Breast Cancer Chemoprevention Is Underrated

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SAN ANTONIO — The efficacy of raloxifene and tamoxifen for pharmacologic prevention of breast cancer in high-risk postmenopausal women rivals the efficacy of statins for prevention of cardiac events, yet enjoys vastly less physician and patient acceptance, Dr. Leslie G. Ford said at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

"I think maybe it's time we got off the dime and started recognizing that cancer in general and breast cancer in particular is a preventable disease. If we don't start thinking like cardiologists, it'll never happen. We have to assume some of the risks, we have to understand that no intervention is risk free, and we have to—instead of looking for every reason why it can't be done—start doing it," said Dr. Ford, associate director for clinical research in the National Cancer Institute's Division of Cancer Prevention.

To illustrate her point that breast cancer prevention and cardiovascular risk–reducing interventions are in the same efficacy ballpark, she turned to numbers-needed-to-treat (NNT) analyses from landmark clinical trials. For primary prevention, the Study of Tamoxifen and Raloxifene (STAR), which involved more than 19,000 randomized postmenopausal women at high risk for breast cancer, demonstrated that 55 patients had to be treated with either tamoxifen or raloxifene for 5 years in order to prevent one case of invasive breast cancer.

That compares favorably with a major placebo-controlled statin primary prevention trial in which 44 patients with markedly elevated total cholesterol needed to be treated with pravastatin for 5 years to prevent one coronary event, broadly defined.

A more stringent cardiovascular end point that would be comparable with invasive breast cancer in STAR might be the prevention of large anterior MIs, in which case pravastatin's NNT would increase considerably. If the NNT in STAR was reanalyzed to include in situ breast cancers that were prevented, the NNT for tamoxifen or raloxifene would drop significantly.

Turning to secondary prevention, she cited a study in which the NNT for 5 years of adjuvant tamoxifen in order to prevent one case of recurrent breast cancer was 8, compared with a large placebo-controlled trial of simvastatin in patients with a prior coronary event and elevated cholesterol, with an NNT of 12.

Dr. Ford finds particularly irksome the low utilization of tamoxifen for primary prevention in younger high-risk women.

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DR. FORD

The reason most often cited is concern about the drug's side effects. However, it's not widely appreciated that these side effects are confined to postmenopausal women.

In the landmark National Surgical Adjuvant Breast and Bowel Project Breast Cancer Prevention Trial, in which more than 13,000 high-risk women were randomized to tamoxifen or placebo, rates of endometrial cancer, pulmonary emboli, deep-vein thrombosis, and stroke in patients younger than age 50 years weren't significantly different with tamoxifen versus placebo. Yet tamoxifen's benefits—a reduction by half in the incidence of both invasive and noninvasive breast cancer—were similar in younger and older patients.

Like most breast cancer experts, Dr. Ford anticipates eventual Food and Drug Administration approval of raloxifene for breast cancer prevention, largely on the strength of STAR. When that occurs, women will have two options for prevention, both of which are selective estrogen-receptor modifiers. In addition, several promising agents with novel mechanisms of action are in the pipeline.

The use of raloxifene will be confined to postmenopausal patients; tamoxifen will remain the only premenopausal option.

In postmenopausal patients, the choice will hinge on whether a uterus is present. If so, raloxifene will be the preferred option based on the 38% reduced risk of endometrial cancer, compared with tamoxifen, in STAR. In the absence of a uterus, the decision will be based on medical history and personal preference, Dr. Ford predicted. ■