

Pregnancy in Polycystic Ovary Syndrome II (PPCOS II)

Purpose of Study

To determine the safety and efficacy of clomiphene citrate, a selective estrogen receptor modulator, compared to letrozole, an aromatase inhibitor, in achieving live birth in infertile women with polycystic ovary syndrome (PCOS)

Study Design

This was a multi-center, prospective, double blind clinical trial of clomiphene citrate (cc) vs. letrozole for 5 cycles (or approximately up to 25 weeks). The randomization scheme was coordinated through the central data coordination center (DCC) and stratified by each participating site. We elected not to stratify by prior exposure to medication as this did not exert significant effects in our previous trial and would add an unnecessary layer of complexity.

Study Population

The population consisted of 750 infertile women with PCOS, age 18<x>40 years, diagnosed by the modified Rotterdam Criteria: subjects must have ovulatory dysfunction and either one or the remaining two criteria, hyperandrogenism (clinical or biological or polycystic ovaries on ultrasound, with exclusion of secondary causes of PCOS. Additionally, the couple will have no other major infertility factor, and the subject will have at least one patent fallopian tube and a normal uterine cavity, and a partner with a sperm concentration of 14 million/mL in at least one ejaculate.

Treatments

After progestin withdrawal, 750 women were equally randomized to two different treatment arms: A) clomiphene citrate 50 mg every day for 5 days (day 3-7 of cycle), or B) letrozole 2.5 mg every day for 5 days (day 3-7 of cycle), for a total of 5 cycles or 25 weeks. Dose will be increased in subsequent cycles in both treatment groups for non-response or poor ovulatory response up to a maximum of 150 mg of clomiphene a day (x 5 days) or 7.5mg of letrozole a day (x 5 days).

Results

Live birth was the primary outcome, and the live birth rate was the efficacy parameter. Secondary efficacy parameters included singleton live birth rate, abortion rate, time to pregnancy, ovulation rate, pregnancy complication rate, birth weight, neonatal complication rate, predictive factors for response including quality of life, and cost effectiveness.