Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

The Safety & Feasibility Study of Intra-Articular Transplantation of Wharton’s Jelly-Derived Mesenchymal Stromal Cells in Patients with Knee Osteoarthritis: Clinical Trial Phase I/IIa

Protocol summary

Study aim

The aim of this study is to evaluate the safety and feasibility of intra-articular transplantation of Wharton’s jelly–derived mesenchymal stromal cells in patients with knee osteoarthritis, within a Phase I/IIa trial.

Design

A two-arm, randomized, controlled Phase I/II clinical trial conducted in 20 patients. Randomization will be performed using a computer-generated random sequence.

Settings and conduct

This study will be conducted at Imam Khomeini Hospital, Karaj. Eligible participants who enter the study will be allocated to one of the two study groups according to the randomization table. The trial will follow a single-blind design.

Participants/Inclusion and exclusion criteria

Inclusion Criteria Age 18–70 years. Both sexes. Knee osteoarthritis Kellgren–Lawrence grade II or III in early stages, confirmed by standing knee radiography. Knee joint malalignment less than 20°, determined by three-joint view radiography. Patient Visual Analog Scale (VAS) ≥ 4. Inadequate response to standard treatment during the previous 3 months. Provision of written informed consent. Exclusion Criteria BMI higher than 35 kg/m². History of recent knee surgery or imminent need for joint replacement. Intra-articular injection within the past 3 months. Coagulopathy or current use of anticoagulant medications. Requirement for systemic corticosteroid therapy. Immunodeficiency disorders. Severe allergy to protein/biologic products. Pregnancy or breastfeeding. Simultaneous participation in another clinical trial. Active systemic infection or infection of the knee joint. Substance abuse. Uncontrolled comorbid diseases.

Intervention groups

Intervention Group: 20 million Wharton’s jelly–derived mesenchymal stromal cells (WJ-MSCs) suspended in 3 mL of normal saline Control Group: A single dose of high-molecular-weight sodium hyaluronate

Main outcome variables

Safety; Feasibility

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20160704028786N3**
Registration date: **2026-06-06, 1405/03/16**
Registration timing: **prospective**

Last update: **2026-06-06, 1405/03/16**
Update count: **0**

Registration date

2026-06-06, 1405/03/16

Registrant information

Name

Hossein Baharvand

Name of organization / entity

Royan Institute

Country

Iran (Islamic Republic of)

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Recruitment status

recruiting

Funding source

Expected recruitment start date

2026-08-07, 1405/05/16

Expected recruitment end date

2027-03-21, 1406/01/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

The Safety & Feasibility Study of Intra-Articular Transplantation of Wharton’s Jelly-Derived Mesenchymal Stromal Cells in Patients with Knee Osteoarthritis: Clinical Trial Phase I/IIa

Public title

Safety and feasibility of intra-articular injection of mesenchymal stromal cells in knee osteoarthritis

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Age between 18-70 years Both Sexes Grade 2 and 3 Kolgren osteoarthritis of the knee joint (diagnosis by standing knee radiograph) Malalignment of the knee joint less than 20 degrees. Diagnosis by radiography (three joint view) Visual analog scale of the patient greater than or equal to 4 Failure to respond to standard treatment in the past 3 months Written informed consent

Exclusion criteria:

Body mass index greater than 35 A history of recent surgery or imminent need for joint replacement History of intra-articular corticosteroid or hyaluronic acid injection within the past 3 months Any coagulopathy or use of anticoagulant medications Any need for corticosteroid use Immunocompromised state Active malignancy or history of malignancy in the last 5 years Severe Allergy to biologic/protein products Pregnancy or breastfeeding Concomitant participation in another clinical trial Active systemic or knee joint infection Substance use disorder Any uncontrolled concomitant disease

Age

From **18 years** old to **70 years** old

Gender

Both

Phase

1-2

Groups that have been masked

- Data analyser

Sample size

Target sample size: **20**

Randomization (investigator's opinion)

Randomized

Randomization description

Allocation method Participants who meet the eligibility criteria and provide informed consent will be assigned in a 1:1 ratio to either the MSC intervention group or the control group using a computer-generated random sequence. Sequence generation The random allocation sequence will be created by an independent statistician who is not involved in participant recruitment, assessment, treatment administration, or data analysis. Randomization will be performed using a block randomization method with variable block sizes to maintain group balance throughout the enrollment period. Implementation After confirming eligibility and obtaining informed consent, the study coordinator will assign the participant to the next available allocation according to the concealed randomization list. The person enrolling participants will not have access to the random sequence. Stratification If applicable, randomization may be stratified by key prognostic factors such as: Baseline radiographic severity of knee OA Study center Age group or sex If no stratification is planned, this should be explicitly stated.

