Alendronate, Risedronate Compared in BMD Trial

The 1-year study did not provide data on fractures; clinical relevance of BMD findings questioned.

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SEATTLE — Alendronate appears slightly more effective than risedronate at increasing bone mineral density, according to the results of a head-to-head trial presented during the annual meeting of the American Society for Bone and Mineral Research.

However, without fracture data, it's unknown whether such BMD findings will translate into a clinically meaningful difference.

In the double-blinded study involving 1,053 postmenopausal women treated for 1 year, alendronate increased BMD at the hip trochanter by a mean of 3.4%, and risedronate increased trochanter BMD by a mean of 2.1%.

The investigation, known as the Fosamax Actonel Comparison Trial, was conducted with patients from 78 different centers, said Clifford J. Rosen, M.D., who is the director of the Maine Center of Osteoporosis Research and Education, Bangor.

Patients received either 70 mg of alendronate and placebo risedronate once weekly or 35 mg risedronate and placebo alendronate once weekly.

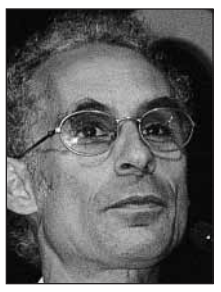
In addition to the hip trochanter, BMD measurements were taken for the total hip, lumbar spine, and femoral neck. BMD was increased a mean 2.2% in the active alendronate group, versus a mean 1.2% in the active risedronate group.

Lumbar spine BMD increased a mean 3.7% with alendronate, versus 2.6% with risedronate. In addition, femoral neck BMD increased a mean 1.6% with alendronate and 0.9% with risedronate, he said.

A greater proportion of patients also either maintained or increased BMD on alendronate. Of the patients on alendronate, 84% at least maintained trochanter BMD and 51% had at least a 3% increase, whereas on risedronate, 68% of patients at least maintained BMD, and 41% had a 3% increase or greater.

In addition, alendronate depressed urine and serum markers of bone turnover to a greater degree than risedronate. There was no difference in the occurrence of adverse events between the two drugs.

Not everyone at the meeting was impressed by the study or its results.



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DR. ROSEN

"Marketing," said Paul D. Miller, M.D., when asked about the trial, which was sponsored by Merck and Co., Inc., the manufacturer of alendronate. It's not clear that the degree of difference reported translates into greater bone strength, he said.

"The problem is that there are no fracture data," said Dr. Miller, medical director for the Colorado Center for Bone Research, Lakewood. "At these differences, the bone strength may not be very different."

A larger study over a longer period of time would be needed to acquire fracture data, said Richard Petruschke, Pharm. D., who is a spokesperson for Merck and one of the investigators in the study.

"There is literature to support using these surrogates as being meaningful when taken together," Dr. Petruschke commented. ■

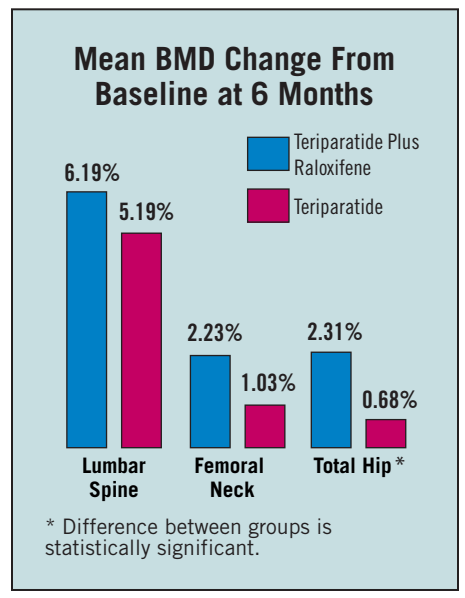
Raloxifene and PTH May Have Synergistic Effect on BMD

SAN ANTONIO — Women who are taking raloxifene for osteoporosis do not need to stop taking the bisphosphonate to begin parathyroid hormone therapy.

In fact, the two drugs may have some synergy, Chad Deal, M.D., said at the annual meeting of the American College of Rheumatology.

In a 6-month study comparing parathyroid hormone (1-34) plus raloxifene with parathyroid hormone monotherapy, the combination increased total hip bone density to a greater degree, observed Dr. Deal, who is the head of the center for osteoporosis and metabolic bone disease at the Cleveland Clinic Foundation.

