

Local Clinical Trials

The Alzheimer's Association, Connecticut Chapter does not officially endorse any specific research study. The following information regarding clinical trials is provided as a service to our readers.

AAB-001-201 in Patients with Mild to Moderate Alzheimer's Disease

The purpose of this study is to assess the safety and tolerability of multiple doses of AAB-001 passive immunization in patients with mild to moderate Alzheimer's disease (AD).

The humanized monoclonal antibody, AAB-001, which binds to and clears beta amyloid peptide, is designed to provide antibodies to beta amyloid directly to the patient, rather than requiring the patient to mount his/her own individual response. It is believed that this approach may eliminate the need for the patient to mount an immune response to beta amyloid. Animal studies have shown that this approach is equally effective in clearing beta amyloid from the brain as traditional active immunization methods.

This is a multi-center, double-blind, placebo controlled, randomized, outpatient, multiple ascending dose study in male and female patients aged 50 to 85 years with mild to moderate AD. Approximately 30 study sites will be involved. Patients will be randomized to receive either AAB-001 or placebo. Each patient's participation will last approximately 2 years.

For more information contact: Yale University School of Medicine, New Haven, CT 06510 - Kristina Estok, (203) 764-8100, Kristina.estok@yale.edu

Anti-Psychotic Discontinuation in Alzheimer's Disease

The purpose of this study is to determine the efficacy and safety of risperidone in Alzheimer's disease patients with behavioral complications.

Antipsychotic medications have been shown to be efficacious in the treatment of patients with Alzheimer's disease who have psychotic symptoms or behavioral dyscontrol (called "behavioral complications" here). However, these medications have a variety of short and long-term side effects. Although their prolonged effects in AD patients are not established, Federal (OBRA) regulations have mandated periodic discontinuation of antipsychotic medications in nursing homes. Surprisingly, there is little empirical evidence to support or refute this approach in nursing homes or in outpatients. A previous study examined the use of haloperidol, a conventional antipsychotic that commonly causes extrapyramidal signs (EPS), and is associated with a high risk of tardive dyskinesia (TD) with prolonged use.

This multi-center study (four academic sites; nursing homes and outpatients) will involve treating a relatively large number of AD patients using an atypical antipsychotic, risperidone. In Phase 1, 200 AD patients (48 patients at the NYSPI site)

with behavioral complications will receive open treatment with risperidone for 16 weeks. Responders will be randomized, double-blind, to one of three arms in Phase 2: (1) continuation risperidone for the next 32 weeks, (2) risperidone for the next 16 weeks followed by placebo for 16 weeks, or (3) placebo for the next 32 weeks. This design will provide useful data on the efficacy and side effects of longer term treatment with risperidone, and provide critical information about the likelihood and time to relapse, as well as predictors of relapse, in patients switched from risperidone to placebo. This information is essential to guide the clinician toward optimal use of such medications in one of the most challenging types of patients: the AD patient with behavioral complications.

For more information contact: Research Center for Clinical Studies, Inc, Darien, CT 06820 - Anju Shrestha, (203) 662-0070

DHA (Docosahexaenoic Acid), an Omega 3 Fatty Acid, in Slowing the Progression of Alzheimer's Disease

The purpose of this study is to determine whether chronic DHA (Docosahexaenoic Acid) supplementation slows the progression of cognitive and functional decline in mild to moderate Alzheimer's disease.

Preliminary studies have shown a reduced risk of Alzheimer's disease (AD) in people consuming increased amounts of fish in their diets. Many of the health benefits of fish are attributed to the abundance of omega 3 fatty acids. Docosahexaenoic Acid (DHA) is the most abundant omega 3 fatty acid in the brain. Data from several animal models supports the hypothesis that DHA may be an effective treatment for AD by means of anti-amyloid, antioxidant, and neuroprotectant mechanisms.

