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# Sustained Improvements in Bone Mineral Density and Health Related Quality of Life in Osteoporosis Patients Two Years Post Teriparatide Treatment: A Retrospective Chart Review

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## Abstract

**Introduction:** The purpose of this study is to determine the effect of teriparatide and subsequent antiresorptive therapy on Health-Related Quality of Life (HRQL) and Bone Mineral Density (BMD) up to two years after completion of teriparatide.

**Methods:** A retrospective chart review of consecutive osteoporosis patients treated with teriparatide for 18 or 24 months was conducted. BMD, Mini-Osteoporosis Quality of Life Questionnaire (mini-OQLQ) data and medications taken were recorded at baseline, during and post-teriparatide therapy up to two years after completion of treatment. A repeated measures mixed-model compared baseline and follow-up measurements for BMD and each of the ten questions (five domains) in the mini-OQLQ.

**Results:** 167 patients (143 women) were included. Significant improvements were also observed at the second follow-up post treatment in the OQLQ domains of pain symptoms, emotional functioning and physical functioning ($p<0.05$ for the first six questions). BMD values significantly improved from baseline to the 3rd follow-up at all three sites: femoral neck (0.30, $p=0.007$), lumbar spine (0.84, $p<.001$) and total hip (0.26, $p=0.003$). Subsequent subgroup analysis showed no significant difference in BMD among patients treated with antiresorptive therapy prior to or post-teriparatide treatment.

**Conclusions:** Our findings suggest sustained improvement in BMD and HRQL up to 2 years after completion of teriparatide.

**Keywords:** Bone Density; Osteoporosis; Parathyroid Hormone; Quality of Life; Teriparatide

## Background

Osteoporosis is defined as a skeletal disorder leading to a systemic decrease in bone mass and an increased susceptibility to fractures [1-3]. This results in considerable impact on patient Health-Related Quality of Life (HRQL) and imposes a significant economic burden on our healthcare system [4-6].

Various drugs are available for the treatment of osteoporosis with the goal of reducing the morbidity and mortality associated with fractures and improving a patient's HRQL. First line treatment

typically involves bisphosphonates followed by denosumab, a monoclonal antibody targeting the Receptor Activator of Nuclear Factor Kappa-B Ligand (RANKL) [7-9]. Teriparatide, a 34-amino acid formulation of recombinant human parathyroid hormone (PTH), is currently the only available anabolic agent for the treatment of osteoporosis.

Although sustained secretion of PTH decreases bone mass, intermittent pulsations of PTH has been shown to increase bone mass as is seen with studies of teriparatide showing increases in the rate of osteoblast development and prevention of osteoblast apoptosis [10-14]. Multiple studies have established the effectiveness of teriparatide in significantly improving Bone Mineral Density (BMD) at most sites including the lumbar spine, femoral neck and total hip as well as reducing the risk of vertebral and non-vertebral fractures [10,15,16]. Also well-established is the significant impact teriparatide has on HRQL during treatment, with some evidence emerging now suggesting that these benefits persist up to 18 months post discontinuation of teriparatide [17-20].

Our retrospective chart review seeks to affirm the existing literature regarding the effects of teriparatide on BMD and HRQL over the duration of the therapy and, additionally, provide evidence demonstrating the sustained effects of teriparatide up to two years following completion of treatment.

## Materials and Methods

### Study Participants

This retrospective chart review was conducted in a single Canadian academic rheumatology practice on 167 osteoporosis patients (143 females and 24 males) who received teriparatide therapy for an 18-month regimen, as recommended at the approval of teriparatide in 2004, or a 24-month regimen, as recommended by current guidelines. Patients undertook treatment regimens from August 2004 to October 2013. Three reviewers (H.B., R.C. and A.B.) extracted data from an Electronic Medical Records (EMR) system and for patients who did not have an EMR, data was extracted via paper records by H.B. Data was abstracted regarding patient demographics, medication history, and mini-OQLQ scores and BMD. The Hamilton Integrated Research Ethics Board approved this study.

### Measurement of Health-related Quality of Life

HRQL was measured through the mini-OQLQ, a shortened version of the 30-item Osteoporosis Quality of Life Questionnaire (OQLQ), comprising of 10 questions that address the 5 domains: symptoms, physical function, activities of daily living, emotional function and leisure. A change of approximately 0.5 within each domain is considered a clinically relevant difference in quality of life [21]. The mini-OQLQ was administered prior to commencement of teriparatide therapy and at each subsequent follow-up visit, during teriparatide therapy as well as post-teriparatide therapy.

