Consider Bisphosphonate Holiday After 5 Years

BY BRUCE JANCIN

ESTES PARK, COLO. — Many bone disease experts are recommending a 1- to 2-year bisphosphonate holiday after 5 years of treatment in response to a recent spate of reports of atypical fractures of the femoral diaphysis.

There are now more than 70 reports of these atypical transverse fractures of the femoral shaft occurring in patients on bisphosphonates for longer than 5 years. Affected individuals have also had severely suppressed bone turnover markers, Dr. Michael T. McDermott said at a conference on internal medicine sponsored by the University of Colorado.

These distinctive fractures have been bilateral in two-thirds of cases. There is no associated history of trauma, just spontaneous thigh pain. Radiographically they look like nonhealing stress fractures that have completed through the bone shaft, said Dr. McDermott, professor of medicine and director of diabetes practice at University of Colorado Hospital, Aurora.

He has informally polled bone experts across the country. Their consensus: a bisphosphonate holiday for 1-2 years is reasonable after 5 years of therapy in low-risk patients (individuals with a current T-score greater than –2.5 and no history of fractures) "Treatment holidays are not advised for high-risk patients," he stressed.

For such patients—those who have a T-score less than –2.5 and/or previous fractures—options include a switch to an anabolic agent such as teriparatide (Forteo) or to a nonbisphosphonate antiresorptive agent such as raloxifene (Evista), estrogen, or calcitonin.

Continuing the bisphosphonate in a high-risk patient is also a reasonable strategy, Dr. McDermott noted. ■

Denosumab's Benefits Seen to Outweigh Risks

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.

Denosumab (Prolia) manufacturer Amgen Inc. also 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 committee did not formally vote on approval for any of the indications but took a series of votes on the risks and benefits of denosumab.

For osteoporosis prevention, advisory committee members expressed particular concern about exposing otherwise healthy women to a therapy that had been shown to have a slightly higher risk of causing serious skin infections and neoplasms. Dr. Scott Emerson, a biostatistician from the University of Washington, Seattle, said he could not say the benefits outweighed the risks, "because there's a lot of uncertainty in this low-risk population."

Committee members also said that Amgen had not shown that denosumab did not affect the underlying disease or tumor progression when used in the breast cancer setting. Dr. Lawrence M. Nelson, a panel member and researcher at the Eunice Kennedy Shriver National Institute of Child Health and Human Development, said he could not support use of the drug in breast cancer, "because of concerns about the need for more data on how this affects the primary disease."

But the committee was more enthusiastic about Amgen's studies in the prostate cancer setting, saying that the company had proved, at least in treating bone loss, that denosumab reduced fracture risk.

The FDA generally follows the advice of its panels.

—Alicia Ault