ForPatients
by Roche

Enfermedad de Alzheimer (EA)

A clinical trial to compare gantenerumab with placebo in people who are at risk for, or are in the earliest stages of, Alzheimer's disease (AD)

A Study to Evaluate the Efficacy and Safety of Gantenerumab in Participants at Risk for or at the Earliest Stages of Alzheimer's Disease (AD)

Trial Status	Trial Runs In	Trial Identifier
Terminado	10 Countries	NCT05256134 2021-001184-25 WN42444

La información se obtuvo directamente de sitios web de registros públicos, como ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., y no se ha editado.

Official Title:

A Phase III, Multicenter, Randomized, Parallel-Group, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Gantenerumab in Participants at Risk for or at the Earliest Stages of Alzheimer's Disease

Trial Summary:

A study to evaluate the efficacy and safety of gantenerumab in amyloid-positive, cognitively unimpaired participants at risk for or at the earliest stages of AD. The planned number of participants for this study is approximately 1200 participants randomized in a 1:1 ratio to receive either gantenerumab or placebo (600 participants randomized to gantenerumab and 600 participants randomized to placebo).

Hoffmann-La Roche	Phase 3
Sponsor	Phase

NCT05256134 2021-001184-25 WN42444
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#60 Years & # 80 Years	No

How does the SKYLINE (WN42444) clinical trial work?

© 2022 F. Hoffmann-La Roche Ltd

This clinical trial is recruiting people who are at risk of developing, or are in the earliest stages of, Alzheimer's disease (AD).

The purpose of this clinical trial is to compare the effects, good or bad, of gantenerumab versus placebo in people who are at risk of developing, or are in the earliest stages of, AD. If you take part in this clinical trial, you will receive either gantenerumab or placebo. A 'placebo' medicine looks the same as the medicine in the clinical trial (active medicine) but does not contain any active ingredients.

How do I take part in this clinical trial?

To be able to take part in this clinical trial, you must be 60–80 years old and be at risk for developing AD or be in the earliest stages of AD (known as preclinical AD). You must be 'amyloid positive', which will be confirmed by either a scan of your brain, or by testing your cerebrospinal fluid, which will be obtained through a procedure known as a lumbar puncture. You must also demonstrate a certain level of brain function (be cognitively unimpaired) to join the clinical trial. Your doctor will confirm this through a number of tests that measure your brain health against certain criteria. You must also choose someone you are close with, for example a family member or friend, who you will have to contact (in person, by telephone, video call, email, or other electronic means) at least twice a week as your 'study partner'. Your study partner will support you throughout the clinical trial and speak to your doctor about your abilities, such as logic and reasoning, attention, memory and processing information.

If you have been diagnosed with some pre-specified medical conditions, or have previously taken pre-specified medications, you may not be able to take part in this clinical trial.

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor. If your doctor thinks that you might be able to take part in this clinical trial, they may refer you to the closest clinical trial doctor. The clinical trial doctor will give you all the information you need to make your decision about taking part in the clinical trial. You can also find the clinical trial locations on this page.

To take part, you must successfully go through the screening process, which lasts for approximately 17 weeks and includes some further tests to confirm this clinical trial is right for you. Some of these tests or procedures may be part of your regular medical care. They may be done even if you do not take part in the clinical trial. If you have had some of the tests recently, they may not need to be done again.

Before starting the clinical trial, you will be told about any risks and benefits of taking part in the trial. You will also be told what other treatments are available so that you may decide if you still want to take part.

© 2022 F. Hoffmann-La Roche Ltd

While taking part in the clinical trial and for at least 17 weeks after the last dose of clinical trial treatment, women (who are not currently pregnant but can become pregnant, and who have not reached menopause) will need to either take contraceptive medicine or not have heterosexual intercourse for safety reasons.

What treatment will I be given if I join this clinical trial?

Everyone who joins this clinical trial will be split into two groups randomly (like flipping a coin). You will have a 1 in 2 chance of receiving either gantenerumab or placebo.

The treatment period will be split into two parts: Part 1 and Part 2. You have up to Week 25 of the clinical trial to give your preference on how you would like to be given treatment in Part 2:

- One injection every week
- OR two injections once every two weeks.

In Part 1 (dose-escalation phase) you will be given either:

- Gantenerumab, as an injection under the skin once every four weeks for at least six months, then one injection every two weeks for three months (if you prefer one injection every week in Part 2) or two injections once every four weeks for three months (if you prefer two injections once every two weeks in Part 2)
    - Your dose will be gradually increased during this time
- OR placebo, as an injection under the skin once every four weeks for at least six months, then one injection every two weeks for three months (if you prefer one injection every week in Part 2) or two injections once every four weeks for three months (if you prefer two injections once every two weeks in Part 2).

Once your clinical trial treatmnet has been escalated to the target dose (the dose believed to have the best effect), you will enter Part 2 (maintenance phase) and you will be given either:

- Gantenerumab, as one injection under the skin every week or two injections under the skin once every two weeks, until the end of the four-year treatment period
- OR placebo, as one injection under the skin every week or two injections under the skin once every two weeks, until the end of the four-year treatment period.

Your first three doses in Part 1 will be administered by the clinical trial doctor. If you want to, you can then ask your clinical trial doctor if you, or your study partner, can administer your injections at home. You or your study partner will be given training by the clinical trial staff on how to do this and they will supervise you at your next four clinic visits to ensure this is being done appropriately. You may also have the option to have your injections administered by a home nurse.

