



Arthritis News

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SERM-ACCOMPANIED TERIPARATIDE OFFERS IMPROVED BONE THERAPY FOR POSTMENOPAUSAL PATIENTS

SAN ANTONIO, TEXAS—The combination of teriparatide (Forteo®), an injectable parathyroid hormone medication, when administered with the selective estrogen receptor modulator, raloxifene (Evista®), improves bone density formation, according to research presented this week at the American College of Rheumatology Annual Scientific Meeting in San Antonio, Texas.

Osteoporosis weakens bones, leaving the over 10 million women who suffer from the disease susceptible to bone fractures of the spine, wrist and hip. These often debilitating fractures, particularly those in the spine or hip, can lead to chronic pain, long-term disability and even death. Therefore, the goal in treating osteoporosis with medications such as teriparatide is to stimulate new bone formation that strengthens the bone and prevents such fractures from occurring.

Previous research had shown that another antiresorptive agent, alendronate (Fosamax®), appeared to diminish the gain in bone density seen with teriparatide alone. To determine if the benefits of teriparatide can be enhanced with the addition of raloxifene, a selective estrogen receptor modulator (SERM) that slows bone loss and slightly increases normal bone growth, researchers conducted a six-month randomized, double-blind study comparing the use of teriparatide against the combination therapy. The 137 postmenopausal women participating in the trial, none of whom had prior osteoporosis treatment, also received calcium and vitamin D supplements throughout the course of the study.

Groups on the single and double agents showed similar significant increases in bone formation in months one, three and six. However, bone resorption was reduced (as measured by markers of bone turnover found through urine and blood tests) in the group taking both medications by month three, an effect which persisted to month six. Those taking both teriparatide and raloxifene had higher bone density at the spine and hip (significantly higher for the hip site) than those on teriparatide alone.

“The results are encouraging since we are looking for agents or a combination of agents given together or sequentially that will further reduce the rate of fracture in high risk patients,” said Chad Deal, MD, Cleveland Clinic Foundation, Cleveland, Ohio, and an investigator in the study. “The most important question is effect on fracture reduction and, although no studies are underway at this time to assess fracture reduction with this combination, the bone density and marker data are a promising start.”

The American College of Rheumatology is the professional organization for rheumatologists and health professionals who share a dedication to healing, preventing disability and curing arthritis and related rheumatic and musculoskeletal diseases. For more information on the ACR’s annual meeting, see www.rheumatology.org/annual.

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Editor’s Notes: Dr. Deal will present this research during a scientific session at the ACR Annual Scientific Meeting from 5:00–5:15 PM CT (6:00–6:15 PM ET) Wednesday, October 20, in Room 006 of the Henry B. González Convention Center. He will be available for media questions during a briefing at 1:30 PM CT (2:30 PM ET) on Tuesday, October 19, in the on-site Press Conference Room, Room 218.

Concomitant Teriparatide plus Raloxifene for the Treatment of Postmenopausal Osteoporosis: Results from a Randomized Placebo-controlled Trial

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PURPOSE: To study whether concomitant raloxifene therapy would impact the bone activity of teriparatide [rhPTH (1–34)].

METHODS: We conducted a 6-month randomized, double-blind, placebo controlled trial comparing teriparatide 20 mcg/day (TPTD20) plus raloxifene 60 mg/day (RLX60) (n=69) with TPTD20 plus placebo (n=68) in postmenopausal women who were osteoporosis treatment naïve and received calcium and vitamin D supplementation. Serum procollagen type I amino-terminal propeptide (PINP) and type I collagen C-telopeptide (CTX) levels were determined. Bone mineral density (BMD) was measured by DXA. Adverse events and calcium, phosphate and uric acid metabolism were assessed.

RESULTS: Similar significant increases in bone formation (PINP) were shown at 1, 3, and 6 months in both groups (TABLE). After 1 month, bone resorption (CTX) was not increased from baseline in either group. After 3 months, CTX was significantly increased from baseline in the TPTD20 but not the concomitant group. At 6 months, CTX was significantly increased from baseline in both groups, but the increase in the concomitant group was significantly less than in the TPTD20 group. Mean BMD (\pm SE) percent changes from baseline to endpoint in the TPTD20 group were: LS $5.19 \pm 6.7\%$ ($P < .001$), FN $1.03 \pm 6.7\%$ (NS), and TH $0.68 \pm 5.9\%$ (NS). In the concomitant group, BMD changes from baseline to endpoint were: LS $6.19 \pm 6.5\%$ ($P < .001$), FN $2.23 \pm 6.4\%$ ($P < .001$), and TH $2.31 \pm 5.6\%$ ($P < .001$). The BMD increase at total hip was significantly ($P = 0.04$) greater in the concomitant group compared to the TPTD20 group. In the TPTD20 group, mean serum calcium levels increased (0.30 ± 0.6 mg/dl, $P < .001$) from baseline to endpoint and mean serum phosphate was unchanged. In the concomitant group, mean serum calcium was unchanged, whereas mean serum phosphate decreased (-0.20 ± 0.6 mg/dl, $P < .001$) from baseline to endpoint. Serum uric acid levels significantly increased versus baseline at study endpoint with TPTD20 (1.28 ± 0.6 mg/dl, $P < .001$) and concomitant therapy (0.94 ± 1.1 mg/dl, $P < .001$). Changes from baseline in serum calcium ($P < .001$), phosphate ($P < .01$) and uric acid ($P < .05$) were significantly different between treatment groups. Therapy in both groups was well tolerated.

CONCLUSIONS: Compared to TPTD20 therapy, concomitant therapy increased bone formation to a similar degree, increased bone resorption to a significantly lesser degree, and significantly increased total hip BMD.

Markers of bone turnover (mean \pm SE) change from baseline. Analysis was by ITT using ANCOVA with baseline marker as a covariate.

	Baseline	Mo. 1 change	Mo. 3 change	Mo. 6 change
PINP (mcg/l)				
TPTD20+Placebo	50 \pm 3	+39 \pm 5 [†]	+51 \pm 7 [†]	+73 \pm 12 [†]
TPTD20+RLX60	59 \pm 3*	+47 \pm 5 [†]	+45 \pm 7 [†]	+65 \pm 12 [†]
CTX (pmol/l)				
TPTD20+Placebo	5097 \pm 871	-257 \pm 281	+1805 \pm 494 [†]	+3704 \pm 646 [†]
TPTD20+RLX60	6313 \pm 874	-145 \pm 287	+648 \pm 499	+1880 \pm 631 ^{†*}
* $P < .05$ vs. TPTD20, [†] $P < .001$ vs. baseline, [‡] $P < .01$ vs. baseline				

Disclosure: C. Deal, Eli Lilly 2, 5, 8; Merck 8; Procter & Gamble 5, 8; M. Omizo, Eli Lilly 2; E.N. Schwartz, Eli Lilly 2; E.F. Eriksen, Eli Lilly 3; P. Cantor, Eli Lilly 3; J. Wang, Eli Lilly 3; E.V. Glass, Eli Lilly 3; S.L. Myers, Eli Lilly 3; J.H. Krege, Eli Lilly 3

Author disclosure legend—Authors' disclosures of third-party relationships are listed in numeric format according to the following listing:

None—Nothing to disclose; 1—Stock options or bond holdings in a for-profit corporation or self-directed pension plan; 2—Research grants; 3—Employment (full or part-time); 4—Ownership or partnership; 5—Consulting fees or other remuneration (payment); 6—Non-remunerative positions of influence such as officer, board member, trustee or public spokesperson; 7—Receipt of royalties; 8—Speakers bureau.