Ketasyn in Mild to Moderate Alzheimer's Disease

This study has been completed.

First Received on September 1, 2005. Last Updated on December 30, 2008

Purpose

The purpose of this study is to evaluate the safety, tolerability and effectiveness of Ketasyn™ administered once a day for ninety days in subjects with mild to moderate, probable Alzheimer's disease.

Sponsor: Accera, Inc.
Information provided by: National Institute on Aging (NIA)
ClinicalTrials.gov Identifier: NCT00142805

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Condition  Intervention  Phase
Alzheimer's Disease  Drug: Ketasyn™ (AC-1202)  Phase 2

Resource links provided by NLM:

Genetics Home Reference related topics: Alzheimer disease
MedlinePlus related topics: Alzheimer's Disease
U.S. FDA Resources

Further study details as provided by National Institute on Aging (NIA):

Primary Outcome Measures:
- Changes measured by Alzheimer's Disease Assessment Scale - Cognitive Subscale (ADAS-Cog) at all 5 visits
- Alzheimer's Disease Cooperative Study - Clinician's Global Impression of Change (ADCS-CGIC) at visits 2 through 5
- Mini-Mental State Exam (MMSE) at all 5 visits

Secondary Outcome Measures:
- Changes measured by Electrocardiogram (ECG) at visits 1 and 5
- Beta-Hydroxybutyrate pre-dose levels at all 5 visits
- Beta-Hydroxybutyrate 2-hour post-dose levels at visits 2, 3, and 4

Estimated Enrollment: 100
Study Start Date: October 2004
Detailed Description:
Substantial scientific evidence has shown that defects in glucose metabolism occur in Alzheimer's disease. Attempts to compensate for the reduced cerebral metabolic rates in AD have met with some success. Treatment of AD patients with high doses of glucose and insulin will raise cognitive scores. However, this effect is slight, and high doses of insulin can have adverse consequences. Administration of ketone bodies or their metabolic precursors such as medium chain triglycerides (MCTs) presents an attractive alternative to glucose and insulin. In a preliminary study, Ketasyn™, an MCT, demonstrated pharmacological activity and statistically significant efficacy in improving short-term memory and attention performance after a single dose.

Participants will be randomized to receive either Ketasyn™ or a matching placebo, administered once a day by mixing powder in a glass of liquid. The treatment period will last 90 days, followed by a 2-week washout period. Each patient will be seen 5 times: at screening, baseline, and post-baseline days 45, 90, and 104. The visits will include physical and/or neuropsychological examinations, electrocardiograms (ECGs) and laboratory tests.

Eligibility
Ages Eligible for Study: 50 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria
Inclusion Criteria:
- Informed Consent Form signed by patient and caregiver
- Diagnosis of probably Alzheimer's disease of mild to moderate severity
- Age 50 or older
- If female, 2 years postmenopausal or surgically sterile
- Hearing, vision, and physical abilities adequate to perform assessments (corrective aids allowed)
- Caregiver to attend all visits, perform assessments, and supervise administration of study medication
- CT or MRI within 24 months prior to screening compatible with a diagnosis of probably Alzheimer's disease
- Modified Hachinski Ischemia Scale score of 4 or less
- ADAS-Cog score between 15 and 35 inclusive at screening
- MMSE score between 14 and 24 inclusive at screening
- Stable medical condition for 3 consecutive months immediately prior to baseline
- No clinically significant abnormal findings on the physical examination, medical history, or clinical laboratory results during screening

