

Clinical Trial Protocol

Iranian Registry of Clinical Trials

19 Sep 2026

The mesenchymal stem cell-derived extracellular vesicles for primary postmenopausal osteoporosis: A safety, feasibility, and efficacy trial.

Protocol summary

Study aim

Determining the safety, feasibility, and efficacy of extracellular vesicles derived from mesenchymal stem cells for postmenopausal osteoporosis

Design

A randomized controlled clinical trial, phase 1-2, with three parallel arms on 30 patients. RAS will be used for randomization.

Settings and conduct

Thirty postmenopausal women suffering from osteoporosis referring to the clinics of physical medicine and rehabilitation at Imam Reza Hospital-Tabriz University of Medical Sciences will be randomly assigned into two interventions and one control group (alendronate sodium) using block randomization method with a 1:1:1 allocation ratio. It is not possible to blind the control group.

Participants/Inclusion and exclusion criteria

Inclusion criteria: Menopausal women aged 50 to 70 years with a bone mineral density less than 2.5 in the lumbar vertebrae, pelvis, or femoral neck. Exclusion criteria: Suffering from renal failure and diseases; Suffering from bone diseases other than osteoporosis; Taking drugs that affect bone metabolism; Suffering from mental illness; Having malignancy.

Intervention groups

The first group will receive intravenous extracellular vesicles (EVs) with alendronate sodium tablets, the second group will receive intravenous EVs and placebo of alendronate sodium, and the control group will receive only alendronate sodium for 1 year. All groups will receive recommendations based on physical activity and food intake. Participants in the first and second groups at the beginning of the study, day 2, day 4, end of the second week, end of the sixth week, and then every 8 weeks for 5 times (total 46 weeks and 10 drug doses) will receive a slow intravenous injection of 15 ml of EVs

Main outcome variables

The rate of enrollment and retention of participants in

study groups, changes in the serum inflammatory and anti-inflammatory factors, Changes in the serum bone turnover markers

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20131009014957N15**

Registration date: **2023-09-26, 1402/07/04**

Registration timing: **prospective**

Last update: **2023-09-26, 1402/07/04**

Update count: **0**

Registration date

2023-09-26, 1402/07/04

Registrant information

Name

Azizeh Farshbaf-khalili

Name of organization / entity

Tabriz university of Medical Sciences

Country

Iran (Islamic Republic of)

Phone

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2023-11-17, 1402/08/26

Expected recruitment end date

2025-05-16, 1404/02/26

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

The mesenchymal stem cell-derived extracellular vesicles for primary postmenopausal osteoporosis: A safety, feasibility, and efficacy trial.

Public title

The mesenchymal stem cell-derived extracellular vesicles for postmenopausal osteoporosis

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

Having the ability to self-care A resident of Tabriz city
Cessation of menstruation for at least 12 consecutive months
Having a bone density of less than 2.5 in the lumbar vertebrae, pelvis, or femoral neck
No history of fracture

Exclusion criteria:

T-score $\leq$ -4 in lumbar vertebrae, T-score $\leq$ -3.5 in pelvic bone and femoral neck, history of hip or vertebrae fractures
Suffering from renal failure and diseases
Having bone diseases other than osteoporosis
Taking drugs that affect bone metabolism
Having a mental illness according to the patient's own statement
Malignancy according to the patient's own statement
Peptic ulcers and malabsorption disorders
25-(OH) Vitamin D levels < 20ng/ml or current hypercalcemia or hypocalcemia

Age

From **50 years** old to **70 years** old

Gender

Female

Phase

1-2

Groups that have been masked

No information

Sample size

Target sample size: **30**

Randomization (investigator's opinion)

Randomized

Randomization description

Thirty eligible postmenopausal women with osteoporosis will be randomized into three groups receiving intravenous extracellular vesicles (EVs) along with sodium alendronate tablets (10 people), intravenous EVs without alendronate sodium, and alendronate sodium without EVs (control group) by blocking method using blocks 3 and 6, and an allocation ratio of 1:1:1 through RAS (Random Allocation Software) and will receive the allocated intervention for one year. The random sequence of allocation will be generated by a person not involved in the research. 30 opaque and identical envelopes will be numbered from 1 to 30, and the type of intervention will be written on paper and placed inside the envelopes based on the generated sequence and will be sealed. Participants in the first and second groups at the beginning of the study, day 2, day 4, the end of the

second week, the end of the sixth week, and then every 8 weeks for 5 times (a total of 46 weeks and 10 drug doses) will receive a slow intravenous injection of 15 ml of EVs.

