Vienna — Alendronate is markedly more effective than 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 alendronate at 2.5 mg/day, 100 mg once per month, 130 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 alendronate 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. 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. (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 were low 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 co-investigator Jean-Yves Reigner, 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 sus 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. Regnier of the University of Liège, Belgium.

### Alendronate Bests Alfalcacidol in Steroid-Induced Osteoporosis

**BY BRUCE JANCIN**

Vienna — Alendronate is markedly more effective than 1-hydroxyvitamin D₃ (alfalcacidol) 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 2:1 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 mg/day of alfalcacidol, an activated vitamin D₃ 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 alfalcacidol group, 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 alfalcacidol, 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 alfalcacidol group. Two 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. 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.

Alfalcacidol was deemed worth studying as an alternative because activated vitamin D₃ is effective for osteoporosis by stimulating 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**

Santa Barbara, Calif. — About half of patients using glucocorticoids for long periods will suffer compression fractures of the vertebrae 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. (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 were low 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.

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“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. Regnier of the University of Liège, Belgium.

### Mean 2-Year Increase in BMD With Ibandronate

<table>
<thead>
<tr>
<th>Site</th>
<th>150 mg once-monthly</th>
<th>2.5 mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar spine</td>
<td>2.5%</td>
<td>3%</td>
</tr>
<tr>
<td>Trochanter</td>
<td>1.5%</td>
<td>2%</td>
</tr>
<tr>
<td>Total hip</td>
<td>1.5%</td>
<td>2%</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>0.5%</td>
<td>1%</td>
</tr>
</tbody>
</table>

Source: Dr. Delmas

With Ibandronate