Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Safety and feasibility study of intra-ovarian injection of bone marrow mesenchymal stromal cells-derived extracellular vesicles in idiopathic premature ovarian failure patients: Clinical trial phase I

Protocol summary

Study aim

Investigating the effect of intraovarian injection of bone marrow-derived extracellular vesicles (MSC-EV) on serum levels of Follicle-Stimulating Hormone (FSH),Anti-Mullerian Hormone (AMH) levels, as well as the return of the menstrual cycle in infertile patients with premature ovarian failure, as well as the evaluation of its possible side effects.

Design

A before/after clinical trial (phase I) on 10 patients

Settings and conduct

For all patients in the infertility clinic of Royan Research Institute, first a basic visit will be done to obtain basic laboratory data, hormone levels and ultrasound examination of the ovaries, and then MSC-EV will be injected into the ovaries with a determined dose.

Participants/Inclusion and exclusion criteria

Infertile women who have been diagnosed with premature ovarian failure and have normal body mass index and normal genetic tests are invited to participate in this project. Patients with early amenorrhea and certain immunological and cardiovascular diseases, as well as a history of ovarian masses or abnormal serological tests will not be included in the study. If the patient has undergone hormone replacement therapy (HRT), the HRT will be stopped for at least two months and then the injection cycle will be started.

Intervention groups

Injection of bone marrow-derived extracellular vesicles with a dose equivalent to 3 times 10 million clonal mesenchymal stem cells in 2 ml will be performed for all patients.

Main outcome variables

Follow-up of patients in order to respond to treatment for 8 months based on evaluation of Follicle-Stimulating Hormone (FSH),Anti-Mullerian Hormone (AMH) levels, return of menstrual cycle, ovarian ultrasound and also check possible complications due to injection (fever, bacteremia, sepsis, Pelvic inflammatory disease, anaphylactic shock and hematoma from the first 24 hours and in the first week) will be done.

General information

Reason for update

Completion of the trial recruitment and follow-up process

Acronym

IRCT registration information

IRCT registration number: **IRCT20080831001141N43**
Registration date: **2023-10-17, 1402/07/25**
Registration timing: **registered_while_recruiting**

Last update: **2026-06-10, 1405/03/20**
Update count: **2**

Registration date

2023-10-17, 1402/07/25

Registrant information

Name
Kiandokht Kiani
Name of organization / entity
Royan Institute
Country
Iran (Islamic Republic of)
Phone
+98 21 2230 7960
Email address
kiandokht.kiani@royaninstitute.org

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2023-02-20, 1401/12/01

Expected recruitment end date

2025-02-18, 1403/11/30

Actual recruitment start date

2023-02-20, 1401/12/01

Actual recruitment end date

2024-10-08, 1403/07/17

Trial completion date

2025-07-08, 1404/04/17

Scientific title

Safety and feasibility study of intra-ovarian injection of bone marrow mesenchymal stromal cells-derived extracellular vesicles in idiopathic premature ovarian failure patients: Clinical trial phase I

Public title

Investigating the effect of intraovarian injection of extracellular vesicles derived from bone marrow mesenchymal stromal cells in patients with premature ovarian failure.

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Women between 20-38 years old Baseline serum level of follicle stimulating hormone (FSH) higher or equal to 25 IU/l at least twice with an interval of 3 or 4 months At least one year has passed since secondary amenorrhea and premature ovarian failure (POF) diagnosis Normal karyotype and fragile X messenger ribonucleoprotein 1 (FMR1) gene

Exclusion criteria:

Primary amenorrhea Congenital anomaly of the ovary Thyroid disease Immune system diseases such as lupus and... Previous and/or family history of ovarian tumor Previous and/or family history of suffering from major diseases in the past and present such as cancer Positive serological evidence regarding previous or current hepatitis B and C, Human T-lymphotropic virus 1, Human immunodeficiency virus (HIV), Syphilis Disturbance in the normal range of laboratory tests as levels of Hemoglobin Subunit Alpha 1 (HbA1), Alanine transaminase (ALT), The aspartate aminotransferase (AST), the number of white blood cells (WBCs), The creatinine (Cr), International normalised ratio (INR) , Platelets (Plt), Hematocrit (Hct) tests. History of specific systemic disease (rheumatology, endocrine, cardiovascular, etc.) Severe endometriosis (stage III and IV) Small and non-injectable ovaries Lack of patient satisfaction The patient's unwillingness to continue participating in the plan

Age

From **20 years** old to **38 years** old

Gender

Female

Phase

1

Groups that have been masked

No information

Sample size

Target sample size: **10**

Actual sample size reached: **10**

Randomization (investigator's opinion)

N/A

Randomization description

Blinding (investigator's opinion)

Not blinded

Blinding description

Placebo

Not used

Assignment

Single

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics Committee of Royan Research Institute

Street address

Shahid Qassem Soleimani Highway, Bani Hashem Street, Bani Hashem Square, Hafez East Alley, Royan Alley, Royan Research Institute

City

Tehran

Province

Tehran

Postal code

1665659911

Approval date

2022-01-04, 1400/10/14

Ethics committee reference number

IR.ACECR.ROYAN.REC.1400.124

Health conditions studied

1

Description of health condition studied

Premature ovarian failure

ICD-10 code

E28.3

ICD-10 code description

Primary ovarian failure

Primary outcomes

1

Description

Ovary abscess

Timepoint

First 24 hours, first week and monthly up to 8 months after injection

Method of measurement

Evaluation of ovarian abscess or any other ovarian lesion formation up to 8 months after intraovarian injection of extracellular vesicles derived from bone marrow mesenchymal stromal cells (any adverse events through follow-up visits (first 24 hours and first week after

transplantation, 1, 2, 3, 4, 5, 6, 7 and 8 months after injection) will be checked and recorded.

