EDITORIAL

Breast Cancer Chemoprevention: The Saga of Underuse Continues

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The American Cancer Society estimates that there will be 232,670 Americans diagnosed with invasive breast cancer this year (1). Several large, well-conducted studies provide Level I evidence that therapies are available to reduce that figure, but they have thus far been underutilized (2).

In this issue of the Journal, Nichols et al. (3) report on the use of tamoxifen among 50,884 women who entered the Sister Study, all of whom were required to have at least one sister diagnosed with breast cancer. Only 1046 reported ever taking tamoxifen for breast cancer chemoprevention. In the substudy of those who did, there were only three women (under age 50 years) who showed no evidence of net benefit.

Although current chemoprevention options are not perfect, there are women who could benefit now and avoid the diagnosis of breast cancer.

In 1999, Gail et al. demonstrated a net benefit and no increase in the risks of either endometrial cancer or clotting in all premenopausal women with a five-year risk of breast cancer greater than 1.67% (4).

It is of note that 25 women with lobular carcinoma in situ (LCIS) were excluded in the Nichols et al. report (3). Because they have a defined histological abnormality and their risk of developing breast cancer is very high, women with LCIS or atypical hyperplasia are likely to adhere to using chemoprevention (5).

Adherence rates to selective estrogen receptor modulator (SERM) therapy were high in both the STAR trial (6) and the Breast Cancer Prevention Trial (7) because of: 1) a defined visit schedule, 2) written risk/benefit information given to all patients prior to enrollment, and 3) both patient and provider education given on a continuing basis during the conduct of the studies.

It is not surprising that nearly half of the women in the Sister Study discontinued use of tamoxifen at 4.5 years. This is to be expected when no systematic efforts are made to maintain adherence to prolonged chemoprevention therapy.

Freedman et al. (8) reported that African American women were less likely to have a favorable risk-benefit profile. Nichols et al. (3) found a lower risk of developing breast cancer in both African American and Hispanic women in this study and report that they derive less net benefit from tamoxifen use. Women with a history of hysterectomy (who make up 40% of the adult female population in the United States) were also found to derive a greater benefit from tamoxifen (odds ratio = 11.8) in the Nichols et al. study (3).

As Nichols and her colleagues note (3), “Until alternative therapies for premenopausal women become available, tamoxifen will continue to have an important role in breast cancer primary prevention.” The American Society of Clinical Oncology has recommended that “in women at increased risk of breast cancer age 35 or older, tamoxifen (20 mg per day for 5 years) should be discussed as an option to reduce the risk of estrogen receptor–positive breast cancer. In postmenopausal women, raloxifene (60 mg per day for 5 years) and exemestane (25 mg per day for 5 years) should also be discussed as options for breast cancer risk reduction” (9).

The important clinical challenge is to identify those women at highest risk and to offer tamoxifen only to those who have either had hysterectomy or to those who are at higher levels of risk. Most of these women will derive greater benefit from using tamoxifen. Raloxifene offers greater safety for postmenopausal women, the benefit ratio of which is related to the level of breast cancer risk, as it is for tamoxifen.

While we wait for further advances in this field, there are women who could obtain substantial benefit from the established options in breast cancer chemoprevention. What actions could be considered to increase the number of women offered the opportunity to receive today’s therapy?

1. The majority of the large breast cancer prevention trials were supported by the National Cancer Institute (NCI), which should take a lead role in supporting and developing a sustained program to promote breast cancer chemoprevention directed at both medical professionals and the general public.

2. As noted, various professional organizations and societies have developed guidelines and position papers relevant to breast cancer chemoprevention. These resources can aid in incorporating training on the topic into residency and fellowship curricula so that the next generation of health care providers are able and willing to identify and treat the
proper candidates for chemoprevention. At the moment, oncologists are familiar with the disease and the current chemoprevention options. The tables in Freedman et al., for example, can help both physicians and patients summarize the benefits and risks of tamoxifen and raloxifene for chemoprevention (8). Although most oncologists do not routinely see “at risk” patients, this may be a “Field of Dreams” moment for preventive oncology; that is, build it and they will come.

3. Additionally, the breast cancer advocacy community could take an even more active role in supporting and promoting breast cancer chemoprevention education for patients and the general public. Advocates could provide a powerful voice in promoting the discussion leading to increased utilization of chemoprevention and a decrease in breast cancer incidence.

**Funding**

The work was supported by grants U10-CA-12027, U10-CA-69651, U10-CA-37377, U10-CA-69974, and U10-CA-44066 from the National Cancer Institute, Department of Health and Human Services, Public Health Service. Eli Lilly and Company; Zeneca Pharmaceuticals, a business unit of ZENECA Inc.

**Note**

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**References**