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Chemoprevention of Breast Cancer

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Breast cancer remains a major public health problem in the United States. An estimated 215,990 women are diagnosed annually with breast cancer, and 40,580 women die from the disease each year (American Cancer Society, 2004). Efforts to improve screening technology and participation in screening continue, and options for the chemoprevention of breast cancer now are available. Oncology nurses often encounter women without a diagnosis of cancer who have questions about the usefulness and safety of chemoprevention agents, including tamoxifen and raloxifene. Currently, three organizations have published formal guidelines about the use of these agents: the American Society of Clinical Oncology (ASCO), the U.S. Preventive Services Task Force (USPSTF), and the Canadian Breast Cancer Initiative (CBCI) (Chlebowski et al., 2002; Levine, Moutquin, Walton, & Feightner, 2001; USPSTF, 2002). Table 1 provides a comparison of the recommendations.

Assessment of Risk

Each of the guidelines is based on accurate assessment of breast cancer risk. Known risk factors for breast cancer are shown in Figure 1. These factors should be summarized and interpreted to women at risk, so that they can understand the magnitude of their risk. Most of the work performed with chemoprevention of breast cancer also has incorporated the Gail model of risk for developing breast cancer (National Cancer Institute, 2001). It can be accessed at http://cancer.gov/bcrisktool or by calling 800-4CANCER.

The Gail model was derived from a sample of women who were undergoing regular mammography as part of the Breast Cancer Detection Demonstration Project (Gail et al., 1989). Subsequently, the Gail model was used to estimate cancer risk for the National Surgical Adjuvant Breast and Bowel Project (NSABP) and has been revised (Costantino et al., 1999). In a validation study, Spiegelman, Colditz, Hunter, and Hertzmark (1994) noted that the Gail model overpredicted absolute breast cancer risk by 33% among women aged 25–61 who did not receive annual screening. The model provides a figure of absolute risk for developing breast cancer at the current age and in five years.

The Gail model excludes some wellknown predictors of hereditary breast cancer: family history of ovarian cancer, ages at which relatives were diagnosed with breast cancer, affected second-degree relatives, and paternal family history (see Figure 2). Because of these limitations, the model underestimates risk for those who have mutations in BRCA1 and BRCA2 and overestimates risk for women who have some family history but no mutation in BRCA1 and BRCA2. The Gail model is used most accurately in women with minimal to moderate family history. Women need to be educated about the benefits and limitations associated with the Gail model. Clinicians should be careful to use the model appropriately.

Chemoprevention Options

Once risk factor assessment is complete, women need education about the strengths and risks associated with the various chemoprevention agents. As shown in Table 1, ASCO, USPSTF, and CBCI have conflicting recommendations about when to use these agents. ASCO recommended that tamoxifen be offered to women with a Gail risk score of greater than 1.66%. The USPSTF and CBCI have recommended that women be educated about the option if they are at higher risk. At present, none of the agencies recommends raloxifene, aromatase inhibitors, or fenretinide (Chlebowski et al., 2002; Levine et al., 2001; USPSTF, 2002). Women need careful teaching to understand the risks and benefits associated with tamoxifen.

Tamoxifen

Healthcare providers should consider the risk for breast cancer and the risk for adverse events in women who are considering chemoprevention. These women usually are healthy, and serious and potentially life-threatening side effects may not be acceptable risks for otherwise healthy women. Tamoxifen appears to block the action of estrogen in the breast. It also appears to have estrogen-like effects on some other tissues, including the uterus and the bones. It is not a new drug. Currently, tamoxifen is the only agent approved by the U.S. Food and Drug Administration for breast cancer risk reduction.

Potential Benefits Associated With Tamoxifen Use

In the Breast Cancer Prevention Trial (BCPT), a large clinical trial conducted by the NSABP and funded by the National Cancer Institute, a group of women were selected because of their high risk for invasive breast cancer. Participating women were randomized to determine whether taking tamoxifen could lower their risk of getting breast cancer. This study of 13,338 women at risk for developing breast cancer showed a significant (42%) reduction in relative risk of developing breast cancer with tamoxifen use (Fisher et al., 1998). Over the course of the trial, 264 women were diagnosed with breast cancer (175 in the placebo group and 89 in the tamoxifen group). The absolute risk reduction

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