

KEEPS TRIAL

Hormone Therapy Has Many Favorable Effects in Newly Menopausal Women:

Initial Findings of the Kronos Early Estrogen Prevention Study (KEEPS)

PHOENIX, (October 3, 2012) – Estrogen /progesterone treatment started soon after menopause

appears safe and relieves many of the symptoms menopausal women face as well as improving

mood and markers of cardiovascular risk, according to a multicenter randomized study presented at the North American Menopause Society (NAMS) Annual Meeting in Orlando, Florida.

The Kronos Early Estrogen Prevention Study (KEEPS) was a four-year randomized, double-blinded, placebo-controlled clinical trial of low-dose oral or transdermal (skin patch) estrogen and cyclic monthly progesterone in healthy women aged 42-58 (mean age, 52) who were within three years after menopause at randomization. 727 women were randomized into the following three arms, along with cyclical micronized progesterone (Prometrium®):

- Oral conjugated equine estrogens (o-CEE) given as Premarin®, 0.45 mg/day (a lower dose than the 0.625 mg/d used in the Women’s Health Initiative [WHI])
- Transdermal Estradiol (t-E2) given by Climara® patch, 50 µg/day
- Placebo

Measurements showed that:

- Neither o-CEE nor t-E2 significantly affected systolic or diastolic blood pressure, in contrast to the higher dose of CEE in the Women’s Health Initiative (WHI), which increased blood pressure levels.
- Oral CEE, but not t-E2, was associated with an increase in HDL (“good”) cholesterol. The o-CEE group had a decrease in LDL (“bad”) cholesterol, but also an increase in triglyceride levels (a lipid fraction that is of uncertain significance as an independent risk factor). t-E2

had neutral effects on these biomarkers.

- Transdermal E2 appeared to improve insulin sensitivity (lower insulin resistance) calculated from glucose and insulin levels as “HOMA-IR.”

- During 48 months of treatment with either type of hormone therapy (HT) vs placebo, there were no apparent effects, either beneficial or deleterious, on atherosclerosis progression assessed by carotid ultrasound and a non-significant trend toward less accumulation of coronary artery calcium (CAC). We conclude that hormone treatment at the doses employed and in this healthy, recently menopausal population neither significantly reduced nor accelerated progression of atherosclerosis as measured by arterial imaging.

- Improvements in hot flashes, night sweats, mood, sexual function, and bone density were observed with HT vs placebo.

- No significant differences in adverse events (breast cancer, endometrial cancer, myocardial infarction, TIA, stroke, or venous thromboembolic disease) were found among groups.

However, the absolute numbers of such events were extremely small in all three treatment groups, making definitive conclusions impossible.

Conclusions: KEEPS found many favorable effects of HT in newly menopausal women.

The results provide reassurance for women who are recently menopausal and taking HT for short-term treatment of menopausal symptoms. KEEPS also highlights the need for individualized decision making about hormone therapy, given that o-CEE and t-E2 may have different profiles of effects and different women have different symptom profiles and priorities for treatment. Additional research on HT in newly menopausal women, including differences in effects according to route of delivery, dose, and formulation of hormone therapy, is needed.