But Drugs Not Widely Used

Tamoxifen *from page 1*

love for that part of my job to go away. These data are a step in that direction" said Dr. Wickerham, chief of the cancer genetics and prevention section at Allegheny General Hospital in Pittsburgh.

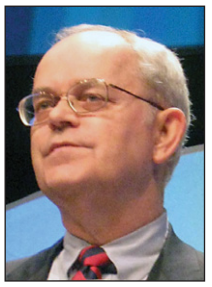
The randomized, double-blind federally funded STAR trial included women at least 35 years of age with a 5-year predicted breast cancer risk of at least 1.66% (based on a modified version of the Gail model). Researchers from the NSABP randomized 19,747 women to receive either tamoxifen or raloxifene (JAMA 2006;295:2742-51).

The update includes 19,490 women—9,736 on tamoxifen and 9,754 on raloxifene. The differences in numbers are due to a combination of loss during follow-up or follow-up data becoming available for women who were lost to follow-up in the original report. Women on tamoxifen received 20 mg/day and those on raloxifene received 60 mg/day.

At an average follow-up of 8 years, the relative risk of invasive breast cancer on raloxifene compared with tamoxifen was 1.24, which was significant. Both drugs reduced the risk of invasive breast cancer by roughly 50% in the original report (median follow-up, 47 months).

In this analysis, "we have estimated, however, that this difference in the raloxifene-treated group represents 76% of tamoxifen's chemopreventive benefit, which translates into a 38% reduction in invasive breast cancers," he said.

In the 2006 report, raloxifene (81 events) did not appear to be as effective as tamoxifen (57 events) in preventing noninvasive breast cancer. "Now with additional follow-up, those differences have narrowed," he said. At 8 years, there was no statistical significance between the two groups with a risk ratio of 1.22. The relative risk of 1.22 favors tamoxifen, but raloxifene preserves 78% of the chemopreventive benefit of tamoxifen.



'The important message is that [both] drugs are options.'

DR. WICKERHAM

This translates to raloxifene's preventing 39% of noninvasive breast cancers.

Raloxifene maintained its toxicity advantage. The relative risk of uterine cancers with raloxifene vs. tamoxifen was 0.55.

In addition, there were twice as many hysterectomies for benign disease in the tamoxifen group. This was due in part to an 80% increase in hyperplasia of the endometrium that occurred in women on tamoxifen, said Dr. Wickerham.

Both drugs increase the risk of thromboembolic complications, but there were significantly fewer of these events in women on raloxifene (154), compared with tamoxifen (202). ■

Disclosures: *The study was supported by the National Cancer Institute. Dr. Wickerham reported that he has consulted for Eli Lilly.*

MY TAKE

The News Is Good; We Need to Get the Word Out

The results of this simple but elegant trial inform our selection of breast cancer chemopreventive agents by confirming the findings of the BCPT (Breast Cancer Prevention Trial), which demonstrated the efficacy of tamoxifen in preventing cancer at a relatively minimal cost of adverse events. It also demonstrates comparable results with raloxifene.

The mature results of the STAR trial presented at this meeting demonstrate the durability of the therapeutic benefit and the long-term safety of these two agents, and clarify some of the differences and similarities. Despite these compelling results, selective estrogen receptor modulators (SERMs) remain largely underutilized for prevention purposes. So the challenge today is how to communicate to the public to enhance the utilization of SERMs and reduce further the incidence of breast cancer.

There is minimal use of these two drugs by women at risk for breast cancer. In clinical practice, data suggest that only 5%-20% of women who were eligible for these randomized trials agreed to take a SERM for risk reduction. Based on recent reports, this number has only declined.

The picture is similar for raloxifene, with use starting to fall after the release of data regarding toxicity of hormone replacement therapy from the Women's Health Initiative study. The use of raloxifene has continued to fall, in part because of the growing use of bisphosphonates for osteoporosis. Raloxifene has also likely suffered from association with tamoxifen, which is perceived by the public as a toxic cancer drug.

I have to ask, why aren't the results of the BCPT and STAR trials more vigorously applied in clinical practice?

