Sequential Romosozumab and Alendronate Decrease Bone Fracture Risk and Increase Bone Density in Postmenopausal Women With Osteoporosis

Postmenopausal women with osteoporosis and a history of bone fracture had decreased fracture risk and increased bone density after a sequential course of romosozumab followed by alendronate compared with alendronate only.

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June 3, 2019 – Postmenopausal women with osteoporosis and a history of fragility fracture had a significant reduction in vertebral and clinical fracture incidence and increased bone density after a sequential 12-month course of romosozumab, then alendronate, compared with alendronate alone.

Kenneth G. Saag, MD, with the Division of Clinical Immunology and Rheumatology, University of Alabama, and colleagues at Amgen, UCB Pharma, and other academic institutions, reported their results in the September 11, 2017, issue of the *New England Journal of Medicine*.

Alendronate, a first-line fracture prevention treatment for patients with osteoporosis, has been shown to decrease the risk of fracture by 50%. Romosozumab (Amgen, UCB Pharma) is a sclerostin-inhibiting antibody shown to decrease vertebral and clinical fracture risks compared with placebo in women with osteoporosis. Few fracture preventative studies have compared these two treatments or used fracture incidence to define end points.

This phase 3 trial enrolled 4093 postmenopausal women, aged 55 to 90 years with a history of osteoporosis and bone fracture, and randomly assigned them to one of two blinded groups that received either romosozumab (monthly subcutaneous injection of 210 mg) or alendronate (weekly oral dose of 70 mg; Merck) for 12 months. Open-label alendronate was then administered to each group in the subsequent 12 months. Primary end points comprised incidence of vertebral fractures at 24 months and clinical fractures at the primary analysis (after clinical fractures occurred in 330 patients and all patients' 24-month follow-ups were completed).

After the 24-month treatment period, there was a 48% reduction in incidence of vertebral fracture in the sequential romosozumab and alendronate group compared with that of the alendronate-only group (6.2% vs 11.9%; risk ratio [RR], 0.52; 95% CI, 0.40-0.66; $P < .001$). Sequential romosozumab and alendronate also decreased clinical fracture risk by 27% compared with alendronate only (hazard ratio [HR], 0.73; 95% CI, 0.61-0.88; $P < .001$).

There were increases in bone mineral density in proximal femur and lumbar spine measurements in the romosozumab group at the 12-month mark that remained stable after the course of alendronate at the 36-month mark ($P < .001$).

Adverse cardiovascular events were reported in 2.5% of the romosozumab group and in 1.9% of the alendronate group (odds ratio, 1.31; 95% CI, 0.85 to 2.00). Adjudicated serious cardiovascular events included cardiac ischemia, cerebrovascular events, and death. Other adverse events such as peripheral vascular ischemia and noncoronary revascularization occurred in fewer numbers in the romosozumab group.

“It is worth noting that romosozumab outperformed [alendronate]…. In our trial, the effect of romosozumab on the risk of fracture was rapid….” concluded the study’s authors. However, “[f]urther evaluation is needed to determine the cause of the observed imbalance in cardiovascular events.”

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