Response to the Letter by Trovas

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We thank Dr. Trovas for his encouraging comment and his help in finding an explanation for these rebound-associated vertebral fractures (RAVFs). According to the FRAX® calculation, 6 of 9 women had a 10-year risk for major osteoporotic fracture below the treatment threshold. Thus, these women should not have received treatment and would not have suffered of the RAVFs after denosumab discontinuation.

As observed by Dr. Trovas, the bone mineral density (BMD) T score at the lumbar spine was lower than at hip sites for most of the patients. However, only the femoral neck BMD is included in the FRAX® calculation. The lumbar spine BMD is not included in the FRAX® algorithm, due to the increasing prevalence of degenerative changes with age (1). In practice, discordance between lumbar spine and femoral neck T scores is a source of confusion. Leslie *et al.* (2) have demonstrated that the fracture risk increases with a hazard ratio of 1.12 (95% confidence interval, 1.06 to 1.18) per each standard deviation (SD) of lumbar spine below femoral neck, independent of the FRAX® probability. Nevertheless, the absolute percentage of 10-year fracture risk change per each SD difference is low. Of the 6 low-risk patients described, only 2 had more than 1 SD difference between lumbar spine and femoral neck BMD.

This being said, it is urgently needed to determine the clinical profile of patients at risk for RAVFs. Dr. Trovas' comment is correct. A very low lumbar spine BMD is a marker of damaged vertebral microarchitecture. As denosumab discontinuation is associated with a severe bone turnover rebound and a rapid loss of BMD, pre-existing low lumbar spine BMD could be one of the factors inducing a particularly high risk of RAVFs.

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Abbreviations: BMD, bone mineral density; FRAX, fracture risk assessment tool; RAVF, rebound-associated vertebral fractures; SD, standard deviation.