Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Jun 2026

Pregnancies following the use of sequential treatment of metformin and incremental doses of letrozole in clomiphen-resistant women with polycystic ovary syndrome

Protocol summary

Summary

Background: Clomiphen citrate (CC) is the first line therapy for women with infertility and poly cystic ovary syndrome(PCOS).However, 20-25% of women are resistant to CC and do not ovulate. Objective: The objective of this study was to evaluate the efficacy of sequential treatment of metformin and incremental doses of letrozole in induction of ovulation in cases of CC- resistant PCOS patients. Material and Methods:In this propective before-after study, we enrolled 106 anovulatory PCOS women who failed to ovulate with CC alone from Amir-Almomenin University Hospital in Semnan, Iran from June 2005 to December 2008. After an initial 6- 8 weeks of metformin treatment, they received 2.5 mg letrozole daily on days 3-7 after menes. If they did not ovulate with 2.5 mg letrozole, the doses were increased to 5 to 7.5 mg daily in subsequent cycles. The main outcomes were ovulatory rate , pregnancy rate and cumulative pregnancy rate. The mean number of follicles≥ 18 mm, the mean of follicular size and endometrial thickness on the day of HCG administration were secondary outcome measures.

General information

Acronym

IRCT registration information

IRCT registration number: **IRCT201109073386N3**
Registration date: **2011-10-09, 1390/07/17**
Registration timing: **retrospective**

Last update:
Update count: **0**

Registration date

2011-10-09, 1390/07/17

Registrant information

Name

Azam Azargoon

Name of organization / entity

Semnan University of Medical Sciences

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Semnan University of Medical Sciences

Expected recruitment start date

2005-06-01, 1384/03/11

Expected recruitment end date

2008-11-30, 1387/09/10

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Pregnancies following the use of sequential treatment of metformin and incremental doses of letrozole in clomiphen-resistant women with polycystic ovary syndrome

Public title

Pregnancies following the use of sequential treatment of metformin and incremental doses of letrozole in clomiphen-resistant women with polycystic ovary syndrome

Purpose

Treatment

Inclusion/Exclusion criteria
Inclusion criteria: women who were 19-42 years of age with period of infertility more than 1.5 years; normal serum prolactin and thyroid function tests; having documented patent tubes by hysterosalpingography; no other infertility factor and failed to ovulate with a dose of CC of 150 mg/day for 5 days from day 3 of the period.The women were excluded from the study if they were diabetic; taking any medication that could influence carbohydrate metabolism; had hypertension or abnormal renal or liver function tests; and undergone ovarian drilling.Hirsutism was diagnosed when the Ferriman and Gallway score is >8 The diagnosis of PCOS was according to the Rotterdam Criteria.

Age
From **19 years** old to **42 years** old

Gender
Female

Phase
N/A

Groups that have been masked
No information

Sample size
Target sample size: **106**

Randomization (investigator's opinion)
N/A

Randomization description

Blinding (investigator's opinion)
Not blinded

Blinding description

Placebo
Not used

Assignment
Single

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Deputy research

Street address
Semnan university of medical sciences-Basij Blvd-Semnan

City
Semnan

Postal code

Approval date
2011-09-27, 1390/07/05

Ethics committee reference number
90/100019

Health conditions studied

1

Description of health condition studied
Poly cystic ovarian syndrome

ICD-10 code
E28.2

ICD-10 code description
Polycystic ovarian syndrome

Primary outcomes

1

Description
Ovulation, Pregnancy and Cumulative pregnancy rates in different doses of letrozole

Timepoint
During and the end of treatment

Method of measurement
Sonography and BHCG

Secondary outcomes

1

Description
The mean number of follicles≥ 18 mm, the mean of follicular size and endometrial thickness on the day of HCG administration

Timepoint
During treatment

Method of measurement
Sonograhy and BHCG

Intervention groups

1

Description
Metformin was started after two months of CC to allow for the washout of the latter. All women were examined clinically and their weight, height and body mass index (BMI) recorded. All patients received 1500 mg metformin (Glocophage, Merck, West Drayton, UK) daily for 6- 8 weeks. The dose of metformin was built up gradually over a 3 weeks period, beginning at 500 mg daily with main meal for 1 week, followed by 500 mg twice daily for 1 week and increased to 500 mg three times daily to minimize side effects. If pregnancy occurred, metformin was continued for another 8 weeks. In case of failure of pregnancy after the end of this period, metformin was continued and patients were given 2.5 mg letrozole (Femara, Novartis, Quebec, Canada) for 5 days starting from day 3 of their menstrual cycle.

Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Amir-AL-Momenin Hospital infertility clinic -Semnan
Full name of responsible person
Azam Azargoon
Street address
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Sponsors / Funding sources

1

Sponsor
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Semnan university of medical scienses
Full name of responsible person
Deputy research
Street address
Semnan university of medical sciense- Basij-Blvd-Semnan
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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
Semnan university of medical scienses
Proportion provided by this source
100
Public or private sector
empty
Domestic or foreign origin
empty
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
empty

Person responsible for general inquiries

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Person responsible for updating data

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
empty
Study Protocol
empty

Statistical Analysis Plan
empty
Informed Consent Form
empty
Clinical Study Report
empty
Analytic Code
empty
Data Dictionary
empty