20. Denosumab Compared with Risedronate in Postmenopausal Women Suboptimally Adherent with Alendronate Therapy: Efficacy and Safety Results from a Randomized Open-Label Study.

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Denosumab (DMAb), a fully human monoclonal antibody that specifically targets RANKL to inhibit osteoclast formation, function, and survival, reduces the risk for new vertebral, nonvertebral, and hip fractures (Cummings NEJM 2009). In subjects who were treatment naïve or previously treated with alendronate, DMAb was associated with greater gains in bone mineral density (BMD) and decreases in bone turnover markers when compared with alendronate-treated subjects (Brown JBMR 2009; Kendler JBMR 2010). The purpose of this open-label trial was to compare the efficacy and safety of DMAb with risedronate over 12 months in postmenopausal women who transitioned from daily or weekly alendronate treatment and were considered to be suboptimally adherent with therapy.

This was a multicenter, international, randomized, open-label, parallel-group study in which postmenopausal women aged 55 and older were randomized 1:1 to receive open-label DMAb 60 mg subcutaneously every 6 months or risedronate 150 mg orally every month (one 75 mg tablet on two consecutive days) for 12 months. The primary endpoint was percent change from baseline in total hip BMD at month 12. Secondary endpoints included percent change from baseline in femoral neck and lumbar spine BMD at month 12, and percent change from baseline in serum CTX at months 1 and 6 (exploratory). Safety endpoints were also assessed.

A total of 870 subjects were randomized (435, DMAb; 435, risedronate) who had a mean (SD) age of 68 (7) years, mean (SD) BMD T-score of –1.6 (0.9), –1.9 (0.7), and –2.2 (1.2) at the total hip, femoral neck, and lumbar spine, respectively, and median CTX of 0.3 ng/mL. DMAb significantly increased BMD at the total hip compared with risedronate at month 12 (2.0% vs. 0.5%, respectively; $p<0.0001$; Figure). DMAb also significantly increased BMD at the femoral neck (1.4% vs. 0%) and lumbar spine (3.4% vs. 1.1%) compared with risedronate ($p<0.0001$ at both sites). DMAb significantly decreased CTX compared with risedronate at month 1 (median change from baseline of –78% vs. –17%; $p<0.0001$) and month 6 (–61% vs.
–23%; $p<0.0001$). In this open-label study, overall adverse events (AEs) and serious AEs were similar between groups.

In postmenopausal women who were suboptimally adherent with alendronate, switching to DMAb is more effective than risedronate based on significantly greater increases in BMD at all measured sites and greater reductions in CTX with DMAb.