A Phase I Study Evaluating the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Immunogenicity of Single and Multiple Doses of AL002 in Healthy Participants and in Participants with Mild to Moderate Alzheimer*s Disease.

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The primary objective of the study is to evaluate the safety, tolerability, PK, and PD of AL002 administered in single ascending doses in healthy participants and multiple doses in participants with mild to moderate AD.

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

Summary

ID

NL-OMON50153

Source
ToetsingOnline

Brief title
AL002-1

Condition

- Demyelinating disorders

Synonym
Alzheimer□s Disease - Neurodegenerative disease - Dementia

Research involving
Human

Sponsors and support

Primary sponsor: Alector Inc.
Source(s) of monetary or material Support: Pharmaceutical Company

Intervention

Keyword: AL002, Alzheimer, Phase I, Safety

Outcome measures

Primary outcome

The safety endpoints of this study are:

* Incidence, nature, and severity of serious adverse event (SAE)s and adverse events of special interest (AESI)

* Incidence of dose limiting adverse events (DLAE)

* Incidence of treatment discontinuations due to AEs

* Incidence of dose reductions due to AEs

* Mean changes in clinical laboratory tests from baseline over time; incidence of treatment emergent abnormal laboratory values and abnormal laboratory values reported as AEs

* Physical and neurologic examination abnormalities

* Ophthalmological examination abnormalities

* Mean change in vital signs from baseline over time and incidence of abnormal vital sign measurements

* Suicidal ideation, suicidal behavior, and self-injurious behavior without suicidal intent, as determined using the Sheehan-STS (for the MD participant cohort only)

* Incidence of ADAs during the study relative to the prevalence of ADAs at baseline (in SAD healthy adult participant cohorts and in MD participant cohort).

AEs of special interest will be tracked and are defined as occurrences of:

* ARIA-E,

* ARIA-H,

* An AE Grade 2 or higher of Uveitis.

6.2.2. Pharmacokinetic Endpoints

Pharmacokinetic endpoints for the study are:

* Serum concentration of AL002 at specified time points,

* Relationship between serum concentration or PK parameters for AL002 and safety endpoints, Relationship between serum, CSF concentration, or PK parameters for AL002 and activity or PD endpoints (relationship with activity is an endpoint only for the MD participant cohort - i.e. participants with AD).

6.2.3. Exploratory Clinical Outcomes

Exploratory clinical outcome endpoints (for the MD participant cohort only - i.e. participants with AD) are:

* Clinical Dementia Rating Sum of Boxes (CDR-SB) score (change after dosing relative to baseline)

* Mini-Mental State Examination (MMSE) score (change after dosing relative to baseline)

* Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) score (change after dosing relative to baseline).

6.2.4. Exploratory Biomarker Endpoints

Analyses of exploratory biomarker endpoints for the study may include the following, or additional exploratory analyses:

* changes in levels of sTREM2 in plasma (all cohorts) and CSF (from selected cohorts) after dosing relative to baseline concentration,

* relationship between biomarkers at baseline, including common and rare genetic variants, identified through whole genome sequencing (WGS) performed on deoxyribonucleic acid extracted from blood, and safety, PK, activity, immunogenicity, or other biomarker endpoints (relationship with activity is an endpoint only for the MD participant cohort only - i.e. participants with AD),

* change in brain amyloid burden as assessed by Amyloid-positron emission tomography (PET) in the MD participant cohort only, i.e. participants with AD,

* changes in markers of neuroinflammation and disease process in CSF and plasma.

Secondary outcome

See above

Study description

Background summary

Alzheimer*s disease (AD) is a degenerative brain disease and is the most common cause of dementia in the United States (US), affecting approximately 5.5 million Americans. Worldwide, 50 million people are living with dementia, and this prevalence is expected to triple by 2050. Of the top 10 causes of death in the US, AD is the only major cause of morbidity and mortality in the US without suitable treatments for prevention, slowing or cure (2017 Alzheimer*s Association Report).
Current therapies for AD such as acetylcholinesterase inhibitors (e.g. donepezil) and N-methyl-D-aspartate (NMDA) receptor antagonists (e.g. memantine) show only modest and transient benefits to cognition and behavior

parameters in AD patients but do not slow or halt the progression of the disease (Cummings, 2004). Given the large number of Alzheimer* disease patients and expected increases in this patient population due to an extended life expectancy and a major worldwide growth in the population of older adults, an effective treatment for AD remains an urgent unmet medical need.

