Genentech
A Member of the Roche Group

GANTENERUMAB PHASE III PIVOTAL CLINICAL TRIALS: GRADUATE I AND II

EVALUATING THE EFFICACY AND SAFETY OF THE INVESTIGATIONAL ANTI-AMYLOID MONOCLONAL ANTIBODY, GANTENERUMAB, IN PEOPLE LIVING WITH EARLY ALZHEIMER'S DISEASE[1,2,3,4]

Evaluating the clinical benefit of subcutaneous gantenerumab for people living with early Alzheimer's, the GRADUATE trials build on learnings from

NEARLY

2 DECADES

of research in the field.[5,6,7,8,9]

ROBUST CLINICAL TRIAL DESIGN[1,2]

2
identical clinical trials

Allows comparison of results between studies

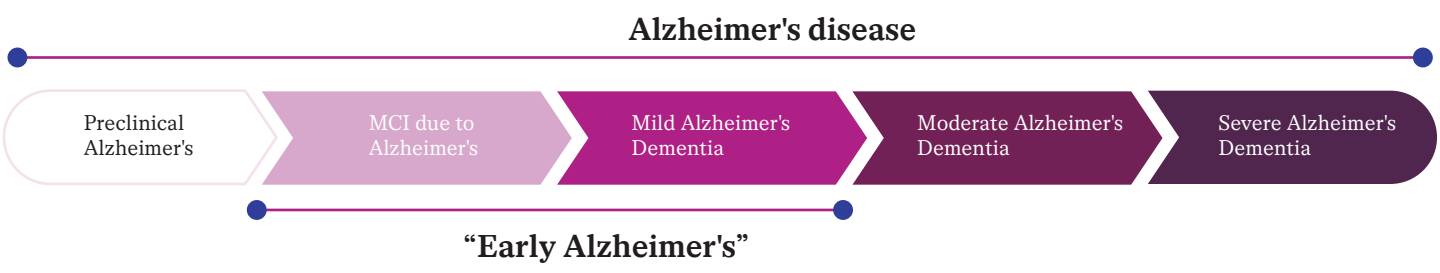
~1,000
participants per study, across 30 countries

Provides sufficient statistical power

27-MONTH
duration

Represents the longest late-stage clinical program to date

ELIGIBLE PARTICIPANTS HAD EARLY ALZHEIMER'S AND WERE AT HIGHER RISK OF THEIR DISEASE PROGRESSING[1,2,10]



WHAT GENENTECH AND THE FIELD HAVE LEARNED FROM PREVIOUS RESEARCH

Previous clinical trials in Alzheimer's have underscored the importance of recruiting participants with the targeted disease pathology to better test potential therapies for efficacy. This is known as enrichment. In the GRADUATE program, the trial population was enriched with participants who had abnormal memory when beginning the trial and evidence of Alzheimer's pathology. As their disease was more likely to progress during the study, this could help researchers measure clinical decline and the potential impact of gantenerumab.

INCLUSION CRITERIA

- Presence of beta-amyloid (build-up of amyloid plaques in the brain is a hallmark of Alzheimer's)
- Scores on cognitive tests that meant the participant was experiencing memory problems
- A partner to support study participation
- Age 50-90 years

RANDOMIZED, DOUBLE-BLIND ADMINISTRATION OF STUDY MEDICINE[1,2]

1:1

Participants were randomly assigned to receive either gantenerumab or placebo

Neither the study participants nor study investigators knew whether participants received gantenerumab or placebo

MEASURING WHAT MATTERS TO PEOPLE LIVING WITH ALZHEIMER'S AND THEIR FAMILIES[1,2]

IMPACT OF TREATMENT ON COGNITION AND ABILITY TO PERFORM ACTIVITIES OF DAILY LIVING[1,2]

PRIMARY ENDPOINT:

Change in Clinical Dementia Rating-Sum of Boxes (CRD-SB) from start of study to Week 116[1,2]

Clinical Dementia Rating-Sum of Boxes (CRD-SB)
A clinician-rated measure of cognition and function: a doctor asks questions designed to measure memory, judgement, problem solving, home and hobbies, orientation and personal care[11]

SECONDARY ENDPOINTS*:

May provide additional clinically meaningful information regarding cognitive and functional decline[1,2]

- Performance-based tests of cognition
- Observer (care partner) reported measures of daily function
- Safety measures

*Key secondary endpoints include: change from Baseline to Week 116 in Mini-Mental State Examination (MMSE), Alzheimer Disease Assessment Scale-Cognition Subscale 11 (ADAS-Cog11), ADAS-Cog Subscale 13 (ADAS-Cog13), Verbal Fluency Task Score, Functional Activities Questionnaire (FAQ) Score, Alzheimer Disease Cooperative Study Group-Activities of Daily Living (ADCS-ADL).

Gantenerumab is an investigational medicine in clinical development and is not approved in any country worldwide.

1. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT03443973. Last accessed: June 2022.
2. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT03444870. Last accessed: June 2022.
3. Klein G, et al. J Prev Alzheimers Dis. 2021;8:3-6.
4. Roche Data on File. Gantenerumab Breakthrough Designation. October 2021.
5. Ostrowitzki S, et al. Alzheimers Res Ther. 2017;9:95.
6. Andjelkovic M, et al. 2018. AAIC Oral presentation.
7. Abi-Saab D, et al. 2018. AAIC Oral presentation.
8. Lane C, et al. 2021. CTAD Oral presentation.
9. Salloway S, et al. Nat Med. 2021;27:1187-1196.
10. Mayo Clinic. Alzheimer's stages: how the disease progresses. Available at: https://www.mayoclinic.org/diseases-conditions/alzheimers-disease/in-depth/alzheimers-stages/art-20048448. Last accessed: June 2022.
11. Morris JC. Neurology. 1993;43:2412-14.