

Treatment of Infertility in Women with Polycystic Ovary Syndrome (PPCOS I)

Purpose of Study

Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder affecting up to 10% of women. The primary symptoms of PCOS are menstrual irregularities, increased body and facial hair, acne, and infertility. The PPCOS I study evaluated the safety and effectiveness of a combination of medications in achieving a successful pregnancy in infertile PCOS women.

Study Design

The PPCOS I study was a double-blind randomized trial of Clomiphene Citrate, Metformin XR, and combined Clomiphene Citrate/Metformin XR for the treatment of infertility in women with PCOS. The primary hypothesis was that combined treatment with metformin and clomiphene was more likely to result in a live birth than single agent/placebo therapy. The primary outcome of the study was the live birth rate. The secondary outcome measures of the study included singleton live birth rate, ovulation rate, cycles to first ovulation, and cycles to conception, cycles to pregnancy, abortion rate and weeks from pregnancy to live birth.

Study Population

Six hundred twenty-six infertile women with PCOS, aged 18-39 years, with elevated testosterone levels and oligomenorrhea, seeking pregnancy, with at least one patent fallopian tube(s), normal uterine cavity, and a partner with sperm concentration of at least 20 million/mL in at least one ejaculate, participated in the study. All subjects were in good health with no major medical disorders and those with other causes of infertility were excluded.

Treatments

Patients will be randomized to one of three different treatment arms: A) Metformin XR 1000 mg twice/day; B) Clomiphene Citrate 50 mg every day for 5 days (day 3-7 of cycle); or C) Metformin XR 1000 mg twice/day with Clomiphene Citrate 50 mg/day for 5 days (day 3-7 of cycle). Women continued on study medications for 30 weeks, 6 treatment cycles, or until they become pregnant. Progesterone levels were drawn weekly to monitor ovulation.

Results

This study has been completed and the result showed that Clomiphene Citrate (alone or combined with Metformin) was superior to Metformin in achieving live birth in infertile women with PCOS, although multiple birth was a complication.

Primary Reference

Richard S. Legro, M.D., Huiman X. Barnhart, Ph.D., William D. Schlaff, M.D., Bruce R. Carr, M.D., Michael P. Diamond, M.D., Sandra A. Carson, M.D., Michael P. Steinkampf, M.D., Christos Coutifaris, M.D., Ph.D., Peter G. McGovern, M.D., Nicholas A. Cataldo, M.D., Gabriella G. Gosman, M.D., John E. Nestler, M.D., Linda C. Giudice, M.D., Ph.D., Phyllis C. Leppert, M.D., Ph.D., and Evan R. Myers, M.D., M.P.H. for the Cooperative Multicenter Reproductive Medicine Network. Clomiphene, Metformin, or Both for Infertility in the Polycystic Ovary Syndrome. *N Engl J Med* 2007; 356:551-566, 2007.