Exclusion Criteria:
- Any condition that would, in the opinion of the Principal Investigator, render the patient or the caregiver unsuitable for the study, or place them at substantial risk of adverse outcome
- Unwillingness or inability of the patient and/or caregiver to fulfill the requirements of the study
- Resident in a skilled nursing facility
- Any significant neurological disease other than probable AD (e.g. Parkinson's disease, Huntington's disease, brain tumor, normal pressure hydrocephalus, progressive supranuclear palsy, seizure disorder, subdural hematoma, multiple sclerosis, history of stroke, or history of head injury requiring hospitalization)
- An alternate cause for dementia other than AD as determined by a required CT or MRI scan within 24 months prior to screening
- Current history of major psychiatric disorder
- Major depression as determined by a Cornell Scale for Depression in Dementia
- Clinically significant hypothyroidism
- Clinically significant B12 deficiency
- Unstable or clinically significant cardiovascular disease
- Diabetes of any type
- History of tertiary syphilis
• Cancer within 3 years prior to baseline, with the exception of squamous and basal cell carcinoma
• Vital sign abnormalities
• Clinically significant renal disease or insufficiency
• Clinically significant hepatic disease or insufficiency
• Alcohol consumption greater than 2 oz of spirits per day or 14 oz per week (1 oz of spirits is equal to 6 oz of wine or 12 oz of beer)
• Current history of alcohol abuse or other substance abuse within 24 months prior to baseline
• Known HIV infection
• Use of any investigational compound within 30 days prior to screening
• Use of prohibited medications (contact site for details)
• Prior or current use of medium-chain triglycerides (MCTs) for medical purposes
• Known allergies to coconut oil

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT00142805

Locations

United States, Arizona
21st Century Neurology, a division of Xenoscience Inc.
Phoenix, Arizona, United States, 85013

United States, California
Comprehensive Neuroscience
Cerritos, California, United States, 90703
Pharmacology Research Institute
Los Alamitos, California, United States, 90720
Pharmacology Research Institute
Newport Beach, California, United States, 92660
Pharmacology Research Institute
Northridge, California, United States, 91324
The Southwest Institute for Clinical Research
Rancho Mirage, California, United States, 92270
Pharmacology Research Institute
Riverside, California, United States, 92506

United States, Florida
Baumel-Eisner Neuromedical Institute
Boca Raton, Florida, United States, 33486
Meridien Research
Brooksville, Florida, United States, 34613
Baumel-Eisner Neuromedical Institute, Inc.
Ft. Lauderdale, Florida, United States, 33321
Sunrise Clinical Research
Hollywood, Florida, United States, 33021
Comprehensive Neuroscience
Melbourne, Florida, United States, 32935
Baumel-Eisner Neuromedical Institute
Miami Beach, Florida, United States, 33154
Anchor Research Center
Naples, Florida, United States, 34102
Renstar Medical Research
Ocala, Florida, United States, 34471
Comprehensive Neuroscience
St. Petersburg, Florida, United States, 33702
Meridien Research
Sponsors and Collaborators
Accera, Inc.

Investigators
Study Director: Sam Henderson, PhD Accera, Inc.

More Information

Additional Information:
Accera Pharmaceuticals Clinical Trials Query Form

Publications:


Additional publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Henderson ST, Poirier J. Pharmacogenetic analysis of the effects of polymorphisms in APOE, IDE and IL1B on a ketone body based therapeutic on cognition in mild to moderate Alzheimer's

ClinicalTrials.gov Identifier: NCT00142805  History of Changes
Other Study ID Numbers:  IA0076
Study First Received:  September 1, 2005
Last Updated:  December 30, 2008
Health Authority:  United States: Institutional Review Board
United States: Federal Government

Keywords provided by National Institute on Aging (NIA):
ketones
Apolipoprotein E
ApoE genotype
cognitive function
glucose metabolism

Additional relevant MeSH terms:
Alzheimer Disease  Tauopathies
Dementia  Neurodegenerative Diseases
Brain Diseases  Delirium, Dementia, Amnestic, Cognitive
Central Nervous System Diseases  Disorders
Nervous System Diseases  Mental Disorders

ClinicalTrials.gov processed this record on May 06, 2012
Experimental Drug Ketasyn(TM) Improves Memory in Age-Associated Memory Impairment Study

BROOMFIELD, Colo., Aug. 29 /PRNewswire/ -- Accera, Inc. announced today that recent data from a Phase II study of its lead compound Ketasyn(TM) (AC-1202) in age-associated memory impairment (AAMI) showed that Ketasyn has a positive and clinically meaningful effect on memory in older adults.

AAMI is the decline in memory that occurs during the natural course of aging. The National Institute of Mental Health criteria for AAMI include complaints of gradual memory loss in everyday problems in persons more than 50 years of age. AAMI affects an estimated 10-15 million people in the U.S., and may be a precursor to Alzheimer's disease (AD), which is expected to afflict 11-16 million Americans in the next 40 years.

AAMI symptoms may be related to declines in glucose metabolism in the brain that are also associated with aging. Glucose is the brain's primary fuel source, so aging brains with impaired glucose metabolism require an alternative source of energy. Ketasyn is an orally available compound that is metabolized into ketone bodies, which the brain can use for energy even when its ability to process glucose is impaired.

"The results of this study support the hypothesis that providing additional energy reserves to the elderly brain improves a variety of cognitive activities. They also provide further evidence of the roles that glucose and insulin metabolism plays in cognition and memory," said Dr. Lauren Costantini, Accera's vice president of clinical development. "As in our earlier successful clinical studies in Alzheimer's disease, Ketasyn was well tolerated by subjects in the AAMI study and we are encouraged by the strong efficacy data."

The randomized, double-blind, placebo-controlled, parallel, multi-center trial was conducted at six centers in the United States. One hundred fifty-nine subjects diagnosed with AAMI received either Ketasyn or placebo for 90 days followed by a two-week washout period. Mean age in this study was 65. Subjects underwent genomic testing for variations in the coding regions of genes known to influence memory and cognition, including the apolipoprotein E gene (APOE), a known genetic risk factor for Alzheimer's disease (AD) that occurs in 15-20% of the general population. On days 0, 30, 60, 90 and 104, subjects were evaluated through a battery of neuropsychometric tests that measure various aspects of memory and cognition.

Ketasyn showed significant efficacy in tests of memory. On average, subjects taking Ketasyn performed significantly better on the 'First-Last Name Association' test (FLN) than subjects taking placebo (p=0.042). "On average, seniors taking Ketasyn remembered more names than those taking placebo," said Dr. Costantini.

In another memory test called Name-Face Recognition (NFA), which associates a person's name and face, Ketasyn subjects under age 59 improved significantly more than placebo subjects at Day 90 (p=0.0217). The efficacy in the NFA test observed with Ketasyn in subjects under age 59 captures a large portion of the AAMI population.

Consistent with the findings of Accera's Phase IIa and IIb AD studies, subjects who did not have the APOE4 genotype (E4(-)) responded particularly well to treatment: E4(-) subjects showed a further significant treatment effect of Ketasyn in FLN at Day 90 (p=0.012). In contrast, and also consistent with the AD trial results, APOE4(+) subjects showed no...
difference between Ketasyn and placebo for FLN scores at Day 90 (p=0.4639).

The safety profile of Ketasyn was excellent, as shown in the previous AD trials with Ketasyn. The incidence of adverse events was low and similar between Ketasyn and placebo groups.

Accera recently completed a Phase IIb clinical trial in AD patients that confirmed Ketasyn's safety and efficacy as measured by improvement in ADAS-Cog scores, the gold standard measure for efficacy in cognition and short-term memory. Accera plans to initiate a pivotal, Phase III multi-center clinical trial in early 2008 in mild-to-moderate AD patients. This study will focus on several measures of efficacy, including ADAS-Cog, safety and the role of insulin regulation in AD.

About Ketasyn(TM) (AC-1202)

Brain imaging techniques performed on aging adults and Alzheimer's patients reveal a dramatically decreased uptake of glucose, the brain's preferred source of energy. Ketasyn(TM) (AC-1202) is an orally available compound that is efficiently metabolized by the liver into ketone bodies, an alternative energy source that the brain can utilize when glucose metabolism is compromised. Ketasyn has disease modifying potential in AD and a number other neurodegenerative diseases characterized by decreased glucose use in the brain, which is known as neuronal hypometabolism.

About Accera, Inc.

Based in Broomfield, CO, Accera, Inc. is a privately held biotechnology company focused on developing novel drugs for neurodegenerative diseases. The company's lead candidate, AC-1202, is a first-in-class molecule that has recently completed Phase II clinical trials for Alzheimer's disease and Age-Associated Memory Impairment. Accera has other small molecule compounds in its product pipeline for a range of other neurodegenerative diseases including Parkinson's disease and Huntington's disease. For more information, visit: http://www.accerapharma.com.

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