# Monthly Oral Boniva Is Safe and Effective

## *Bone mineral density gains continued for 3 years and counting in MOBILE's extension phase.*

BY KERRI WACHTER
*Senior Writer*

PHILADELPHIA — Once-monthly oral ibandronate (Boniva) increases spine and hip bone mineral density beyond 2 years, Dr. Paul D. Miller reported in a poster presented at the annual meeting of the American Society for Bone and Mineral Research.

Dr. Miller, of the department of medicine at the University of Colorado, Denver, and medical director of the Colorado Center for Bone Research, Lakewood, and his colleagues presented 1-year results from the long-term extension phase of the MOBILE (Monthly Oral Ibandronate in Ladies) study. In year 3 of treatment with oral ibandronate, lumbar spine bone mineral density (BMD) increased 1.5% for women receiving 150 mg once monthly and 1.1% for women receiving 100 mg once monthly. In the same period, total hip BMD increased 0.3% in the 150-mg group; total hip BMD did not change for the 100-mg group.

**Bone mineral density increased 2.5% at the femoral neck over 3 years in women on 100 mg monthly and by 3.5% in women taking 150 mg each month.**

In the MOBILE study, 1,609 postmenopausal women with osteoporosis were randomized to receive 100 mg (single dose), 50 mg plus 50 mg (50-mg doses on 2 consecutive days), or 150 mg (single dose) of monthly oral ibandronate, or 2.5 mg of oral daily ibandronate.

At 2 years, once-monthly oral ibandronate provided superior increases in lumbar spine BMD compared with the daily regimen (Ann. Rheum. Dis. 2006;65:654-61). In 2005, the Food and Drug Administration approved the 150-mg, once-monthly dosage of oral ibandronate.

After 2 years, the MOBILE study was extended for another 3 years. In the extension phase, patients in the 100-mg (single dose) or 150-mg oral ibandronate once-monthly groups maintained these regimens. Patients who were originally randomized to daily treatment or the 50 mg plus 50 mg (50-mg doses on 2 consecutive days) per month regimens were rerandomized to receive either 100 mg once monthly or 150 mg once monthly.

All patients received daily calcium (500 mg) and vitamin D (400 IU) supplements.

For 168 women on 150-mg once-monthly oral ibandronate for 3 years (the 2 years of the MOBILE study and 1 year of the extension study), lumbar spine BMD increased 7.6% from baseline.

Likewise, for 173 women on 100 mg ibandronate, lumbar spine BMD increased 6.4% from baseline. Also, total hip BMD increased 4.1% from baseline in women in the 150-mg group, while it increased 3.4% from baseline in the 100-mg group. Over 3 years, there were also gains of 2.5% and 3.5% from baseline at the femoral neck for the 100-mg and 150-mg groups, respectively. In the same period, there were gains of 5.4% and 6.2% from baseline at the trochanter for the 100-mg and 150-mg groups. The long-term extension study was funded by F. Hoffmann-LaRoche Ltd. and GlaxoSmithKline Inc. Dr. Miller reported receiving funding and consulting fees from both companies.

In a separate poster, Dr. Stuart Silverman, a rheumatologist at Cedars-Sinai Medical Center in Los Angeles, and his colleagues reported on adverse events from the MOBILE study.

A total of 719 women—359 in the 100-mg group and 360 in the 150-mg group—were included in the safety analysis.

The rates of drug-related adverse events were generally low and comparable for the two groups (7.8% for the 100-mg group and 7.5% for the 150-mg group). Only one serious adverse event was considered to be possibly related to treatment with 150-mg oral ibandronate once monthly.

The rates of drug-related adverse events leading to withdrawal were also comparable between the two groups (0.3% in the 100-mg group and 0.8% in the 150-mg group).

Gastrointestinal events have often been cited by patients as a reason for discontinuing oral bisphosphonates. The incidence of upper-GI adverse events was 4.5% and 6.9% in the 100-mg and 150-mg groups, respectively. No serious upper-GI adverse events occurred. The five most common upper-GI adverse events reported were dyspepsia, nausea, upper-abdominal pain, gastritis, and vomiting.

Dr. Silverman reported receiving funding from F. Hoffmann-LaRoche Ltd. and GlaxoSmithKline. ■

# *Investigational Cathepsin K Inhibitor Increased BMD in Older Women*

BY KERRI WACHTER
*Senior Writer*

PHILADELPHIA — Balicatib, an investigational agent that belongs to a new class of osteoporosis drugs, appears comparable to bisphosphonate therapy in increasing bone mineral density in postmenopausal women, according to trial results presented at the annual meeting of the American Society for Bone and Mineral Research.