Human genetic studies have identified inherited mutations that underlie familial forms of AD, but these mutations are rare (occurring in less than 5% of all cases). More recently, large human genetic association studies have revealed genetic loci that modify the risk of common sporadic forms of AD (Tanzi, 2012). Interestingly, many of these loci encode for proteins expressed primarily on innate immune cells, including microglia, macrophages, and dendritic cells. Microglia are resident macrophages of the central nervous system and serve protective housekeeping functions such as facilitating clearance of cellular debris through phagocytosis, as well as secretion of growth factors. Thus, in the course of neurodegenerative disease such as AD, these cells may serve an important protective role when activated appropriately.

The most prominent microglial gene that modifies the risk of common sporadic forms of AD encodes for triggering receptor expressed on myeloid cells 2 (TREM2). TREM2 is an immunoglobulin-like receptor that is expressed primarily on myeloid lineage cells, such as macrophages, dendritic cells, and microglia (Colonna, 2016). TREM2 is thought to play a key role in modulating the innate immune response, such as in response to bacteria in the context of infection or to dying neurons and other debris in neurodegenerative disorders including AD (Colonna, 2016).

Heterozygous mutations in the TREM2 gene increases the risk of AD by up to 3-fold (Guerreiro, 2013; Jonsson, 2013), and increases the rate at which brain volume shrinks (Rajagopalan, 2013). Even individuals without AD who carry a heterozygous TREM2 mutation show impaired cognition compared to individuals with 2 normal TREM2 alleles.

Recent mouse genetic model studies strongly support a key role for TREM2 in AD, with loss of TREM2 (through functional mutations and in knockout models) being associated with increased pathology (Cheng-Hathaway, 2018). These findings are suggestive of potential improvements in cognitive function under pathological conditions with the application of TREM2 agonistic antibodies. Wang et al. (Wang, 2015) showed that in the 5xFAD transgenic model of AD, deficiency in TREM2 function exacerbated AD pathology. Subsequent studies went further to detail the pathological changes seen in 5xFAD mice that lack 1 or both copies of TREM2, showing a consistent defect in the ability of TREM2 mutant microglia to effectively surround and engulf amyloid plaques (Wang, 2016; Yuan, 2016; Jay, 2017a). In these TREM2-defective microglia, the reduction in microglia per-plaque was associated with more diffuse plaques and more axonal damage from surrounding plaques.

It has been shown that TREM2 expression enhances microglial cell survival, proliferation and differentiation, and regulates microglial chemotaxis and phagocytosis. In the context of AD pathology, TREM2 expression impacts amyloid pathology, modulates neuritic dystrophy, tau hyperphosphorylation and aggregation, and affects synaptic and neuronal loss (Jay, 2017b). In addition,

it has been shown that TREM2 plays a key role in limiting the development of peri-plaque tau pathologies (Leyns, 2019).
In summary, the loss of TREM2 function is detrimental as demonstrated in human and mouse genetic studies, while conversely, activating TREM2 on microglial cells is protective against damage in the process of neurodegeneration.
The approach of Alector Inc. is to utilize TREM2 agonistic antibodies to ameliorate AD pathology through activation of the innate immune system, thereby improving the clearance and sequestration of the molecular factors causing pathology. Alector Inc. has generated TREM2 selective agonistic antibodies that synergize with endogenous ligands to treat AD. Alector Inc. has subsequently developed a humanized therapeutic TREM2 antibody candidate, AL002, with optimized agonistic activity. As demonstrated in the data from Alector Inc.*s pre-clinical studies, activating TREM2 can effectively suppress AD pathology in vivo, to prevent cognitive decline in animal models. To the best of Alector Inc.*s knowledge, an anti-TREM2 agonistic antibody has not previously been investigated in human clinical studies.
Alector Inc. proposes to evaluate the safety, tolerability, pharmacokinetic (PK) and pharmacodynamic (PD) profiles in plasma and cerebrospinal fluid (CSF) and anti-drug antibody (ADA) responses in normal healthy adult participants and patients with AD following intravenous (IV) administration with AL002.
As mentioned above, defective TREM2 functions play a central role in the pathogenesis of AD. Microglia are efficient sensors of changes in the central nervous system microenvironment, and their neuroprotective role has been hypothesized to be impaired during aging (Mecca, 2018), one of the strongest risk factors for AD. It is well known that TREM2 is required to sustain microglial trophic function in the aging brain, and animal studies showed that an overlap exists between aged microglia phenotype and microglial molecular signatures found in models of AD (Krasemann, 2017). This typical signature of aged microglia includes the TREM2 pathways. In vitro experiments demonstrated that AL002 binds to the R47H mutant form of TREM2, as illustrated in Section 4.1.2.3 of the Investigator*s Brochure, indicating that AL002 can activate the receptor even in the presence of TREM2 coding variants that are associated with AD risk. The rationale for including a cohort with AD patients carrying a R47H or R62H mutation is to characterize and compare the molecular signatures of TREM2 mutations carriers versus non-carriers and their response to treatment with AL002 using blood (plasma and white blood cells [WBC]s), CSF, and imaging biomarkers. This may facilitate a better understanding of the function of TREM2 in AD and will allow evaluation of whether AD patients respond differently to treatment with AL002 based on their genetic status.

