Editorial

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Osteoporosis treatment and breast cancer prevention: Two goals, one treatment?

For postmenopausal women with newly diagnosed osteoporosis, assessing the risk of breast cancer prior to prescribing a bone medicine could maximize the benefits of the selected treatment

CASE Active, healthy, osteoporotic, and at-risk for breast cancer

Your patient, a 58-year-old, G0 healthy and active woman underwent early menopause at 44 years. She recently had a bone mineral density test, results of which showed a T-score of –2.8 at the spine and –2.5 at the hip. She is taking vitamin D and calcium. She is an exceptionally active woman who plays tennis and walks more than 5 miles daily. Two years earlier, at age 56, she had abnormal mammography results, and a breast biopsy revealed atypical hyperplasia. Her mother has a history of Paget disease of the breast.

Prior to selecting a bone medicine to treat this woman's osteoporosis, should you assess her risk of breast cancer?

In this editorial, I make the argument that, yes, you should assess this patient's risk of breast cancer prior to selecting treatment for her osteoporosis, as her level of breast cancer risk can help determine the optimal osteoporosis therapy.

An expert panel convened by the American Society of Clinical Oncology noted that far too few American women are being assessed for their risk of breast cancer, and too few American women at increased risk for breast cancer are being offered pharmacologic preventive therapy.[1] One small step to increase the frequency of risk assessment and counseling regarding preventive therapy is to assess breast cancer risk in women with osteoporosis to help guide the selection of a bone medicine.

Options for osteoporosis treatment

Most experts recommend that menopausal women with osteoporosis (T-score ≤–2.5) should be offered a bone medicine in addition to the standard prescription therapy of vitamin D and calcium, exercise, and smoking cessation.

The most commonly prescribed bone medicines are **bisphosphonates, estrogen, and raloxifene.** Following the publication of the Women's Health Initiative (WHI) in 2002, the use of estrogen and raloxifene for the treatment of osteoporosis decreased significantly. Both the bisphosphonates and estrogen are believed to be slightly more effective at increasing bone density than raloxifene, but there are no direct head-to-head, large-scale fracture-reduction studies comparing these agents.[2] In one large retrospective database study, women taking alendronate or raloxifene were reported to have similar vertebral and nonvertebral fracture rates.[3]

Unlike the bisphosphonates and estrogen, raloxifene has been demonstrated to reduce the risk of breast cancer by about 50%. **For women with newly diagnosed osteoporosis and an above-average risk of developing breast cancer, raloxifene may represent an optimal pharmacologic intervention.** But, how would you know if your patient with newly diagnosed osteoporosis is at increased risk for breast cancer?

Assessing breast cancer risk

The Gail breast cancer risk assessment tool is often used in clinical practice to identify women who are at above-average risk for breast cancer (defined as a 5-year risk of developing breast cancer ≥1.66%).[4] For the patient described in the opening case, the Gail tool predicts that her 5-year risk of breast cancer is 6%, compared with 1.7% for a woman of the same age who is at average risk. In addition, the Gail tool predicts that for the woman in this case, her lifetime risk of breast cancer, to age 90, is 30.1%, compared with 9.5% for a woman of the same age who is at average risk.

CONTINUED ON PAGE 13

CONTINUED FROM PAGE 10

The woman in this case is clearly at increased risk for breast cancer. What are her choices for reducing her risk of developing breast cancer?

Options for preventing breast cancer

There are many strategies to prevent breast cancer, including lifestyle interventions, pharmacotherapy, and mastectomy. **Lifestyle interventions** that may reduce the risk of breast cancer in postmenopausal women include: maintain a body weight in the normal range,[5] reduce or eliminate the consumption of alcoholic beverages,[6] exercise daily,[7] and quit smoking.[8]

Mastectomy has been demonstrated to reduce the risk of breast cancer in women at very high risk (BRCA positive), but it is seldom used in women at moderate risk for breast cancer.

