Micro-CT Images Support Parathyroid's Bone Builder Role in Osteoporotic Women

BY HEIDI SPLETE
Senior Writer

WASHINGTON — New imaging data from a phase III study confirm that treatment with parathyroid hormone significantly improves bone microarchitecture in postmenopausal osteoporotic women, David W. Dempster, Ph.D., reported in a poster at an international symposium sponsored by the National Osteoporosis Foundation.

The Treatment of Osteoporosis with Parathyroid Hormone (TOP) study, sponsored by Salt Lake City–based NPS Pharmaceuticals, included approximately 2,600 women who were treated daily with either 100-mcg injections of PTH or a placebo for 18 months.

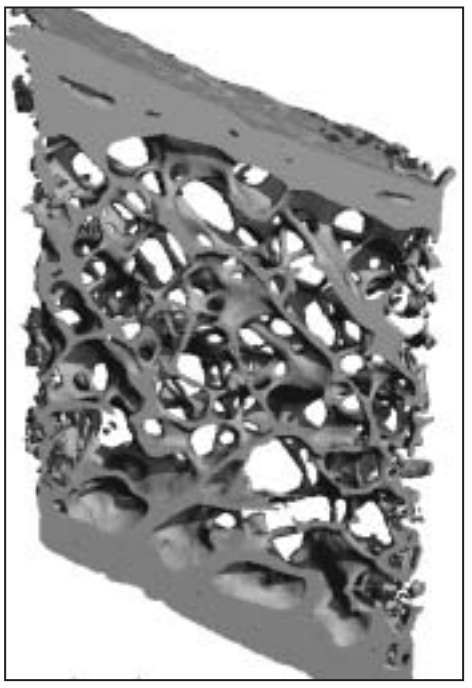
In addition, all patients received 700 mg of calcium and 400 IU of vitamin D daily. The researchers obtained iliac crest biopsies from women in both the PTH and placebo groups.

Based on the micro-CT data, the mean cancellous bone volume was significantly higher (45%) among women treated with PTH, compared with the placebo group. In addition, this increase was associated with 12% and 17% increases in the mean trabecular number and thickness, respectively, in the PTH group, compared with the placebo group.

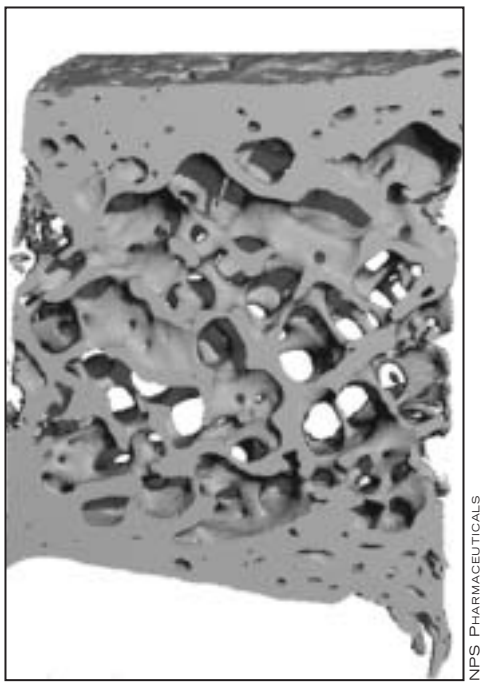
Dr. Dempster, professor of clinical pathology at Columbia University, New York, and director of the regional bone center at Helen Hayes Hospital, West Haverstraw, N.Y., and his colleagues previously reported similar results when they used histomorphometry to assess iliac crest biopsies in the TOP study patients: 48%, 24%, and 17% increases in cancellous bone volume, trabecular number, and trabecular thickness, respectively, among PTH-treated women, compared with placebo-treated women.

Although both techniques similarly illustrated improvements in bone volume and thickness in the PTH group, they each contribute some unique information and thus complement each other. Micro-CT is rapid and nondestructive, and provides quantitative information on the 3-D architecture of the bone, while histomorphometry provides details about the impact of PTH on bone turnover and bone cell populations.

Dr. Dempster is a consultant for NPS Pharmaceuticals. ■



A biopsy of the iliac crest in a placebo-treated patient is shown on Micro-CT.



NPS PHARMACEUTICALS

By contrast, a similar view is shown in a patient after 18 weeks of active therapy.

FDA Okays Once-Monthly Osteoporosis Drug

BY ELIZABETH MECHCATIE
Senior Writer

A once-monthly formulation of the bisphosphonate ibandronate was recently approved by the Food and Drug Administration for treating postmenopausal osteoporosis, 2 years after a daily formulation of the drug was approved but never marketed.

Data from a 1-year study of 1,602 postmenopausal women showed the once-monthly formulation of ibandronate increased BMD in the lumbar spine.