Study objective

The primary objective of the study is to evaluate the safety, tolerability, PK, and PD of AL002 administered in single ascending doses in healthy participants and multiple doses in participants with mild to moderate AD.

Study design

A Phase I Study Evaluating the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Immunogenicity of Single and Multiple Doses of AL002 in Healthy Participants and in Participants with Mild to Moderate Alzheimer*s Disease.

Approximately 22 participants will be enrolled in one of two groups: L and M and will receive multiple doses of AL002 or placebo (fake drug) directly into the blood.

Intervention

Group L
In group L 12 participants will participate of which approximately 10 participants will receive the study drug and 2 participants placebo. Of the first two participants in group L one will receive the study drug and the other placebo. Randomization will determine which treatment you receive.

Group M
In group M all 10 participants will receive the study drug AL002 and no participants will receive placebo.

We will administer study drug or placebo - at 2 visits

Study burden and risks

For the study, you have to visit study hospital 15 times in 26 weeks. A visit will take approximately 4 hours.

- We will measure your vital signs - at 15 visits
- We will perform a physical examination - at 13 visits
- We will perform an electrocardiogram (ECG) - at 5 visits
- We will collect blood samples to:
o Asses your general health - at 10 visits, approximately 2 tubes at a time
o Measure the amount of AL002 in your blood - at 14 visits, approximately 1 tube at a time
o Measure the effect of AL002 on your body - at 14 visits, approximately 1 tube at a time
o Perform Whole Genome Sequencing (WGS) - at 1 visit, approximately 1 tubes at a time
o Measure Anti-drug antibodies - at 7 visits, approximately 1 tube at a time
- We will collect urine samples to:
o Test your general health - at 3 visits
o For a drug screen, the result must be negative for you to continue in the study - at 1 visit

o Perform a urine pregnancy test, if you are able to get pregnant, the result must be negative (not pregnant) for you to continue in the study - at 7 visits
- We will perform an alcohol breath test: when you check into the hospital on Day 1 to see if you have been drinking any alcohol in the past 24 hours. The result must be negative for you to continue in the study - at 1 visit
- We will perform a neurological assessment - at 13 visits
- We will perform eye exams - at 2 visits
- We will administer study drug - at 2 visits
- We will collect brain fluid samples - at 2 visits, approximately 3 tubes at a time.
- We will have you complete a Sheehan-STS (Suicidality Tracking Scale) questionnaire to assess suicidal thoughts and behaviors - at 13 visits. If you are having suicidal thoughts call the study doctor at the telephone number listed on the first page of this form
- We will perform a Mini-Mental State Examination (MMSE) - at 2 visits
- We will perform a Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) - at 2 visits
- We will perform a Clinical Dementia Rating (CDR) - at 2 visits
- We will perform a Brain MRI (magnetic resonance imaging) - at 3 visits
- We will perform an Amyloid PET (positron emission tomography) scan - at 2 visits
- We will perform a Concomitant Medication review - at 15 visits
- We will ask you about Adverse Events - at 15 visits

