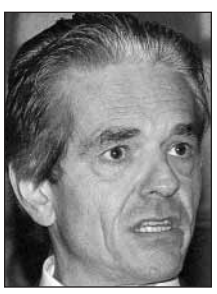
Once-Monthly Ibandronate Effective at 2 Years

BY BRUCE JANCIN
Denver Bureau

VIENNA — Oral ibandronate at 150 mg once monthly showed continued impressive therapeutic efficacy in women with postmenopausal osteoporosis at the 2-year mark in the Monthly Oral Ibandronate in Ladies (MOBILE) trial, Pierre D. Delmas, M.D., said at the annual European congress of rheumatology.

Ibandronate (Boniva) was approved by the Food and Drug Administration this spring as the first once-monthly oral bisphosphonate, in part because of the persuasive 1-year results of MOBILE. The new 2-year data provide reassurance that over the longer term this therapy continues to be a highly effective and well-tolerated alternative to daily or weekly bisphosphonates, said Dr. Delmas, professor of medicine and rheumatology at Claude Bernard University, Lyon, France.



MOBILE is a randomized, double-blind, phase III, Roche- and GlaxoSmithKline-sponsored clinical trial involving 1,609 women with postmenopausal osteoporosis who were placed on oral ibandronate at 2.5 mg/day, 100 mg once per month, 150 mg once per month, or 50 mg on each of two consecutive days per month. The daily-therapy arm served as the comparator group in this trial because 2.5 mg/day was the first FDA-approved ibandronate regimen, and it was previously shown to reduce vertebral fracture risk by 62% compared with placebo in a 3-year trial. Dr. Delmas focused on the once-monthly 150-mg group because this dosage showed the greatest efficacy and is already approved in the United States.

The 150-mg once-monthly regimen was superior to daily therapy in terms of BMD improvement at various sites.

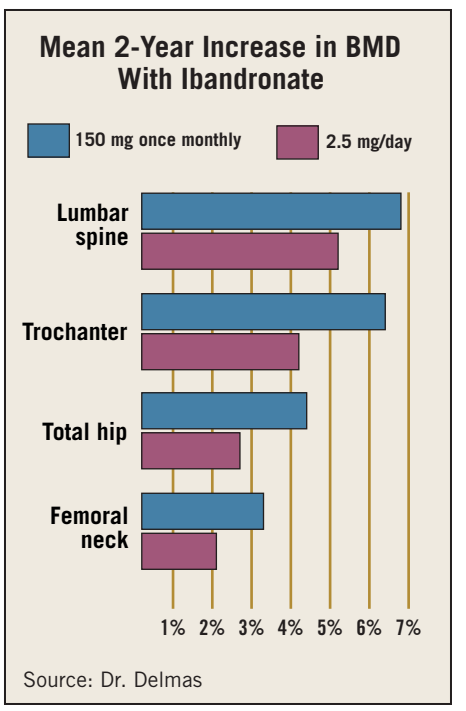
DR. DELMAS

MOBILE wasn't designed or powered to evaluate fracture risk. It was a bridging trial that relied upon the surrogate end points of change in bone mineral density (BMD) and bone resorption markers in an effort to establish that monthly therapy was noninferior to the 2.5-mg/day regimen. In fact, the 150-mg once-monthly regimen proved to be superior to daily therapy in terms of improvement in BMD at various sites at 2 years. (See chart.)

The mean decrease in the bone resorption marker serum C-terminal cross-linking telopeptide of type I collagen (sCTX) was 67.7% in the 150-mg once-monthly group and 61.5% with daily therapy. Tolerability and the incidence of side effects in all of the once-monthly study arms at 2 years were similar to rates with daily therapy, as was also true after 1 year, Dr. Delmas said at the meeting, which was sponsored by the European League Against Rheumatism.

MOBILE coinvestigator Jean-Yves Reginster, M.D., said it's a reasonable hypothesis that once-monthly therapy will result in better therapeutic adherence than weekly or daily therapy, as 1-year adherence to bisphosphonate therapy has been shown to be nearly twice as great with weekly versus daily treatment. This hypothesis is supported by data from a large new European patient survey indicating that four-fifths of women with postmenopausal osteoporosis would be interested in dosing regimens that are less frequent than weekly, and three-fourths of physicians believe that such regimens would have a strong favorable effect upon adherence.

"We're now facing a new challenge in the management of osteoporosis: It's that bisphosphonate compliance and persistence with daily or weekly regimens remain largely suboptimal. More than one-half of patients don't even take their drug for 12 months," according to Dr. Reginster of the University of Liège, Belgium. ■

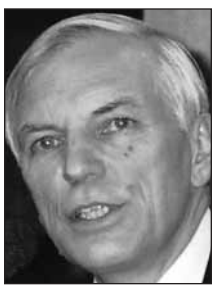


Alendronate Bests Alfacalcidol in Steroid-Induced Osteoporosis

BY BRUCE JANCIN
Denver Bureau

VIENNA — Alendronate is markedly more effective than 1-hydroxyvitamin D_3 (alfacalcidol) as prophylaxis against glucocorticoid-induced osteoporosis, Johannes W.J. Bijlsma, M.D., Ph.D., said at the annual European congress of rheumatology.

