Frail Elderly Reap Most Benefit

Zoledronic Acid *from page 1*

comes were 24-month changes in bone mineral density (BMD) at the lumbar spine, trochanter, femoral neck, distal radius, and total hip. The secondary end points were changes in markers of bone turnover, said Dr. Recknor, an internist specializing in the treatment of osteoporosis in Gainesville, Ga.

At 24 months (1 year after the second infusion), both active groups showed similar BMD increases at all sites that were significantly different from BMD changes with placebo. (See chart.)

Adverse events were most commonly observed in the first 3 days after the first infusion, when they were significantly more common in both active groups (60% vs. 25%). The most frequently reported were pain, fever, chills, myalgia, nausea, and headache.

The study raises a tantalizing possibility, Dr. Recknor said in an interview. "You may be able to give this drug a couple of times to perimenopausal women and prevent the entire problem of bone loss."

A subanalysis of a second HORIZON study has shown that zoledronic acid also benefits patients who have had a hip fracture—particularly the very elderly and those with the poorest bone quality.

The HORIZON Recurrent Fracture Trial included 2,127 patients with a recent hip fracture who were randomized to an annual infusion of 5 mg zoledronic acid or placebo and followed for up to 5 years. HORIZON-RFT concluded that the drug reduced the rate of recurrent fracture by 35% (N. Engl. J. Med. 2007;357:1799-809).

The subanalysis examined response rates within specific patient groups, said Denise Orwig, Ph.D., who presented the trial data during a poster session at the meeting. The analysis showed that patients at the highest risk for a recurrent fracture—those who were at least 85 years old or who had a T score of less than –2.5 at the total hip—benefited the most from the treatment.

Although it's unclear why the oldest, least-dense bones benefited the most, the finding does carry a strongly positive clinical implication, "this study showed us that these individuals can benefit and that we can have a big short-term impact on their bone density and possibly even reduce the risk of more fractures due to continued bone loss," said Dr. Orwig of the department of epidemiology and preventive medicine at the University of Maryland Medical Center, Baltimore.

In a third study presented at the meeting, a single infusion of zoledronic acid suppressed serum markers of bone turnover better than 6 months of daily oral raloxifene in postmenopausal women with low bone mineral density.

Although women who received the 5-mg infusion of zoledronic acid had significantly more immediate adverse events than those receiving a placebo infusion, the long-term adverse event rate was similar in both groups, said Dr. Andrey Kriegman, senior medical director for osteoporosis in the United States for Novartis Pharmaceuticals Corp.

The trial randomized 110 postmenopausal women (mean age, 60 years) to either the active infusion followed by 6 months of daily oral placebo, or a placebo infusion followed by 6 months of daily raloxifene (60 mg). Most (86%) were white; they were a mean of 13 years postmenopausal. About a third (37%) had a mean T score of –2.5 or lower at the lumbar spine, total hip, or femoral neck; the rest had a T score of –2.5 to –1.5.

The study's primary end points were the 6-month measurement of the urine *N*-telopeptide of type I collagen (NTx) corrected for creatinine, and bone-specific alkaline phosphatase (BSAP). Measurements of these markers at 2 and 4 months were the secondary end points.

The mean NTx/creatinine ratio was significantly lower in the zoledronic acid group than in the raloxifene group at all time points. At 6 months, the level had decreased by 14% more in the zoledronic acid group than in the raloxifene group.

The rate of immediate adverse events was significantly higher in the zoledronic acid group, an expected finding, Dr. Kriegman said in an interview.

Novartis sponsored all of the studies. Dr. Orwig has received research funding from the company. Dr. Recknor is on the Novartis speakers bureau. ■

HORIZON Prevention Study: 24-Month Changes in Bone Mineral Density

	2 ZOL Infusions	ZOL + Placebo	2 Placebo Infusions
Lumbar spine	5%	4.4%	–1.3%
Total hip	3%	2.3%	–1.5%
Femoral neck	2%	1.6%	–1.4%
Trochanter	4.8%	4%	–1%
Distal radius	–0.07%	–0.18%	–2.4%

Source: Novartis Pharmaceuticals Corp.

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Even After Hip Fracture, Many Patients Not Told the 'O' Word

BY MICHELE G. SULLIVAN

WASHINGTON — Three-fourths of patients hospitalized for a hip fracture do not receive an osteoporosis diagnosis before discharge, and the majority are not taking a bisphosphonate at discharge or 6 months after the injury, a study has shown.