© 2022 F. Hoffmann-La Roche Ltd

This is a ‘placebo-controlled’ clinical trial, which means that one of the groups will be given a placebo. A placebo is used to show that the doctor or the participants do not sway the results of the clinical trial.

Neither you nor your clinical trial doctor can choose or know the group you are in, but you will be asked to take part in tests throughout the clinical trial to monitor how you are responding to treatment. If you are receiving placebo, have reached ‘target dose’ and show signs of progression due to AD, you will start to receive gantenerumab.

How often will I be seen in follow-up appointments and for how long?

You will be given the clinical trial treatment gantenerumab or placebo for roughly four years. You will have regular clinic visits every six months, which will include tests and brain scans to see how you are responding to the treatment and any side effects that you may be having. You are free to stop this treatment at any time. After the clinical trial, you will have a final clinic visit 16 weeks after your Week 211 safety and efficacy assessments.

What happens if I am unable to take part in this clinical trial?

If this clinical trial is not suitable for you, you will not be able to take part. Your doctor may suggest other clinical trials that you may be able to take part in or other treatments that you can be given. You will not lose access to any of your regular care.

For more information about this clinical trial see the **For Expert** tab on the specific ForPatient page or follow this link to ClinicalTrials.gov

Trial-identifier: NCT05256134

Inclusion Criteria:

- Willing and able to comply with the study protocol and complete all aspects of the study [including cognitive and functional assessments, physical and neurological examinations, MRI, CSF collection, genotyping, and positron emission tomography (PET) imaging].
- Cognitively unimpaired with a screening clinical dementia rating global score (CDR-GS) of 0, and Repeatable Battery for the Assessment of Neuropsychological Status Delayed Memory Index (RBANS DMI) >=80.
- Evidence of cerebral amyloid accumulation.
- Participants who have an available person (referred to as a "study partner").
- Fluent in the language of the tests used at the study site.
- Adequate visual and auditory acuity, sufficient to perform neuropsychological testing (eye glasses and hearing aids are permitted).
- Agreed not to participate in other interventional research studies for the duration of this trial.
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods that result in a failure rate of <1% per year during the treatment period and for at least 17 weeks after the final dose of study treatment.

© 2022 F. Hoffmann-La Roche Ltd

Exclusion Criteria:

- Any evidence of an underlying neurological or neurodegenerative condition that may lead to cognitive impairment other than AD.
- Clinical diagnosis of mild cognitive impairment (MCI), prodromal AD, or any form of dementia.
- History or presence of intracranial or intracerebral vascular malformations, aneurysm, subarachnoid hemorrhage, or intracerebral macrohemorrhage.
- History or presence of posterior reversible encephalopathy syndrome.
- History of ischemic stroke with clinical symptoms or an acute event that is consistent with a transient ischemic attack within 12 months of screening.
- History of severe, clinically significant (i.e., resulting in persistent neurologic deficit or structural brain damage) central nervous system (CNS) trauma (e.g., cerebral contusion).
- History or presence of intracranial mass lesion (e.g., glioma, meningioma) that could potentially impair cognition or lead to progressive neurological deficits.
- Infections that may affect brain function or a history of infections that resulted in neurologic sequelae [e.g., human immunodeficiency virus (HIV), syphilis, neuroborreliosis, and viral or bacterial meningitis and encephalitis].
- History of major depression, schizophrenia, schizoaffective disorder, or bipolar disorder.
- At risk for suicide.
- History of alcohol and/or substance abuse or dependence.
- History or presence of clinically significant systemic vascular disease, atrial fibrillation or heart failure.
- Within the last year, experienced unstable or clinically significant cardiovascular disease (e.g., myocardial infarction).
- Uncontrolled hypertension.
- Chronic kidney disease, indicated by creatinine clearance <30 mL/min.
- Confirmed and unexplained impaired hepatic function.
- History of, or are known to currently have an HIV infection, or hepatitis B or hepatitis C virus infection that has not been adequately treated.
- History or presence of systemic autoimmune disorders that may lead to progressive neurological impairment with associated cognitive deficits.
- Systemic immunosuppression or immunomodulation due to the continuing effects of immunosuppressant or immunomodulating medications.
- Current COVID-19 infection.
- Evidence of folic acid or vitamin B-12 deficiency.
- Any passive immunotherapy (Ig) or other long-acting biologic agent to prevent or postpone cognitive decline within 1 year of screening.
- Any other investigational treatment within 5 half-lives or 6 months (whichever is longer) prior to screening.
- Typical/Atypical anti-psychotic medications or neuroleptic medications.
- Anticoagulation medications within 3 months of screening with no plans to initiate any prior to randomization.
- Any previous treatment with cholinesterase inhibitors and N-methyl-D-aspartate receptor antagonists are exclusionary at screening.
- Pregnant or breastfeeding, or intending to become pregnant during the study or within 17 weeks after the final dose of gantenerumab.
- Impaired coagulation.
- Known history of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric, human, or humanized antibodies or fusion proteins, including gantenerumab and gantenerumab excipients.
- Participants who reside in a skilled nursing facility such as a convalescent home or long-term care facility.

© 2022 F. Hoffmann-La Roche Ltd

- Participants who require residence in such facilities during the study may continue in the study and be followed for efficacy and safety, provided that they have a study partner who meets the study partner requirements.

© 2022 F. Hoffmann-La Roche Ltd