

A nutritional formulation for cognitive performance and mood in Alzheimer's disease and Mild Cognitive Impairment: a phase II multi-site randomized trial with an open-label extension

Ruth Remington^{1*}, Cynthia Bechtel^{2§}, David Larsen^{3§}, Jevin J. Lortie^{4§}, Annemarie Samar^{5§}, Laura Doshanjh⁶, Paul Fishman⁶, Yuan Luo^{6**}, Kathleen Smyers¹, Heather Hoffmann⁴, Constance Barysaukas⁷, Bruce Barton⁷, Thomas B. Shea¹

¹University of Massachusetts Lowell, Lowell, MA 01854, ²Framingham State University, Framingham, MA 01701, ³Advanced Memory Dynamics, Layton, UT 84040, ⁴Knox College, Galesburg, IL 61401, ⁵Worcester State University, Worcester, MA 01602, ⁶University of Maryland, College Park, MD 20740, ⁷University of Massachusetts Worcester, Worcester, MA 01655

CONTACT: TB Shea Thomas_Shea@uml.edu 978-934-2881 Fax 978-934-3044

Funding and Disclosure: This research was funded by the Alzheimer's Association. The nutraceutical formulation utilized herein is marketed by Sevo Nutraceuticals (Waltham, MA); TBS and UMass Lowell have a financial interest in this formulation and the company. TBS is a consultant for Sevo Nutraceuticals.

ABSTRACT

Background

It is increasingly recognized that interventions for dementia must shift towards prevention to obtain maximal efficacy and any significant degree of disease modification. Nutritional supplementation with single agents has shown varied results, suggesting the need for combinatorial intervention.

Methods

We conducted a 3-month, randomized, multi-site, phase II study in which 141 individuals diagnosed with Alzheimer's disease (AD) and 34 individuals with Mild Cognitive Impairment received a nutraceutical formulation (NF; folate, alpha-tocopherol, B12, S-adenosyl methionine, N-acetyl cysteine, acetyl-L-carnitine) or indistinguishable placebo under double-blind conditions, followed by an open-label extension in which all individuals received NF for a total of 1yr. An additional 38 individuals with AD received NF under open-label conditions from baseline for 1yr. The primary outcome was defined as cognitive performance. Secondary outcomes were defined as behavioral and psychological symptoms of dementia and activities of daily living.

Results

Participants randomized to NF improved statistically within 3 months in cognitive performance as ascertained by Clox-1 and the Dementia Rating Scale, and their caregivers reported improvement in Neuropsychiatric Inventory. Participants receiving NF either continued to improve or maintained their baseline performance during open-label extensions. Participants randomized to placebo did not improve, but during open-label extensions displayed similar improvement within 3 months to that of participants initially randomized to NF. Caregivers reported no change in Activities of Daily Living for either cohort.

Conclusions

These findings confirm and extend prior phase I studies in which NF improved or maintained cognitive performance and behavioral symptoms for individuals with AD, and improved cognitive performance for community-dwelling individuals without dementia.

In published studies with transgenic mice NF reduced PS-1 expression, beta and gamma secretase activity, Abeta deposits, phospho-tau, homocysteine and oxidative damage, and increased acetylcholine and glutathione. This comprehensive impact of NF on AD-related neuropathology supports the possibility that NF may harbor disease-modifying properties.