

Clinical Trial Protocol

Iranian Registry of Clinical Trials

14 Jul 2026

Investigation of gene expression and secretion of P53, LIF, IL_10, IL-17 after administration of tacrolimus in endometrial and uterine fluid in patients with repeated implantation failure: Clinical trial

Protocol summary

Study aim

- 1.Evaluate the effect of Tacrolimus on gene expression of P53, IL-10, IL-17 and LIF in endometrial sample
- 2.Evaluate the effect of Tacrolimus on level of secretion of IL-10, IL-17 and LIF in endometrial fluid
3. Evaluate the effect of Tacrolimus on level of secretion of P53 IL-10, IL-17 and LIF in endometrial sample
- 4.Evaluate the effect of Tacrolimus on level of u-NK-cell in endometrial sample
- 5.Evaluate the effect of Tacrolimus on chemical pregnancy rate, implantation rate and live birth rate

Design

In this research, as a first phase of study, 7 eligible patients referring to Al-Zahra Hospital were chosen purposefully. Implantation factors in endometrial and uterine fluid were assessed before and after treatment and finally pregnancy outcomes will be reviewed.

Settings and conduct

Al-Zahra Hospital

Participants/Inclusion and exclusion criteria

patients who have at least three-time implantation failure and normal karyotype and have no anatomical problems, autoimmune disease and clotting disorders and have no history of abortion.

Intervention groups

1. Endometrial sample and uterine fluid are taken in the first menstrual cycle
2. prescription of Tacrolimus and endometrial sample and uterine fluid are taken in the second menstrual cycle
3. prescription of Tacrolimus and embryo transfer

Main outcome variables

1. Gene expression of P-53, IL-10, IL-17 and LIF in endometrial sample
2. Level of secretion of P-53, IL-10, IL-17 and LIF in endometrial sample
3. Level of u-NK-cell in endometrial sample
4. Chemical pregnancy rate, implantation rate and live birth rate

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20171007036623N1**

Registration date: **2017-11-29, 1396/09/08**

Registration timing: **prospective**

Last update: **2018-01-12, 1396/10/22**

Update count: **1**

Registration date

2017-11-29, 1396/09/08

Registrant information

Name

zahra Bahrami asl

Name of organization / entity

Shahid Beheshti university

Country

Iran (Islamic Republic of)

Phone

+98 21 2387 2577

Email address

za.bahrami@sbmu.ac.ir

Recruitment status

Recruitment complete

Funding source

Shahid Beheshti University of Medical Science

Expected recruitment start date

2017-12-11, 1396/09/20

Expected recruitment end date

2018-04-22, 1397/02/02

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Investigation of gene expression and secretion of P53, LIF, IL_10, IL-17 after administration of tacrolimus in endometrial and uterine fluid in patients with repeated implantation failure: Clinical trial

Public title

The Effect of Tacrolimus in patients with recurrent implantation failure

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

History of 3 or more failed IVF/ET cycles with morphologically and developmentally average to good-quality embryo(7 or more blastomeres and less than 10% fragmentation in day 3) into an adequately prepared endometrium (endometrial thickness equal or more than 8 mm); Women who had regular menses (25 to 35 days); Women who had normal karyotype; women who had at least one of these Immunological disorders in their peripheral blood sample between day of 5 to 10 of menstrual cycle: IFN-g/IL-4 equal or more than 10.3 or Nk-cell percentage greater than 12%

Exclusion criteria:

Present of sub mucosal fibroids, endometrial polyps, intrauterine adhesions, congenital anomalies of uterus or hydrosalpinges History of active autoimmune disease (With assessment of ANA, Anti-TG, Anti-TPO, Anti-dsDNA); Women with acquired or inherited thrombophilia (With assessment of Factor2, Factor5, Factor 8, Fibrinogen, Anti- Cardiolipin, Anti-Phospholipid Antibody, Lupus Anti-Coagulate, s-MTHFR gene) Pregnant women; History of miscarriage in a former IVF/ET cycle; Women who received vaccine in the last three months; Women who received steroid hormones in the last 2 months; Women receiving immunotherapy; Women with chronic inflammatory diseases

AgeFrom **20 years** old to **50 years** old**Gender**

Female

Phase

2

Groups that have been masked*No information***Sample size**Target sample size: **10****Randomization (investigator's opinion)**

N/A

Randomization description**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**

