Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Jun 2026

Comparison of the Effectiveness of Letrozole with Estradiol on Frozen Embryo Transfer Cycle Outcomes in Women with Polycystic Ovarian Syndrome

Protocol summary

Study aim
The comparison of letrozole with estradiol on the outcomes of frozen embryo transfer cycles in women with polycystic ovarian syndrome

Design
A randomized controlled clinical trial, with parallel groups, single blinded, phase 3, with simple randomization method on 510 patients.

Settings and conduct
This study will be carried out at Yas Hospital (Tehran, Iran) on women with polycystic ovarian syndrome. The patients, the sonographer and the physician who will be responsible for administration of drugs will know about the interventions; the physician who will be responsible for embryo transferring and the statistician are unaware of the interventions.

Participants/Inclusion and exclusion criteria
Inclusion criteria of study: The women with polycystic ovarian syndrome; 18 - 40 years old; candidate of frozen embryo transfer Exclusion criteria of study: The other causes of hyperandrogenism and ovarian dysfunction; Basal FSH level >10 IU/L; History of recurrent miscarriage; History of congenital or acquired uterine malformations; History of male factor infertility

Intervention groups
In the control group, endometrial preparation will be done by traditional method with estrogen and progesterone containing drugs. In the study group, endometrial preparation will be done by letrozole.

Main outcome variables
Live Birth Rate

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20150105020558N3**
Registration date: **2021-03-02, 1399/12/12**
Registration timing: **prospective**

Last update: **2021-03-02, 1399/12/12**
Update count: **0**

Registration date
2021-03-02, 1399/12/12

Registrant information

Name
Mahbod Ebrahimi

Name of organization / entity
Tehran University of Medical Sciences

Country
Iran (Islamic Republic of)

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+98 21 8882 7794

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Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2021-04-21, 1400/02/01

Expected recruitment end date
2022-10-22, 1401/07/30

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title
Comparison of the Effectiveness of Letrozole with Estradiol on Frozen Embryo Transfer Cycle Outcomes in

Women with Polycystic Ovarian Syndrome

Public title
Letrozole effect in IVF cycles
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
The patients with impression of polycystic ovarian syndrome according to Rotterdam consensus as fulfilling at least two of the three criteria: 1- oligo/anovulation; 2- clinical or biochemical signs of hyperandrogenism; and 3- polycystic ovarian morphology on ultrasound Female age: 18 - 40 years old The candidate of frozen embryo transfer
Exclusion criteria:
The other causes of hyperandrogenism and ovarian dysfunction Basal FSH level >10 IU/L History of recurrent miscarriage History of congenital or acquired uterine malformations History of male factor infertility
Age
From **18 years** old to **40 years** old
Gender
Female

Phase
3
Groups that have been masked

- Care provider
- Outcome assessor
- Data analyser

Sample size
Target sample size: **510**
Randomization (investigator's opinion)
Randomized
Randomization description
Random allocation, there are 255 small envelopes containing letter A and 255 small envelopes in the same shape containing letter B in a bag; and for each patient one envelope is selected randomly.
Blinding (investigator's opinion)
Single blinded
Blinding description
Whilst the patients, the sonographer and the physician who will be responsible for administration of drugs will know about the interventions; the physician who will be responsible for embryo transferring and the statistician are unaware of the interventions.
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Ethics committee of Sina Hospital
Street address
Yas Complex Hospital, Forth Alley Corner, North Ostad Nejatollahi Avenue, Karimkhan Street, Tehran, Iran
City
Tehran
Province
Tehran
Postal code
1597856511
Approval date
2020-12-14, 1399/09/24
Ethics committee reference number
IR.TUMS.SINAHOSPITAL.REC.1399.084

Health conditions studied

1

Description of health condition studied
Polycystic ovarian syndrome
ICD-10 code
E28.2
ICD-10 code description
Polycystic ovarian syndrome