In this study, 400 individuals with mild to moderate AD will participate at approximately 53 study sites throughout the US for 18 months. Participants will be randomized so that 60% will receive approximately 2 grams of DHA, divided into 4 capsules, 2 capsules taken twice a day, while 40% receive an identical placebo.

Potential participants will go to their study site for a screening visit, where eligibility is determined, and if accepted, for a baseline visit where cognitive status, behavioral status, functional status, and global severity of dementia will be assessed. Vital signs and biomarker labs will also be obtained. Subsequent visits will occur every three months for medication checks and, every 6 months, further assessments, physical exams, and labs.

Some participants will also take part in MRI (magnetic resonance imaging) and/or CSF (cerebrospinal fluid) sub-studies. For the MRI sub-study, scans will be done prior to beginning the study medication, and again after 18 months. Likewise, for the CSF sub-study, a lumbar puncture will be done prior to beginning the study medication, and again after 18 months.

Enrollment is restricted to individuals who consume no more than 200 mg of DHA per day, which is almost 300% of the average daily intake in an American diet. Individuals who take fish oil or omega 3 fatty acid supplements are also not eligible. Each visit will include completion of a very brief food frequency questionnaire to monitor dietary DHA levels.

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Rosiglitazone (Extended Release Tablets) As Adjunctive Therapy to Acetylcholinesterase Inhibitors In Mild To Moderate Alzheimer's Disease

Previous research has shown that rosiglitazone, a diabetes drug, in a new extended release formulation, may have benefit in Alzheimer's patients and that this benefit may be related to a patient's genetic makeup. This study will test the efficacy and safety of the new extended release formulation of rosiglitazone when added to standard approved drug treatment with Acetylcholinesterase Inhibitors (AChEI).

Rosiglitazone (RSG) has been tested in clinical studies and is approved by the FDA as a treatment for type II diabetes mellitus, a disease that occurs when the body is unable to effectively use glucose. RSG XR, the investigational drug used in this study, is an extended-release form of RSG.

This study tests whether RSG XR safely provides clinical benefit to people with mild to moderate Alzheimer's disease (AD) when combined with one of the currently approved AD medications, Aricept®, Razadyne® or Exelon®. RSG XR is a new approach to AD therapy and this study tests a new way to treat AD by testing whether one's genetic makeup affects the response to the study drug.

The sugar glucose is used by your cells to make the energy that they need to live. Changes in the way that cells use glucose can lead to disease (e.g., diabetes). It is known that glucose levels may be lowered in the brains of AD patients, and their brain cells also sometimes use glucose less effectively than in unaffected people. The proper function of brain cells is essential for memory and thought, so the inability of brain cells to use glucose may be important in AD. Treatments that help brain cells to properly use glucose may enhance a person's ability to think clearly and to maintain normal memory.

Clinical data suggesting that RSG may benefit AD patients was first seen in a small study performed at the University of Washington and then from a larger GSK study conducted in Europe and New Zealand. In the first study, participants receiving RSG once daily for 6 months scored significantly better on 3 tests of memory and thought than those who did not receive RSG. In the GSK study, those that appeared to benefit most from treatment with RSG XR had a specific genetic pattern. They did not have the gene that caused them to produce the protein apolipoprotein E ϵ 4 (APOE ϵ 4). Participants who have the APOE ϵ 4 gene may have two copies, one from each parent, or they may have only one APOE ϵ 4

gene meaning that they inherited either the APOE ε2 or APOE ε3 version of the gene, instead of APOE ε4, from one of their parents. Participants with one copy of the APOE ε4 gene remained at their same level of thinking ability while those with two copies of the APOE ε4 gene, continued to worsen during the 6-month treatment. The current study will more directly test the effectiveness of RSG XR on people who either have or lack the APOE ε4 gene.

For more information contact: GSK Clinical Trails Call Center, Darien, CT 06820 - Bart Sloan, (877) 379-3718

Vitamin E in Aging Persons With Down Syndrome

The goal of this study is to determine the safety and efficacy of the administration of vitamin E, which has been shown to delay the progression of Alzheimer's disease, in slowing the rate of cognitive/functional decline in older persons with Down syndrome.

