ForPatients
by Roche

Alzheimer's Disease (AD)

A Study of Crenezumab Versus Placebo in Preclinical Presenilin1 (PSEN1) E280A Mutation Carriers to Evaluate Efficacy and Safety in the Treatment of Autosomal-Dominant Alzheimer's Disease (AD), Including a Placebo-Treated Non-Carrier Cohort

Trial Status	Trial Runs In	Trial Identifier
Completed	1 Country	NCT01998841 GN28352

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Double-Blind, Placebo-Controlled Parallel-Group Study in Preclinical PSEN1 E280A Mutation Carriers Randomized to Crenezumab or Placebo, and in Non-Randomized, Placebo-Treated Non-Carriers From the Same Kindred, to Evaluate the Efficacy and Safety of Crenezumab in the Treatment of Autosomal-Dominant Alzheimer's Disease

Trial Summary:

This study consists of 2 periods: [1] Study Period A - evaluating the efficacy and safety of Crenezumab versus Placebo in participants who carry the PSEN1 E280A autosomal-dominant mutation and do not meet the criteria for mild cognitive impairment due to AD or dementia due to AD and are thus, in a preclinical phase of AD. Participants will be randomised in a 1:1 ratio to receive either Crenezumab or Placebo subcutaneously (every 2 weeks) or intravenously (every 4 weeks) for at least 260 weeks. A cohort of participants (non-mutation carriers) will also be enrolled and will be dosed solely on Placebo and [2] Study Period B - Participants will be offered the opportunity to continue to receive study drug until the results of the study are known and post trial access to Crenezumab is started or development of Crenezumab is discontinued.

Genentech, Inc. Sponsor	**Phase 2** Phase

NCT01998841 GN28352
Trial Identifiers

Eligibility Criteria:

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Gender	Age	Healthy Volunteers
All	#30 Years & # 60 Years	No

Inclusion Criteria:

- Membership in PSEN1 E280A mutation carrier kindred
- Agrees to conditions of, and is willing to undergo, genetic testing (for example [e.g.], apolipoprotein E [APOE], PSEN1 E280A, and other genetic testing)
- PSEN1 E280A mutation carrier or non-carrier status has been confirmed prior to or during the screening period
- Mini-Mental Stage Examination (MMSE) greater than or equal to (>=) 24 for participants with less than (<) 9 years of education or MMSE >=26 for participants with 9 or more years of education
- Does not meet criteria for dementia due to AD per the National Institute on Aging and the Alzheimer's Association Workgroup (McKhann et al. 2011) criteria
- Does not meet criteria for mild cognitive impairment (MCI) due to AD per the National Institute on Aging and the Alzheimer's Association Workgroup (Albert et al. 2011) criteria
- Adequate vision and hearing in the investigator's judgment to be able to complete testing
- If female, and not documented (by medical records or physician's note) to be surgically sterile (absence of ovaries and/or uterus) or postmenopausal, willing to undergo pregnancy tests at protocol-specific timepoints
- For women who are not documented (by medical records or physician's note) to be surgically sterile (absence of ovaries and/or uterus) or postmenopausal, agreement to remain abstinent or use two adequate methods of contraception, including at least one method with a failure rate of <1 percent (%) per year (e.g., hormonal implants, combined oral contraceptives, vasectomized partner, tubal ligation) during the treatment period and for at least 16 weeks after the last dose of study drug
- For men with partners of childbearing potential (that is [i.e.], women who are not surgically sterile and are not postmenopausal), agreement to remain abstinent or use a condom as a method of contraception during the treatment period and for at least 8 weeks after the last dose of study drug
- Study partner who agrees to participate in the study and is capable of and willing to: accompany the participant to all required visits; provide information for required telephone assessments; spend sufficient time with the participant to be familiar with his/her overall function and behavior and be able to provide adequate information about the participant including knowledge about domestic activities, hobbies, routines, social skills and basic activities of daily life; work and educational history; cognitive performance including memory abilities, language abilities, temporal and spatial orientation, judgment and problem solving; emotional and psychological state; and general health status
- Participant and study partner have evidence of adequate premorbid functioning (e.g., intellectual, visual, and auditory) and are fluent in, and able to read, the language in which study assessments are administered
- Willing and able to undergo neuroimaging (PET and MRI)
- Serum thyroid stimulating hormone (TSH) and B12 levels within normal or expected ranges for the testing laboratory or if TSH and B12 values are out of range they are judged by the investigator not to be clinically significant. If participant is undergoing thyroid replacement therapy, TSH levels must be within normal or expected ranges for the testing laboratory or, if TSH values are out of range, they do not require any therapeutic actions (treatment or surveillance). If participant is receiving vitamin B12 injections or oral vitamin B12 therapy, B12 levels must be at or above the lower limit of normal for the testing laboratory or, if B12 values are out of range, they do not require any therapeutic actions (treatment or surveillance)
- In good general health with no known co-morbidities expected to interfere with participation in the study

