A double-blinded, randomized, controlled phase 2a safety, proof-of-concept and exploratory end point trial of the drug LM11A-31 in patients with mild to moderate Alzheimers disease.

https://neurodegenerationresearch.eu/survey/a-double-blinded-randomized-controlled-phase-2a-safety-proof-of-concept-and-exploratory-end-point-trial-of-the-drug-lm11a-31-in-patients-with-mild-to-moderate-alzheimers-disease/

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Country

USA

Title of project or programme

A double-blinded, randomized, controlled phase 2a safety, proof-of-concept and exploratory end point trial of the drug LM11A-31 in patients with mild to moderate Alzheimers disease.

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 4,123,729.36

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15/09/2016

Total duration of award in years

1

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)... Brain Disorders... Clinical Research... Clinical Research - Extramural... Clinical Trials and Supportive Activities... Dementia... Effectiveness Research... Neurodegenerative... Neurosciences... Translational Research

Research Abstract

ABSTRACT Extensive preclinical data demonstrate that modulation of the p75 neurotrophin receptor by the small molecule LM11A-31 counteracts multiple neurodegenerative signaling mechanisms and processes associated with AD including: tau phosphorylation-misfolding-mislocalization- oligomer formation; loss of synaptic function/LTP; loss of spines; degeneration of neurites; and cognitive loss. This phase 2a study will consist of a prospective, multicenter, double- blind, placebo-controlled, randomized trial to evaluate proof-of-concept (POC), safety and exploratory end-points for LM11A-31 in mild-moderate AD. The study will include 3 arms each consisting of 40 patients with mild-moderate AD including placebo and two doses treated twice daily for 26 weeks. Given the mechanism of action of prevention/reversal of synaptic impairment and degeneration of basal forebrain, hippocampal and cortical neurite networks, FDG-PET will serve as a key biomarker and proof-of-mechanism outcome measure, testing the hypothesis that a p75 ligand can modulate p75 signaling and thereby restore synaptic mechanisms in human AD, as occurs in mouse models. Additional baseline measures and endpoints will include: Neuropsychological Test Battery (NTB) including ADAS-Cog-14, NPI, and other cognitive assessments; CSF studies (A?, tau, p-tau, acetylcholinesterase activity) and structural MRI. CSF studies will serve to support AD diagnostic accuracy and, in the case of p-tau, tau and acetylcholinesterase activity, provide additional biomarkers. For each endpoint, rates of change between baseline and the 26 week endpoint will be assessed. A full range of safety evaluations are also included. Successful completion of this 2a trial will provide a dose and end-point statistical and power basis for the design and execution of full phase 2b/3 testing and will further validate a novel target in the AD field. This study will be led and directed by Dr. Manfred Windisch (PI) in close collaboration with Drs. Niels Andreasen (Co-Investigator) and Agneta Nordberg (Co-Investigator), who together as co-Investigators will oversee and operate their already established network of approximately 13 sites located in Sweden, Germany, Austria and the Czech Republic. This network will provide a faster enrollment rate, higher lumbar puncture acceptance and lower costs than those available in the US. Moreover, this team is among the world leaders in application of FDG-PET and other biomarkers in AD therapeutic assessment, particularly in the area of novel therapeutics. This grant is proposed to support the clinical trial costs while PharmatrophiX (Menlo Park, CA) will provide cGMP drug in capsule form and close collaboration through Dr. Frank Longo, founder and chairman of PharmatrophiX.

Lay Summary

Project Narrative There are currently no Alzheimer’s disease (AD) treatments known to slow progression of the degeneration of neurons or the loss of their synaptic connections. Recent clinical trials have unfortunately failed. This proposed AD Pilot Trial will make possible the testing of an entirely new drug strategy targeted to underlying degenerative mechanisms. The

trial will assess safety of drug LM11A-31 and explore measurements of brain function that will make possible more advanced testing with the goal of developing a truly effective drug for slowing AD progression.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
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