

# **Comparative Effectiveness of Denosumab versus Zoledronic Acid among Postmenopausal Women with Osteoporosis in the U.S. Medicare Program**

Authors: Jeffrey R. Curtis<sup>1,2</sup>, Tarun Arora<sup>2</sup>, Ye Liu<sup>1</sup>, Tzu-Chieh Lin<sup>3</sup>, Leslie Spangler<sup>3</sup>, Vanessa C. Brunetti<sup>3</sup>, Robert K. Stad<sup>3</sup>, Michele McDermott<sup>3</sup>, Brian D. Bradbury<sup>3</sup>, Min Kim<sup>3</sup>

Affiliations: <sup>1</sup> University of Alabama at Birmingham, Birmingham, AL, USA; <sup>2</sup> Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL, USA; <sup>3</sup> Amgen Inc., Thousand Oaks, CA, USA.

## **Objectives**

Although clinical trials have shown that denosumab (Dmab) significantly increases bone mineral density at key skeletal sites more than zoledronic acid (ZA), evidence from randomized trials evaluating fracture outcomes is lacking. This retrospective cohort study evaluated the comparative effectiveness of Dmab versus ZA in reducing fracture risk among women with postmenopausal osteoporosis (PMO) in the U.S.

## **Methods**

Female Medicare fee-for-service beneficiaries  $\geq 66$  years of age who newly initiated Dmab (n=89,990) or ZA (n=36,861) between Jan 1, 2012 to Dec 31, 2018 with no prior history of osteoporosis treatment were followed from treatment initiation (index date) until the first instance of a given fracture outcome, treatment discontinuation (defined as the end of exposure according to usual dosing intervals + 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 ZA for major osteoporotic (MOP; nonvertebral and hospitalized vertebral), hip, nonvertebral (NV; includes hip, humerus, pelvis, radius/ulna, other femur), non-hip, nonvertebral (NHNV), and hospitalized vertebral (HV) fractures for the overall study period and by year of follow-up.

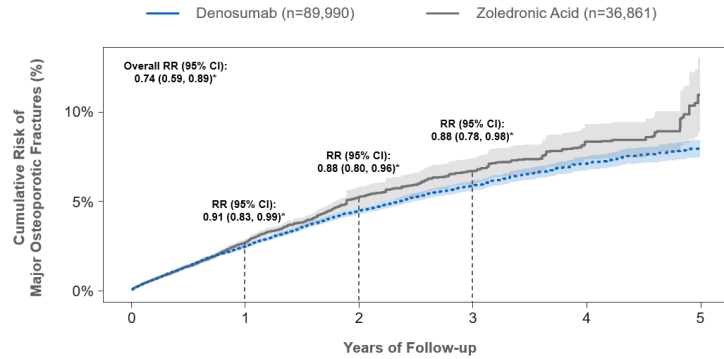
## **Results**

Over a maximum of 5 years of follow-up, Dmab reduced the risk of MOP by 26% (RR=0.74; 95% CI: 0.59-0.89), hip by 34% (0.66; 0.43-0.90), NV by 33% (0.67; 0.52-0.82), and NHNV by 31% (0.69; 0.50-0.88), and HV fractures by 10% (0.90; 0.56-1.24) compared with ZA (Figure). Over time, Dmab reduced the risk of MOP fractures by 9% (0.91; 0.83-0.99) at year 1, 12% (0.88; 0.80-0.96) at year 2, and 12% (0.88; 0.78-0.98) at year 3. An increase in the magnitude of fracture risk reduction with increasing duration of exposure was also observed for other NV outcomes.

## **Conclusion**

In a cohort of over 125,000 treatment-naive women with PMO, we observed robust, clinically meaningful reductions in the risk of MOP, hip, NV, and NHNV fractures for patients on Dmab compared to ZA, with greater reductions in fracture risk with longer duration of exposure.

