Estrogen plus progestin use linked with increased breast cancer incidence and mortality

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Estrogen plus progestin use is linked with increased breast cancer incidence. In addition, prognosis is similar for both users and nonusers of combined hormone therapy, suggesting that mortality from breast cancer may be higher for hormone therapy users as well, according to a study published March 29 in the *Journal of the National Cancer Institute*.

In the Women's Health Initiative (WHI) randomized trial, estrogen plus progestin was associated with an increase in both breast cancer incidence and mortality. However, most observational studies have linked estrogen plus progestin with more positive outcomes.

In order to determine the differences between the WHI trial and other observational studies, Rowan T. Chlebowski, M.D., Ph.D., Los Angeles Biomedical Research Institute (LA BioMed) lead researcher and colleagues, looked at postmenopausal women with no prior hysterectomy with negative mammograms within two years who were either users or non-users of estrogen and progestin combined therapy.

The researchers found that breast cancer incidence was higher in estrogen plus progestin users than incidence in nonusers. Women who started hormone therapy closer to menopause had a higher breast cancer risk with a weakening influence as the time from menopause increased.

"Because survival after breast cancer diagnosis did not differ between
estrogen plus progestin users and nonusers, the higher breast cancer incidence of those using estrogen plus progestin may lead to increased breast cancer mortality on a population basis," the authors write.

In an accompanying editorial, Catherine Schairer, Ph.D., and Louise A. Brinton, Ph.D., both of the National Cancer Institute, write that questions remain about whether the data analyzed from the WHI observational study resolves the differences in tumor prognosis and tumor characteristics when compared to the WHI randomized trial. They write that, "In general, tumors in estrogen plus progestin users in the WHI Observational Study were not significantly different from those in non-hormone users with regard to number of positive lymph nodes or tumor size, but were more likely to be well differentiated and positive for hormone receptors, findings which are similar to other observational studies." This, however, did not translate into a survival benefit. They recommend further analyses in this and other datasets of currency and duration of hormone use in relationship to tumor development to fully resolve the issue of tumor characteristics associated with estrogen plus progestin therapy.

**Author of new breast cancer study comments on its findings of increased risk**

Dr. Rowan Chlebowski, MD, PhD, Los Angeles Biomedical Research Institute lead researcher and author of a study released March 29 by the Journal of the National Cancer Institute, issued the following statement regarding the latest findings from the Women's Health Initiative, the largest-ever study of hormonal therapy in post-menopausal women.

The study Dr. Chlebowski authored reported that estrogen plus progestin use is linked with increased breast cancer incidence. In addition, it said the prognosis is similar for both users and nonusers of combined hormone therapy, suggesting that mortality from breast cancer may be
higher for hormone therapy users as well.

"This study shows that women who begin the hormonal therapy of estrogen plus progestin closer to menopause are at greater risk of breast cancer than those who started the therapy earlier. Because menopause usually is the reason for women to undergo hormonal therapy, this is a very significant finding.

"The study also showed that all categories of breast cancer are increased - not just those with favorable prognosis - among women using estrogen plus progestin. This finding suggests higher mortality from breast cancer among women who use this combined hormonal therapy. As always, women should consult with their physicians and consider the potential risks of any hormonal therapy to help relieve the symptoms of menopause."

More information: DOI:10.1093/jnci/djt043

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