Denosumab Increased BMD in 6-Year Study

BY KERRI WACHTER

DENVER — The investigational agent denosumab continued to increase bone mineral density in osteoporotic postmenopausal women during 6 years of continuous use, based on the results of an extension of a phase II study including 412 women.

"Over a period of 6 years, continuous treatment with denosumab resulted in progressive gains in BMD in postmenopausal women," Dr. Paul Miller said at the annual meeting of the American Society for Bone and Mineral Research.

These findings support earlier ones involving shorter follow-up of twice-yearly injections of denosumab in over 7,000 osteoporotic postmenopausal women.

The 93 patients on denosumab 60 mg for 6 years had a continued increase in spine BMD, with a mean cumulative increase from baseline in spine BMD of 13%. In addition, the reduction in resorption, as measured by serum C-telopeptide (CTX) levels, was sustained and plateaued over the course of continuous denosumab treatment.

The study was sponsored by Amgen Inc., which is developing the drug. Dr. Miller reported significant financial relationships with several pharmaceutical companies that make osteoporosis treatments, including Amgen.

In the parent trial, 412 women were randomized to receive denosumab, open-label oral alendronate (70 mg/wk), or placebo. All participants took daily oral supplements containing elemental calcium (1 g) and vitamin D (400 IU). The 2-year data were published in Bone in 2008 (43:222-9).

At the end of the first 2 years, patients were reallocated. Denosumab-treated patients who continued the study were reassigned based on their randomization group at enrollment. The placebo group was maintained. In the extension phase of the study, all patients received denosumab 60 mg every 6 months for 2 more years.

The 16 patients who had been on placebo for 4 years and were switched to denosumab 60 mg every 6 months for the last 2 years had gains in spine BMD that were comparable to those observed in the first 2 years of the trial for patients on denosumab 60 mg every 6 months. Similar results were obtained for hip BMD. Patients on denosumab for 6 years had an average cumulative hip BMD increase of 6%.

"The forearm data … are interesting because forearm BMD increased in the denosumab groups, unlike the other antiresorptive agents that have consistently shown a decrease," said Dr. Miller, whose group practice in Lakewood, Colo., specializes in treatment of osteoporosis.

In an earlier trial of denosumab, results show a significant decrease in the risk of fractures during 36 months of twice-yearly injections in 7,868 postmenopausal women with osteoporosis, compared with placebo injections (N. Engl. J. Med. 2009 [doi:10.1056/NEJM0a0809493]). The study was funded by Amgen.

Earlier this year, the Food and Drug Administration's Advisory Committee for Reproductive Health Drugs voted that the benefits of denosumab to treat osteoporosis in postmenopausal women outweighed its risks, but the committee did not support use of the drug to prevent osteoporosis.

Amgen was seeking approval of the human IgG2 monoclonal antibody to treat and prevent bone loss in women with breast cancer receiving hormone ablation therapy and to treat and prevent bone loss in men with prostate cancer receiving androgen deprivation therapy.

The committee declined to support most of those uses, primarily because of concerns about long-term safety. Its members did vote 9-4 that the benefits outweighed the risks in treating bone loss in prostate cancer.

The panel voted unanimously that denosumab's benefits outweighed its risks in postmenopausal women, but because of questions about its long-term impact on bone turnover and immunogenicity, suggested that the drug should be limited to those at high risk for fracture or with a history of fracture. ■

Sherry Boschert and Alicia Ault contributed to this report.