

Clinical Trial Protocol

Iranian Registry of Clinical Trials

09 Jun 2026

Molecular evaluation of endometrium obtained from women with repeated implantation failure (RIF) after endometrial injury in compare to women without endometrial injury

Protocol summary

Study aim

Molecular evaluation of endometrium obtained from women with repeated implantation failure (RIF) after endometrial injury in compare to women without endometrial injury

Design

A randomized clinical trial with control group, double blind, two arm parallel group design of 20 patients. Randomization is performed using a computer-generated random assignment schedule for each patient. Sealed and numbered envelopes are used to conceal the treatment allocation until randomization.

Settings and conduct

Female infertility Clinic of ROYAN institute.

Participants/Inclusion and exclusion criteria

- less than 40 years old - Patients had history of 3 failed consecutive cycles of IVF / ICSI. - Patients were good responders in prior ovulation induction cycle. - There were at least two embryos with grade A in each embryo transfer cycle. - Normal uterus in Hysterosalpingography (HSG) or ultrasound or hysteroscopy scans. - The minimum thickness of the endometrium is 7 mm in injection day.

Intervention groups

Intervention: Endometrial injury In the intervention group, endometrial sampling is obtained twice by Pipelle [one in the follicular phase (during 8-9 or 11- 13 day in the beginning of buserelin cycle) and the last in the luteal phase (during 19-21 or 20-23 day) of the same cycle preceding the embryo transfer cycle. **No Intervention:** Control In the control group endometrial sampling will be done only in the luteal phase (during 19-21 or 20-23 day) of the cycle preceding the embryo transfer cycle.

Main outcome variables

Determination of cytokine and chemokine genes expression in endometrial specimens in the intervention group (with local endometrial abrasion) compared with

the control group (without local endometrial abrasion)

General information

Reason for update

Acronym

RIF-Injury

IRCT registration information

IRCT registration number: **IRCT20080831001141N28**

Registration date: **2020-11-25, 1399/09/05**

Registration timing: **retrospective**

Last update: **2020-11-25, 1399/09/05**

Update count: **0**

Registration date

2020-11-25, 1399/09/05

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

2014-06-30, 1393/04/09

Expected recruitment end date

2016-06-29, 1395/04/09

Actual recruitment start date

2014-06-30, 1393/04/09

Actual recruitment end date

2020-09-09, 1399/06/19

Trial completion date

2020-09-09, 1399/06/19

Scientific title

Molecular evaluation of endometrium obtained from women with repeated implantation failure (RIF) after endometrial injury in compare to women without endometrial injury

Public title

Molecular evaluation of endometrium after endometrial injury

Purpose

Other

Inclusion/Exclusion criteria**Inclusion criteria:**

Infertile women with repeated implantation failure (RIF) refers to cases in which women have had three failed in vitro fertilization (IVF) attempts with good quality embryos.

Exclusion criteria:

Women with Sub mucosal myoma Women with Intramural and subserosal myomas larger than 5 cm Women with Endometrioma larger than or equal to 3 cm Women with Hydrosalpinx If the number of available embryos is less than 2 in the current cycle Women with endometrial tuberculosis and those undergoing tuberculosis treatment. Patients with any specific medication Patients with a history of thyroid disease, diabetes and other hormonal disorders and diseases Failure to return the patient to prepare an endometrial sample Inability to obtain tissue samples from patients due to severe pain or the possibility of infection

AgeFrom **18 years** old to **40 years** old**Gender**

Female

Phase

2

Groups that have been masked

- Participant
- Investigator

Sample sizeTarget sample size: **20**Actual sample size reached: **20****Randomization (investigator's opinion)**

Randomized

Randomization description

Consecutive sampling until the required sample size is reached. Women by Balanced Block Randomization method are randomly divided into 2 equal groups of 10 people (intervention group and control group). Block randomization method is designed by epidemiologist using STATA software version 13 and the number of blocks considered is 4. Envelopes are prepared for 20 people and inside each envelope is written the group in which the patient should be placed. The envelopes are prepared in a way that the writing inside is not clear. A nurse before the patient enters the operating room,

removes the envelope and sends the patients in one of the two groups.