Concerns about adverse events have largely been exaggerated in the public eye by the media. Admittedly, there are also concerns in some quarters about risk prediction models, which only modestly enrich populations for chemoprevention.

There has also been insufficient education of physicians and the public about these drugs. The randomized trials were primarily performed by oncologists, but the application of SERM prevention falls largely on the primary care community, which cares for patients at risk for breast cancer. One would think that instead of neglecting to use both agents, candidates for risk reduction would be pleased to have two good options. There are very good reasons to use these two drugs for cancer prevention. The magnitude of risk reduction with tamoxifen and raloxifene is major—larger than those for many other prevention strategies. In fact, the only intervention of greater preventive efficacy in breast cancer is bilateral prophylactic mastectomy. In addition, the safety profiles of these two agents are excellent. Millions of women have taken tamoxifen over the past 3 decades; hundreds of thousands have taken raloxifene over the past 12 years.

There is no perfect drug. Certainly in other areas of preventive medicine, there seems to be greater tolerance for adverse effects for effective preventive interventions. For example, drugs used to treat hypertension and lower cholesterol, both markers of coronary artery disease, have more adverse effects—and more serious ones—than SERMs do. Yet millions of men and women take these drugs daily and for a lifetime.

For a practicing medical oncologist, the adverse effects of SERMs pale in comparison to the complications of and disability caused by breast cancer and the hundreds of thousands of women who die each year worldwide as a result of advanced breast cancer.

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Aspirin Use May Boost Survival After Breast Cancer

BY DOUG BRUNK

Aspirin use after the diagnosis of stage I-III breast cancer was associated with a decreased risk of breast cancer death and distant recurrence, results from the ongoing Nurses' Health Study demonstrated.

The study is believed to be the first to report a survival advantage among women with breast cancer who take aspirin.

"If confirmed, our results may broaden the scope of interventions available to reduce breast cancer–related death and mortality," researchers led by Dr. Michelle D. Holmes of at Harvard Medical School and Harvard School of Public Health, Boston, reported.

They emphasized that the results "may be generalizable only to longer term breast cancer survivors," described as those who have lived long enough after diagnosis to report aspirin use after diagnosis (about 4 years). "Fortunately, almost 90% of women diagnosed with breast cancer live at least 5 years. Thus, our findings have considerable clinical importance."

VITALS

Major Finding: Aspirin use after the diagnosis of stage I-III breast cancer was associated with a multivariate adjusted relative risk of breast cancer death of 1.07 among those who used aspirin 1 day per week, 0.29 for those who used aspirin 2-5 days per week, and 0.36 for those who used aspirin 6-7 days per week.

Data Source: Responses from 4,164 female RNs in the Nurses' Health Study who were diagnosed with stage I-III breast cancer between 1976 and 2002. The women were observed until June 2006 or until they died, whichever came first.

Disclosures: Supported by a grant from the National Institutes of Health. The researchers indicated they had no conflicts of interest.

For the study, the researchers drew from questionnaires to evaluate aspirin use among 4,164 female registered nurses in the Nurses' Health Study who were diagnosed with stage I, II, or III breast cancer between 1976 and 2002, and who were observed until they died or until June 2006, whichever came first (J. Clin. Oncol. 2010 Feb. 16 [doi:10.1200/JCO.2009.22.7918]). The primary outcome measured was breast cancer mortality risk according to the number of days per week of aspirin use, categorized as 0, 1, 2-5, or 6-7 days.

Dr. Holmes and her associates reported that 314 deaths attributed to breast cancer and 400 distant recurrences occurred during the study period. Compared with women who never used aspirin, the multivariate adjusted relative risk of breast cancer death was 1.07 among those who used aspirin 1 day per week, 0.29 for those who used aspirin 2-5 days per week, and 0.36 for those who used aspirin 6-7 days per week. "Results did not differ appreciably when stratified by stage, [body mass index], menopausal status, or [estrogen receptor] status."

Aspirin use had a similar impact on distant recurrence of cancer. Compared with women who never used aspirin, the multivariate adjusted relative risk of distant recurrence was 0.91 among those who used aspirin 1 day per week, 0.40 for those who used aspirin 2-5 days per week, and 0.57 for those who used aspirin 6-7 days per week. ■