Escitalopram for Agitation in Alzheimer Disease

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Country

USA

Title of project or programme

Escitalopram for Agitation in Alzheimer Disease

Source of funding information

NIH (NIA)

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30/09/2016

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)... Behavioral and Social Science... Brain Disorders... Clinical Research... Clinical Research - Extramural... Clinical Trials and Supportive Activities... Dementia... Depression... Mental Health... Neurodegenerative... Neurosciences... Translational Research

Research Abstract

DESCRIPTION (provided by applicant): Agitation is common in Alzheimer's disease (AD), a major burden to patients and caregivers. Finding effective treatments is a priority. The standard of care recommends initial use of non-pharmacologic followed by pharmacologic interventions. This approach has several challenges in the real world including unknown efficacy, sparse use of non-pharmacologic therapies, and widespread, often inappropriate, use of antipsychotics that carry significant risks. There is need for effective therapies for agitation combining non-pharmacologic with novel pharmacologic approaches, reducing antipsychotic use, and targeting therapies to appropriate subgroups of this heterogeneous condition. A hypothesized cause of agitation in AD is neurodegeneration that disrupts, then destroys, brain ascending serotonergic pathways. Attempting to develop a novel therapy targeting the serotonin system, we conducted Citalopram in AD (CitAD), a double blind, controlled trial that administered a real world-usable psychosocial intervention to all and additionally randomized participants to the SSRI citalopram at 30mg/day or placebo. In CitAD, racemic citalopram was effective for agitation with 40% of citalopram-treated participants experiencing substantial clinical improvement vs. only 26% on placebo. However, citalopram was associated with cognitive worsening and prolongation of the ECG-QTc interval. In blood concentration models, cognitive and cardiac changes were associated with the R-enantiomer, while clinical improvements were primarily associated with the S-enantiomer (escitalopram). We propose S-CitAD to build on and extend these findings. We will develop an evidence-based, sequential approach to treating agitation in AD with real world applicability for patients. We will enroll 589 patients with AD and agitation and administer the psychosocial intervention used in CitAD. Patients not showing clinically significant improvement in agitation after 3 weeks will be randomized to drug or placebo. Given the findings of CitAD, since the dose of citalopram used in CitAD may be contraindicated in older patients, we will use S-citalopram (originally marketed as Lexapro(r), now generic) instead of the racemic citalopram used in CitAD. In psychosocial intervention non-responders, we will evaluate for efficacy and safety over 12-weeks (AIM 1). We will also evaluate pre-specified predictors of response suggested by CitAD (AIM 2). Finally, we will follow patients showing significant improvement on the psychosocial intervention to study predictors of response, as well as duration of improvement and frequency, time course, and predictors of subsequent relapse (AIM 3). IMPACT: S-CitAD will provide clinicians and payers practical information about a real world-usable, immediately available approach to treating agitation in AD. S-CitAD findings will also form the basis for later treatment development providing information on non-responders in different phases of this sequential approach, and becoming a model of how to evaluate predictors of response in NPS treatment studies.

Lay Summary

PUBLIC HEALTH RELEVANCE: Agitation is common in Alzheimer's (AD), a major burden to patients and caregivers. Development of new treatments is a public health priority. We propose to study the benefits of a generic drug, escitalopram, while developing a sequential approach to treating agitation with real-world applicability. If successful, study findings will immediately mae available to patients a safer approach to treating agitation in part by understanding the profile of those most likely to benefit.

Further information available at:

Types:

Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

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2016

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