**Zoledronic Acid Sustains Bone in Breast Ca Patients**

San Antonio — Zoledronic acid prevents the profound loss in bone mineral density that often occurs with combined adjuvant chemotherapy in premenopausal breast cancer patients, Michael Gnatin, 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 (ABC-SG-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. Gnatin, 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 inhi- bitor 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 osseous impact of cancer therapies in premenopausal breast cancer patients was much less clear before ABC SG-12. The primary end point in the 1,315-patient Phase-III Austrian study will be relapse-free sur- vival, which awaits longer follow- up. In San Antonio, Dr. Gnatin reported on a secondary study end point—change in BMD—in a 401- patient subset.

The ABC-SG-12 trial is a 4-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 with- out zoledronic acid, BMD at the lumbar spine fell an av- erage of 11.6%, compared with baseline. In patients re- ceiving goserelin plus anastrozole but not zoledronic acid, it fell 9.7%. However, patients on either combination who received the potent intravenous bisphosphonate experi- enced 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 hormo- ne 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 in- creasing or remaining unchanged in the delayed treat- ment arm.

The early findings suggest ad- ministration of zoledronic acid from the onset of adjuvant ar- motase inhibitor therapy may pre- vent cancer therapy–induced bone loss in postmenopausal women. However, longer-term follow-up is needed to fully define the effects of zoledronic acid in this popula- tion. 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 in- fusion time is only 15 minutes, compared with 2 hours or more for pamidronate, and there are some data to sug- gest zoledronic acid is more effective.

Until zoledronic acid receives final indication from the Food and Drug Administration for use in the setting of adjuvant breast cancer therapy, however, many oncolo- gists will continue to follow the American Society for Clinical Oncology’s recent guidelines. Those call for in- creased 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.

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**More Educated Breast Ca Patients Use More CAM**

San Antonio — The more years of formal education a breast cancer patient has, the more likely she is to use complementary and alternative medicine in con- junction with adjuvant chemother- apy, Eleanor Glass reported at the annual breast cancer symposium sponsored by the Cancer Therapy and Research Center.

Her survey of 700 breast cancer patients who received chemother- apy and/or adjuvant hormone ther- apy showed that the majority— 55%—used complementary and alternative medicine (CAM) before, during, or afterward. A total of 27% of patients reported using CAM during all three time periods.

CAM usage was strongly relat- ed to education level. Overall, 39% of patients without a high school degree reported using CAM, as did 50% with a high school de- gree, more than two-thirds of women with a college degree, and 70% with graduate education, said Ms. Glass of the University of Cincinnati.

The most commonly used CAM therapies, in descending order of frequency, were vitamin E, vitamin C, green tea, selenium, echinacea, garlic extract, soy sup- plements, and ginkgo biloba.

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**Switch Out Tamoxifen to Improve Outcomes**

San Antonio — Switching post- menopausal breast cancer patients to an aromatase inhibitor following 2-3 years of ad- juvant tamoxifen results in markedly better disease-free survival than the traditional 5 years of tamoxifen, according to three major randomized trials presented at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

Raimund Jakesz, M.D., recommended that breast cancer pa- tients who fit the profile of partici- pants in two Euro- pean clinical trials he reported on at the conference be rou- ped to 3 years of anastrozole (Arimidex) after 2-3 years of tamoxifen.

He reported on more than 3,100 breast cancer patients in the AstraZeneca-spon- sored Austrian Breast and Colorectal Cancer Study Group Trial 8 and the German Adju- vant Breast Cancer Group ARNO 95 study who were randomized to the standard 5 years of adjuvant tamoxifen or to 2 years of tamoxifen followed by 3 years of anastrozole.

The 3-year rate of freedom from locoregional recurrence, distant metastasis, and contralateral breast cancer was 95.8% with tamoxifen/anastrozole vs. 92.7% with tamoxi- fen. The likelihood of survival free of distant recurrence was 39% greater with tamoxifen followed by anastrozole, said Dr. Jakesz, pro- fessor of surgery at the University of Vienna.

All participants in the two randomized trials were postmenopausal, had hormone re- ceptor–positive disease, and underwent breast-conserving therapy. One-fourth were node positive. None received chemothera- pany. Forty percent were under 60 years old. Most had small, well-differentiated tumors.

In a separate presentation, Charles Coombs, M.D., gave an update on the Inter- group Exemestane Study (IES), in which 4,740 postmenopausal breast cancer patients were randomized to 5 years of adjuvant tamoxifen or switched to exemestane (Arom- anis) after 2-3 years. At a median 37 months’ follow-up, lo- cal or distant recurrence had developed in 264 women treated with tamoxifen and 193 switched to the aromatase inhibitor. That translated into a 27% increase in disease-free survival in patients who switched. Twelve cases of contralateral breast cancer occurred in the tamoxifen/exemestane group vs. 26 in those on tamoxifen alone.

A particularly intriguing finding is that there have been significantly fewer pri- marily hormone-related deaths with exemestane: 46 vs. 59 in the tamoxifen- only arm. There have been 6 cases of lung cancer with tamoxifen/exemestane vs. 13 with tamoxifen, and 2 cases of melanoma vs. 5 cases with tamoxifen only. However, 20 acute MIs have occurred in patients switched to the aromatase inhibitor vs. 8 MIs in the tamoxifen-only group, said Dr. Coombs, di- rector of the Cancer Research UK Labora- tories at Imperial College, London.

Based upon the highly favorable IES data, Pfä- erter announced it has submitted a sup- plemental New Drug Application seeking Food and Drug Administration approval for exemestane as adjuvant therapy in post- menopausal women with hormone recep- tor–positive early-stage breast cancer. At present, tamoxifen and anastrozole are the sole drugs with that indication.

A midcourse switch from tamoxifen to an aromatase inhibitor makes a lot of sense, Hope S. Rugo, M.D., said at a satellite sym- posium held in conjunction with the San An- tonio conference. Tamoxifen is of proven benefit in preventing recurrent breast cancer. It’s a good drug with favorable ancillary ef- fects on bone mineral density and the car- diovascular risk profile. But resistance can occur as early as 12-18 months after starting.

Plus, the most serious side effects associ- ated with tamoxifen—endometrial cancer and thromboembolism—become more like- ly with longer treatment. Stopping tamoxi- fen early might prevent some of these ma- jor adverse events while still providing protection against the increased fracture risk associated with 5 years of anastrozole in the 2006 study of the ATAC (Arimidex, Tamoxifen, Alone or in Com- bination) (ATAC) trial, said Dr. Rugo, direc- tor of the breast oncology clinical trials pro- gram at the University of California, San Francisco, Comprehensive Cancer Center.

To date the switch trials have shown a higher incidence of osteoporosis but not a signifi- cant increase in fractures, compared with 5 years of tamoxifen alone, she noted.