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Continuing ovulation induction with letrozole versus switching to gonadotropins in women with polycystic ovary syndrome

Submission date
01/05/2025

Recruitment status
Recruiting

Registration date
13/05/2025

Overall study status
Ongoing

Last Edited
10/06/2025

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Women who ovulate on letrozole and are not pregnant after 6 months can switch to gonadotrophins or continue with letrozole. Ovulation induction with gonadotrophins is very effective, but has some major disadvantages. It involves injections of gonadotrophins and regular ultrasound scans to monitor the growth of follicles in the ovaries. This is necessary because multiple follicles can develop in PCOS. Letrozole tablets are easier to use and also less harmful to the environment. We believe that both treatments are equally effective and will result in a live birth in 50% of women after a maximum of 6 cycles within 8 months.
Our main study aim is to determine the cumulative live birth rate of continuing with letrozole versus switching to gonadotrophins.
Our secondary objectives are
I) To determine the safety of ovulation induction with letrozole versus switching to gonadotrophins, in terms of side effects, pregnancy complications, and newborn outcome and durability
II) To determine the impact of the treatments on quality of life and mental health of the women
III) To determine the total costs in euros of ovulation induction with letrozole versus switching to gonadotrophins
IV) To determine the environmental burden of both treatments

Who can participate?
Women with PCOS that have been ovulatory for six cycles on letrozole treatment

What does the study involve?
No additional (hospital) visits or laboratory tests are required compared to standard care. Participants will receive digital questionnaires: at randomization (Q1, to assess baseline quality of life and mental health), 3 months after randomization (Q2, quality of life, mental health, side effects), 8 months after randomization (Q3, quality of life, mental health, side effects). Ten months after the end of the treatment period, pregnant women will receive a questionnaire

about pregnancy outcomes and women who did not become pregnant after 6 cycles within 8 months will receive a questionnaire about further treatments (IUI-MOH, IVF) and any pregnancies that resulted from them.

What are possible benefits and risks of participating?
The MOVIN-II study evaluates the effectiveness and safety of continuing ovulation induction with letrozole for another 6 cycles versus switching to gonadotropins. Both interventions are standard treatments in participating clinics in the Netherlands and local treatment protocols are allowed; no additional therapeutic and monitoring procedures will be performed. This study can only be performed in women of reproductive age with PCOS and a desire to have children. The study will provide relevant results that are useful for this specific population.
From the existing large amount of data and literature it is clear that the frequency and severity of side effects and risks of ovulation induction with letrozole for both the woman and the offspring are very limited. We expect that continued treatment with letrozole will provide both individual and collective benefit, as it is expected to result in improved safety in the form of fewer multiple pregnancies, fewer side effects and a better quality of life in comparison to ovulation induction with gonadotropins.
Both letrozole and gonadotropins are reimbursed in the Netherlands.
Patient burden may include: a. Patients being asked to complete multiple questionnaires, b. Patients may be ready for new treatment after 6 cycles of ovulation induction with letrozole without fertilization and therefore refuse to participate.

Where is the study run from?
The study runs in the Netherlands. Main centers are AmsterdamUMC and UMC Groningen. Participating centers are: AmphiaZiekenhuis, Admiraal de Ruyter Ziekenhuis, Albert Schweitserziekenhuis, Catharina Ziekenhuis, Canisius-Wilhelmina ziekenhuis, Deventer Ziekenhuis, Diakonessenhuis, Elkerliek Ziekenhuis, Fertiliteitskliniek Twente, Flevoziekenhuis, Franciscus Gasthuis & Vlietland, Gelderse Vallei, Groene hart Ziekenhuis, Ikazia ziekenhuis, Jeroen Bosch ziekenhuis, Laurentius ziekenhuis, Maasstad Ziekenhuis, Maxima Medisch Centrum, Medisch Spectrum Twente, Nij Geertgen kliniek, Noordwest Ziekenhuisgroep, OLVG, Radboud UMC, St. Antonius ziekenhuis, Tergooi ziekenhuizen, UMC Utrecht, Zuyderland

When is the study starting and how long is it expected to run for?
We expect the study to start recruiting participants in June 2025. We expect to recruit during 36 months, thus until June 2028.