### Statistical Analyses

A repeated measures mixed-model analysis was utilized to compare baseline and follow-up measurements for BMD at three sites (femoral neck, lumbar spine and total hip) as well as each of the ten questions in the mini-OQLQ questionnaire. All analyses were adjusted for sex, baseline age, height and weight.

## Results

### Participant Characteristics

Our study included 167 patients with osteoporosis, 143 of whom were female. The mean age at onset of PTH therapy was 65.13 (SD = 11.36). The mean baseline T scores at the lumbar spine, femoral neck and total hip were -2.79 (SD = 1.30), -2.27 (SD = 0.97) and -1.93 (SD = 0.95) respectively (Table 1).

| Variable | Number of patients | Mean (Standard Deviation) |
|---|---|---|
| Age at onset of PTH (years) | 167 | 65.13 (11.36) |
| Height Baseline (cm) | 153 | 159.78 (9.14) |
| Weight Baseline (kg) | 153 | 63.00 (13.08) |
| Baseline BMD (g/cm$^2$) Lumbar Spine | 159 | -2.79(1.30) |
| Femoral Neck | 147 | -2.27 (0.97) |
| Total Hip | 81 | -1.93 (0.95) |

**Table 1:** Baseline characteristics of patients receiving teriparatide therapy.

Medical histories regarding hysterectomies, oophorectomies and time since last periods were available for 142 of the female patients (Table 2).

| Variable | Number of known patients | Percentage |
|---|---|---|
| Hysterectomy | | |
| No | 98/142 | 69.01% |
| Yes | 44/142 | 30.98% |
| Oophorectomy | | |
| No | 109/142 | 76.76% |
| Unilateral | 5/142 | 3.52% |
| Bilateral | 28/142 | 19.71% |
| Time Since Last Period | | |
| Still having period | 3/142 | 2.11% |
| 10 years or less | 26/142 | 18.31% |
| More than 10 years | 113/142 | 79.58% |
| Bisphosphonates Use | | |

| | | |
|---|---|---|
| Indeterminate | 44/163 | 26.99% |
| No bisphosphonate use | 30/163 | 18.40% |
| 3 years or less | 36/163 | 22.09% |
| Greater than 3 years | 53/163 | 32.52% |
| Prior Alendronate Use | | |
| Yes | 67/163 | 41.10% |
| No | 96/163 | 58.90% |
| Prior Risedronic acid Use | | |
| Yes | 88/163 | 53.99% |
| No | 75/163 | 46.01% |
| Prior Zoledronic acid Use | | |
| Yes | 4/163 | 2.45% |
| No | 159/163 | 97.55% |
| Prior Estrogen Use | | |
| Yes | 14/163 | 8.59% |
| No | 149/163 | 91.41% |
| Prior Calcitonin Use | | |
| Yes | 15/163 | 9.20% |
| No | 148/163 | 90.80% |
| Prior Raloxifene Use | | |
| Yes | 28/163 | 17.18% |
| No | 135/163 | 82.82% |
| Prior Denosumab Use | | |
| Yes | 0/163 | 0% |
| No | 163/163 | 100% |
| Prior Calcium Use | | |
| Yes | 133/163 | 81.60% |
| No | 30/163 | 18.40% |
| Prior Vitamin D Use | | |
| Yes | 139/163 | 85.28% |
| No | 24/163 | 14.72% |

**Table 2:** Medical histories and medications use.

Data regarding prior bisphosphonate use was available for 163 patients, with 30 patients not having previously used a bisphosphonate, 36 patients having used a bisphosphonate for three years or less and 53 patients having used a bisphosphonate for more than three years. The remaining 44 patients had used bisphosphonates in the past but details regarding time of bisphosphonate use were unavailable (Table 2). Table 2 additionally provides a list of prior drugs used by these 163 patients including antiresorptive agents (alendronate, risedronate, zoledronic acid, estrogens, raloxifene, calcitonin and denosumab), calcium and vitamin D.

