

# 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: Clomiphene citrate (CC) is the first line therapy for women with infertility and polycystic 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 prospective 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 menses. 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  $\geq$  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)

##### Phone

+98 23 1446 3401

##### Email address

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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 clomiphene-resistant women with polycystic ovary syndrome

##### Public title

Pregnancies following the use of sequential treatment of metformin and incremental doses of letrozole in clomiphene-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  $\geq 18$  mm, the mean of follicular size and endometrial thickness on the day of HCG administration

#### Timepoint

During treatment

#### Method of measurement

Sonography 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**

Amir-AL-Momenin Hospital-Madar square-Semnan

**City**

Semnan

**Sponsors / Funding sources**

1

**Sponsor**

**Name of organization / entity**

Semnan university of medical sciences

**Full name of responsible person**

Deputy research

**Street address**

Semnan university of medical science- Basij-Blvd-  
Semnan

**City**

Semnan

**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 sciences

**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**

**Contact**

**Name of organization / entity**

Semnan university of medical sciences

**Full name of responsible person**

Azam Azargoon

**Position**

Assistant Professor

**Other areas of specialty/work**

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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*