The combination "could potentially enlarge the anabolic window, maximizing the formation of bone and minimizing the resorption of bone," said Dr. Deal, whose study included measurements of bone turnover markers.



Dr. Deal's double-blind study enrolled 137 subjects who were randomized to daily therapy with either the combination of teriparatide (Forteo), 20 mcg, plus raloxifene (Evista), 60 mg, or to monotherapy with teriparatide, 20 mcg.

All of the study participants also received calcium and vitamin D supplementation.

At 6 months' follow-up, the combination increased bone mineral density over baseline by a mean 6.19% at the lumbar spine, a mean 2.23% at the femoral neck, and a mean 2.31% for the total hip, as measured by dual x-ray absorptiometry. By comparison, teriparatide increased lumbar spine density by a mean 5.19%, femoral neck density by a mean 1.03%, and total hip density by 0.68%.

The differences at the lumbar spine and the femoral neck were not statistically significant, but the difference at the total hip was, Dr. Deal said.

Investigators have been intrigued by the possibility of combination treatment for osteoporosis for some time, he said.

But the only other previous major study of combination treatment looked at the use of parathyroid hormone with alendronate; it suggested that the addition of alendronate appeared to inhibit the ability of parathyroid hormone to stimulate new bone formation.

The two studies differ in several ways that make them difficult to compare.

In the alendronate trial, the addition of alendronate decreased the level of serum procollagen type I N-terminal propeptide (PINP)—a marker of bone formation—by 15% from baseline at 6 months. In the raloxifene trial, PINP in the combination group was increased from baseline to a mean level similar to that seen among patients receiving teriparatide alone.

Moreover, bone resorption was suppressed by both the teriparatide alone and the raloxifene-teriparatide combination, as measured by serum type I collagen C-telopeptide level.

"The limitation of this trial, of course, is that it is too small to assess the important outcome, which is fracture," Dr. Deal said.

The combination was well tolerated. Subjects in both groups had similar increases in serum uric acid levels, but there were no cases of gout, he added.

The trial was sponsored by Eli Lilly & Co., maker of both Evista and Forteo. ■

Investigational SERM Increased Lumbar Spine BMD by 2%

SAN ANTONIO — The next generation selective-estrogen receptor modulator lasofoxifene increased vertebral bone mineral density better than did raloxifene, according to the findings of a company-sponsored trial presented at the annual meeting of the American College of Rheumatology.

In the study, 410 postmenopausal women were randomly assigned to one of two doses of lasofoxifene, 0.25 mg or 1 mg daily; raloxifene at 60 mg daily, or a placebo.

The half-life of lasofoxifene is about a week versus 28 hours for raloxifene, according to Andy Lee, a director with Pfizer Global Research and Development, New London, Conn.

A new drug application for lasofoxifene has been submitted to the Food and Drug Administration for approval.

Lasofoxifene increased bone mineral density (BMD) at the lumbar spine by a mean of about 2% after 2 years of treatment. That compared with no mean improvement in spine BMD—but no density loss—in the patients assigned to raloxifene, and a 2% decrease in density in patients assigned to placebo.

BMD at the total hip improved by a mean of 1% for patients taking either raloxifene or lasofoxifene; total hip BMD remained the same in patients taking placebo.

Although responsiveness to lasofoxifene varied, overall more women responded to lasofoxifene than to raloxifene, Mr. Lee said.

Spine density improved or was at least maintained in 90% and 93% of the patients in the low- and high-dose lasofoxifene groups, respectively. That compared with 77% of the patients who took raloxifene and 65% of the patients who took placebo.

Changes in bone turnover markers were also greater with lasofoxifene. N-telopeptide levels, for example, decreased by a mean 35% in the patients on lasofoxifene, versus 15% in the patients on raloxifene.

And the new drug reduced LDL cholesterol levels by a mean of 20% versus 12% for raloxifene.

Future trials of lasofoxifene will use the 0.25 mg dose, Mr. Lee said.

Some women treated with lasofoxifene experienced hot flashes, leg cramps, and increased vaginal moisture, but overall the two drugs were tolerated similarly.

None of the lasofoxifene trials has shown an increase in endometrial hyperplasia or vaginal bleeding, Mr. Lee said.

Likewise, there have been no reports of urogenital prolapse, a problem that has plagued earlier selective estrogen receptor modulators. ■