

Risk of osteoporotic fractures in new users of denosumab compared with new users of alendronate:
A Danish population- based cohort study

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Background: Head-to-head randomized controlled trials (RCT) have compared efficacy of denosumab versus alendronate in relation to bone mineral density. No RCT has been designed and conducted to compare the anti-fracture efficacy of denosumab and alendronate.

Objectives: We compared the effectiveness of denosumab versus alendronate, measured by clinically manifested fracture risk, using data from population-based Danish health registries.

Methods: We included new users of denosumab or alendronate (with a one year wash-out period with no anti-osteoporosis dispensation/s) aged 50 years or older who started either therapy between May 10, 2010 and December 31, 2015. To control for measured confounding, we used inverse probability of treatment weights. Using the Cox regression and the intention-to-treat approach, we calculated adjusted hazard ratios (aHRs) with 95% confidence intervals (CIs) separately for any fracture, hip fracture, vertebral fracture, and non-vertebral non- hip fracture.

Results: There were 3734 new users of denosumab (median follow-up time: 3.24 years) and 67 765 new users of alendronate (median follow-up time: 3.27 years) sustaining 10.9% and 10.3% any fractures, respectively. Initiation of denosumab versus alendronate was associated with aHRs of 0.94 (CI: 0.84-1.04) for any fracture, 1.07 (CI: 0.90-1.27) for hip fracture, 0.77 (CI: 0.57-1.03) for vertebral fracture, and 0.91 (CI: 0.79-1.05) for non-vertebral non-hip fracture. Similar aHRs were observed after stratification by sex and fracture history. Among patients older than 80 years, aHRs were 1.21 (CI: 0.92-1.48) for hip fracture and 1.17 (CI: 0.92-1.48) for non-vertebral non-hip fracture.

Conclusions: Overall, initiation of denosumab and initiation of alendronate were associated with similar risks of any fracture. Denosumab was associated with a 23% lower risk of vertebral fracture than alendronate. Among patients ages 80 years or older, denosumab was associated with higher risks of hip fracture and non-vertebral non-hip fracture than alendronate. Head-to-head RCT(s) are needed to compare the efficacy of denosumab and alendronate.