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. Total body weight between 50 and 120 kg, inclusive.
2. Clinical laboratory evaluations (including chemistry panel fasted [fasted at least 8 hours], complete blood count, and urine analysis) within the reference range for the test laboratory, unless deemed not clinically significant by the Investigator. A count of the segmented neutrophils and bands should be performed when results from the white blood cells (WBCs) are not within the reference range.
3. Negative test for selected drugs of abuse at screening (does not include alcohol) and at admission (testing at admission does include alcohol breath test). A positive result may be verified by re-testing (up to 1 false positive result permitted) and may be followed up at the discretion of the Investigator.
4. Females must be non-pregnant and non-lactating, and either surgically sterile (e.g. tubal occlusion, hysterectomy, bilateral salpingectomy, bilateral oophorectomy), or use highly effective contraceptive method (oral contraceptives pills [OCPs], long acting implantable hormones, injectable hormones, a vaginal ring or an intrauterine device [IUD]) from screening until study completion, including the follow-up period for at least 16 weeks after the last dose of AL002, or be post-menopausal for *12 months. For healthy volunteers, post-menopausal status will be confirmed through testing of FSH levels (* 40 IU/mL) at screening; for participants with AD, post-menopausal status will be assessed through medical history with assessment of potential alternative causes of amenorrhea as clinically indicated). Females who are abstinent from heterosexual intercourse will also be eligible.
5. Women of child-bearing potential (WOCBP) must have a negative pregnancy test at screening and admission and be willing to have additional pregnancy tests as required throughout the study.
6. Males must be surgically sterile (>30 days since vasectomy with no viable sperm), abstinent, or if engaged in sexual relations with a WOCBP, the participant and his partner must be surgically sterile (e.g. tubal occlusion, hysterectomy, bilateral salpingectomy, bilateral oophorectomy) or using an acceptable, highly effective contraceptive method from screening until study completion, including the follow-up period, for at least 16 weeks after the

last dose of AL002. Acceptable methods of contraception include the use of condoms and the use of an effective contraceptive for the female partner (WOCBP) that includes: OCPs, long acting implantable hormones, injectable hormones, a vaginal ring or an IUD. Male participants whose female partner is post-menopausal, and participants who are abstinent from heterosexual intercourse will also be eligible. Male participants must agree to refrain from donating sperm from screening until study completion, including the follow-up period, for at least 16 weeks after the last dose of AL002.

In addition, for the MD cohorts (i.e. participants with AD):
9. Ages 50-85 years, inclusive.
10. The participant should be capable of completing assessments either alone or with the help of the study partner (where appropriate), per local guidelines.
11. Availability of a person (*study partner*) who, in the Investigator's judgment, has frequent and sufficient contact with the participant and is able to provide accurate information regarding the participant*s cognitive and functional abilities, agrees to provide information at clinic visits, which require partner input for scale completion, and signs the necessary consent form, per local guidelines.
12. Clinical diagnosis of probable AD dementia based on National Institute on Aging Alzheimer*s Association criteria.
13. Screening MMSE score of 16-28 points, inclusive.
14. Screening Clinical Dementia Rating-Global Score (CDR-GS) of 0.5, 1.0, or 2.0.
15. Positive amyloid-PET scan by qualitative read, as defined in the PET Imaging Charter.
16. If already taking cholinesterase inhibitor and/or memantine therapy for AD, on a stable dose for at least 4 weeks prior to screening. There should be no intent to initiate, discontinue, or alter the dose of any therapy for AD for the duration of the study.
In addition, for MD Cohort M (i.e. participants with AD with a TREM2 mutation):
17. The participant must carry at least 1 of the TREM 2 mutations: R47H or R62H.

Exclusion criteria

1. Pregnant, lactating, or intending to become pregnant within 16 weeks after last dose of study drug.
2. Participation in a clinical trial within 30 days before randomization; use of any experimental oral therapy within 30 days or 5 half-lives prior to Day 1, whichever is greater; or use of any biologic therapy within 12 weeks or 5 half-lives prior to Day 1, whichever is greater. Participants who have received an experimental therapy that has no half-life, like a vaccine, should have completed that therapy at least 12 weeks prior to Day 1. Participants who have received an experimental vaccine against a central nervous system target, such

