

CORRESPONDENCE



Breast Cancer and Hormonal Therapy in Postmenopausal Women

TO THE EDITOR: In their article on the Women's Health Initiative (WHI) study of combined hormone therapy, Chlebowski et al. (Feb. 5 issue)¹ describe a marked decrease in the risk of breast cancer after the discontinuation of menopausal treatment. Using a similar approach, we investigated whether a decrease in risk was also seen in the French E3N cohort, in which the use of hormone therapy was self-reported biennially.² Among postmenopausal respondents to the 1997–1998 questionnaire, women receiving combined hormone therapy and those who had never received hormone therapy were followed from January 1999 to the date of diagnosis of any cancer, the last completed questionnaire, or July 2005, whichever occurred first. Hazard ratios for breast cancer among women who received combined hormone therapy, as compared with those who had never received such therapy (in the 1997–1998 period), dropped toward unity after 2002, in parallel with an important reduction in the use of hormone therapy (see Table 1 in the Supplementary Appendix, available with the full text

of this letter at NEJM.org). Our results in a French population corroborate the findings of the WHI study.³

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1. Chlebowski RT, Kuller LH, Prentice RL, et al. Breast cancer after use of estrogen plus progestin in postmenopausal women. *N Engl J Med* 2009;360:573-87.

2. Fournier A, Berrino F, Clavel-Chapelon F. Unequal risks for breast cancer associated with different hormone replacement therapies: results from the E3N cohort study. *Breast Cancer Res Treat* 2008;107:103-11. [Erratum, *Breast Cancer Res Treat* 2008; 107:307-8.]

3. Ringa V, Fournier A. Did the decrease in use of menopausal hormone therapy induce a decrease in the incidence of breast cancer in France (and elsewhere)? *Rev Epidemiol Sante Publique* 2008;56:297-301. (In French.)

THE AUTHORS REPLY: We concur with Fournier and colleagues that their year-to-year results regarding the incidence of breast cancer in the French E3N cohort are similar to our findings in the WHI observational study. Their results support the hypothesis that the recent reduction in the incidence of breast cancer in several countries is related to a decrease in the use of combined hormone therapy. In the two cohorts, the hazard ratios were similar (approximately 2) for breast cancer among women who had received estrogen plus progestin for longer intervals. For women who continued to receive combined hormone therapy for longer than about 5 years, the annual risk of breast cancer was doubled with each subsequent year. These results have implications for women who are already receiving combined hormone ther-

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apy: there are benefits to stopping and risks to continuing with respect to breast cancer.

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Endocrine Therapy plus Zoledronic Acid in Premenopausal Breast Cancer

TO THE EDITOR: Gnant et al. (Feb. 12 issue)¹ report on the Austrian Breast and Colorectal Cancer Study Group trial 12 (ABCSG-12) (ClinicalTrials.gov number, NCT00295646), which looked at the use of goserelin plus either tamoxifen or anastrozole with or without zoledronic acid in premenopausal women with breast cancer. The authors conclude that the addition of zoledronic acid improved disease-free survival and that treatment with tamoxifen and treatment with anastrozole were associated with similar rates of disease-free survival. However, a separate analysis of the group of patients who received anastrozole without zoledronic acid would be of interest.

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1. Gnant M, Mlineritsch B, Schippinger W, et al. Endocrine therapy plus zoledronic acid in premenopausal breast cancer. *N Engl J Med* 2009;360:679-91.

TO THE EDITOR: Gnant et al. report a 4-year rate of 90.8% for disease-free survival in the group of premenopausal women with breast cancer who received endocrine therapy alone and a rate of 94.0% in the group that received endocrine therapy plus zoledronic acid. Data from this trial that were presented at the American Society of Clinical Oncology meeting in 2008 showed that the effect of zoledronic acid was driven almost exclusively by the findings in the cohort of patients who received anastrozole, whereas little effect was discernible for the patients who received tamoxifen. With only 137 events contributing to these analyses, the test for interaction comparing the effectiveness of zoledronic acid between the anastrozole group and the tamoxifen group is expected

to be nonsignificant. What was the effect of zoledronic acid on the anastrozole and tamoxifen groups?

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TO THE EDITOR: Gnant et al. describe the results of the combination of tamoxifen plus goserelin; however, this combined therapy is not a standard option for the typical premenopausal patient with breast cancer enrolled in this study. In most centers, outside the context of a clinical trial, such patients would be offered 5 years of tamoxifen plus or minus chemotherapy,¹ with the possible addition of ovarian ablation for women under the age of 35 years who did not have chemotherapy-induced amenorrhea.^{2,3} The combination of ovarian suppression and tamoxifen is being prospectively addressed in the Suppression of Ovarian Function Trial (SOFT) (ClinicalTrials.gov number, NCT00066690). In addition, the duration of the tamoxifen exposure (3 years) cannot be considered a standard, level I, evidence-based form of adjuvant hormonal therapy.

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1. Goldhirsch A, Wood WC, Gelber RD, Coates AS, Thürlimann B, Senn HJ. Progress and promise: highlights of the international