Sequential Tx Sustains Benefits Of Teriparatide in Osteoporosis

BY NANCY WALSH
New York Bureau

TORONTO — Patients with osteoporosis who took daily raloxifene following a yearlong course of treatment with teriparatide maintained bone mineral density gains, whereas those who had no further therapy rapidly lost bone, Dr. Silvano Adami reported at a world congress on osteoporosis.

Recombinant teriparatide (human parathyroid hormone 1-34) treatment increases bone mass and reduces fracture risk by stimulating bone formation and remodeling, but there are concerns about its long-term safety. The Fracture Prevention Trial was terminated early in 1998 because of the occurrence of osteosarcomas in rats, and although no sarcomas developed in patients in the study, the drug subsequently was not recommended for use for any longer than 2 years.

Clinical experience has shown, however, that once therapy with teriparatide ceases, the bone mineral density (BMD) gains achieved during treatment quickly diminish. Therefore, subsequent antiresorptive therapy has been suggested as a means of maintaining the improvements.

Results of a new study support this concept of sequential therapy, said Dr. Adami of the University of Verona, Italy.

The study included 380 postmenopausal women who had completed 1 year of open-label treatment with 20 mcg/day of teriparatide. They were randomized to an additional year of raloxifene (60 mg/day) or placebo and were followed with dual-energy X-ray absorptiometry.

One year of teriparatide significantly increased BMD at the lumbar spine and femoral neck, by 8.2% and 1.3%, respectively, Dr. Adami said at the meeting, which was sponsored by the International Osteoporosis Foundation. At the end of the second year, patients who had received raloxifene showed a further significant increase in femoral neck BMD of 2.3%. (See chart.)

Correlations also were seen between the changes in bone markers and BMD during the first 3 months after raloxifene therapy, he said.

The sequential approach to therapy is not the first combination strategy to be evaluated for teriparatide. An earlier hypothesis had been that concurrent administration of an antiresorptive drug with parathyroid hormone (PTH) might enhance teriparatide's anabolic effects.

This hypothesis was tested in two studies in which parathyroid hormones were given in combination with alendronate. In one of the studies, 238 postmenopausal women with low BMD were randomized to receive daily parathyroid hormone (100 mcg), alendronate (10 mg), or both for 12 months. The investigators found no evidence of synergy for the combination therapy, reporting that the increase in volumetric density of spinal trabecular bone in the parathyroid hormone group was about double that seen in the other groups. They suggested the concurrent use of alendronate might be attenuating the anabolic effects of teriparatide (N. Engl. J. Med. 2003;349:1207-15).

In the second study, 83 men who had low BMD were randomized to receive parathyroid hormone (40 mcg daily), alendronate (10 mg daily), or both. This study also showed no benefit, with BMD at the femoral neck increasing significantly more in those men who received the parathyroid hormone alone than it did in those who were in the alendronate or combination groups (N. Engl. J. Med. 2003;349:1216-26). ■

BMD Changes With Raloxifene Treatment Following Teriparatide

	Change during year 2		Change from baseline	
	Raloxifene	Placebo	Raloxifene	Placebo
Lumbar spine	–1.0%	–4.0%	+7.6%	+3.7%
Femoral neck	+2.3%	+0.2%	+3.4%	+1.6%

Note: Based on a study of 380 postmenopausal women.
Source: Dr. Adami

ELSEVIER GLOBAL MEDICAL NEWS

Ibandronate Shots Better in Those With GI Intolerance

BY NANCY WALSH
New York Bureau

TORONTO — Women with postmenopausal osteoporosis who had previously discontinued oral bisphosphonate therapy because of gastrointestinal intolerance preferred an intravenous, every-3-month regimen of ibandronate over a monthly oral regimen, Dr. E. Michael Lewiecki said at a world congress on osteoporosis.

Complex dosing instructions designed to maximize bioavailability and address tolerability concerns may affect adherence to oral bisphosphonate therapy, and adherence is crucial to clinical efficacy and fracture prevention, he noted.

Adherence was addressed in a 12-month, open-label multicenter study that included 542 patients with osteoporosis or osteopenia who had stopped daily or weekly treatment with oral alendronate or risedronate because of symptoms such as heartburn and acid reflux. All got supplemental vitamin D (400 IU/day) and elemental calcium (1,000 mg/ day). Patients were given the choice of oral ibandronate, 150 mg once monthly, or 3 mg intravenously every 3 months. The intravenous injection takes 15 to 30 seconds to complete. A total of 396 (73%) of patients chose the intravenous regimen, and 146 (27%) chose the oral route. They were permitted to switch treatment groups once during the study if they experienced adverse effects.

