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# DIANTU001: Phase II/III randomized, double-blind placebo in Alzheimer's

| Submission date | Recruitment status | [ ] Prospectively registered |
|---|---|---|
| 25/02/2014 | No longer recruiting | [ ] Protocol |
| **Registration date** | **Overall study status** | [ ] Statistical analysis plan |
| 25/02/2014 | Completed | [ ] Results |
| **Last Edited** | **Condition category** | [ ] Individual participant data |
| 16/06/2016 | Mental and Behavioural Disorders | [ ] Record updated in last year |

**Plain English summary of protocol**

Background and study aims
Alzheimer's disease is the most common type of dementia, affecting multiple brain functions including memory. This is a study of two drugs (gantenerumab and solanezumab) in patients who are either known to have a mutation causing Alzheimer's disease, or who don't know their gene status but are "at risk" for an autosomal dominant Alzheimer's disease (ADAD) mutation. The aim is to test whether one or both of these drugs prevent, delay or reverse the changes in the brain that are associated with disease symptoms in ADAD.

Who can participate?
People who are at risk of developing ADAD, aged 18-80 (and between 15 years younger to 10 years older than the age of symptom onset in their affected parent), and who are either symptom free or have mild symptoms of dementia.

What does the study involve?
Participants are randomly allocated to either the gantenerumab or solanezumab group. In the gantenerumab group, participants who are mutation carriers receive either gantenerumab or a placebo (dummy) drug by injection under the skin every 4 weeks. In the solanezumab group, participants who are mutation carriers receive either solanezumab or placebo by injection into a vein every 4 weeks. All mutation non-carriers are allocated to take the placebo. The safety and tolerability of gantenerumab and solanezumab are measured throughout the study period.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
University College London (UK)

When is the study starting and how long is it expected to run for?
January 2014 to August 2016

Who is funding the study?
1. Avid Radio Pharmaceuticals

2. Eli Lilly and Company Limited
3. Hoffman LaRoche
4. NIH (USA)
5. The Alzheimer's Association

Who is the main contact?
Jane Douglas
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# Contact information

### Type(s)
Scientific

### Contact name
Ms Jane Douglas

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# Additional identifiers

### EudraCT/CTIS number

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
15734

# Study information

### Scientific Title
A Phase II/III randomized, double-blind, placebo-controlled multi-center study of two potential disease modifying therapies in individuals at risk of and with dominantly inherited Alzheimers disease

### Acronym
DIANTU001

### Study objectives

This is a study of two potential disease modifying therapies (Gantenerumab and Solanezumab) in subjects who are either known to have a mutation causing Alzheimer's disease OR who don't know their gene status but are "at risk" for an autosomal dominant Alzheimer's disease (ADAD) mutation. The purpose is to test whether one or both of these drugs prevent, delay or reverse the changes in the brain that are associated with the development of disease symptoms in ADAD.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
13/SC/0535

## Study design
Randomised; Interventional; Design type: Treatment

## Primary study design
Interventional

## Secondary study design
Randomised controlled trial

## Study setting(s)
Hospital

## Study type(s)
Treatment

## Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

## Health condition(s) or problem(s) studied
Topic: DeNDRoN; Subtopic: Dementia; Disease: Dementia

## Interventions
Participants will be randomised 1:1 to either the gantenerumab or solanezumab arm of the study. Within each treatment arm, subjects who are mutation carriers will be randomised to active treatment or placebo at a 3:1 ratio. All mutation non-carriers will be randomised to placebo.

Gantenerumab arm: Subjects will receive either gantenerumab or placebo via injection under the skin every 4 weeks. Solanezumab arm: Subjects will receive either solanezumab or placebo via injection of the drug into the patients vein every 4 weeks.

Adverse events and serious adverse events will be reported by the investigator to the study sponsor and to regulatory bodies as required. Unblinded data on safety-related endpoints and SAEs will be reviewed quarterly by the Data Safety Monitoring Board (DSMB). Amyloid related

imaging abnormalities (ARIA), which include cerebral vasogenic oedema and microhaemorrhages, are a safety endpoint. MRI scans will be analysed for ARIA changes at the Mayo clinic.

