# Teriparatide Beats Alendronate in Prospective Trial

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The anabolic agent teriparatide outperformed alendronate in patients with glucocorticoid-induced osteoporosis who were at high risk for fractures in a large, randomized, controlled trial.

Study participants taking teriparatide were significantly less likely to sustain new vertebral fractures and showed greater increases in bone mineral density (BMD) at the spine and hip, the investigators wrote in the the New England Journal of Medicine.

International guidelines recommend bisphosphonates like alendronate for patients who either already have or are at risk for glucocorticoid-induced osteoporosis, they noted. But recombinant teriparatide—human parathyroid hormone (1-34)—is thought to stimulate bone formation, increase bone mass, and reduce the risk of vertebral and nonvertebral fractures.

"Teriparatide may be a rational treatment for glucocorticoid-induced osteoporosis because it directly stimulates osteoblastogenesis and inhibits osteoblast apoptosis, thereby counteracting two key mechanisms through which glucocorticoid therapy promotes bone loss," reported Dr. Kenneth G. Saag of the University of Alabama at Birmingham, and his associates.

They are conducting what they called the first randomized, controlled clinical trial comparing teriparatide with a bisphosphonate in this patient population. Dr. Saag reported their results for the first 18 months of a planned 36. The trial is supported by Eli Lilly & Co., which markets teriparatide as Forteo in the United States.

Study participants in 12 countries in North America, South America, and Europe were randomly assigned to either injectable teriparatide plus an oral placebo or oral alendronate plus an injectable placebo every day. All also received daily calcium and vitamin D supplements.

The subjects were 345 women and 83 men aged 22-89 years who had established osteoporosis because of long-term glucocorticoid therapy for a variety of disorders.

After 18 months, BMD at the lumbar spine increased to a significantly greater degree in subjects taking teriparatide (7.2%) than in patients taking alendronate (3.4%). The same was true for total hip bone mineral density (3.8% and 2.4%, respectively).

Markers of bone formation increased almost 70% and those of bone resorption increased about 45% at 6 months in subjects taking teriparatide, while these markers decreased in subjects taking alendronate.

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**DR. SAAG**

New vertebral fractures developed in 10 subjects taking alendronate, compared with only 1 taking teriparatide, a significant difference. The number of subjects who developed new nonvertebral fractures did not differ significantly between the two groups (N. Engl. J. Med. 2007;357:2028-39).

"Safety profiles in the two study groups were similar, with no significant differences in the overall incidence of adverse events, the incidence of serious adverse events, or the incidence of events either leading to withdrawal from the study or considered to be possibly related to the study drug," they added.

However 70 subjects in the alendronate group and 64 in the teriparatide group dropped out of the study. Thirteen (6.1%) of the 214 patients in the alendronate group and 25 (11.7%) of the 214 in the teriparatide group discontinued because of an adverse event.

In an editorial accompanying this report, Dr. Philip N. Sambrook, of the University of Sidney (Australia), noted this "moderately high" dropout rate of 30% may indicate that adherence to either treatment may be limited, particularly because this patient group is "often already unwell.

"The persistence of [adverse] effects in the ongoing 18-month extension of the study will be of interest," he noted (N. Engl. J. Med. 2007;357:2084-6).

Nevertheless, "for patients with low bone mineral density who are receiving long-term low-dose glucocorticoid therapy, the study by Saag et al. suggests that teriparatide should be considered as a potential first-line therapy," he said. ■



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