## Effects of Teriparatide on BMD

At the lumbar spine site, we observed a statistically significant improvement from baseline T-scores at all three follow up visits post teriparatide therapy, showing a 0.84 g/cm$^2$ improvement by the final visit (p = <0.001). Improvements were seen in the two follow-up visits during teriparatide therapy, with the first follow-up demonstrating a 0.58 g/cm$^2$ improvement and second follow-up demonstrating a 0.92 g/cm$^2$ improvement. Both follow-ups were statistically significant (p = <0.001) (Table 3).

| BMD site | Difference between baseline T-score and follow-up (95% confidence intervals) | P-value |
|---|---|---|
| Femoral neck | | |
| 1st follow-up during PTH therapy | 0.05 (-0.04, 0.15) | 0.276 |
| 2nd follow-up during PTH therapy | 0.16 (0.01, 0.32) | 0.040 |
| 1st follow-up after PTH therapy | 0.25 (0.14, 0.37) | <0.001 |
| 2nd follow-up after PTH therapy | 0.23 (0.09, 0.38) | 0.002 |
| 3rd follow-up after PTH therapy | 0.30 (0.09, 0.52) | 0.007 |
| Lumbar spine | | |
| 1st follow-up during PTH therapy | 0.58 (0.44, 0.72) | <0.001 |
| 2nd follow-up during PTH therapy | 0.92 (0.59, 1.25) | <0.001 |
| 1st follow-up after PTH therapy | 0.77 (0.63, 0.91) | <0.001 |
| 2nd follow-up after PTH therapy | 0.92 (0.74, 1.11) | <0.001 |
| 3rd follow-up after PTH therapy | 0.84 (0.43, 1.24) | <0.001 |
| Total hip | | |
| 1st follow-up during PTH therapy | -0.01 (-0.01, 0.08) | 0.91 |
| 2nd follow-up during PTH therapy | 0.00 (-0.13, 0.13) | 0.97 |
| 1st follow-up after PTH therapy | 0.18 (0.09, 0.27) | <0.001 |
| 2nd follow-up after PTH therapy | 0.15 (0.04, 0.26) | 0.008 |
| 3rd follow-up after PTH therapy | 0.26 (0.09, 0.44) | 0.003 |

**Table 3:** BMD changes compared to baseline at all follow-ups during and after teriparatide therapy.

At the femoral neck site, we observed an improvement from baseline T-scores at all three follow up visits up to two years post-teriparatide therapy, showing a 0.30 g/cm$^2$ improvement by the final visit (p = 0.007). Improvements were seen in the two follow-up visits during teriparatide therapy, with the first follow-up demonstrating a 0.05 g/cm$^2$ improvement and second follow-up demonstrating a 0.16 g/cm$^2$ improvement. Only the second follow-up was statistically significant (p = 0.04) (Table 3).

At the total hip site, we observed a statistically significant improvement from baseline T-scores at all three follow up visits

post teriparatide therapy, showing a 0.26 g/cm$^2$ improvement by the final visit (p = 0.003). No changes were seen in the two follow-up visits during teriparatide therapy, with the first follow-up demonstrating a -0.01 g/cm$^2$ decrease in BMD and second follow-up demonstrating a 0.00 g/cm$^2$ change. Both follow-ups were not statistically significant changes (p-values 0.91 and 0.97 respectively) (Table 3). In subgroup analyses comparing previously treated osteoporosis patients to treatment-naïve patients, we noted no statistically significant differences in bone mineral density among patients who were treated with bisphosphonates either prior to or after commencement of teriparatide therapy, or patients who were treated with denosumab after commencement of teriparatide therapy (Table 4).

| BMD site | T-score difference between medication naïve patients and pretreated patients (95% confidence intervals) | P-value |
|---|---|---|
| Femoral neck | | |
| Bisphosphonate use prior (yes) | 0.06 (-0.32, 0.43) | 0.767 |
| Bisphosphonate use after (yes) | 0.08 (-0.34, 0.50) | 0.690 |
| Denosumab use after (yes) | 0.14 (-0.34, 0.62) | 0.569 |
| Lumbar spine | | |
| Bisphosphonate use prior (yes) | 0.16 (-0.39, 0.72) | 0.558 |
| Bisphosphonate use after (yes) | -0.19 (-0.81, 0.42) | 0.530 |
| Denosumab use after (yes) | 0.07 (-.63, 0.77) | 0.842 |
| Total hip | | |
| Bisphosphonate use prior (yes) | 0.21 (-0.26, 0.68) | 0.377 |
| Bisphosphonate use after (yes) | 0.15 (-0.37, 0.68) | 0.569 |
| Denosumab use after (yes) | -0.06 (-0.66, 0.54) | 0.842 |

