# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

22 Jul 2026

## Evaluation of safety and efficacy of intra-articular knee transplantation of three consecutive doses of allogenic umbilical cord mesenchymal stromal cells in patients with knee osteoarthritis: interventional clinical trial, phase I/II

## Protocol summary

**Study aim**
Safety & efficacy evaluation of intra-articular transplantation of 3 consecutive doses of allogenic umbilical cord tissue-derived stromal mesenchymal cells in patients with knee osteoarthritis

**Design**
Randomised controlled trial, with parallel groups, double-blind, phase 1/2 on 30 patients, randomized using Random allocation software

**Settings and conduct**
Patients are transplanted 3 times at intervals of 0, 2 and 4 months in the operating room of Royan Clinic. Patients will be monitored for up to one year. For the purpose of blinding, the biological product will be prepared in the form of disposable 5 cc syringes that look exactly like each other with a special label. Only the doctor and the person in charge of the transplant will know the type of treatment received.

**Participants/Inclusion and exclusion criteria**
- Inclusion criteria: Age 40-70 years Knee osteoarthritis with grades 2 and 3 Diagnosis by radiograph of standing knee VAS Knee pain: ≥4 Complete the informed consent form - Exclusion criteria: Knee deviation more than 15 degrees BMI ≥ 35 Pregnant women, nursing mothers or adults with disabilities Intra-cartilage injection during the last 2 months Arthroscopy in the last 6 months Abnormal hematological or biochemical tests Any type of neoplasm Take aspirin 1 week before the cell injection Coagulopathy or use of anticoagulants Positive viral tests Rheumatoid arthritis or other autoimmune diseases involving the joints Allergy to substances in the culture medium Corticosteroid use in 3 months

**Intervention groups**
Control group: 3 doses of normal saline + hyaluronic acid Test Group: 3 doses of normal saline containing mesenchymal cells derived from non-native umbilical cord tissue + hyaluronic acid

**Main outcome variables**
Adverse events (AEs) and severe adverse events (SAEs) WOMAC VAS SF-36 Articular cartilage thickness

## General information

**Reason for update**
Add information about the new sponsor (Cell-Tech Pharmed) of this clinical trial

**Acronym**

**IRCT registration information**
IRCT registration number: **IRCT20211102052944N1**
Registration date: **2021-11-09, 1400/08/18**
Registration timing: **prospective**

Last update: **2021-11-27, 1400/09/06**
Update count: **1**

**Registration date**
2021-11-09, 1400/08/18

**Registrant information**

**Name**
Elaheh Afzal

**Name of organization / entity**
Royan stem cell technology company

**Country**
Iran (Islamic Republic of)

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+98 21 2763 5735

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e.afzal@rsct.ir

**Recruitment status**
**Recruitment complete**

**Funding source**

**Expected recruitment start date**
2021-11-22, 1400/09/01
**Expected recruitment end date**
2022-05-22, 1401/03/01
**Actual recruitment start date**
empty
**Actual recruitment end date**
empty
**Trial completion date**
empty

**Scientific title**
Evaluation of safety and efficacy of intra-articular knee transplantation of three consecutive doses of allogenic umbilical cord mesenchymal stromal cells in patients with knee osteoarthritis: interventional clinical trial, phase I/II

