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To study the safety of an anti-tau antibody as a therapeutic against Alzheimer's disease

Submission date
06/01/2025

Recruitment status
No longer recruiting

Registration date
08/01/2025

Overall study status
Completed

Last Edited
08/01/2025

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Alzheimer’s disease (AD) is a condition where harmful proteins build up in the brain, leading to memory loss and other cognitive issues. These proteins include β-amyloid, which forms sticky clumps called plaques, and tau, which forms twisted tangles inside brain cells. While both proteins are harmful, recent research suggests that problems with tau might be more closely linked to the disease's progression. Tau normally helps keep brain cells' internal transport systems running smoothly, but when it becomes abnormal, it clumps together and disrupts these systems, eventually causing brain cells to die. Scientists have developed a special antibody, a monoclonal antibody (mAb) that targets the harmful form of tau, showing promise in early tests with mice and human brain cells. This antibody could potentially stop or slow down the damage caused by tau in Alzheimer’s disease, offering hope for new treatments. This study aims to evaluate the safety and efficacy of the mAb in AD patients.

Who can participate?
Mild to moderate-stage AD patients

What does the study involve?
In this phase I study, the safety of the mAb will be assessed through a five-month follow-up period, with long-term follow-ups including periodic cognitive and safety assessments beyond the 6 months to provide insights into sustained efficacy and potential delayed adverse effects of AININ-20. The efficacy of the mAb in treating AD will be evaluated through primary endpoints, including changes in questionnaire scores following AININ-20 infusion, which will assess improvements in cognitive function.

What are the possible benefits and risks of participating?
Benefits:
1. Potential for Symptom Improvement: Participants may experience improvements in cognitive function, memory, and overall quality of life if the mAb proves effective in reducing tau-related pathology in Alzheimer's disease.
2. Contribution to Scientific Knowledge: Participants will be contributing to the advancement of scientific understanding and treatment options for Alzheimer's disease, a condition that currently has limited effective therapies. Their involvement may help researchers identify new

therapeutic targets and strategies.
3. Access to New Treatment: Participants will have access to a potentially novel and promising therapeutic agent that is not yet available outside of clinical trials, which could provide a new treatment option if the mAb shows efficacy.
4. Close Monitoring: Participants will receive regular medical check-ups, monitoring, and assessments as part of the trial, which may help identify any health issues early, even if unrelated to the trial drug.

Risks:
1. Potential Side Effects: Like any medication, the mAb could cause side effects. These may include mild reactions (e.g., headache, fatigue, nausea) or more serious adverse events such as immune system reactions, infusion-related reactions, or increased risk of infection due to immune modulation.
2. Unknown Long-Term Effects: Since the mAb is still being tested, the long-term effects of the treatment are not fully understood. Participants may experience effects that are not yet known or anticipated, and the long-term safety profile of the treatment is still under investigation.
3. Risk of Discomfort from Study Procedures: Participation may involve regular blood draws, imaging studies, cognitive assessments, or lumbar punctures, all of which could cause temporary discomfort or adverse reactions in some individuals.
4. Possibility of No Benefit: There is no guarantee that participants will experience any benefit from the mAb, as its effectiveness has not yet been conclusively proven in this phase of the trial.
5. Unexpected Serious Events: Though rare, the mAb could potentially lead to more severe adverse events such as neurological complications, including increased risk of amyloid-related imaging abnormalities (ARIA), which have been seen in other Alzheimer's trials involving monoclonal antibodies.

Where is the study run from?
Farhikhtegan Hospital - Islamic Azad University, Iran

When is the study starting and how long is it expected to run for?
March 2023 to April 2024

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Dr Koorosh Shahpasand, shahp001@umn.edu

Contact information

Type(s)
Public, Scientific, Principal investigator

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Study information

Scientific Title
To study the safety of Alzheimer's disease passive immunotherapy against pathogenic tau in mild to moderate stage Alzheimer's disease patients: Clinical trial phase I

Study objectives
The administration of AININ-20 (anti-pT231-tau antibody) will significantly reduce neurodegeneration and improve clinical outcomes in AD patients.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 07/05/2023, Research Ethics Committee of Farhikhtegan Hospital, Islamic Azad University (Farhikhtegan Hospital No. 9, Farhikhtegan St., Mirdamad Blvd., Tehran, 19697-74311, Iran; +98 21 8865 5555; nrec@behdasht.gov.ir), ref: IR.IAU.FARHIKHTEGANH.REC.1402.004

Primary study design
Interventional

Study design
No-randomized clinical study

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Treatment of mild to moderate stage Alzheimer's disease patients.

