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A trial of Nilvadipine in mild to moderate Alzheimer's disease

Submission date
22/07/2013

Recruitment status
No longer recruiting

Registration date
22/07/2013

Overall study status
Completed

Last Edited
19/08/2019

Condition category
Nervous System Diseases

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Alzheimers disease (AD) is the most common form of dementia for which currently there is no cure available. Early symptoms include memory loss and mild cognitive impairment, often related to stress or aging. As the disease progresses, symptoms worsen to affect all areas of brain function, such as memory, behaviour, language and motor skills. In the final stages of Alzheimers disease, the patient is completely dependent upon caregivers.
With more than 15 million people affected worldwide (5 million in Europe), Alzheimers disease is an ever-increasing public health concern among the aging population, causing a great burden to patients and their caregivers. The economic costs of Alzheimers disease and other dementias are estimated at more than 180 billion in Europe each year.
Even small advances in treatment that delay the start of disease (onset) or its progression could significantly reduce the global burden of the disease and the level of care required by patients. While there are drug therapies available for AD that treat symptoms, these medications do not delay onset, slow progression or prevent the disease process itself. Therefore it is necessary to develop new treatments for AD that have disease-modifying effects.
The aim of this study is to investigate the effectiveness and safety of the drug nilvadipine in Alzheimers disease. Nilvadipine is a licensed blood pressure medication with a proven safety record in people with high blood pressure and more recently has been shown to be well tolerated and safe in older people with Alzheimers disease. There is preliminary evidence for clinical benefit in individuals with cognitive impairment and strong scientific evidence based on animal model studies of Alzheimers disease.

Who can participate?
The study will recruit 500 people over 50 with mild to moderate Alzheimers disease.

What does the study involve?
Participants will be randomly allocated to receive either nilvadipine or placebo (dummy) for 78 weeks.

What are the possible benefits and risks of participating?
This study tests whether nilvadipine has a disease-modifying effect in mild to moderate Alzheimers disease. If this is found to be correct, patients may benefit from this treatment.

In routine treatment, effects of medication are not monitored as regularly as in this study, so patients may benefit from the routine examinations during study participation.
Subjects administered the nilvadipine drug may experience adverse events, adverse drug reactions or other clinically significant complaints, symptoms or other abnormalities. However, the risk associated with the trial is low. Nilvadipine is a licensed medication for high blood pressure in certain European countries with a reliable safety profile. A successful short-term safety study was carried out on Alzheimers patients in 2008 which showed very good tolerability in this patient population over the 6-week trial period.

Where is the study run from?
The study will be conducted across 23 study sites in nine partner countries (Ireland, UK, Netherlands, Sweden, Greece, Hungary, France, Italy, Germany) and is being coordinated by Prof Brian Lawlor from Trinity College Dublin, Ireland.

When is the study starting and how long is it expected to run for?
The study started in May 2013 and will be recruiting patients until December 2014. The study is expected to complete in July 2016.

Who is funding the study?
The study is funded by the European Commission's Framework 7 programme.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT02017340

Clinical Trials Information System (CTIS)
2012-002764-27

Protocol serial number
14541

Study information

Scientific Title
A European multicenre double-blind placebo controlled phase III trial of nilvadipine in mild to moderate Alzheimer's disease

Acronym
NILVAD

Study objectives
The objective of this study is to investigate the efficacy of Nilvadipine as a disease course modifying treatment for mild to moderate AD in a phase III double-blind placebo-controlled study and to investigate the safety profile of Nilvadipine in patients with mild to moderate AD.

More details can be found at: http://www.nilvad.eu/fileadmin/websites/nilvad/media/NILVAD_Brochure.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee- North London Harrow, 06/02/2013, ref 12/LO/1903

Study design
Randomized double-blind placebo controlled parallel; Design type: Treatment

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Dementias and Neurodegenerative Diseases Research Network; Subtopic: Dementia; Disease: Alzheimer's Disease

Interventions
A total of 500 subjects with Alzheimers disease; 250 in the nilvadipine group and 250 in the placebo group recruited from 31 European centres.

Over encapsulated nilvadipine 8 mg, sustained release capsule, for the treatment group, taken once a day at lunchtime or, matching over encapsulated placebo for the control group, taken once a day at lunchtime.
The total study duration will be 82 weeks. Patients will receive study medication for 78 weeks.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Nilvadipine

Primary outcome(s)
Cognitive and non-cognitive symptoms of Alzheimer's disease are measured using the Alzheimer s Disease Assessment Scale (ADAS) at baseline, 13, 52 and 78 weeks

Key secondary outcome(s)
1. Involvement in activities of daily living are measured using the Disability Assessment for Dementia (DAD) at baseline, 13, 52 and 78 weeks
2. Severity of symptoms is measured using the Clinical Dementia Rating Scale (CDR) Assessments at baseline, 13, 52 and 78 weeks

