Comparative Effectiveness of Denosumab versus Bisphosphonates among Treatment-Experienced Postmenopausal Women with Osteoporosis in the U.S. Medicare Program

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Objectives

Although clinical trials have shown that transitioning from bisphosphonates (BP) to denosumab (Dmab) increases bone mineral density at key skeletal sites more than remaining on BP, evidence from head-to-head studies evaluating fracture outcomes is lacking. This retrospective observational study compared the effectiveness of Dmab versus BP in reducing fracture risk among treatment-experienced women with postmenopausal osteoporosis (PMO) in the U.S.

Methods

Female Medicare fee-for-service beneficiaries ≥ 66 years of age with prior history of treatment with a n oral BP, who newly initiated Dmab (n~108,000), a different oral BP (alendronate, ibandronate, or risedronate; n=100,649), alendronate (Aln; n=53,165), or zoledronic acid (ZA; n=35,100) between Jan 1, 2012 to Dec 31, 2018 were followed from treatment initiation (index date) until the first instance of a fracture, treatment discontinuation (defined as the end of exposure + 60-day gap) or switch, Medicare disenrollment, death, end of available data (Dec 31, 2019), or 5 years post-index date. A doubly robust inverse-probability of treatment (weights estimated from multivariate logistic regression models) and censoring (weights estimated from multivariate Cox Proportional Hazards regression models) weighted function was used to estimate the relative risk (RR) associated with the use of Dmab compared with oral BP, Aln, and ZA for hip, nonvertebral (NV; includes hip, humerus, pelvis, radius/ulna, other femur), non-hip, nonvertebral (NHNV), hospitalized vertebral (HV), and major osteoporotic (MOP; nonvertebral and hospitalized vertebral) fractures for the overall study period and by year of follow-up.

Results

Over a maximum of 5 years of follow-up, Dmab reduced the risk of hip fracture by 45% (RR=0.55; 95% CI: 0.42-0.68), 37% (0.63; 0.51-0.75), and 38% (0.62; 0.32-0.91), and reduced the risk of MOP fracture by 31% (0.69; 0.61-0.76), 25% (0.75; 0.67-0.82), and 31% (0.69; 0.57-0.82) compared with oral BP, Aln, and ZA respectively (Figure). Similar results were observed for NV, NHNV, and HV fractures, with an increase in the magnitude of fracture risk reduction with increasing duration of exposure across all fracture outcomes.

Conclusion

In a large cohort of treatment-experienced women with PMO, we observed robust, clinically meaningful reductions in the risk of hip, NV, NHNV, HV, and MOP fractures for patients on Dmab compared to oral BP, Aln, and ZA; greater reductions in fracture risk were observed with longer duration of exposure.

Figure. Forest Plot of Relative Risk of Fracture Comparing Denosumab to Alendronate, Oral BP, and Zoledronic Acid