Interventions
The study will recruit 12 mild to moderate-stage AD patients to perform 12 interventions, each spaced 3 days apart.

Notably, the study team found the mAb half-life to be approximately 18 hours in the ex vivo system, leading them to conclude that it should be administered to patients every 72 hours (4 × t1/2). Based on their preclinical observations, it was determined that the antibody’s therapeutic effect is dose-dependent. In the absence of detailed pharmacokinetic and pharmacodynamic data, 1 mg of the mAb per 70 kg patient was chosen to administer via IV infusion, based on

preclinical therapeutic target considerations and allometric scaling principles. This dose will serve as a starting dose for assessing safety and efficacy in humans, with further refinement to follow during Phase IIa to determine the optimal therapeutic dose.

Safety assessments will include the recording of all adverse events, physical and neurological examinations, vital signs, and laboratory analysis of blood. The study will evaluate the immune response at baseline, immediately after the final dose, and 5 months following the last infusion. Hematological endpoints will include complete blood count (CBC), white blood cell (WBC) count, red blood cell (RBC) count, and platelet levels. To assess renal and hepatic function, they will include biochemical evaluations such as urea, creatinine, glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase, sodium, and potassium levels. Additionally, baseline urine tests will be conducted to detect any potential infections.

The study will administer 100 mg of hydrocortisone via IV injection. After 10 minutes, they will dilute the investigational medicinal product (1 mg of cGMP grade purified mAb) in 500 mL of normal saline and administer the IMP gradually via IV infusion over 3 hours under monitored conditions. They will repeat the intervention every 3 consecutive days for a total of 12 visits (±1 day interval flexibility).

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
AININ-20 (anti pT231-tau antibody)

Primary outcome(s)
The safety profile of AININ-20 will be assessed using the following methods:
1. Incidence of adverse events (AEs) including cardiovascular, psychiatric, extrapyramidal, injection site reactions, infections, and renal/liver complications measured using data collected in the Case Report Form at the end of the study
2. Evaluation of immediate and long-term AEs post-infusion measured using data collected in the Case Report Form at the end of the study
3. Physical examination, ECG, BMI and vital signs before and after infusion
4. Laboratory test results before and after infusion
5. Overall clinical improvement measured using the Clinical Global Impression (CGI) scale after infusion

Key secondary outcome(s)
The efficacy of AININ-20 in treating AD will be assessed using the following methods:
1. Cognitive function measured using the Mini-Mental State Examination (MMSE) before and after infusion
2. Cognitive function in areas like memory, language, attention, and orientation, measured using the Montreal Cognitive Assessment (MoCA) score before and after infusion
3. Visuo-motor pathway dysfunction measured using the Integrated Cognitive Assessment (ICA) score before and after infusion

Completion date

10/04/2024

Eligibility

Key inclusion criteria
1. Male or female participants aged 55 to 85 years at the time of screening.
2. Participant who is informed of the clinical trial and signs a consent form (if unable to sign, consent from a legally acceptable representative is required).
3. Patient diagnosed with Mild-to-Moderate Stage AD according to the core clinical criteria outlined in National Institute on Aging (NIA) – Alzheimer's Association Diagnostic Guidelines (2011):
3.1. In the mild stage of Alzheimer’s disease, the symptoms might not be apparent; however, the patient may have difficulties performing social and work tasks, remembering recent information or names, choosing the right words, or misplacing valuable objects.
3.2. In the moderate stage, dementia symptoms become more pronounced, and the person may struggle with expressing thoughts and performing routine tasks without assistance (such as dressing, bathing, and eating). Symptoms can vary from person to person and may include forgetfulness, mood changes, confusion, difficulty with daily tasks, incontinence, changes in sleep patterns, wandering, and personality/behavioral changes.
4. Positive findings for AD in CSF (low Aβ42 and high tau, p-tau protein levels) as measured via lumbar puncture at screening (or within 12 months before baseline) or positive amyloid PET scan within 12 months before baseline.
5. MMSE score at screening of 15-24, inclusive.
6. Participants should be maintained on stable doses of their medical therapy for AD for at least 4 weeks before the screening and baseline visits.
7. Willingness and ability to complete all study visits, confirmed by the physician.
8. Availability of a reliable person ("caregiver") who, in the investigator's judgment, has frequent and sufficient contact with the participant and is able to provide accurate information regarding the participant's cognitive and functional abilities, agrees to provide information at clinic visits, which require partner input for scale completion and signs the necessary consent form.
9. Patients with normal clinical laboratory values or, if abnormal, must be judged to be not clinically significant by the physician.
10. Adequate visual and auditory acuity, in the investigator's judgment, sufficient to perform the neuropsychological testing.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
55 Years