Completion date
19/12/2016

Eligibility

Key inclusion criteria
1. Age range: Adult subjects, males and females over age 50 years.
2. Subjects with a diagnosis of probable Alzheimers disease based on the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimers disease and Related Disorders Association, Inc (NINCDS-ADRDA) criteria (McKhann et al, 1984)
3. Subjects with a Standardised Mini-Mental State Examination (SMMSE) (Standish & Molloy, 1991) score of greater than or equal to 12 and less than 27.
4.Subjects on a stable dose (>3 months) of cholinesterase inhibitor or memantine. The dose must be stabilised prior to randomisation. Patients due to begin these medications must not be enrolled until the dose is stabilised. Subjects who are not on cholinesterase inhibitors or memantine due to poor tolerability and/or who will not require treatment with these medications during the course of the study can be included.
5. Subjects who retain capacity will provide written informed consent for participation. The procedure for obtaining informed consent when the subject has reduced decision making capacity will follow national law and will be assessed by the relevant bodies in each of the participating countries.
6. Fluency in relevant language sufficient to reliably complete all study assessments.
7. Subjects with blood pressure values greater than 100/65 mmHg but less than 159/99 mmHg (Grade 1 hypertension, ECS guidelines 2007; escardio.org/guidelines) using an office based BP measurement will be included.
Subjects with blood pressure values greater than 105/70mmHg but less than 140/90 mmHg using an Ambulatory BP measurement will be included.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Subjects with co-morbid dementia due to other neurological disorders such as Parkinson's disease, vascular dementia, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, normal pressure hydrocephalus, brain dementia, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, normal pressure hydrocephalus, brain tumour, progressive supranuclear palsy, seizure disorder, subdural hematoma, or multiple sclerosis, as well as subjects with HIV disease, neurosyphilis, history of significant head trauma with loss of consciousness followed by persistent neurological deficits, known structural brain abnormalities, or any other condition known to interfere with cognitive function.
2. Subjects currently taking any calcium channel blocker or beta-blocker
3. Subjects who in the opinion of the investigator, have a medical condition that would preclude them from participating in the study (e.g.hemodynamically significant coronary artery disease, chronic heart failure, syncope within the past year, significant valvular heart disease i.e. severe aortic and mitral stenosis symptomatic orthostatic hypotension within the last year, subjects requiring more than one agent to control BP), or subjects who in the opinion of the investigator are unlikely to complete per protocol due to care issues etc.
4. Current Axis I diagnosis of schizophrenia, bipolar disorder, major depression. Subjects who are currently or who have within the past year met criteria for drug or alcohol abuse or dependence.
5. Pregnant women or women who may possibly become pregnant.
6. Female subjects who are breastfeeding will be excluded from the study
7. Subjects with a history of hypersensitivity to nilvadipine (Nivadil).
8. Subjects who have taken an investigational or other unapproved drug during the 30 days or five half-lives, whichever is longer, prior to baseline.
9. Subjects who are taking any medication listed in the list of exclusion medication for the study.
10. Subjects with abnormal ECG results which prevent participation in the study.
11. Standardised Mini-Mental State Examination (SMMSE) score of less than 12 or greater than 26.
12. Subjects who are participating in other clinical research studies.
13. Subjects with any clinically significant laboratory blood test abnormality on his/her screening test.
14.Subjects with blood pressure values less than 100/65 mmHg but greater than 159/99 mmHg (Grade 1 hypertension, ECS guidelines 2007; escardio.org/guidelines) using an office based BP measurement will be excluded. Subjects with blood pressure values less than 105/70mmHg but greater than 140/90 mmHg using an Ambulatory BP measurement will be excluded.
15.Subjects with clinically significant abnormalities in their CT/MRI results which would prevent inclusion in the study.
16. Patients with sigificant renal insuffiency (estimated glomerular filtration rate: eGFR <30ml /min) will be excluded .
17. Subjects with severly impaired hepatic function (liver cirrhosis) will be excluded.
18. The medical food stuff Souvenaid® is under exclusion from the study.

Date of first enrolment
23/04/2013

Date of final enrolment

10/04/2015

Locations

Countries of recruitment
United Kingdom

England

France

Germany

Greece

Hungary

Ireland

Italy

Netherlands

Sweden

Study participating centre
St. James's Hospital
James Street
Dublin
Ireland
8

Study participating centre
St Finbarrs Hospital
Douglas Road
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Cork
Ireland
-

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Centre Hospitalier de Béthune
27 Rue Delbecque
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Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre

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Study participating centre
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Study participating centre
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Sponsor information

Organisation
St James Hospital (Ireland)

ROR
https://ror.org/04c6bry31

Funder(s)

Funder type
Government

Funder Name
European Commission Framework 7 programme; Grant Codes: 279093

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	24/09/2018		Yes	No
Results article	results	21/05/2019	19/08/2019	Yes	No
Results article	results	01/08/2019	19/08/2019	Yes	No
Protocol article	protocol	09/10/2014		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes