Benefits of Teriparatide Good While They Last

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LAS VEGAS — Daily teriparatide injections can lower a menopausal woman's risk of fractures, thanks to marked improvement in skeletal mass and structure, Robert Lindsay, M.D., said at the annual meeting of the American Geriatrics Society.

Teriparatide, a synthetic form of human parathyroid hormone, promotes bone remodeling and osteoblast activity. It also enhances calcium absorption during digestion. The end result is "a real increase in bone tissue mass," said Dr. Lindsay, chief of internal medicine at Helen Hayes Hospital, West Haverstraw, N.Y.

The Food and Drug Administration approved teriparatide for treating osteoporosis in men and women in 2002. Eli Lilly & Co. markets the drug under the brand name Forteo. But the FDA gave teriparatide a black box warning because animal studies showed an association between long-term administration and an increased risk of osteosarcoma. The current recommendation is to limit clinical use of teriparatide to 2 years, although so far it has not been associated with any human cases of osteosarcoma, he said.

He recommended daily subcutaneous injections of 20 µg.

Serum markers of bone formation increase by about fourfold within 1 month of starting treatment with teriparatide, and reach peak levels within 6 months. Markers of bone resorption also rise, but more slowly. They start to increase within 6 months of starting teriparatide, and peak at about 12 months.

This is almost the direct converse of normal perimenopausal changes in bone metabolism, which are characterized by a rapid rise in resorption markers and a later, slower rise in markers of formation. Teriparatide may affect osteoblast activity directly, either through cellular recruitment or delayed apoptosis, he said.

Teriparatide exerts its effects more on trabecular bone than cortical bone, making the trabeculae thicker and rendering the bone stronger and more resistant to stress.

These salutary effects don't continue indefinitely. Bone remodeling activity peaks within about 1 year of starting teriparatide treatment and starts to decline until it returns to baseline levels after about 3 years. Longer treatment does not produce further gains.

Patients should limit their use of teriparatide to 2 years and follow it with antiresorptive agents such as bisphosphonates to maintain gains in bone mass.

Termination of teriparatide treatment before 3 years results in a rapid loss of bone mass—unless patients also take an antiresorptive agent, Dr. Lindsay said, citing findings from an observational follow-up study of women who participated in the placebo-controlled clinical trial that demonstrated the efficacy of teriparatide.

That study initially involved 1,637 subjects, of whom 1,093 took 20 µg or 40 µg teriparatide daily (N. Engl. J. Med. 2001;344:1434-41). The trial, which was planned to last 30 months, was terminated after 19 months because of the osteosarcoma finding in rats. At that point, the patients were free to seek treatment with other physicians, but 77% were available for follow-up examinations during the planned 30-month duration. Women who started taking bisphosphonates immediately maintained the benefits they had accrued with teriparatide; those who did not, promptly started losing bone mass.

Given this finding, plus the possible risk of osteosarcoma, patients should limit their use of teriparatide to 2 years and follow it with antiresorptive agents such as bisphosphonates, which can help maintain gains in bone mass, he said.

So far, teriparatide has not been associated with significant adverse effects. Mild hypercalcemia has been reported in rare cases. Dr. Lindsay said he regularly checks patients' serum and 24-hour urine calcium levels. Serum uric acid levels also increase 13%-25%. The clinical significance of this finding isn't clear, but Dr. Lindsay recommended measuring a patient's baseline uric acid levels before starting teriparatide.

All of the studies with teriparatide involved well-nourished individuals with adequate levels of calcium and vitamin D, he added. The findings may not apply to people with nutritional deficiencies. ■