PATIENT INFORMATION AND CONSENT

A Randomized, Double-Blind, Placebo-Controlled Trial of finerenone in women with primary ovarian insufficiency

Version 1.0: 11 Aug 2026

You are cordially invited to participate in the above-named research study. You need to decide whether you want to participate or not. Please take your time to make up your mind. Carefully read the following and feel free to ask the study doctor any question which you may have.

Why is this study being done?

Premature ovarian insufficiency (POI) is defined when women aged less than 40 years have no period or irregular periods for 4-6 months and are found to have raised serum FSH levels. The reproductive potential of women with POI is markedly reduced because of lack of antral follicles and ovulation. However, it remains no effective treatment to stimulate the follicles in the ovary to develop and grow. Hormone replacement therapy (HRT) is given to alleviate vasomotor symptoms associated with low female hormones and to prevent long-term sequelae associated with estrogen deficiency. However, it does not restore ovarian function or improve fertility outcomes. At present, oocyte donation remains the only effective option for achieving pregnancy in women with POI.

Finerenone is a drug originally approved to treat chronic kidney disease in people with type 2 diabetes. Our recent preclinical and early clinical studies have demonstrated that Finerenone may stimulate the follicles to develop and grow, leading to retrieval of mature eggs and development of embryos.

The present study aims to evaluate whether Finerenone treatment increases the proportion of women with POI who are able to have oocytes aspirated during IVF within 24 weeks of Finerenone treatment. We will also evaluate the pregnancy rate/live birth rate.

Who should be in this study?

You will be recruited if

1. Age of women < 40 years.
2. Diagnosis of POI according to ESHRE 2024 guidelines, defined as:
   - Oligomenorrhea or amenorrhea for at least 4 months; and

- Elevated FSH levels (⩾25mIU/ml) on a single measurement.

You cannot join the study if you have any of the following:

1. Known hypersensitivity to Finerenone or any of its excipients.
2. Severe uncontrolled systemic diseases (cardiovascular, hepatic, renal, or endocrine disorders) that may interfere with study participation.
3. An active cancer, or a history of hormone-dependent cancer (e.g., certain types of breast or uterine cancer)—since hormones and study treatments may interact with these conditions.
4. Currently participating in another interventional trial.
5. Known chromosomal abnormalities or clinically significant genetic syndromes associated with POI.

What will we be asked to do?

If you agree to participate in this study, you will be randomly assigned to one of the two groups at a 1:1 ratio through a computer program: (1) the Finerenone group or (2) the placebo group. The placebo is a pill that contains no active pharmaceutical ingredients. Finerenone and the placebo look exactly the same in appearance. In the double-blind trial, neither you nor your doctor knew which treatment group you belonged to. (If the doctor deems it necessary, he/she will be able to know your group.)

Your basic information, including your age, AMH and FSH reports, etc., will be recorded.

You will be asked to stop hormone replacement treatment at least 4 weeks prior to baseline evaluation if you are taking hormonal replacement therapy, to allow accurate assessment of spontaneous ovarian activity and hormone profile.

Finerenone / placebo administration

You will take Finerenone/placebo 20 mg orally, twice per week (eg every Monday and Thursday), for a total duration of 24 weeks. A treatment diary will be provided, and pill counts will be performed at each follow-up visit to monitor adherence.

Follow-up and IVF treatment protocol

You will attend follow-up visits every 4 weeks, during which clinical assessment, ultrasound examination for AFC and serum AMH / FSH measurement will be performed.

If an increase in AFC compared with the individual baseline value is observed, ultrasound monitoring will be performed weekly for four consecutive weeks.

During this period, if follicular development is observed, you can opt for ovarian stimulation for oocyte freezing in unmarried women or embryo freezing in married women. Natural cycle, mild stimulation, low dose FSH ovarian stimulation can be used at the discretion of the physicians or according to the standard protocol of the centre.

Ovarian stimulation, ovulation trigger, oocyte retrieval, and laboratory procedures (including fertilization method and embryo cryopreservation) will be performed in accordance with local standard practice and clinical indications. Oocyte maturation assessment, fertilization outcomes, and embryo development will be recorded as per standard embryology laboratory procedures.

Blood samples obtained at each follow-up visit shall be stored after the AMH and FSH measurements are completed. Should the need arise, these samples may be utilised at a later stage for validating the reliability of the AMH and FSH assay results. Any use of the samples beyond the scope set out in this protocol requires both your prior written informed consent and the approval of the Institutional Review Board of The University of Hong Kong / Hospital Authority Hong Kong West cluster.

Any remaining follicular fluid and granulosa cells (i.e., clinical waste fluid) will be used as biological samples for this study. After processing, the samples will be stored at –80°C or in liquid nitrogen for future use (if applicable). If necessary, these biological samples will undergo cytological and molecular biological testing, and any results will be communicated to you. This can further validate the efficacy of finerenone in women with POI.

The samples will be retained and stored solely within Hong Kong; they will not be transferred to or stored at any location outside Hong Kong.

The above-mentioned biological samples shall be stored for a maximum period of 5 years. Upon expiry of the storage period, all remaining samples will be destroyed in accordance with the institution's standard operating procedures (SOPs).

Pregnancy outcomes will be followed up in your undergoing embryo transfer, with pregnancy testing and ultrasound confirmation performed according to routine clinical practice. Ongoing pregnancy and delivery outcomes will be recorded where applicable.

