Romosozumab Bone Benefits at 1 Year Versus Teriparatide in Postmenopausal Women

Written by Sara Freeman

The investigational drug romosozumab produced significantly greater improvements in volumetric bone mineral density (vBMD) and volumetric bone mineral content (vBMC) compared with both placebo and teriparatide in postmenopausal women with low bone mass in a substudy of an international multicenter randomized Phase 2 trial.

Harry K. Genant, MD, University of California San Francisco, San Francisco, California, USA, reported that greater gains in vBMD and vBMC were seen with romosozumab at the lumbar spine and total hip by 12 months' treatment. This was mainly due to effects on the outer cortical bone in the spine and the cortical and inner trabecular bones of the hip.

Romosozumab is a humanized monoclonal antibody that targets a protein called sclerostin, which is produced by osteocytes and inhibits osteoblast-mediated bone formation. The gene that encodes sclerostin is expressed mainly in skeletal tissue. By targeting this protein, there is the potential to have a positive effect on bone, while minimizing the risk of side effects.

Preclinical data have shown that antibodies directed against sclerostin are associated with increased bone mass and strength [Ominsky MS et al. *J Bone Miner Res* 2010; Li X et al. *J Bone Miner Res* 2009, 2010]. Furthermore, data from a recent Phase 2 trial [McClung M et al. *N Engl J Med* 2014] showed that, compared with placebo, alendronate, and teriparatide, romosozumab not only stimulated bone formation and decreased bone resorption but also significantly increased areal bone mineral density at the lumbar spine, as measured by dual-energy x-ray absorptiometry (DXA). Dr. Genant presented 12-month data from a substudy of this trial that measured volumetric rather than areal bone mineral density using quantitative computed tomography (QCT).

The QCT substudy included 82 of the 419 patients who had participated in the Phase 2 trial, of whom 24 had been treated with romosozumab (210 mg, once monthly, administered subcutaneously), 31 had received open-label teriparatide (20 µg, once daily), and 27 had received placebo. Baseline characteristics were well balanced among the arms, with mean ages of 64.3, 65.8, and 66.1 years, respectively. vBMD at the lumbar spine and total hip, as measured by both DXA and QCT, and markers of bone formation (procollagen type I N propeptide) and resorption (carboxyterminal cross-linking telopeptide of bone collagen) were also comparable among groups at baseline.

At 12 months, vBMD at the lumbar spine increased by 17.7% relative to baseline in romosozumab-treated patients and by 12.9% in teriparatide-treated patients and decreased by –0.8% in patients given placebo. Values for total hip vBMD were a respective 4.1%, 1.2%, and 0.3%. Results for vBMC were similarly higher in romosozumab-treated patients than in teriparatide- or placebo-treated patients, at 17.7%, 12.8%, and –1.0% at the lumbar spine and 4.7%, 0.8%, and 1.1% at the total hip.

Dr. Genant concluded that the improvements in vBMD and vBMC seen in the study with romosozumab would probably result in proportional gains in bone strength. The continued clinical investigation of the drug is warranted, and Phase 3 trials are underway to evaluate the efficacy and safety of romosozumab.

BOW-015 Is Biosimilar to Infliximab With Respect to Efficacy and Safety

Written by Toni Rizzo

Infliximab was the first anti–tumor necrosis factor α monoclonal antibody approved for the treatment of rheumatoid arthritis (RA). In 2013, CT-P13 was the first infliximab biosimilar agent approved by the European Commission. This Phase 3 trial of BOW-015, presented by Jonathan Kay, MD, University of Massachusetts Medical School, Worcester, Massachusetts, USA, is the first study to compare an infliximab biosimilar agent with infliximab in patients with RA, assessing time points before Week 14.

The primary objective of this prospective randomized double-blind study was to determine the equivalence of BOW-015 with reference infliximab during 16 weeks of treatment. The key secondary objectives were to assess the long-term efficacy, safety, and tolerability of BOW-015 and determine BOW-015 serum concentrations and immunogenicity.

Patients with RA were randomly assigned to treatment with BOW-015 (n=127) or infliximab (n=62). The primary endpoint, American College of Rheumatology (ACR) 20 response rate, was assessed at Week 16. A total of 161 responders from both groups received open-label BOW-015 until Week 58. Nonresponders were followed to Week 26 (n=20).

Patients were included if they were aged 18 to 65 years with RA for ≥2 years and on stable medication doses, including methotrexate. Those who previously were treated with biological agents or who had active