Bone loss after denosumab, only partial protection with zoledronate

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Denosumab is a monoclonal antibody which acts as a potent anti-resorptive agent and is now widely used in the treatment of osteoporosis.

However, when treatment is discontinued, bone resorption resumes rapidly and reaches twice baseline levels within 12 months after the last injection. As a result, over the first year off therapy, bone mineral density (BMD) declines significantly and fracture risk increases. To counter this effect, patients may be transitioned from denosumab to other anti-resorptives, primarily alendronate.

This report, a case series of patients involved in the FREEDOM study, addresses whether zoledronate might also be an effective option to prevent bone loss after discontinuation of long-term denosumab treatment.

The six women, who had received continuous denosumab for seven years, had substantial gains in bone mineral density (BMD) - increasing 18.5% in the spine and 6.9% in total hip. The patients were given a single infusion of zoledronate (5 mg) six months after the last dose of denosumab. Post-zoledronate BMDs were measured 18-23 months after treatment. The findings:

- There were significant BMD declines at each site (Pspine = 0.043, Phip = 0.005).
- Spine BMD remained significantly above the pre-denosumab

baseline (+9.3%, P = 0.003), but hip BMD was not significantly different from baseline (?2.9%).
- Serum P1NP levels were between 39 and 60 µg/L (mean 52 µg/L), suggesting that the zoledronate treatment had insufficiently inhibited bone turnover.

The authors conclude that administration of a single infusion of zoledronate six months after the last dose of denosumab is not sufficient to preserve the BMD gains that result from long-term denosumab treatment.

More information: Ian R. Reid et al, Bone Loss After Denosumab: Only Partial Protection with Zoledronate, *Calcified Tissue International* (2017). DOI: 10.1007/s00223-017-0288-x

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