Blinding (investigator's opinion)

Not blinded

Blinding description**Placebo**

Used

Assignment

Parallel

Other design features**Secondary Ids**

empty

Ethics committees**1****Ethics committee****Name of ethics committee**

Ethics committee of Tabriz University of Medical Sciences

Street address

Vice Chancellor for Research and Technology, Third floor, No 2-central building, Tabriz University of Medical Sciences, Golgasht Street

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Tabriz

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East Azarbaijan

Postal code

5165665931

Approval date

2023-05-08, 1402/02/18

Ethics committee reference number

IR.TBZMED.REC.1402.130

Health conditions studied**1****Description of health condition studied**

Postmenopausal osteoporosis

ICD-10 code

M81

ICD-10 code description

Osteoporosis without pathological fracture

Primary outcomes**1****Description**

The rate and severity of adverse events in the study groups

Timepoint

During one year of intervention

Method of measurement

Through recording in the questionnaire and phone calls

2

Description

The rate of enrollment and retention of participants in study groups

Timepoint

During one year of intervention

Method of measurement

Researcher's own follow-up

3

Description

Changes in the levels of some inflammatory and anti-inflammatory factors (TNF- α , HS-CRP, IL-10 and IL-6)

Timepoint

The beginning and end of the intervention

Method of measurement

Using biochemical methods

4

Description

Changes in the levels of serum bone resorption markers (osteocalcin, P1NP, BSAP, CTX)

Timepoint

The beginning and end of the intervention

Method of measurement

Using biochemical methods and ELISA kit

Secondary outcomes

1

Description

Changes in bone density (T-score, BMD Z-score)

Timepoint

The beginning and end of the intervention

Method of measurement

Using a densitometry device

2

Description

Changes in the levels of some oxidative stress factors (TAC, SOD, MDA)

Timepoint

The beginning and end of the intervention

Method of measurement

Using biochemical methods

3

Description

Nutritional status (appetite status, average weight, BMI, waist circumference, ratio of waist circumference to hip circumference)

Timepoint

The beginning, middle and end of the intervention

Method of measurement

Questionnaire and anthropometric methods

Intervention groups

1

Description

Intervention group 1: Receiving intravenous extracellular vesicles derived from stem cells Mesenchymal (MSCs-EV) together with alendronate sodium tablets 70 mg once a week until the end of one year. This group will receive slow intravenous injections of 15 ml MSCs-EV at the beginning of the study, on day 2, day 4, at the end of the second week, at the end of the sixth week, and then every 8 weeks for 5 times (a total of 46 weeks and 10 drug doses) containing 10.5×10^8 EV. This material will be prepared in the clean room of the Stem Cell Innovation Center by the relevant specialist of the project according to the necessary standards.

Category

Treatment - Drugs

2

Description

Intervention group 2: Receiving intravenous extracellular vesicles derived from stem cells Mesenchymal (MSCs-EV) together with placebo tablets of alendronate sodium 70 mg once a week until the end of one year. This group will receive slow intravenous injections of 15 ml MSCs-EV at the beginning of the study, on day 2, day 4, at the end of the second week, at the end of the sixth week, and then every 8 weeks for 5 times (a total of 46 weeks and 10 drug doses) containing 10.5×10^8 EV. This material will be prepared in the clean room of the Stem Cell Innovation Center by the relevant specialist of the project according to the necessary standards.

Category

Treatment - Drugs

3

Description

Control group: Receiving alendronate sodium tablets 70 mg once weekly until the end of one year without extracellular vesicles.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Physical Medicine and Rehabilitation Research Center

Full name of responsible person

Azizeh Farshbaf-Khalili

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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

Tabriz 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
Tabriz University of Medical Sciences
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Azizeh Farshbaf-Khalili
Position
Assistant Professor
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Nutrition

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Sharing plan

Deidentified Individual Participant Data Set (IPD)

Yes - There is a plan to make this available

Study Protocol

Yes - There is a plan to make this available

Statistical Analysis Plan

Yes - There is a plan to make this available

Informed Consent Form

Yes - There is a plan to make this available

Clinical Study Report

Yes - There is 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

Title and more details about the data/document

Data on the main outcome will be published

When the data will become available and for how long

Six months after printing the results

To whom data/document is available

Researchers at institutions have access to data

Under which criteria data/document could be used

In order to help scientific progress in the field of research

From where data/document is obtainable

farshbafa@tbzmed.ac.ir

What processes are involved for a request to access data/document

Scientific approval of the applicant by Tabriz University of Medical Sciences

Comments