Breast Cancer Chemoprevention: A Review of Selective Estrogen Receptor Modulators

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Breast cancer is the most common cancer diagnosis among women in the United States. Chemoprevention plays an important role for women at high risk for developing breast cancer. The use of selective estrogen receptor modulators (SERMs) tamoxifen and raloxifene has demonstrated mixed results in breast cancer prevention clinical trials. In the United States, tamoxifen is approved for use for breast cancer prevention in women at high risk. The continued development of SERMs with improved side-effect profiles is needed. Oncology nurses play a pivotal role in helping patients to understand the current status of breast cancer prevention as well as the future direction of research.

The Physiology of Estrogen Effects on Breast Tissue

The development of breast cancer is complex, involving a multitude of factors. Discussing all factors involved in breast cancer development is beyond the scope of this article, but the influence of estrogen on breast tissue and the role of estrogen in breast cancer development will be highlighted.

Estrogens are steroid hormones that are produced in the ovaries, adrenal glands, and placenta during pregnancy. The hypothalamus secretes gonadotropin-releasing hormone (GnRH), which stimulates the anterior pituitary to release follicle-stimulating hormone (FSH) and luteinizing hormone (LH). FSH and LH act on the ovaries to produce estrogen in the form of estradiol and estrone. These estrogens bind with estrogen receptors in target tissues of the breast, uterus, brain, bone, liver, and heart. Estrogen receptors are molecules inside the cell to which only estrogens or closely related molecules can bind; however, not all cells contain receptors specific for estrogen. Once an estrogen has combined with a receptor in a cell, the shape of the receptor changes to combine with the DNA sites inside the target tissue. The DNA stimulates gene activation and production of RNA, which, in turn, stimulates the synthesis of protein. This protein produces changes in the cell according to tissue type and underlying conditions. The cycle is completed when high levels of estrogen in the blood may be at increased risk for breast cancer from prolonged exposure to estrogen such as with early menarche before age 12, first full-term pregnancy after age 30, late menopause after age 55, or recent long-term use of postmenopausal hormone replacement therapy (HRT) (American Cancer Society, 2003; Clemons & Goss, 2001) (see Figure 1). Women may be at increased risk for breast cancer from prolonged exposure to estrogen such as with early menarche before age 12, first full-term pregnancy after age 30, late menopause after age 55, or recent long-term use of postmenopausal hormone replacement therapy (HRT) (American Cancer Society, 2003; Clemons & Goss, 2001). Prolonged exposure to high levels of estrogen may cause changes in cell proliferation from normal growth to hyperplasia to neoplasia with DNA mutations and uncontrolled cell proliferation (Clemons & Goss, 2001) (see Figure 1). Women...