Delayed Adjuvant Tamoxifen in Postmenopausal Women With Axillary Node-Negative Breast Cancer: Mortality Over 10 Years

Since data on the disease-specific effects of tamoxifen have developed over the past 20 years, from trials that demonstrate a favorable impact in most subgroups given adjuvant tamoxifen therapy (1), and further to the most recent large National Surgical Adjuvant Breast and Bowel Project (NSABP) prevention trial that demonstrates a disease incidence-reducing effect of tamoxifen in women at increased risk for breast cancer (2), concerns about other tissue-specific effects of tamoxifen and effects on overall mortality have grown.

In 1986, we began the Wisconsin Tamoxifen Study to investigate the biologic effects of tamoxifen on lipids, lipoproteins, and bone mineral density (3,4). Women recruited to this placebo-controlled randomized study could be as much as 10 years from diagnoses of axillary node-negative invasive breast cancer, and thus long-term follow-up of these patients will provide data on the impact of delayed adjuvant tamoxifen therapy, clinical events, causes of death, and mortality, which we now report in this correspondence.

After 5 years and again after 10 years, all participating women known to be alive were re-contacted under new, approved protocols. Kaplan–Meier methods were used to describe disease-free and overall survival (see Fig. 1).

The two randomized groups, each containing 70 women, were comparable on several descriptive measures: age (mean age at entry on study = 58.4 years; range = 46–64 years), body mass, amount of exercise per week, percentage smokers, primary breast cancer size, years since breast cancer diagnosis (mean = 7–8 years) (3,4), and primary tumor estrogen and progesterone hormone-receptor status.

Beyond the initial 2 years of the study, the use of tamoxifen in the two groups was comparable. A total of 14 fractures had occurred in women in the placebo group and 12 fractures had occurred in the tamoxifen group (hip, one each; wrist, four and five for the placebo and tamoxifen groups, respectively). There were three deaths in the tamoxifen group and 11 deaths in the placebo group (in the tamoxifen group, one death occurred from breast cancer and two deaths occurred from second primary cancer; in the placebo group, four deaths occurred from breast cancer, one from sudden death, one from stroke, three from second primary cancer, and two from other causes).
One previous specific study of delayed adjuvant tamoxifen therapy has been reported (5,6); a statistically significant increase in disease-free survival but not in overall survival was found. In the updated meta-analysis of tamoxifen adjuvant therapy trials, mortality from breast cancer was less with therapy of longer duration up to 5 years, and increased mortality from endometrial cancer (with a low absolute rate) and non-statistically significant death rate differences (tamoxifen versus no tamoxifen) from nine other causes (for each cause, for cardiovascular causes, and for all causes combined) were found (1). These observations, combined with the observation of major reduction in mortality associated with adjuvant tamoxifen begun promptly after diagnosis, suggest that a major long-term benefit of delayed adjuvant tamoxifen is likely and that this benefit is due to a decreased risk of death from breast cancer.

Our study is small, but it adds to the direct (5,6) and indirect data (1) in support of late adjuvant tamoxifen therapy, particularly in postmenopausal women.

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REFERENCES


NOTES

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