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Increased Risk of Vertebral Fracture After Stopping Denosumab

Denosumab (Prolia) has been shown to reduce the risk of fracture in postmenopausal women and men ≥ 50 years old with osteoporosis. It has also been approved for steroid induced bone loss.

Individuals who were in the FREEDOM study, which evaluated denosumab in comparison to placebo, were followed, and those who stopped denosumab had a subsequent reduction in bone mineral density (BMD) and an increase in the risk of fracture (Bone JCEM 2011).

Analysis of the data from the FREEDOM study as well as the Extension trial of denosumab up to a total of 10 years, confirmed that stopping denosumab was associated with an increase in rate of bone loss as measured by bone turnover markers, which rose 3 months after missing a scheduled dose. BMD decreased back to the baseline level 12 months after missing a scheduled dose of denosumab (Cummings JBMR 2017).

Individuals who had received ≥ 2 doses of denosumab or placebo, and stopped treatment but remained in the study for ≥ 7 months after the last dose, were reviewed. In the 1001 patients who stopped denosumab, the rate of spine fractures increased from 1.2/100 patient-years (while on treatment) to 7.1/100 patient-years, a similar rate to the placebo group. Multiple (>1) vertebral fractures appeared to be more common in the group stopping denosumab than the group stopping placebo (3.4% vs 2.2%). The risk of having multiple (>1) vertebral fractures after stopping denosumab was higher in those people who had already experienced a prior spine fracture, and also in those who had rapid rates of bone loss. The rates of non-spine fractures were similar in those stopping denosumab and those stopping placebo (2.8% denosumab, 3.8% placebo) (Cummings et al JBMR 2017).

Due to the increased risk of vertebral fractures associated with denosumab discontinuation, it is important not to miss scheduled doses of denosumab once treatment has started. Patients need to be advised of the increased risk of bone loss and vertebral fracture when therapy is stopped. If denosumab needs to be stopped, it should be replaced by an alternative osteoporosis medication to help prevent rapid bone loss and risk of fractures (Symonds CMAJ April 2018).

Osteoporosis Canada advises individuals on denosumab therapy to discuss their treatment with their physician prior to stopping therapy or missing a scheduled dose.

1. Bone HG et al JCEM 2011:96:972-980
2. Cummings et al JBMR vol 33, No2, Feb 2018 pp 190-198
3. Symonds C, Kline G CMAJ 2018 April 23 :190 pp E485- 486

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