg] or anti-hepatitis C [HCV]
antibody).Subjects who have evidence of resolved Hepatitis C infection (HCV RNA negative) may be considered following discussion with the Medical Monitor.
11) Clinically significant abnormalities in screening laboratory tests, including:
d) Hematocrit less than 35% for males and less than 32% for females, absolute neutrophil
cell count < 1500/uL (with the exception of a documented history of a chronic benign neutropenia),absolute lymphocyte count <900/ul or platelet cell count of <120,000/uL; INR >1.4 or other coagulopathy,
confirmed by repeat assessment of:
i) Hematocrit.
ii) Neutrophil count.
iii. Lymphocyte count
iv. Platelet count
v. PT/INR
12) Disability that may prevent the subject from completing all study requirements (e.g.
blindness, deafness, severe language difficulty, etc.).
13) Within 4 weeks of screening visit or during the course of the study, concurrent treatment with
antipsychotic agents, antiepileptics, centrally active anti-hypertensive drugs (e.g., clonidine,
l-methyl dopa, guanidine, guanfacine, etc.), sedatives, opioids, mood stabilizers (e.g.,
valproate, lithium); or benzodiazepines, with the following exceptions:
a. Low dose lorazepam may be used for sedation prior to MRI scan for those participants
requiring sedation. At the discretion of the investigator, 0.5 to 1 mg may be given orally
prior to the scan with a single repeat dose given if the first dose is ineffective. No more than
a total of 2 mg lorazepam may be used for the MRI scan.
b) Stable use of eszopiclone or zolpidem for sleep is allowed. Stable use of short-acting benzodiazepines and trazadone specifically as sleep aids are allowed.
14) Any disorder that could interfere with the absorption, distribution, metabolism or excretion of
drugs (e.g. small bowel disease, Crohn*s disease, celiac disease, or liver disease).
15) Nootropic drugs except stable AD meds (acetylcholinesterase inhibitors or memantine.
16) Suspected or known drug or alcohol abuse, i.e. more than approximately 60 g

alcohol
(approximately 1 liter of beer or 0.5 liter of wine) per day indicated by elevated MCV
significantly above normal value at screening.
17) Suspected or known allergy to any components of the study treatments.
18) Enrollment in another investigational study or intake of investigational drug within the
previous 30 days or five half-lives of the investigational drug, whichever is longer.
19) Intake of drugs or substances potentially involved in clinically significant induction or
inhibition of CYP3A4 or P-gp mediated drug interactions with CT1812, within 4 weeks or five
half-lives of the interacting drug prior to administration of CT1812 and throughout the course
of the study. Grapefruit juice should be avoided in the two weeks prior to dosing and throughout the course of the study. See Appendix A for a complete list of prohibited substances. See Section 9.3.1 for handling of Paxlovid * administration for COVID infection during the study.
20) Any prior exposure to immunomodulators, anti Aβ vaccines, or passive Aβ immunotherapies for
AD (e.g. monoclonal antibodies) and/or exposure to BACE inhibitors within the past 30 days.
21) Any vaccination within one week of the baseline visit.
22) Any condition, which in the opinion of the investigator or the sponsor makes the participant
unsuitable for inclusion.

# 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): | 04-11-2022 |
| Enrollment: | 15 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | Elayta |
| Generic name: | n.v.t. |

# Ethics review

| | |
|---|---|
| Approved WMO Date: | 12-07-2022 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 14-09-2022 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 08-10-2022 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 11-10-2022 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 10-11-2022 |

| | |
|---|---|
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 27-01-2023 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 22-08-2023 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 13-10-2023 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 21-01-2024 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 06-03-2024 |
| 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 | EUCTR2022-002326-27-NL |
| CCMO | NL81757.056.22 |