After the study, if your antral follicle counts and AMH levels rise, you will receive treatment based on you wishes and the center's routine procedures. Costs will be handled in accordance with routine clinical practice and the prevailing policies of the hospital. The treatment and

follow-up data will be captured using a Case Report Form (CRF), which will be included as part of the study documentation.

How long will we be in the study?
Up to 24 weeks after participation. Additionally, the diary takes about one minute daily to complete.

How many other people will be participating in the study?
We plan to recruit 46 women in this study.

Will we be paid?
No payment will be made to you for this study.

What is the source of funding for this study?
The source of funding for this study is internal funding from the Department of Obstetrics and Gynaecology, The University of Hong Kong (which falls under the category of departmental funding and is non-commercial). Ownership of the study data belongs to the study team (The University of Hong Kong), and the major right and responsibility of the funding party are management and supervision of this study.

Do I need to pay for this research article/service?
You are not required to pay for the study products (finerenone and placebo), clinical assessments, ultrasound examinations (for antral follicle count, AFC), or blood tests (for AMH and FSH levels) at each follow-up visit. These costs are covered by the above-mentioned funding source.

Costs related to IVF medical procedures, such as ovarian stimulation, triggering of ovulation, oocyte retrieval, and laboratory procedures (including fertilisation method and embryo cryopreservation), will be your own responsibility and will be charged according to routine clinical practice and hospital policies.

What adverse (bad) effects can happen to us by participating in the study?
Potential adverse effects are rare and mostly mild. Use of Finerenone may lead to mild issues including slight electrolyte changes (e.g., high potassium, monitored via blood tests), temporary kidney marker adjustments, or mild symptoms like nausea or fatigue—these often resolve on their own or with medication stops.

The IVF treatment protocol may involve standard risks associated with in vitro fertilization:

slight discomfort from transvaginal ultrasounds or oocyte retrieval (rarely infection/pain), and typical pregnancy risks (e.g., slight miscarriage chance, higher multiple pregnancy risk than spontaneous conceptions). We will monitor your health with regular checks (blood tests, follow-ups) and address any issues promptly.

What benefit can we expect?

Finerenone treatment may help improve your antral follicle count and AMH levels, promote the development of more follicles, leading to a higher chance of pregnancy.

After the study, if your antral follicle count and AMH levels rise, you will receive treatment based on your wishes and the center's routine procedures, fees are charged according to standard medical care procedures/policies.

Can we refuse to be in the study?

Your participation in this study is voluntary. You can choose not to take part in the study, or you can quit at any time. You will not lose any benefit to which you are otherwise entitled. If you quit the study, you can receive the standard treatment as other patients in our Department.

Confidentiality and privacy

The investigators have always maintained a strict privacy policy. We never sell, trade or otherwise share your details with any sources. All correspondence to the department is held confidentially; furthermore, at no time will your personal and/or identifying information be shared outside of our organization, for any reason.

All data will be stored for five years after the study. A designated research nurse will be responsible for data management including data coding, monitoring and verification. Investigators, research assistants, related healthcare providers will have access to your personal and study data during and after the study. The personal and study data after completion of 5 years storage period will be destroyed.

You have the rights of access to personal data and known study results, if and when needed. Under the laws of the Hong Kong Special Administrative Region and, in particular, the Personal Data (Privacy) Ordinance, Cap 486, you enjoy or may enjoy rights for the protection of the confidentiality of your personal data, such as those regarding the collection, custody, retention, management, control, use (including analysis or comparison), transfer in or out of Hong Kong, non-disclosure, erasure and/or in any way dealing with or disposing of any of your personal data in or for this study. For any query, you can consult the Personal

Data Privacy Commissioner or call their office (2827 2827) as to the proper monitoring or supervision of your personal data protection so that your full awareness and understanding of the significance of compliance with the law governing privacy data is assured.

For questions about the study or reporting of adverse events, please call Prof. Ng Hung Yu, Ernest, at telephone no. 2255 4567. The phone number of the Institutional Review Board of The University of Hong Kong / Hospital Authority Hong Kong West cluster is 2255 4086.

If you consent to take part in the research, any of your medical records may be inspected by the research team for purposes of analysing the results. They may also be looked at by people from regulatory authorities to check that the study is being carried out correctly. Your names, however, will not be disclosed outside the hospital.

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY
THE UNIVERSITY OF HONG KONG

PATIENT CONSENT FORM

PROTOCOL TITLE: A Randomized, Double-Blind, Placebo-Controlled Trial of finerenone in women with primary ovarian insufficiency

Name of Principal Investigator: **Professor Ng Hung Yu, Ernest**

1. I confirm that I have read and understood the patient information sheet for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

3. I understand that sections of any of my medical notes may be looked at by responsible individuals who are relevant to my taking part in research. I give permission for these individuals to have access to my medical records.

4. I agree that any archived serum samples, follicular fluid samples, and granulosa cell samples can be retained and used for future cytological and molecular biological testing, and I will be notified of any results.

5. I agree to take part in the above study.

I understand that I will be given a signed copy of this Patient Information and Consent Form.

_____	_____	_____
Patient's signature	Patient's name	Date

_____	_____	_____
Investigator’s signature	Investigator’s name	Date