Blinding (investigator's opinion)

Single blinded

Blinding description

This clinical trial utilizes a single-blind design in which the statistical analyst remains blinded to the treatment allocation, while participants, the administering clinician, and the clinical outcome assessors are aware of the intervention. To maintain the integrity of the statistical analysis, the randomization sequence is generated by an independent statistician, and treatment assignments—comprising either Wharton’s jelly–derived mesenchymal stromal cells or high molecular weight Hyaluronic Acid—are allocated to participants upon enrollment. All clinical data, including VAS scores, WOMAC indices, physical examination findings, and adverse events, are recorded and entered into the database by the clinical team without blinding. Prior to statistical evaluation, the data is pseudonymized using neutral group identifiers (e.g., Group 1 and Group 2), ensuring that the data analyst remains blinded to the nature of the interventions during the analysis phase. Unblinding and the subsequent reconciliation of the group identifiers with the actual interventions will occur only after the primary statistical analysis is finalized and the study database is officially locked.

Placebo

Not used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Research Ethics Committee of Royan Institute

Street address

No. 1270, Central office of the Academic Center for Education, Culture and Research, opposite the main door of the University of Tehran, Enghelab St.

City

Tehran

Province
Tehran
Postal code
4364 - 14155
Approval date
2025-11-19, 1404/08/28
Ethics committee reference number
IR.ACECR.ROYAN.REC.1404.038

Health conditions studied

1

Description of health condition studied
Knee Osteoarthritis
ICD-10 code
M17
ICD-10 code description
Osteoarthritis of knee

Primary outcomes

1

Description
Safety: Safety is defined as the frequency, type, severity, and suspected relatedness of adverse events associated with intra articular injection of mesenchymal stromal cells. All adverse events (AEs) and serious adverse events (SAEs) will be recorded from the time of the first infusion until the end of the follow-up period and will be graded according to the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.
Timepoint
One week, three months and six months after the intervention
Method of measurement
Safety and adverse events are assessed through physical examination, history taking, and questionnaire.

Secondary outcomes

1

Description
Efficacy via the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): defined as "the change in the knee WOMAC score from study entry/baseline to the specified follow-up time point(s) after the intervention."
Timepoint
The study assesses the effectiveness of the intervention on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score at the beginning of the study and 3 months and 6 months after the intervention.
Method of measurement
The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire is used.

2

Description
Efficacy based on the Visual Analogue Scale (VAS) after injection: defined as "the change in the knee joint pain VAS score from study entry (baseline) to the specified follow-up time point(s) after the intervention."
Timepoint
In the study, the effectiveness of the intervention on the Visual Analogue Scale (VAS) criterion is assessed at the beginning of the study and 3 months and 6 months after the intervention.
Method of measurement
Visual Analogue Scale (VAS) is performed using a graduated scale.

3

Description
Efficacy based on the 6-Minute Walking Test (6MWT) after injection: defined as "the change in the distance walked during the 6-minute walk test (in meters) from study entry (baseline) to the specified follow-up time point(s) after the intervention."
Timepoint
In the study, the effectiveness of the intervention on the 6 Minute Walking Test (6MWT) criterion is assessed at the beginning of the study and 3 months and 6 months after the intervention.
Method of measurement
The distance the patient walks in 6 minutes is recorded.

4

Description
Efficacy based on MRI criteria (cartilage and surrounding periarticular structures) after injection: defined as "the change in knee joint MRI findings (including cartilage-related changes and other articular/periarticular structural changes, assessed according to the predefined scoring criterion/system specified in the study protocol) from study entry (baseline) to the specified post-intervention follow-up time point(s)."
Timepoint
In the study, the effectiveness of the intervention will be assessed at the baseline and 6 months after intervention
Method of measurement
Assessment will be done using Magnetic Resonance Imaging (MRI) and scoring will be done with the MRI Osteoarthritis Knee Score (MOAKS)

Intervention groups

1

Description
Intervention group: In this group, 20 million Wharton's jelly-derived mesenchymal stromal cells suspended in 3 mL of sterile normal saline (0.9% sodium chloride), together with 10% albumin serum, will be administered to the patient. This cellular product is prepared under standard conditions in an Cell Processing Facility and is approved with respect to cell viability, sterility, and

phenotypic characteristics.Method of administration: The injection will be performed as a single administration (single-dose) under sterile conditions by an experienced specialist physician into the joint space of the affected knee.

Category

Treatment - Drugs

2

Description

Control group: In this group, patients will receive a single intra-articular injection of high-molecular-weight sodium hyaluronate. The injectable material consists of a sterile high-molecular-weight sodium hyaluronate preparation suitable for intra-articular administration, which will be used at the standard approved dose for intra-articular use in knee osteoarthritis. The injection will be administered intra-articularly into the affected knee in a single session, under sterile conditions, by a qualified physician experienced in intra-articular knee injections.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center
Karaj Imam Khomeini Hospital

Full name of responsible person
Mohsen Emadedin

Street address
Next to Police Station, Shahid Beheshti Street

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Karaj

Province
Alborz

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Email
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Web page address
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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
Royan Institute

Full name of responsible person
Hossein Baharvand

Street address
Hafez st.- Northern Banihashem Ave.- Resalat Exp. Way

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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

Royan Institute

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
Royan Institute

Full name of responsible person
Alireza Beheshti maal

Position
Researcher

Latest degree
Medical doctor

Other areas of specialty/work
Clinical Research Associate

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Person responsible for updating data

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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
No - There is not a plan to make this available
Data Dictionary
No - There is not a plan to make this available