Shahid Beheshti University of Medical Sciences

Street address

Arabi Ave, Daneshjoo Blvd, Velenjak

City

Tehran

Province

Tehran

Postal code

198396-3113

Approval date

2017-02-28, 1395/12/10

Ethics committee reference number

IR.SBMU. MSP.REC.1395. 580

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

Recurrent Implantation Failure

ICD-10 code

N-97.2

ICD-10 code description

Female infertility of uterin

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

Expression of P53 gene

Timepoint

Measure twice: before and after treatment

Method of measurement

qRT-PCR

2**Description**

Expression of LIF gene

Timepoint

Measure twice: before and after treatment

Method of measurement

qRT-PCR

3**Description**

Expression of IL-10 gene

Timepoint

Measure Twice: before and after treatment

Method of measurement

qRT-PCR

4

Description

Expression of IL-17 gene

Timepoint

Measure twice: before and after treatment

Method of measurement

qRT-PCR

Secondary outcomes

1

Description

LIF protein levels in uterine fluid

Timepoint

Measure twice: before and after treatment

Method of measurement

ELISA

2

Description

Level Of IL-10 protein in uterine fluid

Timepoint

Measure twice: before and after treatment

Method of measurement

ELISA

3

Description

Level Of IL-17 protein in uterine fluid

Timepoint

Measure twice: before and after treatment

Method of measurement

ELISA

4

Description

Biochemical Pregnancy Rate

Timepoint

Two weeks after embryo transfer

Method of measurement

Level of B-HCG in blood

5

Description

Live Birth Rate

Timepoint

Nine months after embryo transfer

Method of measurement

Number of newborns

6

Description

Embryo implantation Rate

Timepoint

Two weeks after a chemical pregnancy confirmation

Method of measurement

Observation of Pregnancy Sac by Ultrasound

7

Description

Blood level of Estradiol

Timepoint

Measure twice: before and after treatment

Method of measurement

Measurement in blood

8

Description

Blood level of Progesteron

Timepoint

Measure twice: before and after treatment

Method of measurement

Measurement in blood

9

Description

P53 protein level in endometrium

Timepoint

Measure twice: before and after treatment

Method of measurement

immunohistochemistry

10

Description

LIF protein level in endometrium

Timepoint

Measure twice: before and after treatment

Method of measurement

immunohistochemistry

11

Description

IL-10 protein level in endometrium

Timepoint

Measure twice: before and after treatment

Method of measurement

immunohistochemistry

12

Description

IL-17 protein level in endometrium

Timepoint

Measure twice: before and after treatment

Method of measurement

immunohistochemistry

Intervention groups

1

Description

Prescription of Tacrolimus in the second menstrual cycle for up to 16 days (until 2 days before second biopsy) with 1-3 mg per day upon on IFN-g/IL-4 ratio: Prescription of 1 mg per day if this ratio is equal or more than 10.3 and less than 13 Prescript

Category

Treatment - Drugs

2**Description**

Prescription of Tacrolimus in third cycle of menstruation from 2 days before embryo transfer until 14 days after embryo transfer for overall 16 days with 1-3 mg per day upon on IFN-g/IL-4 ratio. Prescription of 1 mg per day if this ratio is equal or more

Category

Treatment - Drugs

Recruitment centers**1****Recruitment center****Name of recruitment center**

Department of Infertility, Alzahra Hospital

Full name of responsible person

Zahra Bahrami Asl

Street address

Al-zahra Hospital, South-Artesh Ave

City

Tabriz

Province

East Azarbaijan

Postal code

5138665793

Phone

+98 41 3553 6197

Email

dr.za.bahrami@gmail.com

Sponsors / Funding sources**1****Sponsor****Name of organization / entity**

Shahid Beheshti University of Medical Sciences

Full name of responsible person

Dr Afshin Rezaghi

Street address

Arabi Ave, Daneshjoo Blvd, Velenjak, Tehran, Iran

City

Tehran

Province

Tehran

Postal code

1985717443

Phone

+98 21 2387 2577

Email

dr.za.bahrami@gmail.com

Grant name**Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

Title of funding source

Shahid Beheshti 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**

Shahid Beheshti University of Medical Sciences

Full name of responsible person

Zahra Bahrami Asl

Position

PhD student of reproductive biology

Latest degree

Medical doctor

Other areas of specialty/work

Reproductive Biology

Street address

Arabi Ave, Daneshjoo Blvd, Velenjak, Tehran, Iran

City

Tehran

Province

Tehran

Postal code

1985717443

Phone

+98 23872555

Fax**Email**

za.bahrami@sbmu.ac.ir

Web page address**Person responsible for scientific inquiries****Contact****Name of organization / entity**

Shahid Beheshti University of Medical Sciences

Full name of responsible person

Dr. Marefat Gaffari Novin

Position

Professor of Reproductive Biology

Latest degree

Ph.D.

Other areas of specialty/work

Reproductive Biology

Street address

Arabi Ave, Daneshjoo Blvd, Velenjak, Tehran, Iran
City
Tehran
Province
Tehran
Postal code
1985717443
Phone
+98 21 2387 2577
Fax
Email
dr.za.bahrami@gmail.com
Web page address

Person responsible for updating data

Contact

Name of organization / entity
Shahid Beheshti University of Medical Sciences
Full name of responsible person
Zahra bahrami Asl
Position
PhD student of reproductive biology
Latest degree
Medical doctor
Other areas of specialty/work
Reproductive Biology
Street address
School of Medicine, Koodakyar St. Danshjoo Blv,
Velenjak, Shahid Chamran Highway
City
Tehran
Province
Tehran
Postal code
1985717443
Phone
+98 21 2387 2577
Fax
Email

dr.za.bahrami@gmail.com
Web page address

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

Yes - There is 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

Share with other studies and collaborate with other research and clinical centers to increase the effectiveness of the study

When the data will become available and for how long

After the study is completed and 6 months after the results are printed

To whom data/document is available

Research Centers and Study Groups of Basic Sciences and Clinical Sciences

Under which criteria data/document could be used

It is possible to use the analyzed results after receiving written permission from the executor

From where data/document is obtainable

Principal Investigator or corresponding author of study

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

After a written request for the use of results in clinical studies

Comments