Pharmacologic interventions for the prevention of breast cancer include tamoxifen, raloxifene, and exemestane.[1] All three agents reduce the risk of breast cancer by about 50%. In fact, the US Preventive Services Task Force (USPSTF) recently recommended the use of tamoxifen or raloxifene to reduce breast cancer risk in patients at high risk. (See "USPSTF recommends tamoxifen or raloxifene to reduce breast cancer risk in high-risk patients" at obgmanagement.com.)

Exemestane is an aromatase inhibitor that causes bone loss. Consequently, this agent would not be an optimal choice for use in a woman with osteoporosis. Like raloxifene, tamoxifen is thought to increase bone density and decrease the risk of osteoporotic fracture.[9,10] Consequently, for a woman with osteoporosis, with an elevated risk of breast cancer, raloxifene or tamoxifen could be prescribed with the dual goals of reducing the risk of osteoporotic fracture and reducing the risk of breast cancer.

Two good options: Raloxifene and tamoxifen

Raloxifene and tamoxifen are both good choices for treating osteoporosis in women at high risk for breast cancer. **For women with a uterus, raloxifene is the preferred agent because tamoxifen can cause endometrial cancer.** For women without a uterus, either raloxifene or tamoxifen could be utilized.

What is the benefit-to-risk ratio for these agents?

Dr. Gabriel Hortobagyi and Dr. Powel Brown have provided a snapshot of the pros and cons of using raloxifene and tamoxifen for breast cancer prophylaxis by estimating benefits and risks in 1,000 women treated for 5 years with an additional 2 years of follow-up (7 years of observation).[11] In their analysis it was assumed that the women had a 5-year risk of developing breast cancer of 4% (the mean risk for "high risk" subjects entered into the STAR P-2 Trial).

They calculated that after 7 years of observation, treating 1,000 women with tamoxifen 20 mg daily for 5 years will prevent 20 invasive and 20 noninvasive breast cancers and cause 2.25 endometrial cancers and 3.3 thromboembolic events. Treating 1,000 women with raloxifene 60 mg daily for 5 years will prevent 15 invasive and 16 noninvasive breast cancers and cause no cases of endometrial cancer and 2.47 thromboembolic events. They concluded that for these major events, tamoxifen caused 40 beneficial events and 5.55 adverse events for a benefit-to-risk ratio of approximately 7. Raloxifene caused 31 beneficial events and 2.47 adverse events for a benefit-to-risk ratio of approximately 13.

Be aware of treatment-specific adverse effects

Raloxifene and tamoxifen treatment cause different patterns of symptom side effects and gynecologic problems. Tamoxifen treatment results in more vasomotor symptoms, leg cramps, and bladder control problems than treatment with raloxifene. Raloxifene is associated with more dyspareunia, lower libido, and more vaginal dryness, weight gain, and musculoskeletal problems than tamoxifen.[12]

Tamoxifen treatment results in more problems with leiomyomata, endometriosis, endometrial polyps, and endometrial cancer than treatment with raloxifene.[13] In turn, this results in more gynecologic surgical procedures, such as endometrial biopsy, oophorectomy, laparoscopy, and hysteroscopy being performed on women taking tamoxifen than on women taking raloxifene. In the largest clinical trial, adherence to treatment was greater for raloxifene than tamoxifen.[12] For women with an intact uterus, raloxifene is likely the better choice for breast cancer prevention.

CONTINUED ON PAGE 14

Editorial

CONTINUED FROM PAGE 13

CASE **I would recommend raloxifene to the case patient**

For the woman presented in this case—who has osteoporosis and a 5-year risk for breast cancer of 6%, as well as an intact uterus—a 5-year course of raloxifene would be an appropriate treatment both to reduce her risk of breast cancer and to treat her osteoporosis.

To achieve the goal of the American Society of Clinical Oncology to increase the use of chemoprevention in women at increased risk of breast cancer, ObGyns will need to take a lead role in assessing our patients for breast cancer risk and counseling them about chemopreventive options.

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