**Table 4:** Antiresorptive agent effect on BMD compared to naïve patients averaged over all time points.

## HRQL domains

(Table 5) describes changes from baseline during the four follow-up visits during teriparatide therapy, as well as the two follow-up visits post teriparatide therapy.

| Pain Question | Difference between baseline pain score and follow-up (95% confidence intervals) | P-value |
|---|---|---|
| Question 1 (Symptoms) | | |
| 1st follow-up during PTH therapy | -0.46 (-0.77, -0.15) | 0.004 |
| 2nd follow-up during PTH therapy | -0.63 (-0.98, -0.27) | <0.001 |
| 3rd follow-up during PTH therapy | -0.70 (-1.20, -0.20) | 0.006 |
| 4th follow-up during PTH therapy | -0.50 (-1.25, 0.26) | 0.200 |
| 1st follow-up after PTH therapy | -0.48 (-0.82, -0.14) | 0.005 |
| 2nd follow-up after PTH therapy | -0.63 (-1.07, -1.20) | 0.005 |
| Question 2 (Symptoms) | | |
| 1st follow-up during PTH therapy | -0.41 (-0.70, -0.11) | 0.008 |
| 2nd follow-up during PTH therapy | -0.55 (-0.89, -0.22) | 0.001 |
| 3rd follow-up during PTH therapy | -0.54 (-0.97, -0.11) | 0.013 |
| 4th follow-up during PTH therapy | -0.83 (-1.49, -0.16) | 0.015 |
| 1st follow-up after PTH therapy | -0.42 (-0.76, -0.08) | 0.015 |
| 2nd follow-up after PTH therapy | -0.92 (-1.36, -0.47) | <0.001 |
| Question 3 (Emotional Functioning) | | |
| 1st follow-up during PTH therapy | -0.26 (-0.61, 0.10) | 0.153 |
| 2nd follow-up during PTH therapy | -0.33 (-0.73, 0.07) | 0.110 |
| 3rd follow-up during PTH therapy | -0.63 (-1.19, -0.08) | 0.026 |
| 4th follow-up during PTH therapy | -0.09 (-0.95, 0.76) | 0.828 |
| 1st follow-up after PTH therapy | -0.38 (-0.76, 0.01) | 0.051 |
| 2nd follow-up after PTH therapy | -0.90 (-0.90, 0.26) | 0.001 |
| Question 4 (Emotional Functioning) | | |
| 1st follow-up during PTH therapy | -0.11 (-0.39, 0.17) | 0.428 |
| 2nd follow-up during PTH therapy | -0.23 (-0.55, 0.09) | 0.150 |
| 3rd follow-up during PTH therapy | -0.14 (-0.59, 0.31) | 0.537 |
| 4th follow-up during PTH therapy | 0.18 (-0.51, 0.86) | 0.613 |
| 1st follow-up after PTH therapy | -0.12 (-0.43, 0.18) | 0.418 |
| 2nd follow-up after PTH therapy | -0.42 (-0.81, -0.02) | 0.040 |
| Question 5 (Physical Functioning) | | |
| 1st follow-up during PTH therapy | -0.21 (-0.58, 0.16) | 0.265 |
| 2nd follow-up during PTH therapy | -0.42 (-0.82, -0.02) | 0.041 |
| 3rd follow-up during PTH therapy | -0.31 (-0.85, 0.23) | 0.261 |
| 4th follow-up during PTH therapy | -0.58 (-1.43, 0.26) | 0.175 |
| 1st follow-up after PTH therapy | -0.31 (-0.71, 0.10) | 0.134 |
| 2nd follow-up after PTH therapy | -0.84 (-1.36, -0.32) | 0.002 |

