Reducing pathology in Alzheimer’s Disease through Angiotensin TaRgeting – The RADAR Trial

https://neurodegenerationresearch.eu/survey/reducing-pathology-in-alzheimer%c2%92s-disease-through-angiotensin-targeting-the-radar-trial/

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Country

United Kingdom

Title of project or programme

Reducing pathology in Alzheimer’s Disease through Angiotensin TaRgeting - The RADAR Trial

Source of funding information

NIHR

Total sum awarded (Euro)

€ 2,641,182

Start date of award

01/03/2013

Total duration of award in years

4.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords
Research Abstract
Research design: A two arm blinded placebo-controlled randomised controlled trial (RCT). Study population: RADAR will study incident and prevalent cases of mild-to-moderate AD diagnosed according to revised NINCDS-ADRDA criteria. Participants can be hypertensive or

normotensive and on any existing dementia drugs with no age restrictions. Inclusion requires an MMSE score of 15-24; a modified Hachinski score of 4 or less, a previous CT or MRI scan supporting a diagnosis of AD and the presence of care-giver in daily contact. Exclusion criteria include anyone already taking other renin angiotensin acting drugs or potassium diuretics; contraindications or conditions that make MRI unfeasible; a BP of < 120/75 mmHg, > 160/110 mmHg and/or postural hypotension (BP drop of >20/10 mmHg after 3-5 minutes); prior history of stroke or transient ischaemic attacks; unstable congestive heart failure; severe renal or hepatic impairment or a history of gout; other primary neurodegenerative or psychiatric disorders other than AD or other possible primary causes of dementia; a recent history of untreated clinically significant hypothyroidism or hyperthyroidism (patients are euthyroid and stable are eligible). Interventions: Patients will be randomised to either encapsulated 100mg generic losartan or placebo once daily for 12 months after a 1 month open label phase which establish drug tolerability. Outcomes: Primary outcome measures will be the rate of whole brain atrophy as a surrogate measure of cognitive decline. Secondary outcomes: (i) white matter hyperintensities (WMH) volume and cerebral blood flow (CBF) (also surrogate markers of cognitive decline and disease progression); (ii) performance on a standard battery of assessments of memory, cognitive function, activities of daily living and quality of life; (iii) changes to levels of plasma protein markers of AD (Abeta, acetylcholinesterase) and AngII pathway-linked AD-related markers (ACE, NEP, TNFalpha, CRP). Major assessments (for all outcomes) will be at baseline and 12 months while an added interim 6 month visit will include cognitive assessments only. Safety monitoring for blood pressure and side effects will occur at weekly intervals of the open-label phase and at 14 days, 3, 6 and 9 months post-randomisation. Based on recent studies conducted within ADNI to optimise protocols for imaging use in clinical trials of AD, we will recruit a sample size of 228 participants (recruited over 15 months) to provide at least 182 subjects with final assessments to provide 84% power to detect a 25% difference in atrophy rate (therapeutic benefit) change over 12 months at an alpha level of 0.05. We will use intention-to-treat analysis to measure our outcomes, measuring between-group estimates of effectiveness derived from appropriate (linear or logistic) multivariable regression models adjusting for minimisation variables and value of outcome at baseline and at the end of the study (12 month follow-up for all primary and secondary outcomes) and for the 6 month cognitive assessment data.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
United Kingdom

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:

N/A