

**The Endocrine Society Statement in Response to the  
American Society of Bone and Mineral Research Report on Bisphosphonate Therapy and Atypical  
Femur Fractures**  
September 17, 2010

In March 2010, The Endocrine Society released a statement on the potential adverse skeletal effects of long-term bisphosphonate therapy. In that statement, the Society acknowledged that although long-term use of bisphosphonates (alendronate, Fosamax, Actonel, Boniva and Reclast) may be associated with subtrochanteric/diaphyseal femur fractures, there was a lack of conclusive evidence demonstrating a causal link between bisphosphonate therapy and these unusual fractures.

The conclusions at the time were based on a June 2008 review of case reports and clinical trial data by the US Food and Drug Administration (FDA) that found no increased risk of atypical femoral shaft fractures in patients taking bisphosphonates, a finding reiterated by the FDA in March, 2010. An observational study (J Bone Miner Res. 2009 Jun; 24(6):1095-102) also concluded that the ratio between hip and subtrochanteric/diaphyseal femur fractures was indistinguishable in alendronate-treated patients and a control cohort, suggesting that atypical femur fractures are probably a subtype of osteoporotic fracture.

In an important update to our understanding of the topic, the American Society of Bone and Mineral Research (ASBMR) released the report of its task force that conducted a comprehensive scientific investigation of the potential connection between bisphosphonate therapy and atypical femur fractures (<http://onlinelibrary.wiley.com/doi/10.1002/jbmr.253/pdf>). The task force evaluated both published and unpublished data and concluded that the risk for atypical femur fractures appears to increase with longer exposure to bisphosphonates (>5 years). While the precise incidence of atypical femoral fractures is unknown, these fractures are uncommon especially in comparison to the large number of vertebral, non-vertebral and hip fractures that are known to be reduced in those receiving bisphosphonates. The ASBMR report makes it clear that a direct causal connection between bisphosphonate therapy and atypical fractures has not been established.

The ASBMR report reiterates that for patients at high risk for fracture (including those who have undergone organ transplantation, endocrine or chemotherapy for breast or prostate cancer or who are taking aromatase inhibitors or glucocorticoids), the benefits of bisphosphonate therapy in leading to osteoporotic fracture reduction strongly outweigh the potential risks of developing an atypical femur fracture. Patients at low risk for osteoporosis-related fractures should not be started on bisphosphonates.

The Endocrine Society encourages patients to discuss these issues and any concerns they have about their medication with their health care provider, but they should continue taking their medication unless advised to stop by their health care provider. Healthcare professionals should continue to follow the recommendations in the package insert when prescribing bisphosphonates. Patients and healthcare providers should be aware that groin or thigh pain may be an early indicator of an impending femoral shaft fracture. In these patients, since the condition may be bilateral, imaging of both hips with plain radiograph, MRI or bone scan to include the full diaphysis of the femur should be performed. Health care providers and patients should report any adverse events associated with bisphosphonate therapy to the FDA MedWatch program.