



## **FORTEO(R) Increased Spine Bone Mineral Density in Patients with Glucocorticoid-Induced Osteoporosis**

### **Multi-national study compared FORTEO and the currently approved therapy Fosamax for the treatment of Glucocorticoid-Induced Osteoporosis**

INDIANAPOLIS, Nov 14, 2007 /PRNewswire-FirstCall via COMTEX News Network/ -- New data, published today in The New England Journal of Medicine, showed that in patients with glucocorticoid-induced osteoporosis FORTEO(R) (PTH 1-34, teriparatide [rDNA origin] injection) significantly increased lumbar spine bone mineral density (BMD) from baseline (8.2 percent) compared to Fosamax(R) (alendronate, 3.9 percent) at 18 months of therapy.(1)

In this head-to-head comparator study, the increase in lumbar spine BMD was significantly greater in patients receiving teriparatide compared with alendronate at 6, 12, and 18 months of treatment ( $p < 0.001$  at all time points).(1)

Glucocorticoid therapy is the most common cause of secondary osteoporosis,(2) leading to bone loss and an increased risk for fracture. Data indicate that glucocorticoids are used by up to three out of every 100 adults (3 percent) over age 50,(3) and up to 50 percent of individuals on chronic glucocorticoid therapy will eventually have an osteoporotic fracture.(4) Glucocorticoids are prescribed to treat many conditions, including rheumatoid arthritis, chronic obstructive pulmonary disease and inflammatory bowel disease.(4,5)

"Currently, there is a lack of variety in treatment choices for patients receiving chronic glucocorticoid medication who are at high risk for fractures," said lead investigator Kenneth G. Saag, M.D., MSc, professor of medicine and epidemiology at the University of Alabama in Birmingham. "These data are important because they show that teriparatide may have the potential to be a viable therapeutic option in the future for people with this disease."

Teriparatide is not indicated for the treatment of glucocorticoid-induced osteoporosis. Teriparatide is the first osteoporosis therapy approved by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) that rebuilds bone in postmenopausal women with osteoporosis who are at high risk for fracture and increases bone mass in men with primary or hypogonadal osteoporosis who are at high risk for fracture.(5,6) Teriparatide is marketed as FORSTEO in the European Union.

In February and June 2007, Lilly filed applications with the FDA and EMA, respectively, for a supplemental indication for teriparatide for the treatment of men and women with osteoporosis associated with glucocorticoid therapy and who are at high risk for fracture. These patients either have a history of osteoporotic fracture or low bone mineral density.(7)

#### **About the Study**

In a double-blind, active comparator-controlled trial, 428 patients with glucocorticoid-induced osteoporosis were randomized to receive once-daily subcutaneous injections of teriparatide (20 micrograms) plus oral placebo or daily placebo injections plus once-daily oral alendronate (10 mg). The study's primary endpoint was to determine whether the increase in lumbar spine bone mineral density from baseline to 18 months in patients receiving teriparatide was greater than in patients receiving alendronate. (1) Data published in the current issue of The New England Journal of Medicine represent the 18-month primary phase results of this 36-month trial. The 18-month continuation phase is ongoing.

The study included men and women aged greater than or equal to 21 years on sustained glucocorticoid therapy (prednisone equivalent of greater than or equal to 5 mg/day for greater than or equal to 3 months). Patient's spine or hip T-scores were either -2.0 or less, or -1.0 or less with one or more fractures.(1)

#### **Efficacy data after 18-months of therapy:(1)**

- The mean increase in lumbar spine BMD with teriparatide was significantly greater compared with Fosamax after six months through 18 months of therapy
- 8.2 plus or minus 0.6 percent increase with teriparatide and 3.9 plus or minus 0.6 percent increase with alendronate at 18

months ( $P < 0.001$ )