The findings are dismaying, said Dr. Pardeep Bansal, because 24% of patients older than 50 years who sustain an osteoporotic hip fracture die within a year. "The 1-year mortality rate is higher than it is in some cancers, and even higher than it is after a heart attack," said Dr. Bansal, chief resident at the Scranton-Temple Residency Program, Scranton, Pa. "But if you have a heart attack, no physician is going to let you leave the hospital without aspirin, a beta-blocker, and a statin. If you have a hip fracture, you're likely to be discharged without even the underlying diagnosis, much less the appropriate treatment."

'The 1-year mortality rate is higher than it is in some cancers, and even higher than it is after a heart attack.'

DR. BANSAL

The two-part study began with a chart review of 191 patients who were admitted to a hospital with a hip fracture. Most (80%) were white females older than 70 years. At the time of discharge, 25% had been assigned a diagnosis of osteoporosis. Only 30% were taking calcium; patients who had been diagnosed with osteoporosis were significantly more likely to be taking both calcium and vitamin D than were patients without a diagnosis.

Furthermore, only 15% were taking a bisphosphonate at discharge, Dr Bansal said. Clinical contraindications did not appear to play a significant role in the lack of treatment: Only 2% of patients had a glomerular filtration rate of less than 30 mL/min per 1.73 m^2, which could be a contraindication for bisphosphonate therapy.

Dr. Bansal then performed a telephone survey of the 105 patients who could be contacted; 33% of the original cohort had died since their fractures, and another 12% could not be found. All of the patients interviewed reported having seen their primary care physicians within 6 months of the fracture. Yet still, only 50% had received a diagnosis of osteoporosis, 50% were taking calcium, 40% were taking vitamin D, and only 28% were taking a bisphosphonate. "Another painful finding was that 14% of the group had experienced a subsequent fragility fracture."

To help improve the rate of osteoporosis diagnosis at his hospital, Dr. Bansal and his colleagues have instituted a standardized protocol. "It's very simple," he said. "Any patient who comes in with a fracture suggestive of osteoporosis is started on calcium, vitamin D, and a bisphosphonate before discharge. If they have a contraindication to a bisphosphonate, such as an allergy or a low GFR, then we call the family physician and discuss an alternative treatment."

Treatment should not be delayed until a scan can be obtained, said Dr. Bansal, who presented the study at an international symposium sponsored by the National Osteoporosis Foundation. He had no conflicts of interest to declare. ■

Aromatase Inhibitors May Hasten Bone Loss

BY MICHELE G. SULLIVAN

WASHINGTON — Aromatase inhibitors are associated with small but significant levels of additional bone loss in osteopenic women who take the drugs for hormone-sensitive breast cancer, according to a study of 104 women.

After just 1 year of aromatase inhibitor therapy, these women lost a mean of 1.5% in bone mineral density (BMD) at the lumbar spine and 2% at the femoral neck; two of the subjects progressed from osteopenia to osteoporosis, Dr. Pamela Taxel reported in a poster session at an international symposium sponsored by the National Osteoporosis Foundation.

Expected bone loss associated with natural progression generally would be about 0.5%-1% per year, according to Dr. Taxel of the University of Connecticut Health Center, Farmington.

She and her colleagues performed a chart review of 104 women who were taking the drugs for breast cancer and were evaluated for bone health. Of these, 61 (58%) had osteopenia. The patients' mean age was 58 years; they had been on aromatase inhibitor therapy for up to 2 years. Eighteen percent (11 patients) were taking a bisphosphonate at baseline. They were followed for an additional year.

Lumbar spine BMD measurements were available at baseline and at 1 year for 39 women. After 1 year, the women had lost a mean of 1.5% in BMD at this site; 18 women had lost more than 3%. Baseline and 1-year femoral neck BMD measurements were available for 36 women. After 1 year, there was a mean BMD decrease of 2% at this site. Four women lost more than 3% at the spine and more than 5% at the femoral neck.

Two of the 36 women with both lumbar spine and femoral neck data progressed to osteoporosis during the follow-up period. The progression in bone loss occurred despite increased compliance with vitamin D supplements. At baseline, 74% were taking at least 1,000 mg/day of vitamin D, although 41% were still deficient. At the end of the follow-up period, vitamin D intake had significantly increased, with only 25% still deficient, Dr. Taxel noted. ■