Romosozumab-to-Alendronate Treatment Lowers Fracture Risk in Women With Osteoporosis

Treatment with romosozumab for 12 months prior to alendronate treatment lowers fracture risk in postmenopausal women with osteoporosis who are at high risk for fracture.

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February 2, 2019 – Romosozumab treatment for 12 months prior to alendronate treatment resulted in a 48% lower risk of new vertebral fractures in postmenopausal women compared with alendronate treatment alone, according to the results of a phase 3 trial.

Kenneth Saag, MD, with the Department of Medicine, University of Alabama at Birmingham School of Medicine, and colleagues reported their findings in the October 2017 issue of *The New England Journal of Medicine*.

According to the researchers, the antiresorptive agent, alendronate, is commonly used as a first-line treatment for osteoporosis. Romosozumab is a bone-forming monoclonal antibody that binds to and inhibits sclerostin, increasing bone formation and decreasing bone resorption.

In a randomized, controlled trial that enrolled a low-risk population of postmenopausal women with osteoporosis, romosozumab treatment resulted in significantly lower fracture risk compared with the placebo treatment. However, the effectiveness of romosozumab remains unclear among postmenopausal women with osteoporosis at high-risk for fracture.

A total of 4093 postmenopausal women with osteoporosis and a fragility fracture were randomly assigned to receive monthly subcutaneous romosozumab or weekly oral alendronate for 12 months in this double-blind trial. Treatment with open-label alendronate followed for an additional 12 months in both groups.

Primary end points were the cumulative incidence of new vertebral fracture at 24 months and the cumulative incidence of clinical fracture at the time of primary analysis. Secondary end points included bone mineral density at 12 and 24 months and the incidence of nonvertebral and hip fracture at primary analysis.

After 24 months, a 48% lower risk of new vertebral fractures was observed in the romosozumab-to-alendronate group compared with the alendronate-to-alendronate group (6.2% vs 11.9%; $P < .001$). Furthermore, the risk of nonvertebral fractures decreased by 19% (8.7% vs 10.6%, $P = .04$) and the risk of hip fracture decreased by 38% (2.0% vs 3.2%, $P = .02$) with the romosozumab-to-alendronate treatment relative to the alendronate-only treatment.

Overall, the incidences of adverse events and serious adverse events were balanced between the two groups. However, an imbalance in adjudicated serious cardiovascular events was observed during the first 12 months in patients receiving romosozumab (odds ratio, 1.31; 95% CI, 0.85–2.00).

Dr. Saag and colleagues concluded that “rapid gains in bone mineral density from bone-forming therapy with romosozumab were associated with a lower risk of fracture than with alendronate” and that the study results challenged “the common treatment practice of first-line use of alendronate in women who have had a previous fracture.”

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