Blinding (investigator's opinion)

Double blinded

Blinding description

In this study, a doctor scratches the endometrium in the intervention group on days 8-9 or 11-13. The biopsy specimen is prepared in the luteal phase of the same cycle during days 19-21 or 20-23 by the same doctor or other. Therefore, in this study, it is not possible to blind the doctor. In order to blind the patients participating in this study, all conditions will be the same between the two groups, so patients in the control group also referred to the center on the day of scratching (on days 8-9 or 11-13) and due to the blindness of the study, all sampling steps except scratching The endometrium will be performed for the control group as well as the intervention group. The endometrial biopsy specimen of both groups is transferred to the Laboratory, which also does not know information about whether the tissue sample received is for the intervention or control group and examines it only based on the received code (researcher blindness).

Placebo

Not used

Assignment

Parallel

Other design features**Secondary Ids****1****Registry name**

مرکز ثبت کارآزمایی های بالینی ایالات متحده آمریکا
(www.clinicaltrial.gov)

Secondary trial Id

NCT02480127

Registration date

2015-06-24, 1394/04/03

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

Ethics Committee of Royan Institute

Street address

Royan Institute, Number 12, East Hafez Avenue,
Banihashem Street, Resalat Highway.

City

Tehran

Province

Tehran

Postal code

148- 16635

Approval date

2014-08-12, 1393/05/21

Ethics committee reference number

EC/93/1070

Health conditions studied

1

Description of health condition studied

repeated implantation failure (RIF)

ICD-10 code

N97.9

ICD-10 code description

Female infertility, unspecified

Primary outcomes

1

Description

Evaluation of gene expression

Timepoint

In the endometrial sample obtained in the luteal phase during days 19-21 or 20-23

Method of measurement

Using PCR Array method and based on the copy number

Secondary outcomes

1

Description

clinical pregnancy rate

Timepoint

Only once; 6 weeks after embryo transfer.

Method of measurement

Vaginal ultrasound

Intervention groups

1

Description

Intervention group: In the intervention group, endometrial sampling is obtained twice by Pipelle [one in the follicular phase (during 8-9 or 11- 13 day in the beginning of buserelin cycle) and the last in the luteal phase (during 19-21 or 20-23 day) preceding the embryo transfer cycle.The endometrial injury which is induced with pipelle.

Category

Treatment - Other

2

Description

Control group: In the control group endometrial sampling will be done only in the luteal phase of the cycle preceding the embryo transfer cycle.

Category

Treatment - Other

Recruitment centers

1

Recruitment center

Name of recruitment center

Infertility Center of ROYAN

Full name of responsible person

Mahnaz Ashrafi

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Royan Institute, Number 12, East Hafez Avenue, Banihashem Street, Resalat Highway.

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

ROYAN Institute

Full name of responsible person

Parvaneh Afsharian

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Royan Institute, Number 12, East Hafez Avenue, Banihashem Street, Resalat Highway.

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pafshar@royaninstitute.org

Grant name

Grant code / Reference number

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

Yes

Title of funding source

ROYAN Institute

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

ROYAN Institute

Full name of responsible person

مهناز اشرفی

Position

Professor

Latest degree

Subspecialist

Other areas of specialty/work

Gynecology and Obstetrics

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Person responsible for scientific inquiries

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Latest degree

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Person responsible for updating data

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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

Not applicable

Informed Consent Form

Undecided - It is not yet known if there will be a plan to make this available

Clinical Study Report

Yes - There is a plan to make this available

Analytic Code

Not applicable

Data Dictionary

Not applicable

Title and more details about the data/document

Clinical study report (published article)

When the data will become available and for how long

After the publication of the article

To whom data/document is available

Available to the public

Under which criteria data/document could be used

Scientific use by citing the source

From where data/document is obtainable

Dr. Mahnaz Ashrafi

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

Request via e-mail

Comments