Title: Prevent rebound effect after RANKL mAb cessation

Introduction (Background and rationale)

Denosumab, a fully human monoclonal antibody against the receptor activator of nuclear factor k-B ligand, is a potent antiresorptive drug to treat osteoporotic postmenopausal women and men. Beyond the randomized controlled trial, however, the persistence of denosumab treatment for 2 years in the "real world" is about 50% in most studies. And discontinuation of denosumab results in a rebound response of bone turnover markers (BTM) and rapid loss of bone mineral density (BMD) gains, and BMD values return to baseline after 2 years off-treatment. Even after a long-term treatment for up to 7 to 10 years, large and rapid bone loss still occurred because of the reversible nature of denosumab.

Not only loss of BMD, several case reports and case series aroused the attention of multiple vertebral fractures after cessation of denosumab with and without subsequent osteoporosis therapy. Two systematic reviews had concluded that BTM increased above baseline 3 to 6 months after denosumab discontinuation and all multiple vertebral fracture cases occurred 2 to 10 months after the last dose effect was depleted, therefore the first year off-treatment seems to be the most critical period. Unlike the rare condition of MVF, whether the risk of all vertebral fractures or nonvertebral fractures is increasing or not is probably more important in clinical practice and needs more attention. Previous studies had showed conflicting findings which underestimation of the incidence rate due to short follow up period and prior exposure to long-term bisphosphonate treatment might bias the results.

This talk sought to introduce the background knowledge of this phenomenon, the incidence of osteoporosis-related fragility fractures among patients who had discontinue denosumab treatment, and the possible solution.

Thanks for your kindness to give me the chance to talk.

Best regards,
Shau Huai
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