Stick With Antiresorptives, Even in Nonresponders

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SAN FRANCISCO — Antiresorptive therapy should be continued even in patients showing no apparent response, Dr. Douglas C. Bauer said at a meeting on osteoporosis sponsored by the University of California, San Francisco.

Monitoring response with periodic bone mineral density (BMD) testing may be misleading, said Dr. Bauer, of UCSF. Furthermore, studies show that antiresorptive therapy decreases fracture risk even when BMD declines. And a patient whose BMD declines in the first year of therapy will often see an improvement in subsequent years.

Those advocating periodic monitoring cite several potential advantages of the practice, including increases in patient satisfaction, improvements in adherence, and the ability to change to more effective therapy in the presence of a nonresponse.

But Dr. Bauer pointed out that there are no studies demonstrating that monitoring improves patient satisfaction or adherence. Although it is true that many patients stop taking drugs to prevent osteoporosis, more than half of those who discontinue do so within 6 months of beginning therapy, he said. Measuring BMD 1-2 years following diagnosis is therefore unlikely to encourage adherence in the majority of patients.

In addition, changes in BMD on subsequent measurements may be misleading. Although BMD is usually considered a very precise measurement, with precision errors in the neighborhood of 1%-2%, some apparent changes in BMD may be due to noise or to small differences in patient position, Dr. Bauer said.

To figure out what changes in BMD measurements are due to chance, Dr. Bauer recommended using the "least significant change" formula. The least significant change in any measurement is defined as three times the measurement's long-term reproducibility. For example, if a dual-energy x-ray absorptiometry instrument has a long-term coefficient of variation of 1.5%, then its least significant change would be 4.5%, meaning that changes of less than 4.5% from measurement to measurement may well be due to chance.

But even if a patient's BMD truly is declining, that does not necessarily mean that the patient is failing to respond to treatment, since he or she may well have lost more bone without treatment, he added.

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And an initial loss of bone during treatment doesn't mean that this loss will continue. Dr. Bauer quoted one study that showed that of patients who lost more than 4% of their BMD during the first year of treatment, 92% gained BMD in the second year, and the average increase during the second year was 4.8%. On the other hand, of patients who gained more than 8% in BMD during the first year, only 36% continue to gain BMD in the second year, and as a whole that group lost 1% of their BMD during that second-year.

An analysis of a clinical trial of alendronate versus placebo compared the patients who lost most BMD while taking alendronate with those who lost most BMD while taking placebo. Fracture risk was reduced by about 50% in those taking alendronate despite their loss of BMD.

Clinicians should consider secondary causes of osteoporosis in patients who are losing BMD despite antiresorptive therapy, Dr. Bauer said. Among the common secondary causes of bone loss are weight loss; medications such as corticosteroids, aromatase inhibitors, and glitazones; inflammatory diseases or myeloma; or malabsorption.

"It's very useful to have these conversations [with patients] about follow-up measurements at the time you start therapy as opposed to having these conversations a year later or 2 years later," Dr. Bauer said.

"I always make a point … to say that bone mineral density is a terrific test to decide who should be treated or who shouldn't be treated. But it's a lousy test to tell us whether you're benefiting from the therapy or not," he said. ■