# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

31 May 2026

## Intradermal lymphocyte therapy in recurrent pregnancy loss patients with immunologic abnormalities

### Protocol summary

**Study aim**

This study investigates the immunomodulatory effects of intradermal lymphocyte therapy in patients with RPL with immunological abnormalities such as imbalance of immune system cells including Treg and Th17, as well as other immunological parameters such as transcription factors related to these cells. Changes in the cytokine production and microRNAs involved in their function compared to before treatment will be examined in this study.

**Design**

200 patients with RPL with immunological disorders are randomly divided into two groups of 100, one group will receive intradermal lymphocyte therapy and other group will not receive intervention.

**Settings and conduct**

Tabriz Valiasr Hospital

**Participants/Inclusion and exclusion criteria**

After receiving informed consent from people with RPL and also a control group consisting of healthy and fertile women with a history of successful previous pregnancies, heparinized blood is taken and mononuclear blood cells are isolated. Flow cytometry technique will then be used to count the number of T reg, Th-17, NK and B cells. The results of flow cytometry studies will be compared, and 200 patients with RPL with immunological disorders and 100 people as a healthy control group will be included in this study. The group of 200 patients with RPL was randomly divided into two groups of 100, one group receiving lymphocyte therapy and the other group not receiving treatment.

**Intervention groups**

According to the standard protocol, 2 × 107 of the husband's lymphocytes will be injected subcutaneously on the forearm or arms of patients with recurrent miscarriages. The number of injections is three times and at intervals of one month.

**Main outcome variables**

Immunological parameters such as Treg and Th17 cell frequency, gene and protein expression of Foxp3 and RORyt, gene expression of cytokines and the expression of microRNAs, including mir-146a, mir-155 and mir-326.

### General information

**Reason for update**

**Acronym**

RPL

**IRCT registration information**

IRCT registration number: **IRCT20160422027520N19**
Registration date: **2021-10-12, 1400/07/20**
Registration timing: **prospective**

Last update: **2021-10-12, 1400/07/20**
Update count: **0**

**Registration date**

2021-10-12, 1400/07/20

**Registrant information**

**Name**

Mehdi Yousefi

**Name of organization / entity**

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**Recruitment status**

**Recruitment complete**

**Funding source**

**Expected recruitment start date**

2021-10-22, 1400/07/30

**Expected recruitment end date**

2022-05-20, 1401/02/30

**Actual recruitment start date**
empty
**Actual recruitment end date**
empty
**Trial completion date**
empty

**Scientific title**
Intradermal lymphocyte therapy in recurrent pregnancy loss patients with immunologic abnormalities

**Public title**
Intradermal injection of lymphocytes in recurrent pregnancy loss patients
**Purpose**
Treatment
**Inclusion/Exclusion criteria**
**Inclusion criteria:**
Having at least three consecutive abortions Having regular menstrual cycles BMI of people below 30 Have no uterine pathology Our patients will be selected only from Azerbaijan. Patients were selected whose semen analysis and DNA fragmentation test were normal.
**Exclusion criteria:**
Patients under the age of 18 and over 40 years Patients who themselves or their spouse have abnormal karyotypes or genetic or chromosomal abnormalities. Patients with chronic underlying disease who have to take certain medications. Patients with intrauterine anomalies. Having polycystic ovary syndrome Patients who test positive for HIV, HCV or HBV
**Age**
From **18 years** old to **40 years** old
**Gender**
Both

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

- Participant
- Data analyser

**Sample size**
Target sample size: **200**
**Randomization (investigator's opinion)**
Randomized
**Randomization description**
At first, the sample size of 200 patients with RPL 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 200. 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**

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**
**Name of ethics committee**
Ethics committee of Tabriz University of Medical Sciences
**Street address**
Tabriz University of Medical Sciences , Daneshghah st, Tabriz
**City**
Tabriz
**Province**
East Azarbaijan
**Postal code**
5166614766
**Approval date**
2021-10-06, 1400/07/14
**Ethics committee reference number**
IR-TBZMED.REC.1400.597

## Health conditions studied

### 1

**Description of health condition studied**
Recurrent Pregnancy Loss(RPL)
**ICD-10 code**
**ICD-10 code description**

## Primary outcomes

### 1

**Description**
Frequency of Treg and Th17 cells
**Timepoint**
Before and after the intervention
**Method of measurement**
Flow cytometry

### 2

**Description**
Gene expression levels of Foxp3 and RORyt
**Timepoint**
Before and after the intervention

**Method of measurement**
Real-time PCR

**3**

**Description**
Protein expression levels of Foxp3 and RORyt
**Timepoint**
Before and after the intervention
**Method of measurement**
Western blot

**4**

**Description**
Gene expression levels of IL-10, IL-17, IL-21, IL-23, TGF-β
**Timepoint**
Before and after the intervention
**Method of measurement**
Real-time PCR

**5**

**Description**
Secretion levels of IL-10, IL-17, IL-21, IL-23, TGF-β
**Timepoint**
Before and after the intervention
**Method of measurement**
ELISA

**6**

**Description**
Gene expression levels of mir-146a و mir-155 و mir-326
**Timepoint**
Before and after the intervention
**Method of measurement**
real-time PCR

## Secondary outcomes

empty

## Intervention groups

**1**

**Description**
Intervention group: The group of 200 patients with recurrent miscarriage was randomly divided into two groups of 100, one group receiving lymphocyte therapy and the other group not receiving treatment. Is injected. According to the standard protocol, 2 × 107 of husband's lymphocytes are injected subcutaneously into patients with recurrent miscarriages. The number of injections is three times and at intervals of one month.
**Category**
Treatment - Other

## Recruitment centers

**1**

**Recruitment center**
**Name of recruitment center**
Infertility center at Valiasr Hospital
**Full name of responsible person**
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## Sponsors / Funding sources

**1**

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**Web page address**
**Grant name**
**Grant code / Reference number**
**Is the source of funding the same sponsor organization/entity?**
Yes
**Title of funding source**
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**
Academic

## Person responsible for general inquiries

**Contact**

**Name of organization / entity**
Tabriz University of Medical Sciences

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**Position**
PhD in Medical Immunology

**Latest degree**
Ph.D.

**Other areas of specialty/work**
Immunology

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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**
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