Ibandronate, which is being marketed as Boniva by Roche, is the third oral bisphosphonate and the first monthly formulation marketed in the United States for osteoporosis. It was approved in late March.

A 2.5-mg daily formulation was approved in 2003, based on a 3-year study that showed a reduction in vertebral fracture risk, but it was never marketed because of the availability of the more convenient, weekly bisphosphonate formulations, alendronate (Fosamax) and risedronate (Actonel).

Approval of the once-monthly 150-mg formulation of ibandronate was based on a 1-year noninferiority study of 1,602 postmenopausal women. The study showed that bone mineral density (BMD) increases in the lumbar spine in patients on monthly ibandronate were significantly higher than in those on 2.5 mg of ibandronate daily (4.85% vs. 3.86%). BMD increases at other skeletal sites also were "consistently higher" among those on the monthly dose, according to the drug's label.

Approval of the daily formulation was based on a 3-year study of almost 3,000 women with postmenopausal osteoporosis; the risk of having a vertebral fracture was 4.7% among those on ibandronate, vs. 9.6% among those on placebo, a highly significant difference.

Over the past decade, several new choices for osteoporosis treatment and prevention have become available, each a little different from the others, providing more opportunities to individualize therapy, said Ethel Siris, M.D., director of the Toni Stabile Osteoporosis Center at New York–Presbyterian Hospital and the Madeline C. Stabile professor of clinical medicine, Columbia University, New York.

The fracture data in the trials of these three drugs are somewhat different, she observed, noting that in the initial 3-year study, daily ibandronate was found to reduce the vertebral fracture risk "quite substantially" but did not reduce the risk of nonvertebral fractures. Alendronate, on the other hand, has been shown to reduce vertebral and hip fractures, and risedronate has been shown to reduce vertebral and nonvertebral fractures, reflected in approved indications, she added in an interview.

In a subgroup of patients with very low T scores in the initial ibandronate study, there was a reduction in nonvertebral fracture risk among those on 2.5 mg, compared with placebo, but that was a post hoc analysis and not a prespecified end point, she said.

Another difference between ibandronate and the other two oral bisphosphonates is that a patient needs to sit or stand for 1 hour after taking ibandronate, compared with only 1/2 hour for the other two agents, she said.

Dr. Siris, a consultant to the manufacturers of alendronate and risedronate, has served on an advisory board for GlaxoSmithKline, which is copromoting ibandronate with Roche.

The recommended dosage of monthly ibandronate is one 150-mg tablet taken on the same day once a month, swallowed with a 6- to 8-ounce glass of water, while standing or sitting. The patient should then wait 60 minutes before lying down or eating, drinking, or taking other medications (to reduce the risk of esophageal irritation). Esophagitis, the main side effect of bisphosphonates, is reduced with less frequent dosing but can still occur. ■

Preserve Bone After Heart Transplants

BY MITCHEL L. ZOLER
Philadelphia Bureau

PHILADELPHIA — Weaning heart transplant patients aggressively from steroids and prophylactic treatment with alendronate led to a reduced incidence of osteoporosis in a series of 28 patients, compared with a historic control group.

The alendronate regimen was well tolerated by all 28 patients, Gerald Yong, M.B., said at the annual meeting of the International Society for Heart and Lung Transplantation.

And survival rates among the patients managed with steroid weaning and alendronate were similar to the historic control group that had been treated with full-dose steroids, suggesting that the regimen designed to prevent bone loss did not compromise immunosuppression, said Dr. Yong, a physician in the cardiac transplant unit at Royal Perth Hospital in Australia.

He and his associates reviewed bone mineral density scores, obtained with dual-energy x-ray absorptiometry (DXA) of the femoral neck and lumbar spine, for 28 heart-transplant patients who were treated at Royal Perth since June 1999, when the bone-preserving regimen was instituted, and compared them with a similar group of 28 patients treated at the same center from 1995 to 1999.

Among the 28 patients in the historic control group, 26 were on prednisolone at the time they underwent bone mineral density studies.

Two patients in this group received treatment with either estrogen or vitamin D to prevent osteoporosis.

The patients in the bone-preserving group were all treated with either 10 mg alendronate daily or 70 mg weekly. Steroid weaning was begun at least 6 months after transplantation, and by the time of their DXA scans 16 of the 28 patients were completely off of prednisolone.

The average *z* scores and T scores at the femoral neck were 0.4 and –0.7 among the patients in the bone-preserving group, compared with –0.6 and –1.2 in the historic controls. The average scores in the lumbar spine were 0 and –0.6 among patients in the bone-preserving group, and –0.9 and –1.3 in the controls.

On the basis of their average z scores and T scores in the femoral neck, osteoporosis was diagnosed in five of the patients on the bone-preserving regimen (18%), compared with eight patients in the control group (29%). ■

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