**Public title**
Intra-articular transplantation of umbilical cord stromal mesenchymal cells in patients with knee osteoarthritis
**Purpose**
Treatment
**Inclusion/Exclusion criteria**
**Inclusion criteria:**
40-70 years Unilateral knee osteoarthritis Kellgren and Lawrence grade of both knees between 2 and 3 Evidence of x-ray imaging findings compatible with knee osteoarthritis knee pain for at least 4 months that has not responded to common medical and physical therapies. Visual analogue score ≥ 4 Informed consent
**Exclusion criteria:**
Pregnancy or lactation Inflammatory or infectious arthritis Intra-articular injection during the last 2 months Body Mass Index ≥ 35 Haematological and biochemical analysis with significant alterations that contraindicates intervention Known and uncontrolled chronic disease (including diabetes (HbA1c ≥ 8), heart failure (EF <45%), renal failure (Cr> 2), liver failure (AST, ALT> 100) History of any type of neoplasm Take aspirin one week before the cell injection History of coagulopathy or use of anticoagulants Positive viral tests (HIV, CMV, HTLV1 & 2, HBV, HCV) Having a movement disorder Having serious illnesses with a life expectancy of less than 1 year Drug or alcohol abuse History or clinical diagnosis of any psychological disorder Arthroscopy in the last 6 months Rheumatoid arthritis or other autoimmune diseases that affect the joints. Immunosuppression or taking systemic immunosuppressant Allergy to proteins or substances in culture medium (gentamicin, bovine or equine serum) History of corticosteroid use 3 months before enrolment Knee joint misalignment ≥15 degree
**Age**
From **40 years** old to **70 years** old
**Gender**
Both

**Phase**
1-2
**Groups that have been masked**

- Participant
- Investigator
- Outcome assessor
- Data analyser

**Sample size**
Target sample size: **30**
**Randomization (investigator's opinion)**
Randomized
**Randomization description**
Patients will be randomly assigned to the control and MSC groups. The method of random assignment of these two groups is block randomization. The size of the blocks is 6 people and using Random allocation software, the sequence of assigning patients to the groups is determined, and this sequence will be kept by the transplant manager.
**Blinding (investigator's opinion)**
Double blinded
**Blinding description**
This study is a double-blind study. Patients and study analysts will be unaware of the type of treatment assigned. To achieve this goal, by using a biological product in the form of disposable 5 cc syringes that are already filled by the nurse and are completely "similar" to the type of treatment received, to blind the participants in the study. Also, the people who apply the treatment will be different from the people who are responsible for examining and evaluating the patients, and the biological product packages will be labeled according to a specific code. Only the doctor and the person in charge of the transplant will know the type of treatment the patients receive.
**Placebo**
Not used
**Assignment**
Parallel
**Other design features**

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**
**Name of ethics committee**
Research Ethics Committees of Royan Institute-Academic Center for Education, Culture and Research
**Street address**
No. 24, East Hafez Alley, Bani Hashim Square, Bani Hashim St, Resalat Highway, Tehran, Iran.
**City**
Tehran
**Province**
Tehran
**Postal code**
1665666311
**Approval date**
2021-09-21, 1400/06/30
**Ethics committee reference number**
IR.ACECR.ROYAN.REC.1400.079

## 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**
Adverse events and severe adverse events
**Timepoint**
2, 4, 6, 9, and 12 months after intervention
**Method of measurement**
Clinical signs and questionnaire

## Secondary outcomes

### 1

**Description**
Visual analog scale
**Timepoint**
Baseline and 2, 4, 6, 9, and 12 months after intervention
**Method of measurement**
Visual Analogue Scale Questionnaire

### 2

**Description**
Western Ontario and McMaster Universities Osteoarthritis Index
**Timepoint**
Baseline and 2, 4, 6, 9, and 12 months after intervention
**Method of measurement**
WOMAC Questionnaire

### 3

**Description**
Disability index
**Timepoint**
Baseline and 6, 9, and 12 months after intervention
**Method of measurement**
Short Form Health-36 Questionnaire

### 4

**Description**
Articular cartilage thickness
**Timepoint**
Baseline and 6, 9, and 12 months after intervention
**Method of measurement**
Magnetic resonance imaging

## Intervention groups

### 1

**Description**
Control group: Patients receiving 3 doses of normal saline + Hyaluronic acid The procedure will be performed in such a way that patients are injected intra-articular injection of 2 cc of normal saline with 2 cc of hyaluronic acid in three times at 0, 2 and 4 months intervals in the operating room of Royan Clinic. At the time of injection, the patient's knee is sterilized and the orthopedic surgeon will inject into the joint space under sterile conditions. After the injection, the patient is monitored for 2 hours and after this period, if there is no problem with the necessary medication and care instructions and explanation of warning signs will be discharged.
**Category**
Treatment - Drugs

