Most At-Risk Women Ineligible for Tamoxifen

BY SHARON WORCESTER
Tallahassee Bureau

Tamoxifen probably won't prevent many cases of breast cancer in women at risk for the disease because most are ineligible for treatment and those most likely to be eligible are the least likely to develop cancer, according to Carmen L. Lewis, M.D., of the University of North Carolina at Chapel Hill and colleagues.

Of 605 women studied, more than 90% of those found to be at risk for developing breast cancer (based on their responses to a questionnaire about their health and family history) would be ruled out for chemoprevention with tamoxifen due to the risk of adverse events such as blood clots and stroke associated with the drug, the investigators found.

Using the Gail model, they estimated that the percentage of white women in the study with an increased 5-year breast cancer risk (defined as a risk of at least 1.66%) was 9% among those in their 40s, 24% among those in their 50s, and 53% of those in their 60s. Among black women, 3% of those in their 40s, 7% of those in their 50s, and 13% of those in their 60s had this level of risk.

In a hypothetical cohort of 10,000 women similar to those in the study (calculations were made only for white women due to the small number of black women in the study) only 7% of those in their 40s, 6% of those in their 50s, and 10% of those in their 60s met the requirement for discussions about tamoxifen. It is recommended that discussion about chemoprevention take place only with those who have a high potential of benefit and a low potential of harm from using tamoxifen. Those with conditions, such as high blood pressure and diabetes, would be excluded from such discussions because of the increased risk of adverse effects.

With the same hypothetical cohort, and if it is assumed tamoxifen would result in a 49% reduction in the number of invasive breast cancers in high-risk women as demonstrated in the 1998 placebo-controlled National Surgical Adjuvant Breast and Bowel Project (NSABP) Breast Cancer Prevention Trial , a maximum of only 6%-8% of invasive cancers would be prevented (Arch. Intern. Med. 2004;164:1897-1903).

This is likely an inflated figure because it is based on the assumption that 100% of eligible women would use tamoxifen; studies have shown that 24%-40% of such women discontinue treatment, they noted.

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The study, which was sponsored by the National Cancer Institute, doesn't question the drug's ability to prevent breast cancer, but does illustrate the limitations of its use for women in different age groups. For women in their 40s, the overall effect of chemoprevention is likely to be small because the proportion of breast cancers occurring in those with increased risk in this age group is small. For those in their 50s and 60s, the potentially larger number of women with increased risk for breast cancer who could benefit from chemoprevention is reduced by the increased number with a substantial likelihood of adverse effects associated with tamoxifen, the investigators explained.

The findings underscore the need for proper identification of chemoprevention candidates and for studies on how to improve the efficacy—and reduce the side effects—of chemopreventive drugs, Larry Wickerham, M.D., said in an interview.

Dr. Wickerham of the NSABP was an investigator and served as the protocol officer on the Breast Cancer Prevention Trial, which established the efficacy of tamoxifen for preventing invasive breast cancer in high-risk women.

For those who can benefit from chemoprevention with tamoxifen, the benefit is "real and impressive," Dr. Wickerham said, stressing that the findings of the University of North Carolina study don't contradict those of the Breast Cancer Prevention Trial.

"The take-home message isn't to throw out tamoxifen—it's that clinicians should become familiar with how to identify women who can benefit from this drug," he said. ■