Bisphosphonates May Reduce Breast Cancer Risk

BY BETSY BATES

SAN ANTONIO — Two differently designed studies found a nearly identical, roughly 30% reduction in the risk of breast cancer in postmenopausal women who took bisphosphonates to prevent or remediate bone loss.

The results of a retrospective analysis of data from the Women's Health Initiative (WHI) in the United States and a case-control study conducted in Israel were presented at the annual San Antonio Breast Cancer Symposium.

In both studies, cancer incidence was sharply lower among women prescribed bisphosphonates for low bone mineral density, suggesting that the impact of these agents may extend beyond bone.

In the 151,592-patient database for the WHI, breast cancer development was explored only after controlling for baseline bone mineral density, since women at risk for osteoporosis are known to be at lower risk for breast cancer, likely due to a lower lifetime exposure to estrogen.

Following that statistical adjustment, researchers found that only 64 of 2,216 bisphosphonate users developed breast cancer after a mean 8 years of follow-up, and that 50 of the cancers were estrogen receptor positive.

This represents a 32% lower incidence of breast cancer than was seen among non–bisphosphonate users, reported Dr. Rowan Chlebowski, a medical oncologist at the Harbor-University of California, Los Angeles Medical Center.

"This is a cohort study, not a definitive randomized, controlled trial, but I think it provides a strong signal," said Dr. Chlebowski during a press conference preceding his podium presentation. "Oral bisphosphonate use may directly inhibit breast cancer incidence."

No advantage was seen with respect to ductal carcinoma in situ (DCIS) in women taking bisphosphonates. Indeed, women taking bisphosphonates were slightly more likely to develop DCIS. This perhaps implies that the effects of bisphosphonates occur later in the development of breast cancer, Dr. Chlebowski said.

In Israel, women with breast cancer who reported taking bisphosphonates for at least a year prior to their diagnosis were matched to demographically similar women who were not taking bisphosphonates and without cancer. (Controls were selected by age, neighborhood, and ethnicity.)

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"Oral bisphosphonate use may directly inhibit breast cancer incidence," said Dr. Rowan Chlebowski.

To ensure against recall bias, researchers used prescription records to confirm a prediagnosis history of bisphosphonate use, said Dr. Gad Rennert, chairman of community medicine and epidemiology at the Clalit National Cancer Control Center in Haifa, Israel.

Among the 4,575 subjects, those who took bisphosphonates for at least a year were 34% less likely to be diagnosed with breast cancer.

Risk reduction remained significant at 29% after controlling for other risk factors for breast cancer, including age, ethnicity, family history, fruit and vegetable intake, exercise, body mass index, pregnancy history, and use of calcium supplements and hormone replacement therapy.

"The tumors we saw were more commonly estrogen receptor positive, and more precisely, strongly estrogen receptor positive," Dr. Rennert said during his podium presentation. "They were more commonly well differentiated."

Both estrogen receptor positivity and cell differentiation are associated with re-

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sponse to treatment and a better prognosis, he noted.

No effect on breast cancer risk was seen in women who took bisphosphonates for less than a year, but after 1 year, the risk was reduced at a fairly steady rate. "Five years of use was not dramatically better than 4 years of use," he said. This finding corresponds with the drugs' pharmacokinetic profile, characterized by a slow and steady cumulative effect on bone that stabilizes after a period of time.

"We are seeing an association here. It's a very strong and robust association," Dr. Rennert said.

Initially, a hint of cancer protection arose in small studies comparing breast cancer patients receiving bisphosphonates for cancer- and treatment-related bone loss to those who did not receive the drugs. The evidence seemed to show that those receiving the bone-protecting drugs also developed fewer new cancers in their contralateral breasts.

Possible biologic explanations may lie in the ability of bisphosphonates to reduce angiogenesis and stimulate immune cells responsible for tumor cell detection, Dr. Chlebowski said in an interview.

Dr. Theresa Guise, professor of medicine and oncology at Indiana University, Indianapolis, said the studies may hold "very important implications for a large population of patients."

The possibility that a "simple oral drug" could prevent both osteoporosis and breast cancer represents a "step forward in the prevention of … common health problems of women today," Dr. Guise commented during a discussion of the papers at a press conference.

Bisphosphonates, which can be taken either orally or in an intravenous infusion, are prescribed to about 30 million patients each year. ■

Disclosures: *Dr. Chlebowski disclosed that he has been a consultant for, or served on speakers bureaus for AstraZeneca, Novartis, Pfizer, Amgen, and Eli Lilly. Dr. Rennert disclosed no relevant financial relationships. Dr. Guise said she has been a consultant for or served on speakers bureaus for Amgen, Novartis, Eli Lilly, and Roche Pharmaceuticals.*

A related video is at www.youtube.com/InternalMedicineNews (search for 71010).