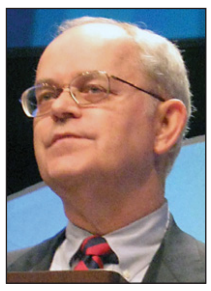
Tamoxifen, Raloxifene Upheld for Prevention

BY KERRI WACHTER

WASHINGTON — Tamoxifen and raloxifene offer women at high risk of developing breast cancer two effective options to prevent the disease, based on 8 years of follow-up data for more than 19,000 women in the STAR trial.

While tamoxifen proved significantly more effective in preventing invasive breast cancer, there was no significant difference between the two drugs in preventing noninvasive breast cancer. And raloxifene (Evista) had significantly less toxicity, including endometrial cancer, thromboembolic complications, and cataracts.

"These data are good news for postmenopausal women who want to reduce their risk of breast cancer," said Dr. D. Lawrence Wickerham, associate chairman of the National Surgical Adjuvant Breast and Bowel Project (NSABP). "The important message is that both [drugs] are options. The decision is a shared one between the patient and her physician."



'These data are good news for postmenopausal women who want to reduce their risk of breast cancer.'

DR. WICKERHAM

Dr. Wickerham presented the latest results for the Study of Tamoxifen and Raloxifene (STAR) trial during a late-breaker session at the annual meeting of the American Association for Cancer Research. The results were also published in the journal Cancer Prevention Research (April 19, 2010; doi: 10.1158/1940-6207.CAPR-10-0076).

Oncologists at the meeting expressed frustration that more women at high risk are not on the drugs, given the proven efficacy of the two selective estrogen receptor modulators (SERMs) in preventing breast cancer.

"I have to ask, why aren't the results of the BCPT [breast cancer prevention trial] and STAR trials more vigorously applied in clinical practice?" said Dr. Gabriel N. Hortobagyi, who was the discussant.

Dr. Wickerham echoed this frustration during a press conference. "I see women each week, at a high risk of breast cancer, and I will end up telling one or two of them…all too often…that they have breast cancer. I'd 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 ($P = .01$). Both drugs reduced the risk of invasive breast cancer by roughly 50% in the original report (median follow-up 47 months).

"We have estimated, however, that this difference in the raloxifene-treated group represents 76% of tamoxifen's chemopreventative benefit, which translates into at 38% reduction in invasive breast cancers," Dr. Wickerham said.

In the 2006 report, raloxifene (81 events) did not appear to be as effective as tamoxifen (57 events) in preventing noninvasive breast cancer ($P = .052$). "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 ($P = .12$). The relative risk of 1.22 favors tamoxifen, but raloxifene preserves 78% of the chemopreventative benefit of tamoxifen. This

translates to raloxifene preventing 39% of noninvasive breast cancers.

Raloxifene maintained its toxicity advantage. The relative risk of uterine cancers with raloxifene vs. tamoxifen was 0.55. There also 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, Dr. Wickerham said.

Both drugs increase the risk of thromboembolic complications, but there were significantly fewer ($P = .007$) of these events in women on raloxifene (154), compared with tamoxifen (202).

Dr. Hortobagyi, director of the breast cancer research program at the University of Texas M.D. Anderson Cancer Center in Houston, identified factors that may be responsible for limited use of tamoxifen and raloxifene for prevention. He cited misinformation about the drugs, fears about toxicities, limited high-risk prediction tools, lack of a marker or measurement to monitor for risk reduction, cost, and insufficient public and professional education about the drugs.

'The challenge today is how to communicate to the public to enhance the utilization of SERMs.'

DR. HORTOBAGYI

"There is no perfect drug. Certainly in other areas of preventive medicine, there seems to be greater tolerance for adverse effects for effective preventative interventions," he said, noting discrepancy between what is considered acceptable risk for other preventative drugs and SERMs. For example, drugs used to prevent hypertension and coronary artery disease have more and more serious adverse events than SERMs, he said.

"The challenge today is how to communicate to the public to enhance the utilization of SERMs and reduce further the incidence of breast cancer," he said. ■

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