Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Investigating the safety and efficacy of engineered exosomes containing BDNF in the treatment of Alzheimer's disease

Protocol summary

Study aim
Aim: To determine the safety and early therapeutic benefits of BDNF-loaded exosomes in mild-to-moderate Alzheimer’s disease patients

Design
Single-centre, phase I/II, parallel-group, randomised clinical trial including 18 participants with mild-to-moderate Alzheimer’s disease. Participants will be randomly allocated (simple stratified randomisation) to receive either weekly intranasal BDNF-loaded exosomes for 9 weeks (n=9) or standard care alone (n=9). Allocation concealment will be applied; no blinding is planned.

Settings and conduct
This single-centre trial will be conducted at Bou Ali Hospital in Sari, affiliated with Mazandaran University of Medical Sciences. Patients with mild to moderate Alzheimer’s disease will be screened, consented, and randomized to receive either weekly intranasal BDNF-loaded exosomes for 9 weeks or standard care. All procedures and follow-ups will be performed on site by trained staff. The study is not blinded; standardized assessments will be used to minimize bias.

Participants/Inclusion and exclusion criteria
Inclusion Diagnosis of mild to moderate Alzheimer's Age 55 to 80 years MMSE score between 10 and 24 Presence of a reliable caregiver Informed consent Exclusion Severe Alzheimer's Other neurological disease (e.g., Parkinson's, MS) Severe heart/liver/kidney disease or immunodeficiency Active infection (e.g., HIV, HBV, HCV) Participation in another trial within the last 6 months Pregnancy or breastfeeding

Intervention groups
Intranasal BDNF-loaded exosomes will be administered once per week for 9 weeks to evaluate safety and early clinical benefit compared to standard Alzheimer’s therapy.

Main outcome variables
Safety and tolerability Cognitive function

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20210228050535N8**
Registration date: **2025-12-06, 1404/09/15**
Registration timing: **prospective**

Last update: **2025-12-06, 1404/09/15**
Update count: **0**

Registration date
2025-12-06, 1404/09/15

Registrant information

Name
Amirali Khodashenas limoni

Name of organization / entity

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Iran (Islamic Republic of)

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Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2026-02-19, 1404/11/30

Expected recruitment end date
2026-06-21, 1405/03/31

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title

Investigating the safety and efficacy of engineered exosomes containing BDNF in the treatment of Alzheimer's disease

Public title

Exosome therapy for Alzheimer's

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

• Definite diagnosis of Alzheimer's disease based on DSM-5 criteria and confirmed by brain scans (MRI). • Definite diagnosis of mild or moderate Alzheimer's disease based on NIA/AA (2018) criteria. • Patients must have a low to moderate score (usually between 20 and 35) on the QoL-AD test, which indicates a decrease in quality of life due to the disease. • Patients must have an ADAS-Cog score in the range of early to moderate Alzheimer's disease (usually between 15 and 40). • MMSE score between 10 and 24 (inclusive). • Score less than or equal to 4 on the Modified Hashinsky Ischemic Scale (MHIS). • Age between 55 and 80 years. • Body mass index (BMI) between 18.5 and 30. • Written informed consent obtained from the patient and legal representative or close family before the study began. • The patient's general condition is appropriate based on medical history, physical examination, vital signs, laboratory tests, and electrocardiogram (ECG) results. • Ability to walk independently or with assistive devices (such as a wheelchair, walker, or cane) and no vision or hearing problems that would prevent them from following the study (using glasses or hearing aids is permitted). • Presence of a designated and reliable caregiver who meets the following requirements: o Ability to read and understand research-related documents and communicate with the investigator. o Ability to follow research instructions and provide accurate information about the patient's condition during the study. o Living with the patient or providing care at least 3 days a week and at least 2 hours a day.

Exclusion criteria:

• Non-cooperation during the study. • Serious treatment-related adverse events. • Active infectious diseases or autoimmune disorders. • Severe hypersensitivity to therapeutic compounds. • Receiving treatment with mesenchymal stem cells or their derived exosomes. • The following laboratory results: o Neutrophil count less than 100×10^9/L o Platelet count less than 100×10^9/L o Serum albumin level less than 30 g/L. o Serum creatinine level above the normal range. o Total bilirubin, ALT, and AST levels greater than twice the upper limit of normal. • Underlying medical conditions, including (but not limited to) cardiovascular, cerebrovascular, hepatic, renal, pulmonary, or endocrine diseases. • Severe Alzheimer’s. (Score less than 10 on MMSE and MoCA questionnaires) • Severe depression (score greater than 29 on standard questionnaires such as Beck Depression Inventory (BDI-II) or score 24–35 on the 24-item version of the Hamilton Depression Scale (HAM-D)). • Having diseases such as Parkinson's, vascular dementia, Huntington's, hydrocephalus, progressive supranuclear palsy, multiple sclerosis, epilepsy, mental retardation, or a significant history of brain injury. • Having a history of malignant neoplasm. • Contraindications to MRI for reasons such as the presence of implanted electronic devices, agoraphobia, or critical condition. • Positive results for HIV, HBV, HCV, and syphilis. • Participation in another clinical study in the past 6 months. • Pregnancy, breastfeeding, or pregnancy in the past 6 months. • Any other conditions that the investigator deems inappropriate, including factors that reduce compliance with follow-up.

