

# Zoledronic Acid Slows Bone Loss in Osteopenia

BY MICHELE G. SULLIVAN

WASHINGTON — A single yearly infusion of zoledronic acid appears to prevent further bone loss in postmenopausal women with osteopenia and in women who have already had a hip fracture, two randomized controlled trials have concluded.

This is the first time the drug has been shown to be an effective preventive agent in treating osteopenic patients, said Dr. Chris Recknor, who presented the data in a poster session at an international symposium sponsored by the National Osteoporosis Foundation.

Using the drug prophylactically “allows clinicians a little more lead time in treating these patients, many of whom are at increased risk of a low-stress fracture,” said Dr. Recknor, an internist specializing in the treatment of osteoporosis in Gainesville, Ga.

The 2-year Health Outcomes and Reduced Incidence With Zoledronic Acid Once Yearly (HORIZON) prevention study cohort comprised 531 postmenopausal women with low bone mineral density (T scores of  $-1$  to  $-2.5$ ). They were randomized to one of three treatment regimens: two placebo infusions, given 12 months apart; two infusions of zoledronic acid 5 mg, given 12 months apart; or one infusion of 5 mg zoledronic acid, followed 12 months later by a placebo infusion.

The subjects’ mean age was 60 years. Most (93%) were white. The study’s main outcomes 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. 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 box.)

Both zoledronic acid regimens showed significant reductions in bone turnover markers compared with placebo. Markers in the double-infusion group were significantly lower than those in the single-infusion group.

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. Adverse events were significantly lower after the second infusion, occurring in 18% of the double-infusion group, 11% of the single-infusion group, and 12% of the placebo group.

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., 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 Dr. Orwig said it’s unclear why the oldest, least-dense bones benefited the most, the finding does carry a strongly positive clinical implication. “These patients who are at the highest risk are also the ones who are the least likely to be treated,” said Dr. Orwig of the depart-

ment of epidemiology and preventive medicine at the University of Maryland Medical Center, Baltimore. “The thought may be that they have already had multiple fractures and there is probably not a lot more that can be done. But 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.”

In a third study presented at the meeting, a single infusion of zoledronic acid was shown to suppress serum markers of bone turnover significantly better than 6 months of daily oral raloxifene in postmenopausal women with low bone mineral density. (See story on p. 29.)

Novartis Pharmaceuticals Corp. sponsored the studies. Dr. Orwig has received research funding from the company, and Dr. Recknor is on the 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.

ELSEVIER GLOBAL MEDICAL NEWS

## Even After Hip Fracture, Osteoporosis Diagnosis and Treatment Overlooked

BY MICHELE G. SULLIVAN

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

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 two-part study began with a chart review of 191 patients admitted to a hospital with a hip fracture. Most (80%) were white females older than

70 years. At discharge, 25% had been assigned a diagnosis of osteoporosis. Only 30% were taking calcium.

Furthermore, only 15% were taking a bisphosphonate at discharge, Dr. Bansal said. Clinical contraindications did not appear to play a significant role: Only 2% of patients had a glomerular filtration rate of



**‘If you have a hip fracture, you’re likely to be discharged without even the underlying diagnosis.’**

DR. BANSAL

less than 30 mL/min per 1.73 m<sup>2</sup>, which could be a contraindication for bisphosphonate therapy.

A telephone survey revealed that 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 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,” he said.

To improve the rate of osteoporosis diagnosis at his hospital, Dr. Bansal and his colleagues instituted a standardized protocol. “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.”

Although a dual-energy x-ray absorptiometry scan is a helpful diagnostic tool, Dr. Bansal said treatment should not be delayed until a scan can be obtained. “You have to wait for the fracture to heal and then schedule that as an outpatient, and during that time the patient can be lost to follow-up. ... Don’t delay the treatment while waiting for the scan.”

Dr. Bansal presented the study in a poster session at an international symposium sponsored by the National Osteoporosis Foundation. He had no conflicts of interest to declare. ■

## Osteoporosis Often Present in Older Black Women

RIO GRANDE, P.R. — Approximately one in four elderly black women have osteoporosis, findings from a small study suggest.

Physicians should not ignore the possibility of osteoporosis in their older black female patients, although these women are not usually considered at high risk, compared with other demographic groups, said Dr. Sally P. Weaver, research director of the McLennan County Medical Education and Research Foundation, Waco, Tex.

Previous studies of osteoporosis in women have focused mainly on whites because of evidence of an elevated risk for osteoporosis in that population. Yet older women of any ethnicity are prone to age-related fractures if their bone mineral density (BMD) is low, she said in an interview.

Dr. Weaver and her colleagues measured BMD scans from the electronic health records of 44 black women aged 70 years and older. Patients with conditions that could affect bone turnover, vitamin D absorption, or calcium absorption were excluded.

About 50% of the study participants met the criteria for osteopenia, and 10% met the criteria for osteoporosis at the left femoral neck. Approximately 25% met criteria for osteopenia or osteoporosis at the lumbar spine.

Dr. Weaver presented the results in a poster at the annual meeting of the North American Primary Care Research Group. She had no financial conflicts to disclose.

—Heidi Splete