### Intervention Type
Drug

### Phase
Phase II/III

### Drug/device/biological/vaccine name(s)
Gantenerumab, solanezumab

### Primary outcome measure
Safety and tolerability of gantenerumab and solanezumab measured throughout the study period (104) weeks

### Secondary outcome measures
Not provided at time of registration

### Overall study start date
01/01/2014

### Completion date
11/08/2016

# Eligibility

### Key inclusion criteria
A subject may be included if the answer to all of the following statements is yes:
1. Written consent is signed and dated by the subject, Study Partner (if applicable) and/or by the subjects legally acceptable representative according to local regulations for both the core trial ICF and the drug-specific ICF
2. Subject is 18-80 years of age (inclusive)
3. For women able to have children, the subject must agree to use effective contraceptive measures (e.g., hormonal contraception, intrauterine device, sexual abstinence, barrier method with spermicide) if partner is not sterilised. Men must agree to use effective contraceptive measures
4. Mutation status
4.1. Subject is a carrier 1 of a mutation in PSEN1, APP or PSEN2 gene that is associated with dominantly inherited Alzheimers disease 2 OR at 50% risk for such a mutation (e.g. does not know their mutation status AND is a child or sibling of known mutation carrier)
4.2. Subject is within 15 to +10 years of the age of cognitive symptom onset in the affected parent (refer to Manual of Operations for calculation of estimated age of onset).
4.3. Subjects who are aware that they are mutation negative are not eligible for enrolment.
5. Cognitively normal or with mild cognitive impairment or mild dementia, CDR 01 (inclusive)
6. Fluency in DIAN trial approved language and evidence of adequate pre-morbid intellectual functioning
7. Adequate visual and auditory abilities to perform all aspects of the cognitive and functional

assessments
8. Receiving stable doses of medication(s) for the treatment of non-excluded medical condition (s) for at least 30 days prior to baseline visit (V2) with the exception of medications taken for episodic conditions (e.g., migraine abortive therapy, antibiotics and other medications for upper respiratory and gastrointestinal ailments), AND, if treated with cholinesterase inhibitors and/or memantine, all of the following conditions are also met:
8.1. The subject has been maintained on a stable dose regimen for at least 90 days prior to screening¿
8.2. The subject is free of any clinically important side effects attributable to the drug.
Side effects that are intermittent, stable or well-tolerated by the subject are not exclusionary.
9. Has a Study Partner who in the investigator's judgment is able to provide accurate information as to the subject's cognitive and functional abilities, who agrees to provide information at the study visits which require study partner input for scale completion, and who signs the necessary consent form if applicable
10. Agrees not to donate blood or blood products for transfusion for the duration of the study and for one year after the final dose of study drug
11. In the opinion of the investigator, the subject will be compliant and have a high probability of completing the study

## Participant type(s)
Patient

## Age group
Adult

## Lower age limit
18 Years

## Upper age limit
80 Years

## Sex
Both

## Target number of participants
Planned Sample Size: 10; UK Sample Size: 10

## Key exclusion criteria
Subject will be excluded if answer to any of following statements is yes.

CNS Disorder
1. Significant neurologic disease (other than AD) or psychiatric disease that may currently or during the course of study affect cognition or subjects ability to complete study.
2. At high risk for suicide.
Current stable mild depression or current use of antidepressant medications is not exclusionary.
3. History of clinically evident stroke or history of clinically important carotid or vertebrobasilar stenosis, plaque, or other prominent risk factor for stroke or cerebral hemorrhage.
Low dose aspirin (≤ 325 mg daily) is not exclusionary.
4. Alcohol or drug dependence sufficient to meet DSM-IV criteria currently or in past 1 year.
Imaging related exclusion criteria
5. History of or baseline visit brain MRI scan indicative of other significant abnormality

Note: For subjects who have participated in the DIAN observational study, site staff should work with DIAN Observational Imaging Core to review results of MRIs done in the observational study so that those with pre-existing exclusionary findings on MRI are not unnecessarily subjected to screening & baseline visit procedures.
6. Presence of pacemakers, aneurysm clips, artificial heart valves, ear implants, or foreign metal objects in eyes, skin or body which would preclude MRI scan.

Cardiovascular Disorders
7. Uncontrolled hypertension within 6 months prior to screening
8. Myocardial infarction or other myocardial ischemic events in last 2 years
9. Heart failure resulting in limitation of physical activity
10. History of atrial fibrillation except if only episode which resolved more than three years ago & which treatment
is no longer indicated
11. 12-lead ECG: Clinically significant abnormalities in subjects over 65 years of age.
A discrepancy between local & central read will not be considered a protocol deviation.

