Study Protocol

Official Title: Semaglutide Improves Metabolic Abnormalities and Fertility in Obese Infertile Women With Polycystic Ovary Syndrome: a Prospective, Randomized, Open, Controlled Study

NCT number: Not assigned yet

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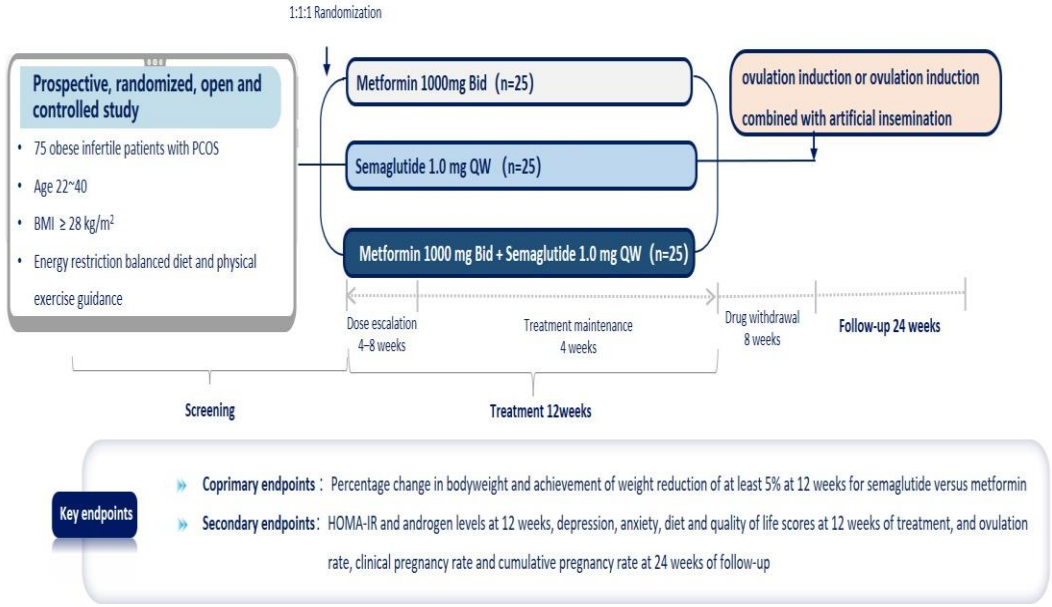
Study Protocol

This study is a prospective, randomized, open and controlled study. 75 obese infertile patients with polycystic ovary syndrome (PCOS) will be recruited , and all will receive energy restriction balanced diet and physical exercise guidance. In a 1:1:1 ratio, all subjects will be randomized to three groups: metformin single, semaglutide single and metformin combined with semaglutide group, with 25 subjects in each group.

Metformin and semaglutide are administered in a dose-increasing mode. The initial dose of metformin is 500mg Bid (twice daily), increased to 1000mg Bid after 2 weeks, and then maintained until the end of 12 weeks of treatment. Semaglutide is injected subcutaneously. The initial dose is 0.25 mg QW (once a week), increased to 0.5 mg QW after 4 weeks, and increased to 1.0 mg QW after another 4 weeks, and then maintained until the end of 12 weeks of treatment. All patients will be treated for 12 weeks, and the metabolism-related indexes will be evaluated. After 8 weeks of drug withdrawal, all patients will start ovulation induction or ovulation induction combined with artificial insemination treatment, and then followed up for another 24 weeks to record the pregnancy and evaluate the fertility related indicators.

Coprimary endpoints are percentage change in bodyweight and achievement of weight reduction of at least 5% at 12 weeks for semaglutide versus metformin. The secondary endpoints include HOMA-IR and androgen levels at 12 weeks, depression, anxiety, diet and quality of life scores at 12 weeks of treatment, and ovulation rate, clinical pregnancy rate and cumulative pregnancy rate at 24 weeks of follow-up.