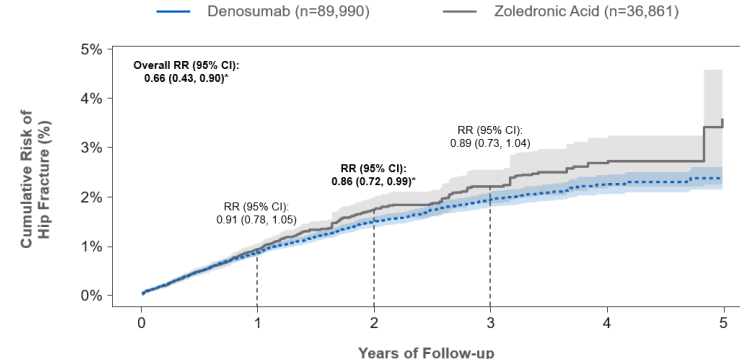
### Major Osteoporotic Fractures



Persons at risk	0	1	2	3	4	5
Denosumab	89,990	53,979	22,946	10,184	4,458	1,725
Zoledronic Acid	36,861	31,167	7,693	2,880	1,018	354

CI, confidence interval; RR, risk ratio. \*P < 0.05

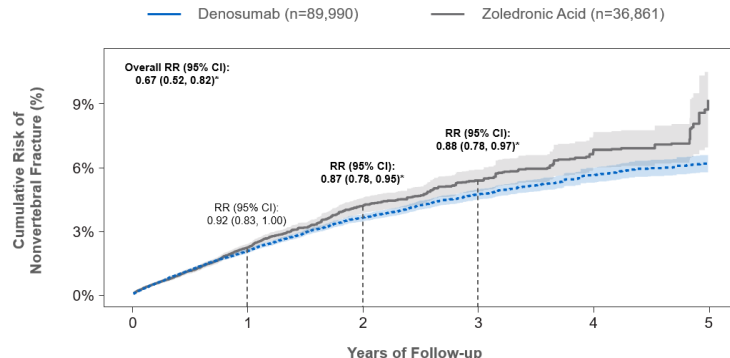
### Hip Fracture



Persons at risk	0	1	2	3	4	5
Denosumab	89,990	54,679	23,447	10,494	4,629	1,808
Zoledronic Acid	36,861	31,662	7,879	2,972	1,056	380

CI, confidence interval; RR, risk ratio. \*P < 0.05

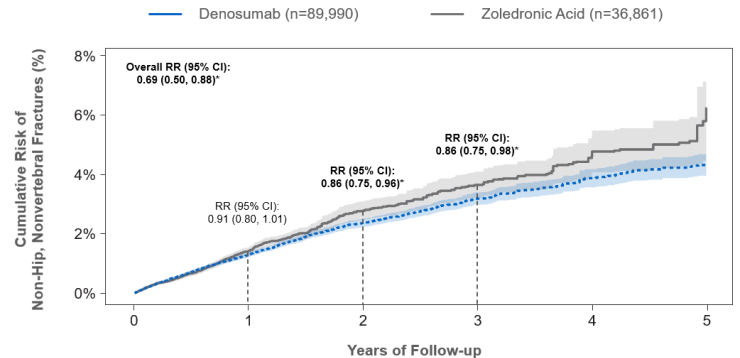
### Nonvertebral Fracture



Persons at risk	0	1	2	3	4	5
Denosumab	89,990	54,133	23,060	10,253	4,490	1,741
Zoledronic Acid	36,861	31,282	7,723	2,895	1,024	358

CI, confidence interval; RR, risk ratio. \*P < 0.05

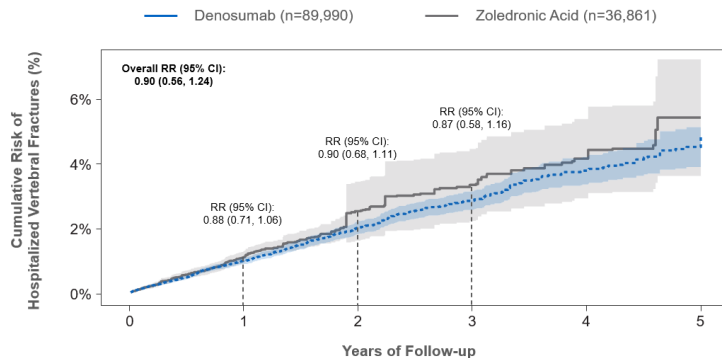
### Non-Hip, Nonvertebral Fractures



Persons at risk	0	1	2	3	4	5
Denosumab	89,990	54,405	23,216	10,328	4,529	1,756
Zoledronic Acid	36,861	31,462	7,795	2,920	1,038	364

CI, confidence interval; RR, risk ratio. \*P < 0.05

### Hospitalized Vertebral Fractures



Persons at risk	0	1	2	3	4	5
Denosumab	89,990	54,824	23,514	10,523	4,645	1,809
Zoledronic Acid	36,861	31,749	7,926	2,979	1,066	381

CI, confidence interval; RR, risk ratio.