

NSCLC Mortality Higher for Smokers on HT

BY MARY JO M. DALES

ORLANDO — Hormone therapy with estrogen plus progestin for more than 5 years increased the risk of death in women diagnosed with non-small cell lung cancer, based on secondary analyses from the Women's Health Initiative reported at the annual meeting of the American Society of Clinical Oncology.

The increased risk was most notable in women who were current smokers. One in 100 current smokers on combined hormone therapy (HT) in the trial experienced an avoidable death from non-small cell lung cancer during the 8 years of this study, said Dr. Rowan Chlebowski, a medical oncologist at the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, and the study's lead author.

The findings "should influence discussions between physicians and women considering hormone therapy use, especially for those with a smoking history," Dr. Chlebowski said. Women who

smoke and are seeking or already receiving HT should be strongly advised to quit smoking.

The Women's Health Initiative (WHI) was a randomized, placebo-controlled clinical trial that examined the health effects of continued use of conjugated equine estrogen plus medroxyprogesterone in 16,608 mostly healthy postmenopausal women. In current practice, HT is recommended for brief use in the treatment of menopausal symptoms, offers alternative hormone sources, and is given at doses that are about half of those used in the WHI. The WHI was launched in 1993; the estrogen-progestin arm of the WHI was stopped in 2002.

This is the first study to examine a specific correlation between non-small cell lung cancer (NSCLC) and HT in a randomized, double-blind design and with a large, ethnically diverse population. A limitation of this study was the secondary nature of the analyses. The findings on the risk and outcome of lung cancer were not a primary objective of the WHI.

NSCLC incidence and mortality were studied during the 5.6 years of HT or placebo and 2.4 years of follow-up. While the incidence of NSCLC diagnosis was not significantly different for controls and women on HT, survival after di-



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agnosis was significantly lower in the HT group. There were 67 deaths among 96 women on HT and 39 deaths in 72 cases among controls. Median survival was 9.4 months in the HT group and 16.1 months in the control group.

The HT and control groups were evenly matched for smoking history with 50% never smokers, 40% former smok-

ers, and 10% current smokers. But when the data on NSCLC deaths were analyzed by tobacco use, the risk was higher in current smokers and considerably higher in smokers also taking HT.

Of the 67 NSCLC deaths in the HT group, 27 occurred in 800 current smokers. The other deaths included 9 in 4,178 never smokers and 29 in 3,362 former smokers. Of the 39 NSCLC deaths in the control group, 19 occurred in 838 current smokers. The other 20 deaths occurred in 5 of 3,999 never smokers and in 15 of 3,157 past smokers.

Dr. Chlebowski said in an interview that a prospective randomized trial of women on current regimens would be preferable, but that study would be large and costly and therefore unlikely.

Dr. Chlebowski is a consultant for numerous pharmaceutical companies, none relevant to the WHI analysis. ■

To see an interview with Dr. Chlebowski, visit www.youtube.com/user/ClinicalEndoNews.

No Link Seen Between PCOS and Fetal Growth, Androgen Levels

BY JEFF EVANS

WASHINGTON — Female infants born to women with polycystic ovary syndrome do not appear to have high levels of androgens or to be small for gestational age, according to the results of a prospective, case-control study.

In fact, offspring born to mothers with polycystic ovary syndrome (PCOS) were more likely than were controls to be large for gestational age, according to the study.

Findings from clinical and animal-based studies suggest that PCOS may originate during fetal development. Prenatal exposure to androgens has been shown to induce a PCOS phenotype in sheep, monkeys, and rats. In humans, retrospective studies have shown that girls with PCOS features and premature menarche had been significantly small for their gestational age, according to Helen Anderson of the division of endocrinology, metabolism, and molecular medicine at Northwestern University, Chicago.

To determine if the intrauterine environment of women with PCOS alters fetal growth and androgen levels, Ms. Anderson and her associates compared singleton pregnancies in 39 women with PCOS and 31 healthy controls. The participants were non-His-

panic white women who met National Institute of Child Health and Human Development criteria for PCOS. None of the participants had a history of gestational diabetes, preexisting medical conditions, or complications during pregnancy.

Compared with healthy con-



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MS. ANDERSON

controls, a larger percentage of women with PCOS were nulliparous (64% vs. 39%) or had undergone ovulation induction or in vitro fertilization (77% vs. 6%). Women with PCOS were slightly, but significantly, younger than were the healthy control women (30 years vs. 32 years). Although PCOS women had a slightly higher mean body mass index than did controls, they had comparable maternal weight gains.

The birth cohort consisted of more females (43) than males (27) because the investigators were primarily interested in female offspring, and they excluded women known to be carrying a male fetus.

Overall, the gestational age and birth weight of infants did not differ between women with and

without PCOS. However, when Ms. Anderson and her colleagues stratified the analysis according to size at gestational age, a significantly greater proportion of the infants born to women with PCOS were large for gestational age compared with healthy controls (23% vs. 3%).

"This may be secondary to the increased nutritional flow across the placenta," as elevated levels of insulin and glucose have been demonstrated in pregnant women with PCOS, Ms. Anderson said at the annual meeting of the Endocrine Society.

Analyses of the steroid hormones in whole (mixed arterial and venous) cord blood showed that the female offspring of PCOS women had significantly lower levels of androstenedione and estradiol.

However, female offspring had no differences in levels of testosterone, dihydrotestosterone, and dehydroepiandrosterone, although Ms. Anderson said that many of the testosterone and dihydrotestosterone values were at the low end of detectability for the assays.

Female offspring from either group of women showed no differences in levels of 17-hydroxyprogesterone or in the ratio of testosterone to estradiol levels.

The National Institutes of Health funded the study. Ms. Anderson reported having no conflicts of interest to disclose. ■

OC/Metformin Combo Improves Lipids in PCOS

BY JOYCE FRIEDEN

WASHINGTON — A combination of metformin and the oral contraceptive Ortho Tri-Cyclen improves lipid profiles more than does an oral contraceptive alone in patients with polycystic ovary syndrome, according to preliminary data from a small pilot study.

"Insulin resistance with compensatory hyperinsulinemia plays a critical role in PCOS," Dr. Paulina Essah said at the annual meeting of the Androgen Excess and PCOS Society. "Traditionally, oral contraceptives have been the treatment for PCOS, but oral contraceptives may worsen or have no effect on insulin sensitivity. There are also very little data on the effects of the combination of metformin and oral contraceptives on insulin resistance and cardiovascular risk," said Dr. Essah of the division of endocrinology and metabolism at Virginia Commonwealth University, Richmond.

In this randomized, double-blind, placebo-controlled study, Dr. Essah and colleagues assigned 17 women with PCOS to an oral contraceptive plus 500 mg of metformin three times daily or an oral con-

traceptive plus a placebo three times daily. Ortho Tri-Cyclen (ethinyl estradiol 35 mcg/norgestimate 0.25 mg) was chosen because it is commonly used in the United States, Dr. Essah said.

All subjects underwent 2-hour oral glucose tolerance testing, frequently sampled intravenous glucose tolerance testing, and brachial artery flow-mediated dilatation at baseline and after 3 months. The subjects' mean age was 24.9, and their mean body mass index was 33.7.

After 3 months, the researchers found no difference between the two groups in weight, BMI, fasting insulin, or fasting glucose measurements. However, the combination oral contraceptive-metformin group experienced a trend toward higher HDL cholesterol (55.6 vs. 47.6 mg/dL) and lower triglyceride levels (86.8 vs. 152.7 mg/dL) compared with the group that took oral contraceptives alone. The combination group also demonstrated a significant increase in acute insulin response to glucose.

The study was funded by the National Institutes of Health. Dr. Essah said she had no financial conflicts of interest. ■