Who is funding the study
ZonMw (https://www.zonmw.nl/en) (Netherlands)

Who is the main contact?
Madelon van Wely, movin2@amsterdamumc.nl

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2024-519354-36-00

Protocol serial number
2024-12-10-MOVIN-II

Study information

Scientific Title
Effectiveness of continuing ovulation induction with letrozole versus switching to gonadotropins in terms of pregnancy outcomes in women with polycystic ovary syndrome

Acronym
MOVIN-II

Study objectives
Women that ovulate on letrozole often switch to gonadotropins after 6 cycles but may also continue with letrozole. We hypothesize that in women who ovulate on letrozole but did not yet conceive, continuing with letrozole and switching to gonadotropins will result in a similar cumulative live birth rate of 50% following 6 cycles within 8 months.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 30/05/2025, METC Amsterdam UMC (Meibergdreeg 9, Amsterdam, 1109AZ, Netherlands; +31 20-4445585; metc@amsterdamumc.nl), ref: 2024-519354-36-00 MOVIN-II

Primary study design
Interventional

Study design
Multicenter interventional open-label randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Women with PCOS and child-wish that require ovulation induction in order to conceive and that have ovulated for 6 cycles on letrozol

Interventions
We will randomise online using Castor EDC software, stratified for BMI group and using random blocks (size 2, 4 and 6).

The intervention group will continue ovulation induction with letrozole at a dose of 2.5 mg, 5 mg or 7.5 mg per day for five days. The dose at which the last ovulatory treatment cycle was done will be the starting dose. The dose will be increased in subsequent cycles in cases of nonresponse using the standard ovulation induction protocol. The maximum daily dose will be 7.5 mg given for 5 days. If patients do not ovulate on the highest letrozole dose anymore, they will be treated according to local protocol.

The comparator group will switch to ovulation induction with gonadotropins starting at the 2nd to 5th cycle day with 50 or 75 IU daily in a low-dose step-up protocol. Monitoring and cancellation will be performed according to local protocol and national guideline. When at least one follicle with a diameter of ≥ 16 mm is present, ovulation is induced by administering human chorionic gonadotropin according to local protocol followed by timed intercourse or by intra-uterine insemination in single women and when indicated.

There are no additional (hospital) visits or laboratory tests when compared to standard care.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Letrozole, follitropin

Primary outcome(s)
Pregnancy within 8 months after randomization, leading to a live birth, measured using patient records

Key secondary outcome(s)
Measured using patient records unless noted otherwise:
1. Clinical pregnancy, ongoing pregnancy, biochemical pregnancy loss and miscarriage rates within 8 months after randomisation.
2. For each participant, the number of treatment cycles initiated, completed and cancelled are evaluated within 8 months after randomisation.
3. Of all achieved (ongoing) pregnancies occurring within 8 months after randomization (including spontaneous pregnancies) the following outcomes are assessed; multiple pregnancy rate, time to pregnancy, pregnancy complications, perinatal outcomes, type of delivery and outcomes
4. Side effects and compliance to therapy assessed during treatment using a medication dairy and a questionnaire, sent out at 3 months and 8 months after randomization.
5. Quality of life and mental health assessed at time of randomization, and at 3 months and 6 months after randomization, using the FertiQoL questionnaire and the HADS questionnaire.

6. Progression to IVF/ICSI within 8 months after randomization
7. Budget impact, Cost-effectiveness analyses using live birth rates, costs and quality of life

Completion date
31/12/2029

Eligibility

Key inclusion criteria
1. Couples or single women with child-wish diagnosed with PCOS according to international guidelines
2. Aged between 18 and 42 years
3. Women have been ovulatory for six cycles on letrozole treatment, with a maximum of 7.5 mg daily for five days, but did not reach an ongoing pregnancy.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
42 Years

Sex
Female

Key exclusion criteria
Women will be excluded if they:
1. have a contraindication to letrozole
2. are pregnant
3. have no patency of at least one fallopian tube
4. have a major medical morbidity (like poorly controlled Type I or Type II diabetes, undiagnosed liver disease or dysfunction based on serum liver enzyme testing, renal disease or abnormal serum renal function)
5. are unable to give informed consent.

Date of first enrolment
01/06/2025

Date of final enrolment
01/06/2028

Locations

Countries of recruitment
Netherlands

Study participating centre
AmsterdamUMC
Meibergdreeg 9
Amsterdam
Netherlands
1109AZ

Study participating centre
UMC Groningen
Hanzeplein 1
Groningen
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9713GZ

Sponsor information

Organisation
Amsterdam University Medical Centers

ROR
https://ror.org/05grdyy37

Funder(s)

Funder type
Research council

Funder Name
ZonMw

Alternative Name(s)
Netherlands Organisation for Health Research and Development

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Netherlands

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository and will be available upon request.
movin2@amsterdamumc.nl

IPD sharing plan summary
Stored in non-publicly available repository, Available on request