Romosozumab Followed by Alendronate Reduces the Risk of Fractures in Postmenopausal Women

Postmenopausal women who were treated with romosozumab followed by alendronate were at lower risk for fractures.

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July 7, 2020 – Postmenopausal women with osteoporosis are at high-risk for fractures. A phase 3 study with romosozumab followed by alendronate reduces the incidence of these fractures compared with alendronate alone.

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

Romosozumab, a new human monoclonal antibody, binds to and inhibits sclerostin, increases bone formation, and decreases bone resorption. In a previous randomized controlled trial, treatment with romosozumab for one year considerably lowered the risks of new vertebral fracture and clinical fracture (a composite of nonvertebral fracture and symptomatic vertebral fracture) than placebo in postmenopausal women with osteoporosis.

According to the study authors, only a few studies about osteoporosis therapy have fractures as endpoints. Also, there is "only one trial evaluating bone-building versus antiresorptive therapy with fracture as the primary endpoint," according to the study authors. The goal of this randomized, double-blind phase 3 trial was to lower the risk of fractures by comparing the efficacy of romosozumab followed by alendronate than with alendronate alone.

A total of 4093 postmenopausal women with osteoporosis and a previous incidence of fracture were enrolled in the trial. The patients were randomized in a 1:1 ratio to receive a monthly dose of subcutaneous romosozumab (210 mg) or a weekly dose of oral alendronate (70 mg) in a blinded fashion for 12 months followed by open-labeled alendronate after that for another 12 months. The trial's primary endpoints resulted in the cumulative incidence of new vertebral fracture at 24 months and the cumulative incidence of clinical fracture.

During the 24 months, there was a 48% lower risk of new vertebral fractures in the romosozumab-to-alendronate group compared with the alendronate-to-alendronate group (6.2% vs. 11.9%; P<.001). Clinical fractures were also less incident in the romosozumab group (9.7% vs. 13.0%; P<.001).

The risk of nonvertebral fractures was lesser by 19% in the romosozumab-to-alendronate group than the alendronate-to-alendronate group (P=0.04). The risk of hip fracture was lower by 38% in the romosozumab group than the alendronate group (P=0.02). However, during the first year, serious cardiovascular adverse events were reported more commonly with romosozumab group than with alendronate group (2.5% vs. 1.9%).

Alendronate is routinely used as the first-line treatment for osteoporosis in postmenopausal women with previous incidence of fractures. "Hip fractures were less frequent with romosozumab followed by alendronate than with alendronate alone," the study authors noted. The trial outcome suggests an important benefit of romosozumab-to-alendronate treatment and challenges the first-line standard treatment. Due to the observed imbalance in acute cardiovascular adverse events, further evaluation is required to determine its cause, the authors concluded.

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