He reported on 200 patients—40% men, the rest postmenopausal women—in an 18-month randomized double-blind 23-center Dutch trial sponsored by the Netherlands Health Council.



Participants had various rheumatic diseases for which they were placed on systemic steroids at a mean starting dose of 23 mg/day of prednisolone or its equivalent. Over 18 months their cumulative dose was nearly 6 g.

Patients were randomized at the outset of steroid therapy to 10 mg/day of alendronate plus placebo or 1 mcg/day of alfacalcidol, an activated vitamin D, plus placebo.

The primary study end point was change in lumbar spine bone mineral density over the 18 months.

It increased by 2.3% in the alendronate group and decreased by 1.9% in the alfacalcidol group, for a net 4.2% difference between the regimens.

Similarly, total hip bone mineral density increased by 0.7% in the alendronate group while declining by 2.5% with alfacalcidol, said Dr. Bijlsma, professor and head of the department of rheumatology and clinical immunology at University Medical Center, Utrecht, the Netherlands.

Three asymptomatic vertebral fractures occurred in three patients in the alendronate group, compared with 13 vertebral fractures in eight patients in the alfacalcidol group; 5 of them were in three patients who were symptomatic.

Glucocorticoid-induced osteoporosis is an enormous problem. In various epidemiologic studies 0.5%-1.7% of women over the age of 55 are on prolonged systemic steroid therapy. Fifty percent develop osteoporosis. One-third experience vertebral fractures. Marked trabecular bone loss, mainly due to reduced bone formation, is observed within the first 6 months of steroid therapy.

Lumbar spine BMD rose by 2.3% in the alendronate group and dropped by 1.9% in the alfacalcidol group.

DR. BIJLSMA

Steroids decrease osteoblasts, reducing bone formation, and encourage release of parathyroid hormone, stimulating bone resorption. Bisphosphonates are known to protect against steroid-induced osteoporosis, Dr. Bijlsma said.

Alfacalcidol was deemed worth studying as an alternative because activated vitamin D stimulates osteoblasts, thereby encouraging bone formation, he explained at the meeting, sponsored by the European League Against Rheumatism. ■

Patients Taking Steroids Require Multiple Bone-Saving Measures

BY ROBERT FINN
San Francisco Bureau

SANTA BARBARA, CALIF. — About half of patients using glucocorticoids for long periods will suffer compression fractures of the vertebrae if nothing is done to intervene, Barbara P. Lukert, M.D., said at a symposium sponsored by the American College of Rheumatology.

Bisphosphonate therapy is clearly effective in reducing fractures, whether started when initiating glucocorticoids or after a patient has been on them for a while. But bisphosphonates aren't enough, and other steps should be taken to manage these patients, said Dr. Lukert of the University of Kansas Medical Center in Kansas City.

Other opportunities to intervene include:

► **Diet is critical.** Since glucocorticoids are catabolic, patients need adequate protein intake, not just calcium and phosphorus.

► **Heavily encourage patients to exercise,** not only because of its benefits on bone. Glucocorticoids often cause myopathy, ranging from mild to severe, and exercise can stave this off. Strengthening the quadriceps and related muscle groups has been shown to prevent falls.

► **Control urinary calcium.** A very large percentage of patients on glucocorticoids will develop hypercalciuria, and restricting sodium in the diet will go a long way toward resolving this.

► **Replace hormones as appropriate.** Glucocorticoids inhibit pituitary gonadotropin, and men taking steroids often have low testosterone levels. If there's no contraindication, this testosterone should be replaced, Dr. Lukert said.

Women taking steroids often have low estrogen levels. If premenopausal women become amenorrheic on glucocorticoids, consider prescribing estrogen or progesterone. Dr. Lukert noted that estrogen replacement in postmenopausal women remains controversial.

Patients who have a bone mineral density (BMD) T score of less than –1.5 or are taking more than 10 mg/day of prednisone or the equivalent should receive bisphosphonate therapy as soon as corticosteroids are started.

Patients with a higher BMD taking lower doses of prednisone may hold off on starting bisphosphonate therapy at first and retest BMD after 6 months.

Another reasonable strategy is simply to give a bisphosphonate to all patients who anticipate taking steroids for several weeks or longer.

This strategy is certain to prevent fractures, but at the cost of treating 40%-50% of patients who would not have suffered a fracture even without the bisphosphonate prescription, Dr. Lukert said. ■