PHASE II/III trial for Slowing Progression in Mild Cognitive Impairment

https://neurodegenerationresearch.eu/survey/phase-ii-iii-trial-for-slowing-progression-in-mild-cognitive-impairment/

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Contact information of lead PI
Country

USA

Title of project or programme

PHASE II/III trial for Slowing Progression in Mild Cognitive Impairment

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 6,970,424.77

Start date of award

15/09/2015

Total duration of award in years

2

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Behavioral and Social Science... Brain Disorders... Clinical Research... Clinical Research - Extramural... Clinical Trials and Supportive Activities... Comparative Effectiveness Research... Dementia... Diagnostic Radiology... Effectiveness Research... Neurodegenerative... Neurosciences... Prevention... Translational Research

Research Abstract

? DESCRIPTION: No therapy has FDA approval for amnestic MCI, a symptomatic stage of Alzheimer’s disease when patients are at increased risk for progression to dementia. Using an agent with proven safety/tolerability, we propose a novel approach for slowing progression in MCI due to AD. The use of the atypical antiepileptic levetiracetam (LEV) is indicated by evidence that hippocampal hyperactivity is characteristic of this stage of disease, predicts subsequent longitudinal cognitive decline/conversion to a dementia diagnosis, and is correlated with the extent of neuronal injury as measured in structural MRI. Supporting the proposed therapy, low dose treatment with LEV reduces hippocampal hyperactivity in both animal models and aMCI subjects, concurrently improving cognitive function. In the longer-term, treatment with LEV is expected to reduce degenerative processes driven by failure to control excess neural activity in the vulnerable entorhinal/hippocampal network. The proposed randomized, placebo-controlled 24 month trial will test the efficacy of LEV therapy on a sole primary outcome, the CDR sum of boxes, and a key secondary measure of entorhinal cortex thinning to assess neuronal injury. The trial will also acquire a rich database, e.g. genetic/DNA, additional imaging modalities (resting state fMRI, and diffusion tensor imaging scans), along with both standardized neuropsychological testing and novel cognitive assessments as secondary measures. Funding under this application would provide partial support (approximately 15% of total trial cost) in a public/private partnership for this Phase II/III trial, which would be the first to target hippocamal hyperactivity and will be registered with the FDA. A pre-IND meeting with the FDA (March 2014) on the proposed protocol provided supportive background on all aspects of the trial plan including appropriate enrollment criteria, adequacy of outcome measures, drug safety, and CMC formulation of an extended release medication. Importantly, the FDA confirmed that no further preclinical or clinical data are required to proceed with the trial. The Hopkins investigators under this award, who have exceptional expertise in biostatistics, imaging, clinical trial design, and data analysis have worked together with the Sponsor (AgeneBio, Inc) and its CRO to develop the protocol and plans to implement it. NIH support would not only contribute to the main purpose of the trial, but also ensure an open resource for data sharing to advance clinical trial design in AD prevention, including biomarker development.

Lay Summary

PUBLIC HEALTH RELEVANCE: Prevention or slowing the progression of Alzheimer’s dementia would address a critical unmet need that will otherwise significantly burden patients, caregivers and the healthcare system in the decades ahead. Using a low dose of levetiracetam in a once-a- day formulation, a drug approved as safe and well-tolerated at much higher dosing in epilepsy patients, this clinical trial assesses the efficacy of two-year therapy in slowing the progression of amnestic mild cognitive impairment due to AD. The study uses endpoints consistent with regulatory guidance for this indication and will produce publically available data that can be used to advance AD prevention trial design and biomarker development, in addition testing a novel approach to Alzheimer’s disease in patients at high risk for dementia.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:
N/A