- The mean increase in total hip BMD with teriparatide was significantly greater compared with alendronate after 12 months (first measurement at the hip) through 18 months of therapy
  - 3.8 plus or minus 0.6 percent increase with teriparatide and 2.4 plus or minus 0.6 percent increase with alendronate at 18 months ( $P < 0.01$ )
- A preliminary analysis of new radiographic vertebral fractures in patients with baseline and 18 month radiographs showed that one patient receiving teriparatide (0.6 percent; 1 out of 171 patients) and 10 patients receiving alendronate (6.1 percent; 10 out of 165 patients) had greater than or equal to 1 new vertebral fracture
- A preliminary analysis of nonvertebral fracture showed that 12 patients receiving teriparatide (5.6 percent; 12 out of 214 patients) and eight patients receiving alendronate (3.7 percent; 8 out of 214 patients) had greater than or equal to 1 new nonvertebral fracture

There was no significant difference overall in the number of patients reporting adverse events in patients receiving teriparatide compared with alendronate.<sup>(1)</sup> Significant differences between groups in individual adverse events included nausea, insomnia, pharyngitis, and viral infection reported by more patients receiving teriparatide than alendronate, and rash, weight decrease, sciatica, and asthma reported by more patients receiving alendronate than teriparatide.<sup>(1)</sup> A significantly higher proportion of teriparatide than alendronate patients had at least one post-baseline calcium in the hypercalcemia range (18.0 percent [38 out of 211 patients] for teriparatide and 5.7 percent [12 out of 207 patients] for alendronate ( $P < 0.001$ )).<sup>(1)</sup>

To view the published manuscript, please visit [www.nejm.org](http://www.nejm.org).

#### Information about FORTEO(R)

As part of drug testing, teriparatide, the active ingredient in FORTEO(R), was given to rats for a significant part of their lifetime. In these studies, teriparatide caused some rats to develop osteosarcoma, a bone cancer. Osteosarcoma in humans is a serious but very rare cancer. Osteosarcoma occurs in about four out of every million older adults each year. It is not known if humans treated with FORTEO also have a higher chance of getting osteosarcoma.

FORTEO should be prescribed only to patients for whom the potential benefits are considered to outweigh the potential risk. The drug should not be prescribed for patients at increased baseline risk for osteosarcoma, including patients with Paget's disease of bone or unexplained elevations of alkaline phosphatase, children or growing adults, or those who have had prior external beam or implant radiation therapy involving the skeleton. Additionally, patients with bone metastases or a history of skeletal malignancies, and those with metabolic bone diseases other than osteoporosis, should not receive FORTEO. Patients with high levels of calcium in their blood should not receive FORTEO due to the possibility of increasing their blood levels of calcium.

In clinical trials, the most frequent treatment-related adverse events reported at the 20-microgram (mcg) dose approved for marketing were mild, similar to placebo and generally did not require discontinuation of therapy. Reported adverse events that appeared to be increased by FORTEO treatment were leg cramps and dizziness (2.6 and 8 percent, respectively), compared with placebo (1.3 percent and 5.4 percent, respectively).

FORTEO is supplied in a disposable pen device that can be used for up to 28 days to give once-daily self-administered injections. FORTEO is available in a 20-mcg dose and should be taken for a period of up to 24 months. Lilly has implemented a risk management program that includes comprehensive measures regarding the appropriate use of FORTEO in the target patient population. A Medication Guide explaining the details of the drug to the patient also accompanies the product. FORTEO also has a "boxed warning" in its package insert about the osteosarcoma findings in rats during preclinical testing. For full prescribing information, please visit <http://www.FORTEO.com>.

#### About Lilly

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of first-in-class and best-in-class pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers -- through medicines and information -- for some of the world's most urgent medical needs. Additional information about Lilly is available at [www.lilly.com](http://www.lilly.com).

## Forward Looking Statement

This press release contains forward-looking statements about the safety and efficacy of FORTEO and reflects Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. There is no guarantee that FORTEO will continue to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filings with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

- (1) N Engl J Med. 2007; TBD
- (2) 2 Trends in Endo. And Meta. 2006;17(4); 144-149.
- (3) Clin Rheumatol. 2007; 26: 144-153.
- (4) Endocrinol Metab Clin N Am. 2003; 32; 135-157.
- (5) N Engl J Med. 2001; 344: 1434-1441.
- (6) Prescribing information for FORTEO.
- (7) Draft prescribing information for FORTEO.

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