Romosozumab Followed by Alendronate Lowers Risk of Fracture in Women With Osteoporosis

Romosozumab treatment followed by alendronate results in lower fracture risk in women with osteoporosis compared with alendronate alone.

Xiomara M. Santos, MD

November 5, 2018- Postmenopausal women with osteoporosis who are at high risk for fracture had a significantly lower incidence of fractures with romosozumab treatment followed by alendronate than with alendronate alone, a phase 3 study showed.

Kenneth G. Saag, MD, with the Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, and colleagues reported their findings in the September 11, 2017, issue of *The New England Journal of Medicine*.

Romosozumab is a new monoclonal antibody that inhibits sclerostin, increasing bone formation and decreasing bone resorption. In a prior randomized controlled trial, romosozumab treatment in postmenopausal women with osteoporosis resulted in a lower risk of new vertebral fracture and clinical fracture (a composite of nonvertebral fracture and symptomatic vertebral fracture) compared with placebo.

Few studies comparing osteoporosis therapies included fracture as end points, “and only one trial evaluating bone-building versus antiresorptive therapy was designed with fracture as the primary end point,” according to study authors. This randomized, double-blind trial compared the efficacy of romosozumab followed by alendronate with alendronate alone in reducing fracture risk among postmenopausal women with osteoporosis and a previous fracture.

A total of 4093 patients were randomized in a 1:1 ratio to receive monthly subcutaneous romosozumab (210 mg) or weekly oral alendronate (70 mg) for 12 months, followed by open-label alendronate in both groups. The primary end points were the cumulative incidence of new vertebral fracture at 24 months and the cumulative incidence of clinical fracture.

The incidence of new vertebral fractures was 48% lower in the romosozumab-to-alendronate group compared with the alendronate-to-alendronate group (6.2% vs 11.9%; $P < .001$). The incidence of clinical fractures was also significantly lower in the romosozumab group (9.7% vs 13.0%; $P < .001$).

In addition, the romosozumab group had a 19% lower risk of nonvertebral fractures ($P = .04$) and 38% lower risk of hip fracture ($P = .02$). However, during the first year, serious cardiovascular adverse events were reported more frequently with romosozumab than with alendronate (2.5% vs 1.9%).

“Hip fractures were less frequent with romosozumab followed by alendronate than with alendronate alone, suggesting an important benefit and challenging the common treatment practice of first-line use of alendronate in women who have had a previous fracture,” the authors noted. “Further evaluation is needed to determine the cause of the observed imbalance in cardiovascular events,” the authors concluded.

The study was supported by Amgen, Astellas Pharma, and UCB Pharma. A full list of disclosures is provided in the journal article.

New England Journal of Medicine. Published September 11, 2017.