Phase 3 trial of inosine for Parkinsons disease – DCC

https://neurodegenerationresearch.eu/survey/phase-3-trial-of-inosine-for-parkinsons-disease-dcc/

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Country

USA

Title of project or programme

Phase 3 trial of inosine for Parkinsons disease - DCC

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 3,230,077.06

Start date of award

01/09/2015

Total duration of award in years

4

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Inosine, Urate, Data Coordinating Center, Phase III Clinical Trials, Parkinson Disease

Research Abstract

? DESCRIPTION (provided by applicant): Convergent laboratory, epidemiological and clinical observations have identified urate – the end product of purine metabolism in humans – as a neuroprotectant and the first molecular predictor of both reduced risk and slower progression of

typical Parkinson’s disease (PD). Urate is also a potent antioxidant and confers protection in cellular and animal models of PD. Epidemiological studies of prospectively followed healthy populations have repeatedly demonstrated serum urate to be an inverse risk factor for PD. These findings led to the discovery that among people with early PD serum and CSF urate levels are predictors of slower progression, assessed clinically or by neuroimaging of dopamine transporter (DAT) loss over years. Phase 2 Progress: Based on urate’s properties as a neuroprotectant and favorable prognostic biomarker in PD, urate elevation was proposed as a candidate disease-modifying strategy. Inosine, an orally bioavailable precursor of urate, was investigated in a phase 2 study, the Safety of Urate Elevation in Parkinson’s Disease (SURE-PD) trial. It demonstrated that inosine can safely produce well-tolerated elevations of serum and CSF urate for months or years in early PD. Secondary analyses of long-term clinical data support advancing to a pivotal efficacy trial. Results also suggested refinements in dosing and other design features. Phase 3 Aims: The primary aim of the study is to determine whether oral inosine dosed to persistently elevate serum urate (from =5.7 mg/dL to 7.1-8.0 mg/dL) slows clinical progression over two years in early PD. Secondary aims include assessing long-term safety and effects on a) the development of disability warranting dopaminergic medication, b) short-term changes in parkinsonian symptoms, c) changes in functional disability and quality of life, and d) non-motor measures of cognition, mood and autonomic function. The operational aim of the Clinical Coordinating Center (CCC) is to safely, effectively and efficiently manage all study activities and training of ~60 participating Parkinson Study Group (PSG) clinical sites and to integrate clinical management by the CCC with data and drug management by the partnered Data Coordinating Center (DCC). Methods: A placebo-controlled, double-blind randomized trial of inosine will enroll 270 subjects with early PD, lower serum urate and DAT deficiency by neuroimaging and will randomize them 1:1 to treatment with placebo or inosine dosed to elevate urate for 2 years with a 3-month wash-out. Our primary outcome of change in the Movement Disorders Society Unified PD Rating Scale (MDS-UPDRS) total score will be assessed quarterly to measure patient- and investigator-reported and motor and non-motor features of the disease. Significance: Slowing the progressive clinical decline of PD remains a critical unmet goal of neurotherapeutics development. If the established association between higher urate and favorable outcomes in PD patients are due to neuroprotective properties, then this study is designed to provide direct evidence that urate-elevating inosine treatment slows clinical progression of the disease.

Lay Summary

PUBLIC HEALTH RELEVANCE: Parkinson’s disease imposes a growing burden not only on the individuals in whom it inexorably progresses, but also on our population as the proportion who are older rises. Although no treatment has been found yet to slow disease progression, urate elevation has emerged as a compelling candidate strategy for protection based on an unprecedented convergence of laboratory and human findings. The proposed trial will determine whether treatment with a urate-elevating drug can slow the rate of worsening in people with early Parkinson’s disease. NOTE: The critiques and criterion scores from individual reviewers are provided below in an essentially unedited form. These were prepared prior to the review meeting and may not have been updated or revised subsequent to the discussion at the meeting. Therefore, they may not fully reflect the final opinions of the individual reviewers at the close of group discussion or th final majority opinion of the group.

Further information available at:

Types:

Investments > €500k

Member States:
United States of America

Diseases:
Parkinson's disease & PD-related disorders

Years:
2016

Database Categories:
N/A

Database Tags:
N/A