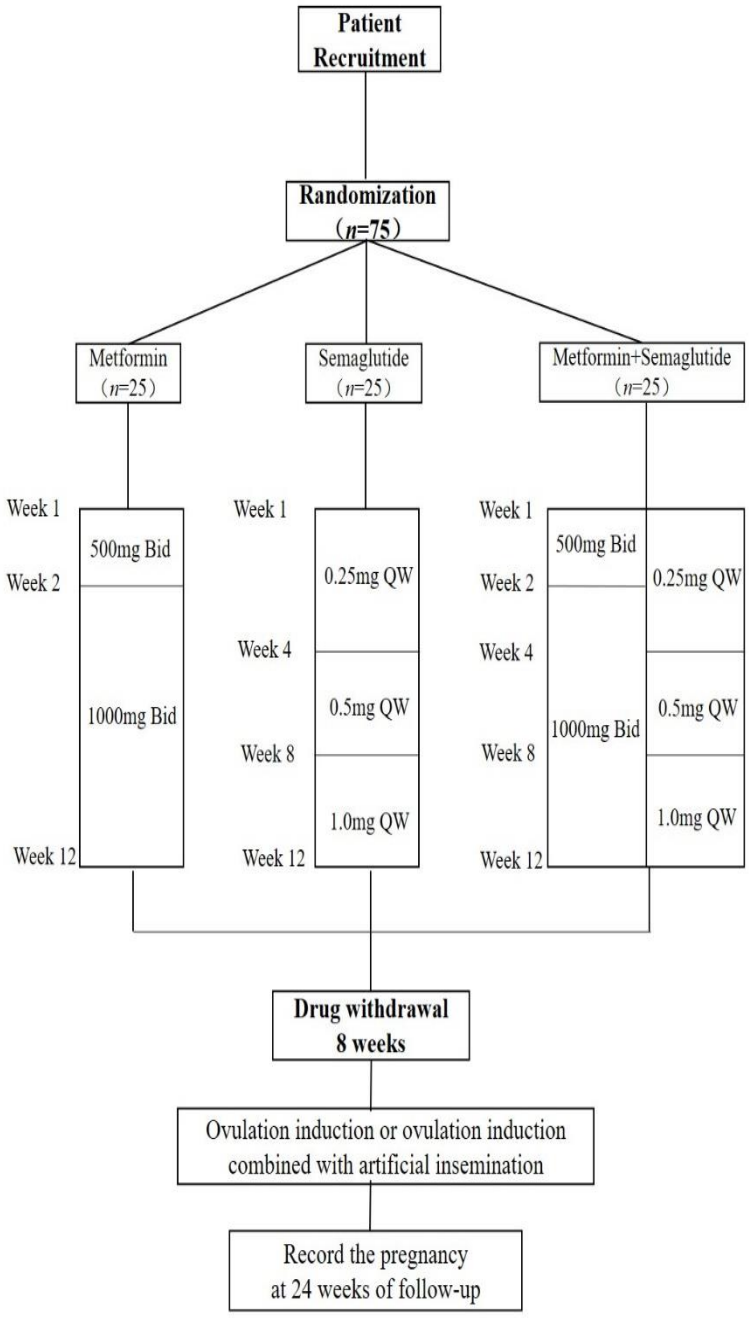
Inclusion Criteria:

- Age 22-40
- Meet the PCOS diagnostic criteria (Rotterdam)
- BMI ≥ 28 kg/m^2
- Infertility: having normal sexual life and failing to conceive without contraception for more than 1 year

- Willing to be pregnant, and her husband has no serious infertility

Exclusion Criteria:

- History of acute pancreatitis, individual or family history of medullary thyroid cancer and multiple endocrine adenomas
- Type 1 diabetes and special type diabetes
- History of tumor
- Serious cardiovascular and cerebrovascular disease, mental disease, liver or kidney disease
- Metformin, GLP-1 RA and other drugs affecting reproductive and metabolic functions were used within 90 days before the study
- Known allergy to metformin, GLP-1 RA and excipients
- Severe endometriosis, low ovarian reserve, premature ovarian failure
- Inability to tolerate pregnancy and ovulation induction therapy
- Other conditions considered unsuitable for this study by researchers



Outcome measures

- **Baseline and Week 12:** body weight, BMI, waistline, body fat rate, visceral fat area, OGTT (blood glucose and insulin), HOMA-IR, androgens level (testosterone, androstenedione), SHBG, FAI, depression, anxiety, diet and quality of life scores
- **Follow-up 24 weeks**: ovulation rate, clinical pregnancy rate and cumulative pregnancy rate