Primary outcomes

1

Description
Live Birth Rate
Timepoint
After pregnancy termination
Method of measurement
The number of deliveries that resulted in a live born neonate, expressed per 100 embryo transfers

Secondary outcomes

1

Description
Clinical Pregnancy Rate
Timepoint
4 to 6 weeks after frozen embryo transfer
Method of measurement
A visible gestational sac by transvaginal ultrasound

2

Description
Ongoing Pregnancy Rate
Timepoint
After 20th weeks of pregnancy
Method of measurement
The number of fetuses with heart activity beyond 20 weeks of gestation

3

Description
Cycle cancellation rate
Timepoint
from 15th until 21th days of cycle
Method of measurement
The number of cancelled cycles

4

Description
Endometrial thickness
Timepoint
On the day of HCG injection
Method of measurement
The measuring of endometrial thickness by transvaginal ultrasound

5

Description
Abortion rate
Timepoint
From 5th until 24th gestational weeks
Method of measurement
The detection of lack or loss of fetal heart activity by ultrasound

6

Description
Premature delivery rate
Timepoint
From 25th until 36th gestational weeks
Method of measurement
The delivery of fetus(es)

Intervention groups

1

Description
Intervention group: In this group, two letrozole tablets (2.5 mg, Aburaihan pharmaceutical co) is prescribed orally for 5 days initiating on day 3 of spontaneous menses or progesterone-induced withdrawal bleeding. Ultrasound monitoring are performed from cycle day 10 onwards. if the leading follicle reaches a mean diameter of ≥ 14mm on cycle day 10, ultrasound is repeated every 2 days. In case of a mean dominant follicle diameter < 14mm on day 10, a daily dosage of 75 IU hMG is supplemented to stimulate follicle growth. When the dominant follicle reaches a mean diameter of ≥17mm and endometrial thickness reaches ≥ 7mm, a bolus of urinary hCG 5000 IU will be injected. According to embryo staging (cleavage stage or blastocyst), embryo transferring will be scheduled 4 or 6 days later.
Category
Treatment - Drugs

2

Description
Control group: In this group, three Estradiol Valerate tablets (2 mg, Aburaihan pharmaceutical co) are prescribed orally from day 3 of spontaneous menses or progesterone-induced withdrawal bleeding. Ultrasound monitoring are performed 12 to 14 days later. ultrasound examination is carried out to measure endometrial thickness as well as to ensure there is no dominant follicle. When the endometrial thickness attained ≥ 7mm, progestrone vaginal suppositories (Fertigest, 400mg, Aburaihan pharmaceutical co) twice daily are initiated. According to embryo staging (cleavage stage or blastocyst), embryo transferring will be scheduled 4 or 6 days later.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Yas Hospital
Full name of responsible person
Mahbod Ebrahimi
Street address
Yas Hospital, Ostad Nejatolahi Ave., Karimkhan Blvd.
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Tehran University of Medical Sciences
Full name of responsible person
Mahbod Ebrahimi
Street address
Keshavarz Blvd , Khods St , Tehran University of Medical Sciences
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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

Tehran 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

Tehran University of Medical Sciences

Full name of responsible person

Mahbod Ebrahimi

Position

Associate 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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Name of organization / entity

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Full name of responsible person

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Position

Associate professor

Latest degree

Subspecialist

Other areas of specialty/work

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Person responsible for updating data

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Latest degree

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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

Yes - There is a plan to make this available

Title and more details about the data/document

Project report to Deputy of Research of TUMS, every researcher who needs data for research

When the data will become available and for how long

5 years

To whom data/document is available

Deputy of Research of TUMS, every researcher who

needs data for research.

Under which criteria data/document could be used

After final report and publishing the results

From where data/document is obtainable

Miss Moamaei-Deputy of Research of TUMS,fifth floor,Central building of TUMS,Ghods ave., Tel:00982164431

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

Miss Moamaei-Deputy of Research of TUMS or send the request to maeb214@yahoo.com, responsible author, after one month they will be responded

Comments