KRONOS LONGEVITY RESEARCH INSTITUTE

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Join us for a tele-pres call 12:30 ET Thurs, Oct 4th to speak to researchers
Speakers: S. Mitchell Harman, MD PhD; JoAnn Manson MD Dr DrPH, FAHA; Sanjay Asthana MD
866-952-1906; conference ID KLRI

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 KEEPS provides invaluable information for women close to menopause and their clinicians," said S. Mitchell Harman, MD PhD, director of the the Kronos Longevity Research Institute, the organization that sponsored the study. "The data showed improvements in cognition, mood, menopausal symptoms, and sexual function in younger women. In addition, some measures showed slight evidence that hormone therapy might be cardio-protective in this age group, although results were not definitive and would require additional study."

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.

About Funding

The core KEEPS was funded by the Phoenix-based Kronos Longevity Research Institute which is supported by the not-for-profit Aurora Foundation and carried out at nine U.S. academic medical centers (see appendix). The Cognitive and Affective Study is National Institutes of Health funded ancillary study of KEEPS that was coordinated by investigators based at the University of Wisconsin in Madison, WI.

About KLRI

KLRI is a not-for-profit 501(c)(3) organization that conducts state-of-the-art clinical translational research on the prevention of age-related diseases and ways to increase longevity. Translational research is the critical link between findings from the basic research laboratory and corresponding improvements in clinical care. For more information on KEEPS, visit www.keepstudy.org or call 1(866) 878-1221.

The nine KEEPS study centers

- Kronos Longevity Research Institute (the Sponsor) (Dr. Mitch Harman, PI)
- Albert Einstein College of Medicine/Montefiore Medical Center (New York City; Drs. Nanette Santoro and Genevieve Neal-Perry, PIs)
- Columbia University College of Physicians and Surgeons (New York City, Dr. Rogerio Lobo, PI)
- Harvard Medical School/Brigham and Women's Hospital (Boston, Dr. JoAnn Manson, PI)
- Mayo Clinic College of Medicine (Rochester, MN, Dr. Virginia, Miller, PI)

- University of California, San Francisco/Center for Reproductive Health (Dr. Marcelle Cedars, PI)
- University of Utah School of Medicine (Salt Lake City, Drs. Eliot Brinton and Paul Hopkins, PIs)
- University of Washington School of Medicine (Seattle, Dr. George Merriam, PI)
- Yale University School of Medicine (New Haven, CT, Dr. Hugh Taylor, PI)

Evaluation of arterial imaging was coordinated by

- Atherosclerosis Research Unit, Keck School of Medicine of USC (CIMT, Dr. Howard Hodis)
- St. Johns Cardiovascular Research Center and the UCLA School of Medicine (CAC, Dr. Matthew Budoff)

Statistical Analysis

- University of California, San Francisco (Dr. Dennis Black)

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