

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

20 Jun 2026

### The effect of peripheral blood mononuclear cells (PBMC) on pregnancy outcomes in patients with recurrent implantation failure (RIF): randomized control trial study

#### Protocol summary

##### Study aim

Investigation the effect of Intrauterine administration of autologous hCG- activated peripheral blood mononuclear cells (PBMC) on pregnancy outcomes in patients with recurrent implantation failure (RIF)

##### Design

This study is a double-blind, randomized control trial with parallel groups, that the sample size allocated to each group is equal. Each patient was first immunologically advised to receive treatment, and after flow cytometry tests were selected if they were eligible. The patient selected would then, after completing the informed consent form, took a random envelope from the box containing the envelopes and gave it to the scientist.

##### Settings and conduct

This study was conducted in Valiasr Hospital, Tabriz. The participants and data analyzer were blinded. After patients selection, blood sampling was done five days before embryo transfer. Then PBMCs were isolated using Ficol. PBMCs were administered into the uterine cavity after culturing 48 hours in the presence of hCG. PBS was inseminated in the control group as a placebo.

##### Participants/Inclusion and exclusion criteria

The target population in this study was 100 women less than 45 years old who experienced at least three repeated implantation failures and lower Th-17 to Treg ratio than the healthy women.

##### Intervention groups

There were 50 women in the treatment group who received intrauterine administration of PBMCs two days before embryo transfer (ET) and another 50 patients in the control group who received an intrauterine injection of PBS as placebo.

##### Main outcome variables

Pregnancy rate Live birth rate Miscarriage rate

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT2017081227520N8**

Registration date: **2017-09-15, 1396/06/24**

Registration timing: **prospective**

Last update: **2019-08-21, 1398/05/30**

Update count: **1**

##### Registration date

2017-09-15, 1396/06/24

##### Registrant information

##### Name

Mehdi Yousefi

##### Name of organization / entity

Department of Immunology, Faculty of Medicine,  
Tabriz University of Medical Sciences, Tabriz, Iran

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Iran (Islamic Republic of)

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##### Recruitment status

**Recruitment complete**

##### Funding source

Stem Cell And Regenerative Medicine Institute, Tabriz  
University of Medical Sciences, Tabriz, Iran

##### Expected recruitment start date

2017-09-23, 1396/07/01

##### Expected recruitment end date

2018-05-22, 1397/03/01

##### Actual recruitment start date

2017-10-07, 1396/07/15

**Actual recruitment end date**

2018-09-25, 1397/07/03

**Trial completion date**

2018-09-27, 1397/07/05

**Scientific title**

The effect of peripheral blood mononuclear cells (PBMC) on pregnancy outcomes in patients with recurrent implantation failure (RIF): randomized control trial study

**Public title**

PBMC-therapy and treatment of recurrent implantation failure (RIF)

**Purpose**

Treatment

**Inclusion/Exclusion criteria****Inclusion criteria:**

Having at least three implantation failures after IVF  
Having primary infertility Age under 45 years old  
Having regular menstrual cycles BMI under 30

**Exclusion criteria:**

Having polycystic ovarian syndrome The presence of uterine pathology; Poor ovarian reserve  
Having chromosomal abnormalities Presence of auto anti-bodies such as anti-TPO, anti-TG, ACA, APA, ANA, and anti-dsDNA  
Presence of mutations involving the coagulation system such as deficiency of factor XII, Pro C, Pro S  
Positive HIV, HCV or HBV tests

**Age**

From **20 years** old to **45 years** old

**Gender**

Female

**Phase**

1-2

**Groups that have been masked**

- Participant
- Data analyser

**Sample size**

Target sample size: **100**

Actual sample size reached: **100**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

At first, the sample size of 100 patients with RIF that met our inclusion criteria was considered as the total sample size. 'Random allocation rule' method was used for randomization, where numbers were randomly assigned to cards on a random order of one to 100. Even numbers were assigned to the treatment group and odd numbers to the placebo group. In this method, the balance will be reached at the end of the study in the number of people assigned to each group. Each card was placed in sealed and opaqued envelopes to hide the random assignment.

**Blinding (investigator's opinion)**

Double blinded

**Blinding description**

The participants and the person who analyzed the results were blinded in this study. Participants were aware of the study before being randomized and informed consent was obtained from them. It should be noted that the person analyzing the results had no other role in this

study.

**Placebo**

Used

**Assignment**

Parallel

**Other design features**

From 248 volunteer patients, after immunologic consultation and flow cytometry analysis, 100 women were finally selected. These 100 patients were randomly divided into two groups: 50 patients for intrauterine injection of PBMC activated by hCG before embryo transfer (ET) and 50 patients as control group undergoing intrauterine insemination of phosphate buffer saline (PBS) as a placebo before ET. One hundred healthy women were selected as the healthy control group for the selection of enrolled women

**Secondary Ids****1****Registry name**

-WWW.clinicaltrial.gov

**Secondary trial Id**

-NCT03267797

**Registration date**

2017-08-30, 1396/06/08

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

Ethics committee of Tabriz University of Medical Sciences

**Street address**

Tabriz University of Medical Sciences , Daneshgah st, Tabriz,

**City**

Tabriz

**Province**

East Azarbaijan

**Postal code**

6446-14155

**Approval date**

2018-01-01, 1396/10/11

**Ethics committee reference number**

IR.TBZMED.REC.1396.937

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

Recurrent implantation failure

**ICD-10 code**

N98.9

**ICD-10 code description**

Complication associated with artificial fertilization, unspecified

## Primary outcomes

1

### Description

Pregnancy rate

### Timepoint

After positive beta-hCG test, clinical pregnancy was evaluated at 5-6 week

### Method of measurement

Laboratory tests and ultrasound

## Secondary outcomes

empty

## Intervention groups

1

### Description

Intervention group: blood sampling was done (20ml) five days before embryo transfer. Then PBMCs were isolated by Ficol and 20-30 million cells were cultured 48 hours in the presence of hCG. After 48 hours, 15-20 million PBMCs in 500 microliters PBS was administered into the uterine cavity two days before embryo transfer using embryo transfer catheter.

### Category

Treatment - Other

2

### Description

Control group: Similar to study group, blood sampling was done in this group but only 500 microliters PBS two days before embryo transfer was injected into uterine cavity.

### Category

Placebo

## Recruitment centers

1

### Recruitment center

#### Name of recruitment center

Infertility center at Valiasr Hospital

#### Full name of responsible person

Dr. Mehdi Yousefi

#### Street address

Infertility center at Valiasr Hospital, Aflak-nama Sq, Zaferaniyeh Ave, Tabriz

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## Sponsors / Funding sources

1

### Sponsor

#### Name of organization / entity

Stem Cell And Regenerative Medicine Institute, Tabriz University of Medical Sciences

#### Full name of responsible person

Mehdi Yousefi

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Stem Cell And Regenerative Medicine Institute, Madani Hospital, Golbad Ave, Tabriz

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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

Stem Cell And Regenerative Medicine Institute, 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

Other

## Person responsible for general inquiries

### Contact

#### Name of organization / entity

Stem Cell And Regenerative Medicine Institute

#### Full name of responsible person

Mehdi Yousefi

#### Position

PhD in Medical Immunology

#### Latest degree

Ph.D.

#### Other areas of specialty/work

Immunology

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## Person responsible for scientific inquiries

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## Person responsible for updating data

### Contact

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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

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