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New Study Provides In-Depth Look at How Osteoporosis Treatments Function Within Bone

Demonstration of different mechanisms of action is important step in defining how best to use FORTEO (R) and Fosamax(R) in treating postmenopausal osteoporosis patients

INDIANAPOLIS, Ind., Aug 08, 2005 /PRNewswire-FirstCall via COMTEX/ -- A new study comparing the head-to-head effects of teriparatide [rDNA origin] injection, (20 mcg), marketed in the US as FORTEO, the first and only FDA approved bone formation agent that actually forms new bone in postmenopausal women with osteoporosis at high risk for fracture, and Fosamax (10 mg alendronate sodium(1)), an inhibitor of bone resorption, gives new information on how the two osteoporosis therapies affect bone cell activity. These data were published in the August 2005 issue of Archives of Internal Medicine.

The study, which provides more in-depth information than previously available about these two treatments, found that both therapies increase bone mineral density (BMD), but to different degrees and through different means. While FORTEO builds new bone by increasing the rate of bone formation, Fosamax increases bone density by preventing bone loss -- different mechanisms of action on bone remodeling.

"This is the first head-to-head study to give us important information about how two osteoporosis therapies can work through diametrically opposite mechanisms of action," said Dr. Michael McClung, M.D., founding director of the Oregon Osteoporosis Center and lead investigator of the study. "Both treatments cause bone density to increase, but the skeleton responds differently to each. By gaining knowledge about how different therapies work, we can understand the nature of changes in bone density and make more informed treatment decisions based on the individual patient's needs."

What is bone cell activity?

In addition to preventing fractures, understanding how therapies impact the body's natural bone cell activity is an emerging but important focus for determining how to treat osteoporosis. Bone is a living tissue that continually breaks down (resorption) and replenishes (formation) itself in order to maintain strength and fracture resistance. This process is called bone turnover or remodeling, and is the foundation for bone health. When bone turnover is thrown out of balance, which is often seen in women of menopausal age due to the decrease in estrogen, the resorption process surpasses the formation process. If not corrected, this can lead to osteoporosis or low bone mass.

"The main goal of a physician who treats a patient with osteoporosis is to reduce the patient's risk for suffering an osteoporotic fracture. Increasing BMD is an important part of the process, but so is the method by which it's improved," said Dr. McClung. "This study assesses these skeletal changes through several measurements -- BMD and markers of bone turnover -- to give us a better understanding of how those skeletal changes occur."

The Study

Two hundred and three postmenopausal women between 45 and 84 years of age participated in this 18-month randomized, parallel, double-blind study. Women included in the study were 5 or more years past menopause and had a bone mineral density T-score between -2.5 and -4.0 at either the lumbar spine or femoral neck. Patients were randomized to receive once-daily injections of FORTEO(R) 20 mcg/day and oral placebo or oral Fosamax(R) 10 mg/day and once- daily injectable placebo. Each woman was given daily calcium supplements and vitamin D (1000 milligrams and 400-800 IU, respectively).

Markers of bone turnover and areal BMD were assessed for all 203 women. Areal BMD was assessed using a dual energy x-ray absorptiometry (DXA) of the lumbar spine at baseline and 3,6,12 and 18 months and femoral neck at baseline, 12 and 18 months. Volumetric BMD of the lumbar spine and the femoral neck was assessed in a subset of 56 patients by quantitative computed tomography (QTC) at baseline and 6 and 18 months.

Results

This study shows the following effects on BMD and bone turnover:

* At 18 months, FORTEO(R) increased volumetric spine BMD by 19.0 percent, while Fosamax increased volumetric spine BMD by 3.8 percent)

* At 18 months, FORTEO increased areal spine BMD by 10.3 percent, while FOSAMAX increased areal spine BMD by 5.5 percent

* At 18 months, FORTEO increased areal BMD at the femoral neck 3.9 percent, while Fosamax increased areal BMD at the femoral neck by 3.5 percent

* At 18 months, femoral neck trabecular BMD increased 4.9 percent in patients taking FORTEO while femoral neck trabecular BMD increased 2.2 percent in patients taking Fosamax

* At 18 months, cortical bone density at the femoral neck increased 7.7 percent in patients receiving Fosamax, while in those receiving FORTEO, cortical bone density at the femoral neck decreased 1.2 percent

* After 6 months of treatment, PINP serum procollagen type I N-terminal propeptide, a marker of bone formation, peaked at 6 months with teriparatide by 218%; while Fosamax decreased PINP by 67%

* Fosamax significantly decreased NTx, urinary N - telopeptide, a marker of bone resorption at 6 months by 72 percent while FORTEO increased NTx by 58 percent at 6 months

* 26 patients receiving FORTEO reported new or worsening back pain as an adverse event after 18 months of treatment while 39 patients receiving Fosamax reported new or worsening back pain as an adverse event during treatment

* After 18 months, eight patients taking Fosamax experienced fractures while nine patients taking FORTEO experienced clinical fractures

Important Safety Information about FORTEO

In two-year studies in rats, FORTEO(R) caused an increase in the incidence of osteosarcoma, a malignant bone tumor, which was dependent on dose and duration of treatment. Although no case of osteosarcoma has been reported in the patients who received FORTEO in clinical trials, it is not known if humans treated with FORTEO are at increased risk for this cancer.

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 black box 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 Osteoporosis

More than 50 percent of all women over the age of 75 are estimated to have osteoporosis, and due to their advanced age, have a high risk of fracture. In fact, most American women over the age of 50 will experience one or more osteoporosis-related fractures during their lifetimes, and women with osteoporosis who have two or more previous fractures have up to a nine times greater risk of future fracture compared with women who have not suffered a previous fracture.

About Lilly

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(1) Fosamax(R) is a prescription medication manufactured by Merck & Co.

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