as beta-amyloid or tau, are not eligible for this study.
3. Any non-experimental vaccine within 2 weeks of randomization, until 2 weeks after the last dose. It is advised that prospective participants receive their annual influenza vaccine as early as possible in advance of the flu season, and then wait 2 weeks prior to randomization. It is permitted to receive the annual influenza vaccine during the screening period.
4. Surgery or hospitalization during the 4 weeks prior to screening.
5. Planned procedure or surgery during the study.
6. Blood transfusion within 8 weeks prior to screening.
7. Donation or loss of blood (excluding the volume of blood that will be drawn during screening procedures) as follows: 50-499 mL of blood within 30 days or > 499 mL of blood within 56 days prior to study drug administration.
8. Poor peripheral venous access.
9. History of major depression (within the past 5 years) unless effectively treated at enrollment and for the duration of the study, at the discretion of the Investigator. History of schizophrenia, schizoaffective disorder, or bipolar disorder.
10. Alcohol and/or substance abuse or dependence (according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition) within the past 2 years.
11. Within the last 2 years, unstable or clinically significant cardiovascular disease (e.g. myocardial infarction, angina pectoris, New York Heart Association Class II or more cardiac failure).
12. Uncontrolled abnormal blood pressure
a. For healthy volunteers, as indicated by sustained supine systolic blood pressure (BP) > 140 or < 90 mm Hg or supine diastolic blood pressure > 90 or <50 mm Hg at screening or admission. Duplicate assessments will be performed and the average of the 2 assessments of BP will be used to exclude a participant.
b. For MD participants with AD, sustained diastolic blood pressure >95 mm Hg performed either sitting or supine. No repeated measurements for eligibility are required for multidose participants.
13. Resting heart rate at screening of >100 or < 40 beats per minute.
14. Chronic kidney disease as indicated by a screening creatinine clearance < 30 mL/min as calculated by the central laboratory using the Cockcroft Gault formula, which remains < 30 mL/min if retested.
15. Impaired hepatic function as indicated by screening aspartate aminotransferase (AST) or alanine aminotransferase (ALT) * 2 or total bilirubin * 1.5 x the upper limit of normal, which remains above these limits if retested due to a slightly elevated initial result or abnormalities in synthetic function tests that are judged by the Investigator to be clinically significant.
16. History of, or known to currently have, Human Immunodeficiency Virus (HIV) infection, hepatitis B or hepatitis C infection that has not been adequately treated in the opinion of the Investigator.
17. History or presence of infections of the central nervous system (e.g. syphilis, Lyme, or borreliosis, viral or bacterial meningitis/encephalitis, HIV encephalopathy).

18. History or presence of central nervous system or systemic autoimmune disorders including but not limited to rheumatoid arthritis, multiple sclerosis, lupus erythematosus, anti-phospholipid antibody syndrome, Behçet disease.
19. Present or past history of uveitis requiring medical intervention, chronic inflammatory or degenerative condition of the eye, current eye infection, any ongoing eye disorder requiring injectable medical therapy (e.g. ranibizumab or aflibercept for macular degeneration) or planned invasive eye procedure during the study period.
20. Systemically, clinically significantly immunocompromised patients, owing to continuing effects of immune suppressing medication.
21. Positive for Hepatitis C virus (HCV) antibody, Hepatitis B surface antigen (HBsAg), or HIV antibody.
22. History of cancer except:
a. if considered likely to be cured,
b. is not being actively treated with anti-cancer therapy or radiotherapy and, in the opinion of the Investigator, is not likely to require treatment in the ensuing 3 years,
c. considered to have low probability of recurrence (with supporting documentation from the treating oncologist if possible),
d. for prostate cancer or basal cell carcinoma, no significant progression over the last 2 years,
e. Adequately resected squamous cell skin cancer.
23. Known history of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric, human, or humanized antibodies or fusion proteins.
24. Past history of seizures, with the exception of childhood febrile seizures.
25. At risk of suicide in the opinion of the Investigator.
26. Any serious medical condition or abnormality in clinical laboratory tests that, in the Investigator*s judgment, precludes the participant*s safe participation in and completion of the study.
27. History or presence of an abnormal ECG that is clinically significant in the Investigator*s opinion, including complete left bundle branch block, second- or third-degree heart block, evidence of prior myocardial infarction (except if due to a myocardial infarction that occurred more than 2 years before screening).
28. History of ventricular dysrhythmias or risk factors for ventricular dysrhythmias such as structural heart disease (e.g. severe left ventricular systolic dysfunction, left ventricular hypertrophy), coronary heart disease (symptomatic or with ischemia demonstrated by diagnostic testing), clinically significant electrolyte abnormalities (e.g. hypokalemia, hypomagnesemia, hypocalcemia), or family history of sudden unexplained death or long QT syndrome.
29. Current treatment with medications that are well known to prolong the QT interval, at the Investigator*s discretion.
30. Immunosuppression caused by disease (such as HIV) or medications, immunosuppressive therapy (such as long-term systemic corticosteroid therapy) within 12 months before screening through the entire study period.

