Practical Guidance on Bone Health in Breast Ca

BY BRUCE JANCIN

SAN ANTONIO — Current American Society of Clinical Oncology guidelines for maintenance of bone health in breast cancer patients are outdated and do not sufficiently protect against fractures, a prominent European expert asserted at the San Antonio Breast Cancer Symposium.

"Nothing against ASCO, but their guidelines were developed in 2002 and published in 2003. Back then people in the osteoporosis field thought bone mineral density was the main contributor to fracture risk, so the ASCO guidelines restrict bisphosphonate therapy to breast cancer patients with a T score of –2.5 or less," said Dr. Peyman Hadji, professor of endocrinology and reproductive medicine at Philipps University of Marburg (Germany).

"The osteoporosis world has turned around since then. We don't treat T scores anymore, we treat absolute fracture risk. We calculate the absolute risk of a hip or spinal fracture in the next 10 years based on the T score and also using clinical risk factors," he continued.

Dr. Hadji is the lead author of a contemporary alternative set of evidence-based guidelines developed by expert panel consensus (Ann. Oncol. 2008;19:1407-16).

Those guidelines significantly lower the threshold for bisphosphonate therapy (see sidebar).

"In Europe, these guidelines have had a big uptake. They're very easy for gynecologists and oncologists to use," he said.

But physicians keep asking me, 'What proportion of breast cancer patients do we have to treat?' Their big fear was they'd have to give [zoledronic acid] to everyone on an aromatase inhibitor. That's why we did this new study," he explained in an interview.

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DR. HADJI

He reported on 402 postmenopausal women with hormone receptor–positive breast cancer on tamoxifen or an aromatase inhibitor. This group of women had a calculated 10-year fracture risk of about 25%.

Yet under the ASCO guidelines (J. Clin. Oncol. 2003;21:4042-57), which recommend antiresorptive therapy in patients with a T score of –2.5 or lower, only 9% of the women would have qualified. In contrast, under the new guidelines, which call for treatment initiation in the presence of two or more risk factors, 29% of patients were bisphosphonate eligible.

To estimate how many fractures would be prevented in postmenopausal women with hormone receptor–positive breast cancer, Dr. Hadji and his coinvestigators turned to the 150,000-woman-strong database for the National Osteoporosis Risk Assessment study.

Using the ASCO guidelines to initiate bisphosphonate therapy in 9% of patients, only 18% of fractures would be prevented. Using the guidelines developed by Dr. Hadji and his associates, roughly 29% of women would be treated and at least 45% of fractures would be prevented. And that 45% figure is probably an underestimate, since women with breast cancer have a higher fracture risk than do healthy age-matched controls, Dr. Hadji said.

"This again indicates that restricting the risk assessment to bone mineral density is not good enough to identify the women at highest risk of fracture. Until ASCO comes out with new guidelines similar to ours, ours are much superior," he declared.

The multidisciplinary international panel that joined Dr. Hadji in developing the guidelines for prevention and management of aromatase inhibitor–associated bone loss included Dr. Adam M. Brufsky of the University of Pittsburgh Cancer Institute, Dr. Theresa A. Guise, an endocrinologist at the University of Virginia, Charlottesville, and Dr. Allan Lipton, a medical oncologist at Pennsylvania State University, Hershey.

The guideline-development project was funded by Novartis. Dr. Hadji disclosed that he has received honoraria, unrestricted educational grants, and research funding from Novartis and a dozen other pharmaceutical companies. ■

Who Gets the Bisphosphonate?

The new practical guidelines recommend that all breast cancer patients on an aromatase inhibitor should receive calcium and vitamin D supplements, and that in addition, bisphosphonate therapy is warranted in those with any two of the following validated fracture risk factors:

- A T score below –1.5.
- Age greater than 65 years.
- History of oral corticosteroid use for longer than 6 months.
- Body mass index below 20 kg/m^2.
- Family history of hip fracture.
- Positive smoking history.
- Personal history of a fragility fracture after age 50.