Severity and frequency of gastrointestinal symptoms and other side effects were evaluated with surveys administered at baseline and at months 1, 4, 7, and 10.

Available data indicate that adherence to both regimens at 6 months was high, at 94.5%. Actual duration of study medication intake divided by maximum duration of intake and a threshold of 75% or more was used to define adherence, according to Dr. Lewiecki of New Mexico Clinical Research and Osteoporosis Center, Albuquerque.

Among patients receiving the oral drug, adherence was 87.7%, while adherence was 94.9% among those receiving the intravenous formulation, Dr. Lewiecki wrote in a poster session at the meeting, which was sponsored by the International Osteoporosis Foundation.

In patients who chose the intravenous route of administration, 147 (37.1%) had a history of fracture as an adult, compared with 36 (24.7%) of those who chose the oral drug.

So far, 26 patients have switched their route of administration. Eleven switched from oral to intravenous ibandronate because of gastrointestinal intolerance; 15 went from intravenous to oral for reasons including influenzalike symptoms and injection-site reactions. By month 4, 28.1% and 36.6% of patients on the oral and intravenous drugs, respectively, reported improvements in gastrointestinal tolerance compared with baseline.

"Patients who had previously discontinued weekly or daily oral bisphosphonates because of gastrointestinal intolerance [seem to] prefer intravenous dosing, and patients with a previous fracture are even more likely to do so than patients without a previous fracture," Dr. Lewiecki said. The study was sponsored by Roche Laboratories. Dr. Lewiecki made no disclosures. ■

Periodic Ibandronate Injections Improve Bone Density at 2 Years

BY KERRI WACHTER
Senior Writer

PHILADELPHIA — Intermittent intravenous injections of ibandronate continue to improve bone mineral density of the spine and hip at 2 years, according to data presented at the annual meeting of the American Society for Bone and Mineral Research.

Two-year results from the Dosing IntraVenous Administration (DIVA) study show that IV ibandronate injections every 2 or 3 months were superior to oral daily ibandronate (Boniva) in terms of increased bone mineral density (BMD) at the lumbar spine. The periodic IV injections were also superior to oral daily ibandronate at 1 and 2 years in terms of increased BMD for the total hip, trochanter, and femoral neck.

"IV ibandronate injections improve BMD at the spine and the hip [and] they produce superior BMD gains to oral dosing," said Dr. E. Michael Lewiecki, osteoporosis director of the New Mexico Clinical Research and Osteoporosis Center and professor of medicine at the University of New Mexico in Albuquerque.

The study was funded in part by F. Hoffmann-La Roche Ltd. and GlaxoSmithKline. Dr. Lewiecki disclosed that he has received research grants from both.

DIVA was a randomized, double-blind, active-control study involving women aged 55-80 years, who were at least 5 years postmenopausal and who had a lumbar spine T score less than –2.5.

Overall 1,395 women were randomized to receive 2-mg IV ibandronate injections every 2 months (454 women), 3 mg IV ibandronate every 3 months (472 women), or 2.5 mg daily oral ibandronate (469 women). All received daily calcium (500 mg) and vitamin D (400 IU) supplements.

The study's primary end point was mean percent change from baseline in lumbar spine BMD at 1 year, and these results were presented at the 2005 annual meeting of the American College of Rheumatology. Secondary end points included mean percent change from baseline in lumbar spine BMD at 2 years, and mean percent change from baseline in total hip, femoral neck, and trochanter BMD at 1 and 2 years.

In early 2006, the Food and Drug Administration approved the 3-mg trimonthly ibandronate IV injection for treating postmenopausal osteoporosis. "These data support the use of the every-3-month regimen in clinical practice," Dr. Lewiecki said. ■

Mean Percentage Increase From Baseline in BMD With Ibandronate

	Daily oral (n = 469)	Bimonthly injection (n = 454)	Trimonthly injection (n = 472)
Lumbar Spine			
Year 1	3.8	5.1	4.8
Year 2	4.8	6.4	6.3
Total Hip			
Year 1	1.8	2.5	2.4
Year 2	2.2	3.4	3.1
Femoral Neck			
Year 1	1.6	2.0	2.3
Year 2	2.2	2.7	2.8
Trochanter			
Year 1	3.0	4.0	3.8
Year 2	3.5	5.0	4.9

Source: Dr. Lewiecki

ELSEVIER GLOBAL MEDICAL NEWS