### 2

**Description**
Intervention group: Patients receiving 3 doses of normal saline containing 20 million Mesenchymal cells derived from allogenic umbilical cord tissue + Hyaluronic acid The method of intervention will be that patients in three times at intervals of 0, 2 and 4 months in the operating room of Royan Clinic, injected with 2 cc of normal saline containing 20 million mesenchymal stem cells derived from non-native umbilical cord tissue with 2 cc of hyaluronic Acids are placed. On the day of cell transplantation, it is sent to this center for injection by the clean room of Cell Tech Pharmed factory in a vial and inside a box. The patient's knee is sterilized and the orthopedic surgeon will inject into the joint space under sterile conditions. After the injection, the patient is monitored for 2 hours and after this period, if there is no problem with the necessary medication and care instructions and explanation of warning signs will be discharged.
**Category**
Treatment - Other

## Recruitment centers

### 1

**Recruitment center**
**Name of recruitment center**
Royan Cell Therapy Center
**Full name of responsible person**
Masoud Vosough
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No.9, Shaghayegh Dead End, Bani Hashem Sq., Bani Hashem St., Resalat St.,
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## Sponsors / Funding sources

### 1

**Sponsor**
**Name of organization / entity**
Royan Stem Cell Technology Company
**Full name of responsible person**
Morteza Zarrabi
**Street address**
No. 24, East Hafez Alley, Bani Hashim Square, Bani Hashim St, Resalat Highway, Tehran, Iran.
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Info@rsct.ir
**Grant name**
**Grant code / Reference number**
**Is the source of funding the same sponsor organization/entity?**
Yes
**Title of funding source**
Royan Stem Cell Technology Company
**Proportion provided by this source**
80
**Public or private sector**
Private
**Domestic or foreign origin**
Domestic
**Category of foreign source of funding**
*empty*
**Country of origin**
**Type of organization providing the funding**
Other

### 2

**Sponsor**
**Name of organization / entity**
Cell-Tech Pharmed
**Full name of responsible person**
Mohammad Hossein Zirak Saz
**Street address**
Cell-Tech Pharmed Company, Drug Production Factory, Kermani St., Moallem Blvd., Yaftabad,
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**Province**
Tehran
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**Phone**
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**Email**
info@celltech.co
**Grant name**
**Grant code / Reference number**
**Is the source of funding the same sponsor organization/entity?**
Yes
**Title of funding source**
Cell-Tech Pharmed
**Proportion provided by this source**
20
**Public or private sector**
Private
**Domestic or foreign origin**
Domestic
**Category of foreign source of funding**
*empty*
**Country of origin**
**Type of organization providing the funding**
Other

## Person responsible for general inquiries

**Contact**
**Name of organization / entity**
Royan Institute
**Full name of responsible person**
Morteza Zarrabi
**Position**
Assistant Professor
**Latest degree**
Specialist
**Other areas of specialty/work**
Cell & molecular biology
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## Person responsible for scientific inquiries

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Assistant professor
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## Person responsible for updating data

**Contact**
**Name of organization / entity**
Royan Stem Cell Technology Company
**Full name of responsible person**
Elaheh Afzal
**Position**
Researcher
**Latest degree**
Master
**Other areas of specialty/work**
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## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**
Yes - There is 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
**Title and more details about the data/document**
The information and data will be published as an article after reviewing and verifying them. All data is potentially shareable after unidentified individuals.
**When the data will become available and for how long**
After following the patients and collecting data, checking the safety and efficiency of cell injection and then writing the article, which is done about 3 months after the follow-up, the data file will be published.
**To whom data/document is available**
Access to the documents of this research is not limited to academic and scientific researchers, and specialists working in other centers can also access these documents.
**Under which criteria data/document could be used**
Designing similar studies in other academic centers
**From where data/document is obtainable**
e.afzal@rsct.it
**What processes are involved for a request to access data/document**
Within 1-2 months after application. Applicants for access to the research documents must provide evidence of their activity in the relevant field and their need for this data along with their application email.
**Comments**