Zoledronic Acid Protects Bone in Premenopausal Patients With Breast Ca

BY BRUCE JANCIN
Denver Bureau

San Antonio — Zoledronic acid prevents the profound loss in bone mineral density that often occurs with combined adjuvant endocrine therapy in premenopausal breast cancer patients, Michael Gnant, M.D., reported at the annual breast cancer symposium sponsored by the Cancer Therapy and Research Center.

Based on new data from the Austrian Breast and Colorectal Cancer Study Group Trial 12 (ABCSG-12), all premenopausal breast cancer patients receiving combination adjuvant therapy with a luteinizing hormone–releasing hormone analog, such as goserelin plus either tamoxifen or an aromatase inhibitor, should undergo annual bone mineral density (BMD) testing. Those showing a treatment-related decline should be considered for intravenous zoledronic acid (Zometa) administered once every 6 months, said Dr. Gnant, professor of surgery at the University of Vienna.

In a separate study presented at the conference, it was reported that zoledronic acid also effectively prevents cancer therapy–induced bone loss in postmenopausal women with early-stage breast cancer on adjuvant aromatase inhibitor therapy.

In clinical practice, the aromatase inhibitors increasingly are replacing tamoxifen, long the standard adjuvant hormonal therapy, because they provide a markedly greater reduction in recurrence along with less risk of endometrial cancer and thromboembolic events.

The price for these advantages has been the greater risk of osteoporosis and fractures associated with aromatase inhibitor therapy. But prophylactic zoledronic acid appears to erase that downside.

While it is widely appreciated that postmenopausal breast cancer patients face increased risk of accelerated bone loss, the osseus impact of cancer therapies in premenopausal breast cancer patients was much less clear before ABCSG-12. The primary end point in the 1,315-patient Phase-III Austrian study will be relapse-free survival, which awaits longer follow-up. In San Antonio, Dr. Gnant reported on a secondary study end point—change in BMD—in a 401-patient subset.

Patients on either combination who received zoledronic acid had no significant change in BMD.

DR. GNANT

The ABCSG-12 trial is a four-part study that randomized patients to 3 years of adjuvant goserelin plus either tamoxifen or anastrozole, with or without 3 years of zoledronic acid given at 4 mg IV every 6 months. After 3 years of goserelin and tamoxifen without zoledronic acid, BMD at the lumbar spine fell an average of 11.6%, compared with baseline.

In patients receiving goserelin plus anastrozole but not zoledronic acid, it fell 17.4%. However, patients on either combination who received the potent intravenous bisphosphonate experienced no significant change in BMD, the surgeon said.

Separately, Adam Brufsky, M.D., presented preliminary 6-month results from Z-FAST, a multicenter U.S. trial in which 415 postmenopausal women with early-stage hormone receptor–positive breast cancer receiving adjuvant letrozole (Femara) were randomized to zoledronic acid administered every 6 months either upfront or beginning 1 year after the start of the aromatase inhibitor.

BMD at the lumbar spine and hip increased in patients who got zoledronic acid upfront and decreased in those assigned to delayed bisphosphonate therapy. Biochemical markers of bone turnover decreased from baseline to 6 months in the upfront zoledronic acid group, while increasing or remaining unchanged in the delayed treatment arm.

These early findings suggest administration of zoledronic acid from the onset of adjuvant aromatase inhibitor therapy may prevent cancer therapy–induced bone loss in postmenopausal women. The Novartis-sponsored Z-FAST trial is scheduled for 5 years of follow-up, said Dr. Brufsky of the University of Pittsburgh.

Zoledronic acid is more expensive than pamidronate (Aredia), the other intravenous bisphosphonate, but its infusion time is only 15 minutes, compared with 2 hours or more for pamidronate, and there are some data to suggest zoledronic acid is more effective.

Until zoledronic acid receives an indication from the Food and Drug Administration for use in the setting of adjuvant breast cancer therapy, however, many oncologists will continue to follow the American Society for Clinical Oncology's recent guidelines.

Those call for increased diligence in screening breast cancer patients for bone loss, advising them on the importance of calcium and vitamin D supplementation and bone-healthy lifestyle measures, and the early use of the clearly less potent oral bisphosphonates in women who show cancer treatment–related decline in BMD. ■

Pap Smears May Predict Bone Health

BY DIANA MAHONEY
New England Bureau

Harrogate, England — Women whose Pap smears reveal atrophic cell patterns may be at greater risk for osteopenia and osteoporosis than women whose smears show mature cell patterns, a study has shown.

The findings suggest that routine Pap testing could be a useful and inexpensive screening tool for identifying women at risk for the degenerative bone disorders, Alenka Repse-Fokter, M.D., reported in a poster presentation at the annual conference of the National Osteoporosis Society.

Given limited medical resources, the ability to use an already existing and widely performed screening protocol to help identify women with osteoporosis "would be highly appreciated," she said.

Dr. Repse-Fokter and colleagues at Celje (Slovenia) General Hospital assessed the Pap smear results and dual-energy x-ray absorptiometry (DXA) bone density measurements of 66 women between 46 and 67 years old. The women had received the Pap smears for routine cervical cancer screening and were invited to undergo bone mineral density measurement as part of the investigation. None used hormonal contraception or hormone therapy.

The investigators grouped the smears into atrophic and mature cell patterns, which can be easily recognized during the screening for cervical dysplasia or cancer, Dr. Repse-Fokter said. "In routine light microscopy, atrophic cells appear much smaller than cells in mature smear patterns," she noted. The smear patterns were then compared with the patients' T values measured by DXA on the femoral neck and lumbar spine.

Overall, the T scores were significantly lower in the atrophic smear group. Of the 33 women with atrophic smears, 13 had osteopenia and 15 had osteoporosis. Among the 33 women whose smears showed mature cell patterns, 9 had osteopenia and 24 had normal bone density. The sensitivity, specificity, and positive predictive value of the findings were, respectively, 76%, 83%, and 85%.

The correlation between smear patterns and degenerative bone disease support the investigators' findings from a previous study that revealed a highly significant association between atrophic smear patterns and low bone mineral density.

"This means that a significant number of women with low bone mineral density who are at high risk [for osteoporotic disease] could be identified in parallel with routine Pap testing for cervical cancer screening without added costs," Dr. Repse-Fokter said.

Although further studies on larger populations are needed, "we strongly suggest that women with atrophic Pap smear patterns be closely followed as recommended by the American National Osteoporosis Foundation," according to Dr. Repse-Fokter and her colleagues. ■