31. Smoking more than 5 cigarettes, 1 cigar, or 1 pipe daily.
32. Contraindication to lumbar dural puncture, including coagulopathy, concomitant anticoagulation (except for platelet inhibitor such as aspirin or clopidogrel), thrombocytopenia, or other factor that precludes safe lumbar puncture in the opinion of the Investigator.
In addition, for SAD cohorts (i.e. healthy adults):
33. QT interval corrected using Fridericia*s formula (QTcF) > 450 msec demonstrated by at least 2 ECGs > 30 minutes apart.
34. The use of all prescribed medication is not allowed (unless discussed and agreed upon by both the Sponsor and the PI) at least 30 days prior to admission to the clinical research center until follow-up. The use of all over the counter medication, vitamin preparations and other food supplements or herbal medications (e.g. St. John*s Wort) is not allowed (unless discussed and agreed upon by both the Sponsor and the PI) for at least 14 days prior to admission to the clinical research center until follow-up. The use of paracetamol/acetaminophen (up to 2000 mg/day) is allowed for the treatment of headache or any other pain. Other medication to treat AEs may only be prescribed if deemed necessary by the Investigator.
In addition, for the MD cohorts (i.e. participants with AD):
35. A lack of ability to consent, in accordance with the local regulations, guidelines, and independent ethics committee (IEC) or institutional review board (IRB).
36. Dementia due to a condition other than AD, including, but not limited to, Frontotemporal Dementia, Parkinson*s disease, dementia with Lewy bodies, Huntington disease, or vascular dementia.
37. History or presence of clinically evident vascular disease potentially affecting the brain (e.g. clinically significant carotid, vertebral stenosis or plaque; aortic aneurysm; intracranial aneurysm; cerebral hemorrhage; arteriovenous malformation) that in the opinion of the Investigator has the potential to affect cognitive function.
38. History or presence of stroke within the past 2 years or documented history of transient ischemic attack within the last 12 months.
39. History of severe, clinically significant (persistent neurologic deficit or structural brain damage) central nervous system trauma (e.g., cerebral contusion).
40. Inability to tolerate MRI procedures or contraindication to MRI, including, but not limited to, presence of pacemakers (with the exception of MRI-safe pacemakers), aneurysm clips, artificial heart valves, ear implants, or foreign metal objects in the eyes, skin, or body that would contraindicate an MRI scan; or any other clinical history or examination finding that, in the judgment of the Investigator, would pose a potential hazard in combination with MRI.
41. MRI evidence of:
a. more than 2 lacunar infarcts,
b. any territorial infarct > 1 cm3, or
c. significant FLAIR hyperintense lesions in the cerebral white matter that may, in the Investigator*s opinion, contribute to cognitive dysfunction.
42. Any other severe or unstable medical condition that, in the opinion of the

Investigator or Sponsor, could be expected to progress, recur, or change to such an extent that it could put the participant at special risk, bias the assessment of the
clinical or mental status of the participant to a significant degree, interfere with the participant*s ability to complete the study assessments, or would require the equivalent of institutional or hospital care.
43. Residence in a skilled nursing facility such as a convalescent home or long-term care facility. Participants who subsequently require residence in these facilities during the study may continue in the study and be followed for efficacy and safety, provided that they have a study partner who meets the minimum requirement.
44. The following medications are prohibited as daily treatment from 1 month prior to screening until the end of the study. They are, however, permitted on an intermittent, as needed basis at any point during the study, provided that no dose is taken within 2 days before any neurocognitive assessment:
a. typical anti-psychotic or neuroleptic medication,
b. narcotic analgesics,
c. sedative, hypnotic, or benzodiazepine medication,
d. tricyclic antidepressant medications,
e. any sedating antihistamine medication (diphenhydramine or other similar over the counter antihistamine therapy).
45. QT interval corrected using Fridericia*s formula (QTcF) > 470 msec demonstrated by at least 2 ECGs > 30 minutes apart for male participants and QT interval corrected using Fridericia*s formula (QTcF) > 480 msec demonstrated by at least 2 ECGs > 30 minutes apart for female participants.

Study design

Design

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):	24-02-2020
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AL002
Generic name:	AL002

Ethics review

Approved WMO Date:	07-01-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-02-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-03-2020
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	EUCTR201900020630-NL
CCMO	NL71749.056.19