Raloxifene, PTH Are Good Osteoporosis Combo

Together, the two drugs could potentially maximize the formation and minimize the resorption of bone.

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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, 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 of raloxifene and parathyroid hormone 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.

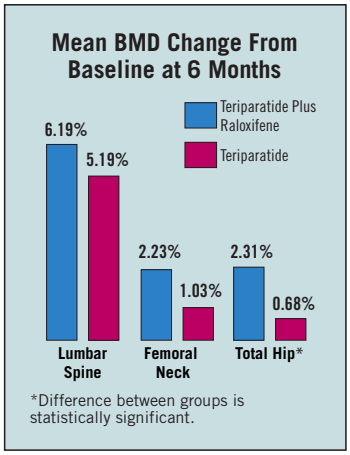
Investigators have been intrigued by the possibility of combination treatment for osteoporosis for some time, he said.

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 clinical trial was sponsored by Eli Lilly & Co., which makes both Evista and Forteo. ■

Alendronate Edged Risedronate In BMD Trial, but Some Skeptical

Seattle — Alendronate appears slightly more effective than risedronate at increasing bone mineral density, according to the results of a head-to-head trial presented at 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%.

A greater proportion of patients either maintained or increased BMD on alendronate.

DR. ROSEN

The investigation, known as the Fosamax Actonel Comparison Trial, was conducted with patients from 78 different centers, said Clifford J. Rosen, M.D., 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, and femoral neck BMD increased a mean 1.6% with alendronate and 0.9% with risedronate.

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 adverse events.

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

"Marketing," said Paul D. Miller, M.D., medical director for the Colorado Center for Bone Research, Lakewood, when asked about the trial, 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," Dr. Miller said. "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., a spokesperson for Merck and one of the study's investigators. "There is literature to support using these surrogates as being meaningful when taken together," he said. ■

Calcium Supplements Cut 5-Year Fracture Risk for Elderly Women

Seattle — Calcium supplementation appears to reduce by 34% the 5-year risk of fracture among elderly women, according to the findings of a population-based study presented at the annual meeting of the American Society for Bone and Mineral Research.

The benefit was seen as early as 13 months despite the fact that all women were deemed at baseline to be getting adequate calcium—a mean of about 960 mg per day, said Richard Prince, M.D., of the department of endocrinology and diabetes at Sir Charles Gairdner Hospital, Perth, Australia.

"On the basis of these data, we believe that an increased emphasis on calcium supplementation should be a first-line, public-health approach to fracture prevention," Dr. Prince said.

Extrapolating from the findings, the data suggest elderly women who use calcium supplementation can cut their fracture risk from 16% to 10% over 5 years.

The 1,460 healthy ambulatory women, aged 70 or older, were randomly assigned to receive 600 mg of calcium carbonate twice daily or placebo.

Calcium intake was assessed and dual x-ray absorptiometry (DXA) scans were taken at baseline and again at least 1 year later.

Possible fractures were flagged on the basis of diaries that were submitted by the women every 4 months and were confirmed by x-ray.

During the 5-year study, the rates of death, withdrawal, and treatment cessation were similar between the two groups: 465 and 458 patients remained in the placebo and calcium groups, respectively.

In all, 235 individuals sustained 296 fractures; 118 fractures occurred among those taking calcium, and 178 occurred among those taking placebo, for an overall 34% reduction in fractures among patients in the calcium group who stuck to the protocol for the entire study period.

Upper-appendage fractures were most common.

Calcium appeared to improve bone mineral density at cortical bone sites, according to DXA findings.

At 13 months, there were early indications of a reduction in fracture rates among patients in the calcium group.

Calcium supplementation did not appear to have an effect on spinal bone mineral density or on the vertebral fracture rate.

Extrapolating from these findings, the data suggest that elderly women who use calcium supplementation, 1,200 mg daily, can cut their fracture risk from 16% to 10% over 5 years, Dr. Prince said. ■