Source: Dr. Hadji

Proposal Based on 'Arcane' Diagnoses

Vitamin D *from page 1*

disease (CKD), hypercalcemia, and end-stage renal disease (ESRD). The decision also would deny all coverage for 1,25-dihydroxy vitamin D assay as not being medically necessary for any diagnosis, including CKD and ESRD. The list omits "historically acceptable" medical conditions for testing for 25-hydroxyvitamin D such as osteoporosis and secondary hyperparathyroidism, according to the AACE Web site.

The draft decision itself provides a short explanation for the proposed change in policy. "Vitamin D deficiency may lead to a variety of disorders, the most infamous of which is rickets," it says. "Treatment of vitamin D deficiency is relatively straightforward, negating the need for measuring vitamin D levels in many cases. Evaluating patients' vitamin D levels is accomplished by measuring the level of 25-hydroxyvitamin D. Measurement of other metabolites is not medically necessary."

This appears to be one of the first attempts by an insurance carrier to restrict testing for vitamin D deficiency, said Dr. Steven M. Petak, past president of the American Association of Clinical Endocrinologists. "If other carriers are doing it, I've never heard of it; we order vitamin D levels frequently for patients at risk for deficiency and have never had a problem." A search of the Medicare Web site yielded no local or national coverage decisions related to vitamin D testing.

Vitamin D is a critical nutrient for a variety of functions, said Dr. Petak, who is also an endocrinologist at the Texas Institute for Reproductive Medicine and Endocrinology, in Houston. "In addition to the benefits of adequate vitamin D on bone health, it has been implicated in an increased risk of cardiovascular disease, in multiple sclerosis, possibly in some cancers, and a growing list of other disorders. The risk of falls and resultant fractures is increased with vitamin D deficiency because of changes in muscle tone and balance."

He continued, "The limitations in this proposed coverage decision are incredibly restrictive, and they don't include major disorders such as osteoporosis, hypocalcemia, celiac disease, bariatric surgery patients, and patients who have a history of falls. The list of acceptable diagnoses represents an arcane group of diagnoses that doesn't include what we've known for the past decade about vitamin D."

The coverage proposal doesn't seem to be based on clinical judgment, he added. "It's a monetary thing. Medicare has probably seen that tests for vitamin D levels are being done in increasing numbers because appropriate awareness among physicians has gone way up, and they are trying to put a lid on it. Unfortunately, the real victims here are the patients."

When asked for a comment on the draft coverage decision, Todd Siesky, spokesman for WellPoint, the parent company of NGS, said that NGS was still reviewing comments it received on the proposal; the comment period ended on Feb. 21. "We expect to post all comments with responses to each one on April 15, 2009." ■

The draft coverage decision is available online at www.ngsmedicare.com/NGSMedicare/lcd/dl29510_c_lcd.htm.

Framingham Score Predicts Stroke Risk in Women Treated With Raloxifine

ORLANDO — The Framingham stroke risk score can predict a high-risk postmenopausal woman's likelihood of a future cerebrovascular event with raloxifene use.

Investigators in 26 countries enrolled 10,101 women at risk for a major coronary event in the Raloxifene for the Heart Study (RUTH). A total of 5,031 women had documented coronary heart disease and the remaining 5,070 had multiple coronary heart disease risk factors. Although overall stroke risk was not significantly different between women randomized to raloxifene versus placebo, a higher number of fatal stroke events occurred in the treatment group, 59, compared with 39 in the placebo group during a mean of 5.6 years follow-up.

To see how this increased risk associated with raloxifene (hazard ratio, 1.49; absolute risk increase, 0.7 per 1,000 woman-years) would apply to women stratified by baseline Framingham stroke scale score, David Cox, Ph.D., and colleague retrospectively calculated 10-year cumulative risk. They presented findings at the annual meeting of the North American Menopause Society. Eli Lilly & Co. supported the study, and Dr. Cox is a clinical research scientist for the company.

As expected, risks congregated in the third- and fourth-highest quartiles of Framingham score risk. However, there were no significant differences between treatment groups in either all strokes or nonfatal strokes, regardless of baseline Framingham score. Regarding fatal stroke, Dr. Cox said, "after 2 years, you start to see a split between placebo and raloxifene for risk of fatal stroke by Framingham stroke risk score in RUTH." Specifically, women who scored a 13 or greater on the Framingham tool at baseline were at increased risk of stroke death.

—Damian McNamara