Age

From **55 years** old to **80 years** old

Gender

Both

Phase

1-2

Groups that have been masked

No information

Sample size

Target sample size: **18**

More than 1 sample in each individual

Number of samples in each individual: **9**

For each participant, clinical and functional assessments will be performed at predefined time points to monitor safety and evaluate treatment response.1. Baseline (prior to first injection)Neurocognitive assessments:MMSE, ADAS-Cog, QoL-AD Functional status evaluation, Brain MRI to document baseline brain structure and amyloid burden (if applicable)Vital signs and full clinical examination. After each injectionClinical monitoring for adverse reactions(neurological status, vital signs, general tolerance)Functional and behavioral observation3. End-of-treatment evaluation: Neurocognitive tests: MMSE, ADAS-Cog, QoL-ADMRI for comparing structural and functional changes with baselineClinical safety assessment and adverse event reporting4. Long-term follow-up (3–6 months)Cognitive function reassessmentFunctional status checkSafety monitoring and documentation of delayed adverse eventsAll data will be recorded in coded forms, stored confidentially, and analyzed to assess clinical outcomes and treatment tolerability.

Randomization (investigator's opinion)

Randomized

Randomization description

In this study, the randomization process was performed as simple randomization at the individual level. In order to control for confounding variables, participants were first stratified by disease severity (mild/moderate) and age group (55–65 and 66–80 years), and then assigned to groups within each stratum using a random list generated in Excel software. To maintain the impartiality of the allocation process, opaque, sealed, and numbered envelopes were used, which were opened only after final confirmation of the patient's entry into the study. Given the nature of the intervention and the necessity of direct clinical supervision of the treatment process, blinding of participants and the treatment team was not performed.

Blinding (investigator's opinion)

Not blinded

Blinding description

Placebo

Not used

Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Research Ethics Committee of Mazandaran University of Medical Scienc
Street address
Deputy of research and technology. Moallem sq., Sari
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Mazandaran
Postal code
4816633131
Approval date
2025-10-29, 1404/08/07
Ethics committee reference number
IR.MAZUMS.REC.1404.393

Health conditions studied

1

Description of health condition studied
Alzheimer's
ICD-10 code
G30.0
ICD-10 code description
Alzheimer's disease with early onset

Primary outcomes

1

Description
Quality of life of Alzheimer’s patients
Timepoint
Three to six months after the last injection, on a monthly basis
Method of measurement
Using the QoL-AD, ADAS-Cog, and MMSE questionnaires

2

Description
Amyloid plaques in the brains of Alzheimer’s patients
Timepoint
Before the injection and three months after the last injection
Method of measurement
MRI

3

Description
Evaluation of the safety of BDNF-containing exosome injections
Timepoint
Three days after each injection
Method of measurement
The changes in TNF-α and IL-6 levels, as well as liver enzyme tests and BUN, using ELISA and biochemical assays.

Secondary outcomes

empty

Intervention groups

1

Description
Intervention group: 50 micrograms of exosomes twice a week for 4 weeks.
Category
Treatment - Other

2

Description
Control group: Taking medication from the acetylcholinesterase inhibitor group.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Bu Ali Sina Hospital, Sari
Full name of responsible person
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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
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Full name of responsible person
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Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?
Yes

Title of funding source
Mazandaran University of Medical Sciences

Proportion provided by this source
100

Public or private sector
Public

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin

Type of organization providing the funding
Academic

Person responsible for general inquiries

Contact

Name of organization / entity
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Full name of responsible person
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Position
Assistant professor

Latest degree
Specialist

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Undecided - It is not yet known if there will be a plan to make this available

Study Protocol
Undecided - It is not yet known if there will be a plan to make this available

Statistical Analysis Plan
Undecided - It is not yet known if there will be a plan to make this available

Informed Consent Form
Undecided - It is not yet known if there will be a plan to make this available

Clinical Study Report
Undecided - It is not yet known if there will be a plan to make this available

Analytic Code
Undecided - It is not yet known if there will be a plan to make this available

Data Dictionary
Undecided - It is not yet known if there will be a plan to make this available