Exclusion Criteria:

- Significant medical, psychiatric, or neurological condition or disorder documented by history, physical, neurological, laboratory, or electrocardiogram (ECG) examination that would place the participant at undue risk in the investigator's judgment or impact the interpretation of efficacy
- History of stroke. Participants with a history of transient ischemic attack may be enrolled if the event occurred >=2 years prior to screening
- History of severe, clinically significant (persistent neurological deficit or structural brain damage) central nervous system trauma (e.g. cerebral contusion)
- Body weight <45 or >120 kilograms (kg)
- History or presence of atrial fibrillation that poses a risk for future stroke in the investigator's judgment
- Clinically significant laboratory or ECG abnormalities (e.g., abnormally prolonged or shortened QTc interval) in the investigator's judgment
- Current presence of bipolar disorder or other clinically significant major psychiatric disorder according to Diagnostic and Statistical Manual of Mental Disorders 4th Edition Text Revision (DSM-IV-TR) or symptom (e.g., hallucinations, agitation, paranoia) that could affect the participant's ability to complete evaluations
- Clinically significant depression, based in part by a Geriatric Depression Scale (short form) (15-point scale) score >9 at screening
- History of seizures (excluding febrile seizures of childhood, or other isolated seizure episodes that were not due to epilepsy in the judgment of the investigator, and required at most time-limited anticonvulsant treatment, and which occurred more than 7 years prior to the screening visit)
- Myocardial infarction within 2 years, congestive heart failure, atrial fibrillation, or uncontrolled hypertension
- Pregnant or nursing women, or women who intend to become pregnant or to nurse infants during the conduct of this trial
- Clinically significant infection within the last 30 days prior to screening
- Positive urine test for drugs of abuse at screening
- History of alcohol or substance dependence within the previous two years
- Use of any other medications with the potential to significantly affect cognition; intermittent or short-term use of these medications may be allowed if deemed medically necessary for the treatment of a non-excluded medical condition with approval from the Medical Monitor. In addition, use of tricyclic antidepressants or benzodiazepines will be permitted if used in stable, low doses for the treatment of a non-excluded medical condition with approval from the Medical Monitor
- Use of typical anti-psychotics or barbiturates
- Use of non-anti-cholinergic antidepressant medications or atypical anti-psychotics unless maintained on a stable dose regimen for at least 6 weeks prior to screening
- Use of any Food and Drug Administration (FDA)/Instituto Nacional de Vigilancia de Medicamentos y Alimentos (INVIMA)-approved medications for treatment of late onset Alzheimer's disease (LOAD) at screening/baseline. Cholinesterase inhibitors and/or memantine are prohibited during the study except in participants enrolled in the study that develop AD dementia
- Use of anti-coagulant medication (heparinoids, heparin, warfarin, thrombin inhibitors, Factor Xa inhibitors), or known coagulopathy or platelet count <100,000 cells/microliter, within 4 weeks of the screening visit; Anti-platelet medications (e.g., aspirin, clopidigrel, dipyridamole) are permitted if on a stable dose for 4 or more weeks prior to screening. Short-term, peri-operative use of anti-coagulants may not result in discontinuation from the study; however, any such use must be discussed with the Medical Monitor
- Treatment with any biologic therapy within five half-lives or 3 months prior to screening, whichever is longer, with the exception of routinely recommended vaccinations, which are allowed
- Use of anti-seizure medication (except in childhood for febrile seizures or if used for non-seizure indications), anti-parkinsonian, or stimulant (e.g., methylphenidate) medications
- Use of investigational drug, device, or experimental medication within 60 days (or five half-lives, whichever is longer) of the screening visit
- Previous treatment with crenezumab or any other therapeutic that targets A-beta

- History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric, human, or humanized antibodies or fusion proteins
- Contraindication to MRI scan procedures or clinically significant claustrophobia that would contraindicate a brain MRI scan
- Contraindication to PET scan procedures