Secondary outcomes

1

Description
Basal follicle-stimulating hormone (FSH) serum level
Timepoint
Baseline,1 week as well as one, two, three, four , five, six, seven and eight months after transplantation
Method of measurement
Laboratory test

2

Description
Serum anti-mullerian hormone (AMH) levels
Timepoint
Before the intervention (baseline) and also three, six and eight months after transplantation
Method of measurement
Laboratory test

3

Description
Menstruation recurrence rate
Timepoint
one, two, three, four , five, six, seven and eight months after transplantation
Method of measurement
Through monthly follow-up and asking the questions

Intervention groups

1

Description
Intervention group: The patient is anesthetized and placed in a lithotomy position, after preparing and washing the vagina with normal saline, under transvaginal ultrasound guidance (Aloka-40000 vaginal probe, Japan) using needle puncture (Reproline medical Gmbh, Rheinbach/Germany). , The injection of 2 ml of extracellular vesicles derived from MSCs (equivalent to 50 million cells) will be performed into one ovary of the patient (the accessible ovary).
Category
Treatment - Other

Recruitment centers

1

Recruitment center
Name of recruitment center
Royan Institute
Full name of responsible person
Mehri Mashayekhi
Street address
No. 12, East Hafez Avenue, Bani Hashem Street, Shahid Soleimani Highway, Tehran, Iran.
City
Tehran
Province
Tehran
Postal code
1665659911
Phone
+98 21 2356 2640
Email
dr.mashayekhy@yahoo.com

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Lotus Royan Charitable Fundation
Full name of responsible person
Amirreza Adib Azar
Street address
Tehran, Shahid Soleimani Highway, Bani Hashem Street, Bani Hashem Street, Shahid Kishori Alley, No. 6, Shahid Kishori Building, 2nd Floor, Unit 4
City
Tehran
Province
Tehran
Postal code
1665659911
Phone
+98 21 2233 8290
Email
tejarisazi.royan@gmail.com
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Lotus Royan Charitable Fundation
Proportion provided by this source
25
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
Vice Presidency for Science and Technology’s Department of Development of Stem Cell Sciences
Full name of responsible person

Amirali Hamidieh

Street address
No. 20, Laden St., North Sheikh Bahai St., Molla Sadra St., Vanak Square, Tehran

City
Tehran

Province
Tehran

Postal code
1991745681

Phone
+98 21 8804 6289

Email
h.amini@stemcell.isti.ir

Grant name

Grant code / Reference number

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

Title of funding source
Vice Presidency for Science and Technology's Department of Development of Stem Cell Sciences

Proportion provided by this source
75

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
Faezeh Shekari

Position
Assistant professor

Latest degree
Ph.D.

Other areas of specialty/work
Reproductive Biology

Street address
No. 12, East Hafez Avenue, Bani Hashem Street, Shahid Soleimani Highway, Tehran, Iran.'

City
Tehran

Province
Tehran

Postal code
1665659911

Phone
009821223562724

Email
faezehshekari@gmail.com

Person responsible for scientific inquiries

Contact

Name of organization / entity
Royan Institute

Full name of responsible person
Hossein Baharvand

Position
Professor

Latest degree
Ph.D.

Other areas of specialty/work
Reproductive Biology

Street address
No. 12, East Hafez Avenue, Bani Hashem Street, Shahid Soleimani Highway, Tehran, Iran.'

City
Tehran

Province
Tehran

Postal code
1665659911

Phone
+98 21 2233 9906

Email
hossein.baharvand@gmail.com

Person responsible for updating data

Contact

Name of organization / entity
Royan institute

Full name of responsible person
Arezoo Arabipoor

Position
Researcher

Latest degree
Master

Other areas of specialty/work
Midwifery

Street address
No. 12, East Hafez Avenue, Bani Hashem Street, Shahid Soleimani Highway, Tehran, Iran.'

City
Tehran

Province
Tehran

Postal code
1665659911

Phone
+98 21 2356 2640

Email
arezoo.arabipoor@gmail.com

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

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

Information regarding main consequence

When the data will become available and for how long

6 months after paper publication

To whom data/document is available

Researchers in academic institutes

Under which criteria data/document could be used

Systematic review and meta-analysis articles

From where data/document is obtainable

The scientific principal of the project whose information is registered on the site.

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

Sending request to principle investigator

Comments