# BMD at Bisphosphonate's End Predicts Fractures

BY MITCHEL L. ZOLER

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TORONTO – The stronger a patient's bones are when bisphosphonate treatment is stopped, the less likely the bones are to fracture later, based on an analysis of 437 patients.

In contrast, changes in bone mineral density following the end of bisphosphonate therapy had no significant link with subsequent fracture risk, Dr. Douglas C. Bauer said at the meeting.

The finding calls into doubt the common practice of running annual dual-energy x-ray absorptiometry examinations on patients who have withdrawn from bisphosphonate treatment.

Routine BMD measurement "1-2 years after stopping prolonged alendronate therapy may not be useful for predicting the patient's fracture risk," said Dr. Bauer, professor of medicine, epidemiology, and biostatistics at the University of California, San Francisco. BMD at the time of alendronate discontinuation "was highly predictive of who was going to fracture."

Patients who stopped alendronate therapy with a total hip BMD T score of –1.4 or greater had a 9% rate of clinical fracture during 5 years of follow-up. Patients with a T score of –2.1 to –1.5 when they stopped bisphosphonate treatment had a 23% fracture rate during 5 years of follow-up, and those who stopped with a T score lower than –2.1 had a 33% fracture rate over the next 5 years. The between-group differences were statistically significant.

These data "are helpful as I try to decide which of my patients I should leave on a bisphosphonate," commented Dr. Elizabeth Shane, a professor of medicine at Columbia University in New York. "Patients below –2.1 were at very high risk of fracture, but even those in the middle tertile, with less than –1.5, were at a risk almost as high." Dr. Bauer's study "provides me with some comfort [on whom] I can stop safely."

**Measurement of BMD '1-2 years after stopping prolonged alendronate therapy may not be useful.'**

DR. BAUER

The investigators used data collected in the FLEX (Fracture Intervention Trial Long-Term Extension) study, which randomized 1,099 postmenopausal women who had completed 5 years of treatment with alendronate to either continue on alendronate for another 5 years or switch to placebo (JAMA 2006;296:2927-38). They focused on the 437 patients who switched to placebo, and assessed the BMD measures that were associated with fracture risk during follow-up.

Even among patients who had relatively substantial bone loss during 1 year of follow-up, the amount of lost BMD did not significantly correlate with their follow-up fracture rate. The researchers saw no significant link to fracture rate among the 21% of patients who lost at least 3% of their BMD during the first year of follow-up, or among the 8% of patients who lost at least 5% of their BMD during 1 year of follow-up.

When a patient starts bisphosphonate treatment, the BMD typically rises sharply for a couple of years, and then plateaus and remains stable, Dr. Bauer said. After patients stop bisphosphonate treatment, their BMD usually declines gradually. Prior analysis of the FLEX data showed that patients who failed to reach a BMD of at least –2.5 usually benefited with fewer fractures when they remained on bisphosphonate treatment. The new findings suggest that patients with T scores of less than –1.5 may also benefit from continued treatment, On the other hand, when patients reach an adequate BMD (greater than –1.5), "it's not unreasonable to talk with the patient about the potential risks and benefits of a drug holiday," Dr. Bauer said.

The FLEX study was funded by Merck, the company that markets alendronate (Fosamax). Dr. Bauer said that he has received research funding from Amgen, Merck, and Novartis. ■