Upper age limit
85 Years

Sex

All

Total final enrolment
12

Key exclusion criteria
1. A diagnosis of dementia due to causes other than probable AD.
2. History of a clinically significant stroke (i.e., in the judgment of the investigator, could be a contributing cause of the participant's dementia).
3. Current evidence or history in the past two years of epilepsy, focal brain lesion, head injury with loss of consciousness, or DSM V criteria for any major psychiatric disorder, including psychosis, depression, bipolar disorder, alcohol, or substance abuse.
4. Sensory impairment that would preclude the participant from participating in the study or cooperating with the investigator.
5. Current evidence of any significant clinical disorder or laboratory finding, including severe or uncontrolled medical condition (including hematologic, hepatic, or renal conditions).
6. For participants who will undergo lumbar puncture, the contraindications include prior lumbosacral spine surgery, severe degenerative joint disease or deformity of the spine, history of bleeding, or platelet count 100000.
7. History of any type of malignancies within the past five years, except for appropriately treated carcinoma in situ of the cervix, stable prostate cancer, or non-melanoma skin carcinoma.
8. Use of an investigational agent or participation in any trial within the last two months prior to the screening visit.
9. Have had prior or current treatment with ADUHELM® (Aducanumab).
10. History of or positive test result at Screening for hepatitis C virus antibody (HCV Ab), hepatitis B virus, positive PPD (defined as positive for hepatitis B surface antigen [HBsAg], hepatitis B core antibody [HbcAb]), or human immunodeficiency virus (VDRL-HIV-TFD).
11. Current drug abuse or alcohol addiction.
12. Chronic uncontrolled hypertension (average of 3 systolic blood pressure (SBP) and diastolic blood pressure (DBP) readings at Screening >165/≥100 mmHg) or severe orthostatic hypotension.
13. Evidence of hydrocephalus or presence of a ventriculoperitoneal shunt.

Date of first enrolment
10/05/2023

Date of final enrolment
09/09/2023

Locations

Countries of recruitment
Iran

Study participating centre
Farhikhtegan Hospital
No. 9, Farhikhtegan St.,
Mirdamad Blvd.
Tehran

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19697-74311

Sponsor information

Organisation
Islamic Azad University Medical Branch of Tehran

ROR
https://ror.org/00eaebe27

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan
1. Data Access and Sharing
Data collected during the trial were de-identified and made available to authorized users through a secure data-sharing platform (Research Electronic Data Capture). External researchers can request access to the datasets by submitting a formal request, which includes a signed Data Use Agreement (DUA) to ensure compliance with privacy regulations. All data will be anonymized before sharing to protect patient confidentiality.

2. Data Documentation and Metadata
Comprehensive metadata and a data dictionary will accompany the de-identified datasets. The metadata include detailed descriptions of the study variables, the methods used to collect data, and the data's intended use.

3. Ethical and Privacy Considerations
Patient data are fully anonymized and handled in accordance with [HIPAA/GDPR] regulations. Informed consent were obtained from all participants, clearly explaining the scope of data usage for research purposes and any potential sharing with third parties. All personal identifiers have been removed to ensure confidentiality.

4. Data Retention and Long-Term Preservation
The collected data will be securely stored for a minimum of 10 years following the completion of

the trial, in compliance with applicable regulatory guidelines. Data will be preserved in a publicly accessible, long-term data repository (REDCap) to ensure future access by researchers. The data will remain accessible for non-commercial, academic purposes, unless specified otherwise in the DUA.

5. Monitoring and Data Quality Control
Site monitoring and data quality control were conducted for the active site. Monitoring included on-site inspections and phone-based quality control (QC). The DSMB oversaw the quality control procedures, which were documented in the study manual.

6. Data Access Procedure for External Researchers
External researchers can request access to the de-identified data. The request must be submitted through the secure data-sharing platform, and a Data Use Agreement (DUA) will need to be signed to ensure ethical use of the data. Access will be granted for non-commercial, academic purposes only, and the researcher will be required to adhere to the confidentiality and privacy requirements set forth in the agreement.

7. Additional Considerations
Safety Monitoring: The DSMB reviewed safety data on a weekly basis, ensuring participant well-being and making recommendations regarding the continuation or modification of the study.

8. Final Reporting: Findings will be shared in publications and presentations, adhering to ethical guidelines for data transparency.

IPD sharing plan summary
Stored in non-publicly available repository