Hepatic/Renal Disorders
12. Alanine aminotransferase (ALT) ≥ 2 times the upper limit of normal or aspartate aminotransferase (AST) ≥ 3 times the upper limit of normal or baseline total bilirubin ≥ 2 times the upper limit of normal
13. Creatinine clearance lower than 30 mL/min according to Cockcroft-Gault formula (if confirmed at retest)
14. Clinical significant abnormalities in urinalysis.

Infections/Immune Disorders
15. History of Human Immunodeficiency Virus infection, history of Hepatitis B infection within past year, history of Hepatitis C infection which has not been adequately treated or history of spirochete infection of central nervous
system
16. Allergies to humanised monoclonal antibodies or to components of formulations of these antibodies
17. Treatment with immunosuppressive medications within 90 days prior to baseline visit or chemotherapeutic agents for malignancy in last 3 years.

Metabolic/Endocrine Disorders
18. Current clinically significant abnormalities of thyroid function studies, clinically significant deficiency in B12
19. Screening HgbA1C >8% (retesting is permitted if slightly elevated) or poorly controlled insulindependent
diabetes. Subject may be rescreened after 3 months to allow optimisation of diabetic control
20. Morbid obesity with significant comorbidities or would preclude MRI imaging.

Co-Medications
21. Anticoagulants except low dose (≤ 325 mg) aspirin
22. Have been exposed to monoclonal antibody targeting beta amyloid peptide in past six months
23. Received any other investigational treatment within 3 months of screening or 5 half-lives whichever is longer
24. Ever participated in study of an active vaccine or other long-acting biological agent which was being evaluated to prevent or postpone cognitive decline¿

Note: use of approved treatment for AD & other medications is permitted in this study in accordance with Concomitant Medications guidelines (Section 5.3 protocol).

Other:
25. Lack of sufficient venous access
26. Clinically relevant abnormalities in hematology, coagulation studies or clinical chemistry
27. History of cancer in last 5 years, except basal cell carcinoma, non-squamous skin carcinoma, prostate cancer or carcinoma in situ with no significant progression over past 2 years
28. Any other medical condition that could be expected to progress, recur, or change to such an extent that it could bias assessment of clinical or mental status of the subject to a significant degree or put the subject at special risk
29. Currently, or within last month prior to screening, participated in a clinical trial including a nonpharmacological trial with a key objective of improving cognition
30. Positive urine or serum pregnancy test or plan or desire to become pregnant during the course of trial.

### Date of first enrolment
01/01/2014

### Date of final enrolment
11/08/2016

## Locations

### Countries of recruitment
England

United Kingdom

United States of America

### Study participating centre
**University College London**
London
United Kingdom
WC1N 3BG

## Sponsor information

### Organisation
Washington University in St Louis (USA)

### Sponsor details
660 South Euclid Avenue
Campus Box 8111
Saint Louis

United States of America
MO 63130

**Sponsor type**
University/education

**ROR**
https://ror.org/01yc7t268

# Funder(s)

**Funder type**
Industry

**Funder Name**
Avid Radio Pharmaceuticals

**Funder Name**
Eli Lilly and Company

**Alternative Name(s)**
Lilly, Eli Lilly & Company, Eli Lilly & Co., Eli Lilly And Co

**Funding Body Type**
Government organisation

**Funding Body Subtype**
For-profit companies (industry)

**Location**
United States of America

**Funder Name**
F. Hoffmann-La Roche

**Alternative Name(s)**
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

**Funding Body Type**
Private sector organisation

**Funding Body Subtype**
For-profit companies (industry)

**Location**
Switzerland

**Funder Name**
National Institutes of Health

**Alternative Name(s)**
Institutos Nacionales de la Salud, US National Institutes of Health, NIH

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**Location**
United States of America

**Funder Name**
Alzheimer's Association

**Alternative Name(s)**
Alzheimer's Disease and Related Disorders Association, Inc., Alzheimer's Disease & Related Disorders Association, Inc., AA

**Funding Body Type**
Government organisation

**Funding Body Subtype**
Associations and societies (private and public)

**Location**
United States of America

# Results and Publications

**Publication and dissemination plan**
Not provided at time of registration

**Intention to publish date**

**Individual participant data (IPD) sharing plan**

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| HRA research summary | | | 28/06/2023 | No | No |