

Relationship Between Total Hip BMD T-Score and Incidence of Nonvertebral Fracture with up to 8 Years of Denosumab Treatment

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Session Time: 9:00AM-11:00AM

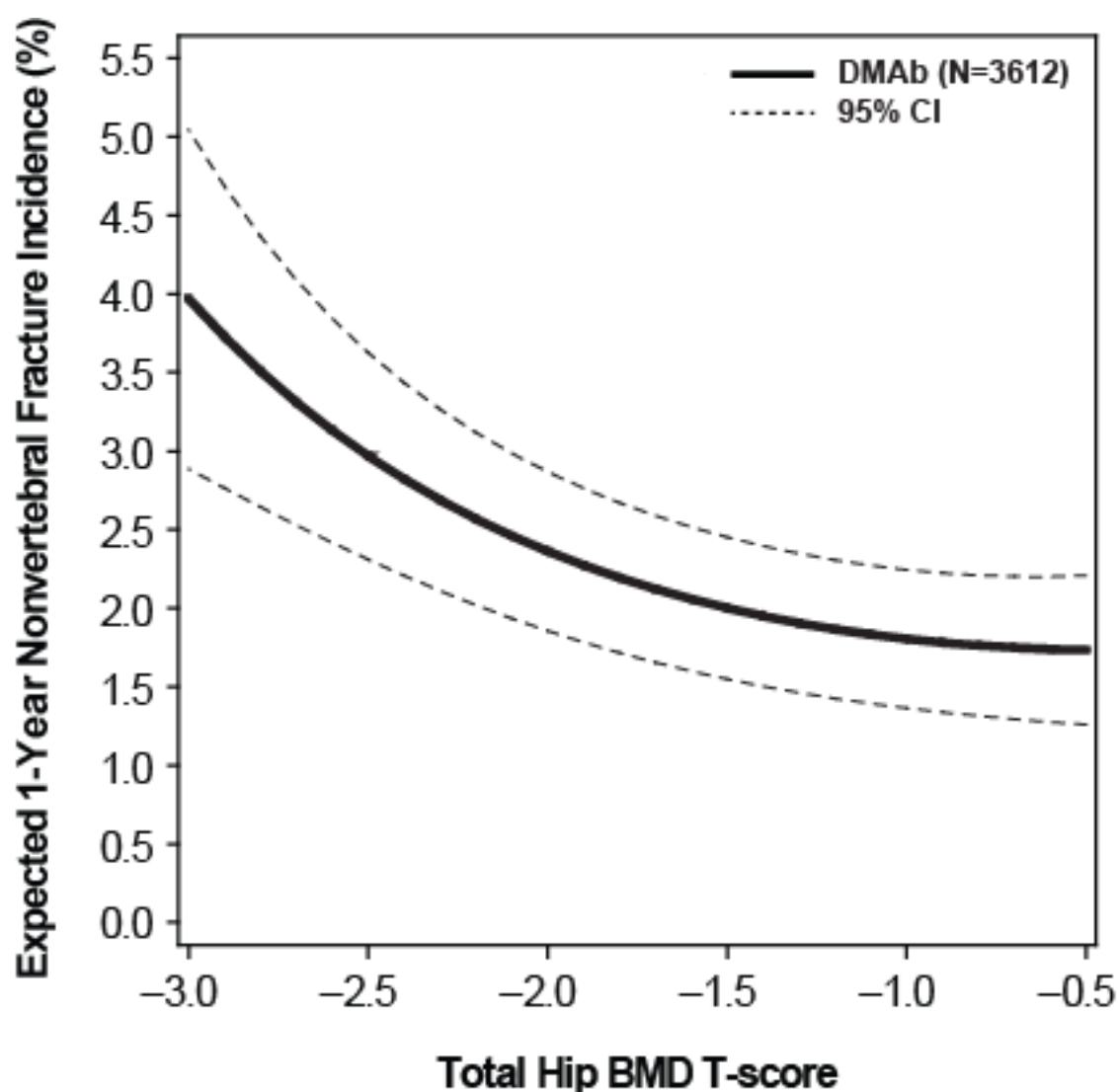
Background/Purpose: The relationship between BMD T-score and fracture risk has not been established in patients on therapy. We previously reported that denosumab (DMAb) treatment over 8 years enabled a substantial proportion of women with osteoporosis to achieve non-osteoporotic BMD T-scores (Ferrari, ASBMR 2014). Further improvement in T-score would only be meaningful if it were associated with fracture reductions; thus, we investigated the relationship between total hip BMD T-score and the incidence of nonvertebral fracture through 8 years of DMAb therapy.

Methods: For these analyses, women received DMAb for 3 years during the FREEDOM trial (N=3902). A large subset of these women enrolled in the Extension and received DMAb for up to an additional 5 years, for a total of up to 8 years of continued treatment (N=2343). A repeated-measures model was first used to estimate each subject's BMD T-scores during the entire follow-up, specifically at each unique nonvertebral fracture time among all subjects at risk at the time of each fracture. Cox's proportional-hazards model was then fitted with time to nonvertebral fracture as the response and total hip BMD T-score time course as a time-dependent covariate.

Results: The incidence of nonvertebral fracture was lower with higher total hip BMD T-score throughout a wide and clinically relevant T-score

interval (Figure). For example, total hip BMD T-scores of -2.5 and -1.5 were associated with 1-year nonvertebral fracture incidences of about 3.0% and 2.0%, respectively. The relationship flattened at a T-score somewhere between -2.0 and -1.0, similar to what is known to occur in untreated subjects. This inverse relationship between total hip BMD T-score and nonvertebral fracture incidence was maintained regardless of age or prior fracture (data not shown).

Conclusion: Higher total hip BMD T-scores during DMAb treatment were associated with a lower incidence of nonvertebral fracture, which is similar to the relationship previously established in treatment-naïve patients. Improvements of similar magnitude in BMD would result in different reductions in fracture risk depending on the baseline BMD value. Our findings highlight the importance of BMD measurement in patients on osteoporosis treatment as a predictor of fracture risk and support the concept that a specific T-score should be further evaluated as a practical goal for therapy.



N=number of subjects randomized to DMAb in FREEDOM who had an observed total hip BMD T-score at FREEDOM baseline and ≥ 1 observed total hip BMD T-score during FREEDOM or the Extension.

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Theramex, Nycomed, Novo-Nordisk, Nolver, 9, Bristol Myers Squibb, Merck Sharp & Dohme, Rottapharm, Teva, Lilly, Novartis, Roche, GlaxoSmithKline, Amgen, Servier, 2; **N. Daizadeh**, Amgen, 1, Amgen, 3; **A. Wang**, Amgen, 1, Amgen, 3; **R. Wagman**, Amgen, 1, Amgen, 3; **E. Lewiecki**, Amgen, Lilly, Merck, 2, Amgen, Lilly, Merck, Radius Health, AgNovos, Theranova, Alexion, NPS, AbbVie, 5.

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