

A Randomized, Double-Blind, Placebo-Controlled and Delayed-Start Study of LY3314814 in Mild Alzheimer*s Disease Dementia (The DAYBREAK Study)

Published: 13-06-2016

Last updated: 17-04-2024

To test the hypothesis that LY3314814, administered orally at doses of 20 and 50 mg daily for 78 weeks, will slow the decline of AD ascompared with placebo in patients with mild AD dementia.

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

Summary

ID

NL-OMON47043

Source

ToetsingOnline

Brief title

The DAYBREAK Study

Condition

- Dementia and amnestic conditions

Synonym

Alzheimer, Mild dementia

Research involving

Human

Sponsors and support

Primary sponsor: Eli Lilly

Source(s) of monetary or material Support: Eli Lilly and Company

Intervention

Keyword: Alzheimer, Mild dementia

Outcome measures

Primary outcome

Change from Baseline in Alzheimer*s Disease Assessment Scale- Cognitive Subscale (ADAS-Cog-13) Score

Secondary outcome

- Change from Baseline in Alzheimer*s Disease Cooperative Study Activities of Daily Living Inventory (ADCS-iADL) Instrumental Items Score
- Change from Baseline in Functional Activities Questionnaire (FAQ) Score
- Change from Baseline on the Integrated Alzheimer's Disease Rating Scale (iADRS) Score
- Change from Baseline in the Clinical Dementia Rating - Sum of Boxes (CDR-SB) Score
- Change in Clinical Dementia Rating (CDR) Global Score
- Change from Baseline in Neuropsychiatric Inventory (NPI) Score
- Change from Baseline on the Mini-Mental State Examination (MMSE)
- Change from Baseline in Concentration of Cerebrospinal fluid (CSF) Biomarker A β 1-42
- Change from Baseline in Concentration of CSF Biomarker A β 1-40
- Change from Baseline in CSF Biomarker Total Tau
- Change from Baseline in CSF Biomarker Phosphorylated Tau

- Change from Baseline in Brain Amyloid Burden using Florbetapir Amyloid Scan
- Change from Baseline in Regional Cerebral Blood Flow (rCBF) using Florbetapir Perfusion Scan
- Change from Baseline in Whole Brain Volume
- Population Pharmacokinetics (PK): Apparent Oral Clearance of LY3314814
- Population PK: Central Volume of Distribution of LY3314814

Study description

Background summary

Alzheimer's disease is a progressive and fatal neurodegenerative disease manifested by cognitive deterioration in addition to progressive impairment of activities of daily living. Current treatments are seen as minimally effective, with only minor symptomatic improvements for a limited duration, and they do not slow the progression of the disease.

Study objective

To test the hypothesis that LY3314814, administered orally at doses of 20 and 50 mg daily for 78 weeks, will slow the decline of AD as compared with placebo in patients with mild AD dementia.

Study design

Study I8D-MC-AZET is a multicenter, randomized, parallel-group, 78-week double-blind, placebo-controlled, study of 2 fixed doses of LY3314814 in patients with mild AD dementia and abnormal levels of amyloid, followed by a 78-week Delayed-Start period.

Intervention

There are 4 treatment arms. The randomization ratio is 2:2:1:1 (LY3314814 20 mg: LY3314814 50 mg: Placebo for 78 weeks then LY3314814 20 mg; Placebo for 78 weeks then LY3314814 50 mg). The three treatment groups in the 78-week Placebo-Controlled period include 2 fixed doses of LY3314814 (20 mg or 50 mg) or placebo. In the 78-week Delayed-Start period, there are the same 2 fixed doses of LY3314814 (20 mg or 50 mg) and all patients previously on placebo will

then initiate either dose of LY3314814 based on their randomization.

Study burden and risks

To date, no safety issues have been identified that would create an unfavorable benefit-risk balance for LY3314814. The potential benefits are not established but expectation for an effect in slowing AD progression is described above in the Section 3.2 of the protocol. Potential risks include but are not limited to elevated liver enzymes, QT-prolongation with overdose, skin or hair hypopigmentation, rash, retinal changes, and potential interactions with other drugs. The potential risks are monitored with scheduled labs, electrocardiograms (ECGs), skin exams, eye exams, and restrictions on some concomitant medications.

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

- Participant must meet the National Institute on Aging (NIA) and the Alzheimer's Association (AA) (NIA-AA) criteria for probable AD dementia.
- MMSE score of 20 to 26 inclusive at screening visit.
- For a diagnosis of mild AD dementia, participant must have a CDR global score of 0.5 or 1, with the memory box score ≥ 0.5 at screening.
- Evidence of amyloid pathology.
- The participant must have a reliable study partner with whom he/she cohabits or has regular contact.

Exclusion criteria

- Significant and/or current neurological disease affecting the central nervous system, other than AD, that may affect cognition or ability to complete the study, including but not limited to, other dementias, repetitive head trauma, serious infection of the brain, Parkinson's disease, epilepsy, or cervicocranial vascular disease.
- Participants with any current primary psychiatric diagnosis other than AD if, in the judgment of the investigator, the psychiatric disorder or symptom is likely to confound interpretation of drug effect, affect cognitive assessment, or affect the participant's ability to complete the study. Participants with history of schizophrenia or other chronic psychosis are excluded.
- Within 1 year before the screening visit or between screening and randomization, any of the following: myocardial infarction; moderate or severe congestive heart failure, New York Heart Association class III or IV; hospitalization for, or symptoms of, unstable angina; syncope due to orthostatic hypotension or unexplained syncope; known significant structural heart disease (such as, significant valvular disease, hypertrophic cardiomyopathy); or hospitalization for arrhythmia.
- Congenital QT prolongation.
- Intermittent second- or third-degree atrioventricular (AV) heart block or AV dissociation or history of ventricular tachycardia.
- A corrected QT (QTcF) interval measurement >470 milliseconds (men and women) at screening (as determined at the investigational site).
- History of malignant cancer within the last 5 years.
- History of vitiligo and/or current evidence of post-inflammatory hypopigmentation.
- Calculated creatinine clearance <30 milliliters per minute (Cockcroft- Gault formula; Cockcroft and Gault 1976) at screening.
- Currently enrolled in any other clinical trial involving an investigational product or any other type of medical research judged not to be scientifically or medically compatible with this study.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL	
Recruitment status:	Recruiting
Start date (anticipated):	11-05-2017
Enrollment:	89
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	LY3078786
Generic name:	Florbetapir (18F)
Product type:	Medicine
Brand name:	LY3191748
Generic name:	18F-AV-1451
Product type:	Medicine
Brand name:	NA
Generic name:	LY3314814

Ethics review

Approved WMO	
Date:	13-06-2016

Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	
Date:	23-11-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	
Date:	26-01-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	
Date:	03-02-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	
Date:	14-02-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	
Date:	24-02-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	
Date:	20-04-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	
Date:	26-04-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO	
Date:	27-04-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	
Date:	14-08-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	
Date:	23-11-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	
Date:	24-01-2019
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	EUCTR2015-005625-39-NL
CCMO	NL56998.056.16