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Author's Response to Letter to the Editor

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Letter to the Editor

Author's Response to Letter to the Editor

Re: Anagnostis P, Karras SN, Goulis DG. Monitoring the efficacy of once-weekly teriparatide. Are bone turnover markers useful in predicting fracture risk? Curr Med Res Opin 2014;30:1177-8

Dear Editor,

We appreciate the important suggestions raised by Drs. Anagnostis, Karras, and Goulis[1] related to our analysis of bone mineral density (BMD) and bone turnover markers (BTMs) as surrogate endpoints for incident vertebral fracture[2,3]. The proportion of the treatment effect of once-weekly teriparatide on vertebral fracture explained by the change in lumbar BMD was estimated to be 83% (Freedman's method) or 66% (Chen's method) in our study[2], and the estimate of the recent meta-analysis was 25–32% (Chen's method)[4] for the once-daily teriparatide formulation, although the magnitude of lumbar BMD changes after teriparatide treatment for 1 year was larger with the once-daily than with the once-weekly preparation (8% in the FPT study[5] versus 6% in TOWER study[3]). In addition, the fracture risk reduction in the TOWER trial (RR 0.20, 95% CI 0.09–0.45) was equal to that in the FPT study (RR 0.29, 95% CI 0.20–0.43[6]). These differences in the two formulations of teriparatide may be explained by plausible factors, such as differences in ethnicity, improvement of bone quality, or changes in BTMs.

Firstly, Tsujimoto *et al.* examined whether the pharmacokinetics of once-daily teriparatide and the effects of the drug on BMD differ between Japanese and non-Japanese populations[5]. The pharmacokinetic parameters (*AUC* and *Cmax*) were not different between Japanese and Caucasian postmenopausal women. Similarly, the time course and dose–response change in BMD between Japanese and Caucasian populations were not significantly different. Therefore, no ethnic difference in teriparatide effects was observed, at least with once-daily teriparatide.

Once-weekly teriparatide treatment is associated with improved material properties (mineral contents and collagen cross-links) of bone in ovariectomized monkeys[7]. Moreover, increases of bone strength parameters (section modulus and buckling ratio) were observed in humans by CT analysis[8]. Therefore, it is theoretically reasonable to expect that the bone quality improvements produced by once-weekly teriparatide may account for the anti-fracture efficacy.

The change in BTMs by once-daily teriparatide treatment has been well established as the 'anabolic window'[9]. However, a significant relationship between the change in BTMs and anti-fracture efficacy was not observed with once-weekly teriparatide[2] and was not reported with once-daily teriparatide treatment. The meaning of the change in BTMs produced by teriparatide treatment may be different between the once-weekly and once-daily treatment regimens. However, we would like to emphasize that a difference in the timing of sampling exists between once-daily and once-weekly preparations. In the case of once-daily teriparatide, the BTM samples were taken 24 hours after the injection, while with once-weekly teriparatide, they were taken one week after the injection. These differences arise because it has been reported that bone resorption markers were increased shortly after the injection, followed by around a 10% decrease during the subsequent 14 days, while bone formation markers were decreased shortly after the injection, followed by a 10% increase during the subsequent 14 days[10]. These changes were repeatedly observed at every weekly injection for 24 weeks[11]. Therefore, measurements of BTMs with once-weekly teriparatide could not represent the total bone turnover changes after the injection.

In conclusion, both once-weekly and once-daily teriparatide treatments increase lumbar BMD (by 6% and 8%, respectively). Changes in BTMs after once-weekly teriparatide were spiky, and the changes were repeated to the same extent during the treatment. On the other hand, the changes in formation markers with once-daily teriparatide increase in a time-dependent manner. The changes in bone resorption markers also increase in a time-dependent manner with a slight delay from the changes in bone formation markers. Therefore, the effects of teriparatide on BTMs are quite different between the once-daily and once-weekly preparations. Although differences in bone effects exist between the two teriparatide preparations,

fracture risk reduction seems to be the same with both preparations. Further study is needed to explore the mechanisms of action on fracture risk reduction with both preparations.

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Transparency

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References

1. Anagnostis P, Karras SN, Goulis DG. Monitoring the efficacy of once-weekly teriparatide. Are bone turnover markers useful in predicting fracture risk? Curr Med Res Opin 2014: published online 6 March 2014;30:1177-8
2. Tanaka S, Kuroda T, Sugimoto T, et al. Changes in bone mineral density, bone turnover markers, and vertebral fracture risk reduction with once weekly teriparatide. Curr Med Res Opin 2014;30:931-6
3. Nakamura T, Sugimoto T, Nakano T, et al. Randomized Teriparatide [human parathyroid hormone (PTH) 1-34] Once-Weekly Efficacy Research (TOWER) trial for examining the reduction in new vertebral fractures in subjects with primary osteoporosis and high fracture risk. J Clin Endocrinol Metab 2012;97:3097-106
4. Nakamura T, Tsujimoto M, Hamaya E, et al. Consistency of fracture risk reduction in Japanese and Caucasian osteoporosis patients treated with teriparatide: a meta-analysis. J Bone Miner Metab 2012;30:321-5
5. Tsujimoto M, Uenaka K, Iwata A, et al. Effects of teriparatide in Japanese and non-Japanese populations: bridging findings on pharmacokinetics and efficacy. J Bone Miner Metab 2012;30:326-37
6. Neer RM, Arnaud CD, Zanchetta JR, et al. Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. N Engl J Med 2001;344:1434-41
7. Saito M, Marumo K, Kida Y, et al. Changes in the contents of enzymatic immature, mature, and non-enzymatic senescent cross-links of collagen after once-weekly treatment with human parathyroid hormone (1–34) for 18 months contribute to improvement of bone strength in ovariectomized monkeys. Osteoporos Int 2011;22:2373-83
8. Ito M, Oishi R, Fukunaga M, et al. The effects of once-weekly teriparatide on hip structure and biomechanical properties assessed by CT. Osteoporos Int 2013;25:1163-72
9. Girotra M, Rubin MR, Bilezikian JP. The use of parathyroid hormone in the treatment of osteoporosis. Rev Endocr Metab Disord 2006;7:113-21
10. Shiraki M, Sugimoto T, Nakamura T. Effects of a single injection of teriparatide on bone turnover markers in postmenopausal women. Osteoporos Int 2013;24:219-26
11. Sugimoto T, Nakamura T, Nakamura Y, et al. Profile of changes in bone turnover markers during once-weekly teriparatide administration for 24 weeks in postmenopausal women with osteoporosis. Osteoporos Int 2013;25:1173-80