"Balicatib was able to increase [bone mineral density] at both the spine and hip, with changes very similar to those seen with bisphosphonates," said Dr. Silvano Adami.

Balicatib inhibits cathepsin K, a cysteine protease that plays an important role in the pathologic process of bone resorption. Cathepsin K is highly and selectively expressed by osteoclasts. Selective cathepsin K inhibitors provide a new method of action for reducing bone resorption and improving BMD.

In this randomized, placebo-controlled trial, 675 postmenopausal women with lumbar spine BMD T scores of less than –2 were randomized to receive 5 mg, 10 mg, 25mg, or 50 mg of daily oral balicatib or placebo, said Dr. Adami, head of gastroenterologic, rheumatologic, and vascular rehabilitation at the University of Verona (Italy). All patients received calcium and vitamin D supplements.

The women were assessed with dual-energy x-ray absorptiometry (DXA) measurements of spine and hip BMD, and levels of bone formation and resorption biomarkers were measured.

At baseline, the average patient age was 62 years. The average lumbar spine and total hip T scores were –2.6 and –1.4, respectively; 87% of the women had no morphometric vertebral fractures.

Following 1 year of treatment with balicatib, "the changes in BMD were quite remarkable," said Dr. Adami. "With the highest dose [50 mg/day], the change in spine BMD was similar to that which [can be] achieved with bisphosphonate therapy." Overall there was a dose-related increase in both spine and hip BMD (see table).

In terms of bone resorption, the researchers looked at levels of urinary N-terminal cross-linked telopeptides of type I collagen (normalized with respect to urine creatinine) and serum C-terminal collagen I telopeptide (CTX).

In the first month of treatment, a decrease was observed in serum CTX levels. However, over the next 11 months, there was a trend of rising CTX levels in all patients—even those in the placebo group. "We do not have an explanation," said Dr. Adami. Overall, there was also a dose-related decrease in serum CTX and urinary NTX levels.

In terms of biomarkers of bone formation, the researchers measured serum osteocalcin and NTX. Serum osteocalcin and NTX decreased somewhat during the early stages but at 12 months, no differences were observed between the treated and placebo patients. Overall, bone resorption markers were decreased, while bone formation markers remained the same.

**BMD Improvement After 1 Year of Balicatib Treatment**

| | 5 mg | 10 mg | 25 mg | 50 mg | Placebo |
|---|---|---|---|---|---|
| **Lumbar Spine** | | | | | |
| Mean % change | 1.20 | 3.16 | 4.41 | 4.46 | 0.25 |
| **Total Hip** | | | | | |
| Mean % change | 0.07 | 1.77 | 2.21 | 2.25 | 0.29 |

Note: Based on a study of 675 patients.
Source: Dr. Adami

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The numbers of adverse events were very similar between all of the groups. Two patients developed sclerodermic/morphea-like lesions, which improved when the treatment was stopped, Dr. Adami reported. ■

# Spinal Bone Mineral Density Preserved Despite Dalteparin Use in Pregnancy

LISBON — Long-term treatment with low-molecular-weight heparin during pregnancy did not cause a drop in spinal bone mineral density in a study with 62 women, Dr. Marc A. Roger said at the third World Congress of the International Society of Obstetric Medicine.

The findings are from a subgroup analysis of data collected in the Thrombophilia in Pregnancy Prophylaxis Study (TIPPS), an ongoing, multicenter trial designed to compare prophylaxis using LMWH with placebo for pregnancy outcomes in women with a thrombophilia, explained Dr. Roger, Ottawa Hospital.

TIPPS enrolled women with thrombophilia at less than 20 weeks gestation who were at risk for thromboembolism or had a history of pregnancy complications. They were randomized to placebo or to 5,000 U dalteparin daily through week 20, followed by a regimen of 5,000 U b.i.d. through delivery. All women in the study received dalteparin post partum for 6 weeks. In the substudy of 62 women, the primary end point was the absolute lumbar-spine bone mineral density measured at 6 weeks post partum. Because of crossovers, 33 women received dalteparin and 29 women received placebo.

The average bone mineral density was 1.15 g/cm$^2$ in the LMWH group and 1.20 g/cm$^2$ in the control group, a difference that was not statistically significant. In addition, the 95% confidence interval for bone mineral density in the dalteparin group did not enter the range that defines osteopenia (less than one standard deviation below the mean). Both TIPPS and the subanalysis were sponsored by Pfizer, which markets dalteparin (Fragmin), the LMWH used in the studies. Dr. Roger has received research support from and is on a scientific advisory board for Pfizer.

**—Mitchel L. Zoler**