The growing success of therapeutic interventions (including the antioxidant Vitamin E) for Alzheimer's disease in the general population requires a solution to the methodological problems so that therapeutic trials can be conducted in the aging population with Down syndrome which will ultimately improve their quality of life as well as that of their families and caregivers. The experience gained in this trial will be useful to the design of appropriate cognitive measures of Alzheimer's disease in persons with Down syndrome in subsequent trials.

The goal of this international three-year study is to determine whether the administration of vitamin E, which has been shown to delay the progression of Alzheimer's disease, will slow the rate of cognitive/functional decline in persons age 50 or older with Down syndrome. Persons with Down syndrome functioning at all levels of intellectual disability will be eligible. Men and women of approximately equal numbers and people from minorities and ethnic groups other than Caucasian will be included. A total of 400 individuals with Down syndrome, 50 years of age and older, will be recruited at approximately 27 trial sites. The study is a randomized, double-blind, placebo-controlled, parallel group design with stratification by geographic site and presence of Alzheimer disease according to DSM-IV (American Psychiatric Association) criteria for diagnosing this disease.

The primary outcome measure is a brief test of praxis, measuring cognitive functions expressed as performances of simple, short, sequences of voluntary movements in persons with Down syndrome with mild to profound levels of mental retardation. A vitamin E regimen (1,000 international units twice daily, plus a multivitamin) or a placebo will be compared to a multivitamin alone in a two-arm parallel group design. Apolipoprotein E (Apo E) genotype will be determined at the screening visit to allow secondary analyses of the impact of Apo E genotype (that may influence Alzheimer's disease risk) on outcome measures and the response to treatment. DNA specimens will also be stored for possible future genetic analyses, with trial sites allowing for non-

participation in this procedure. Visits will occur at baseline and then at 6 monthly intervals, with each visit including interval medical history, current and interval medications, side effects checklist, adverse events, pill count, institutionalization status, cognitive, functional, and behavioral measures, and DSM-IV diagnostic assessment for Alzheimer's disease.

For more information contact: University of Connecticut Health Center, Farmington, CT 06030 - Cindy Gruman, (860) 545-7012, cgruman@harthosp.org

ADNI: Alzheimer's Disease Neuroimaging Initiative

The purpose of this study is to examine how brain imaging technology can be used with other tests to measure the progression of mild cognitive impairment (MCI) and early Alzheimer's disease (AD). This information will aid future clinical trials by providing a standard assessment tool to measure the effects of treatments being studied.

This study will test whether serial magnetic resonance imaging (MRI), positron emission tomography (PET), other biological markers, and clinical and neuropsychological assessment can be combined to measure the progression of mild cognitive impairment (MCI) and early Alzheimer's disease (AD). The information obtained by studying changes in the brain images of MCI and AD patients and healthy individuals, as well as other assessment tools, will be used to determine the best methods for measuring treatment effects in patients with MCI and AD.

Approximately 800 participants, ranging in age from 55 to 90, will be recruited for the study: 400 patients with MCI, 200 with early AD, and 200 normal controls. Patients with MCI and normal controls will be followed for 3 years, and those with AD will be followed for 2 years. At 6-month intervals, all participants will be seen in person or contacted by telephone. All participants will undergo repeated scanning and blood and urine biomarkers will be collected at the time of each scan. All patients will be asked if they are willing to undergo lumbar puncture at baseline and year one, with the goal of a minimum of 20% and as many as 50% of each group providing CSF (cerebrospinal fluid) samples for analysis and storage for future analyses.

For more information contact: Yale University School of Medicine, New Haven, CT 06510 - Martha MacAvoy, PhD, (203) 764-8100. Martha.macavoy@yale.edu; Kristina Estok, (203) 764-8100, Kristine.estok@yale.edu