| | | |
|---|---|---|
| Question 6 (Physical Functioning) | | |
| 1st follow-up during PTH therapy | -0.17 (-0.53, 0.20) | 0.369 |
| 2nd follow-up during PTH therapy | -0.38 (-0.78, 0.02) | 0.059 |
| 3rd follow-up during PTH therapy | -0.18 (-0.71, 0.35) | 0.508 |
| 4th follow-up during PTH therapy | -0.77 (-1.59, 0.05) | 0.067 |
| 1st follow-up after PTH therapy | -0.41 (-0.81, -0.01) | 0.046 |
| 2nd follow-up after PTH therapy | -0.67 (-1.18, -0.16) | 0.011 |
| Question 7 (Activities of Daily Living) | | |
| 1st follow-up during PTH therapy | -0.29 (-0.74, 0.16) | 0.207 |
| 2nd follow-up during PTH therapy | -0.44 (-0.95, 0.06) | 0.085 |
| 3rd follow-up during PTH therapy | -0.49 (-1.15, 0.17) | 0.146 |
| 4th follow-up during PTH therapy | -0.98 (-2.03, 0.08) | 0.069 |
| 1st follow-up after PTH therapy | -0.48 (-0.99, 0.03) | 0.064 |
| 2nd follow-up after PTH therapy | -0.66 (-1.33, 0.01) | 0.052 |
| Question 8 (Activities of Daily Living) | | |
| 1st follow-up during PTH therapy | 0.09 (-0.27, 0.44) | 0.638 |
| 2nd follow-up during PTH therapy | -0.04 (-0.44, 0.36) | 0.838 |
| 3rd follow-up during PTH therapy | -0.38 (-0.90, 0.14) | 0.150 |
| 4th follow-up during PTH therapy | -0.66 (-1.49, 0.16) | 0.115 |
| 1st follow-up after PTH therapy | -0.33 (-0.74, 0.08) | 0.113 |
| 2nd follow-up after PTH therapy | -0.44 (-0.95, 0.07) | 0.094 |
| Question 9 (Leisure) | | |
| 1st follow-up during PTH therapy | -0.08 (-0.41, 0.26) | 0.652 |
| 2nd follow-up during PTH therapy | -0.38 (-0.77, 0.00) | 0.050 |
| 3rd follow-up during PTH therapy | -0.49 (-1.00, 0.00) | 0.051 |
| 4th follow-up during PTH therapy | -0.58 (-1.31, 0.15) | 0.120 |
| 1st follow-up after PTH therapy | -0.48 (-0.86, -0.10) | 0.013 |
| 2nd follow-up after PTH therapy | -0.34 (-0.82, 0.14) | 0.165 |
| Question 10 (Leisure) | | |
| 1st follow-up during PTH therapy | -0.07 (-0.47, 0.32) | 0.715 |
| 2nd follow-up during PTH therapy | -0.33 (-0.79, 0.14) | 0.169 |
| 3rd follow-up during PTH therapy | -0.41 (-0.99, 0.17) | 0.169 |
| 4th follow-up during PTH therapy | -0.42 (-1.24, 0.40) | 0.317 |
| 1st follow-up after PTH therapy | -0.56 (-1.03, -0.08) | 0.023 |
| 2nd follow-up after PTH therapy | -0.50 (-1.08, 0.08) | 0.093 |

**Table 5:** Quality of life scores compared to baseline at all follow-ups during and after teriparatide therapy.

**Symptoms:** Questions 1 and 2 (Appendix) address the HRQL domain of symptoms. We noted statistically significant improvements from baseline of -0.63 for question 1 and -0.92 for question 2 at the second follow-up post teriparatide therapy ($p = 0.005$ and $<0.001$, respectively). All other follow-up scores showed statistically significant improvements except for questions 1 at the fourth follow-up during teriparatide therapy, which showed an improvement of -0.5 ($p = 0.2$).

**Emotional functioning:** Questions 3 and 4 (Appendix) address the HRQL domain of emotional functioning. We noted statistically significant improvements from baseline of -0.9 for question 3 and -0.42 for question 4 at the second follow-up post teriparatide therapy ($p = 0.001$ and 0.04 respectively). All other follow-up scores were not statistically significant, except for question 3 at the third follow-up during teriparatide therapy, which showed an improvement of -0.63 ($p = 0.026$).

**Physical functioning:** Questions 5 and 6 (Appendix) address the HRQL domain of physical functioning. We noted statistically significant improvements from baseline of -0.84 for question 5 and -0.67 for question 6 at the second follow-up post teriparatide therapy ($p = 0.002$ and 0.011 respectively). All other follow-up scores were not statistically significant, except for question 5 at the second follow-up during teriparatide therapy, which showed an improvement of -0.42 ($p = 0.041$) and question 6 at the first follow-up after teriparatide therapy, which showed an improvement of -0.41 ($p = 0.046$).

**Activities of daily living:** Questions 7 and 8 (Appendix) address the HRQL domain of activities of daily living. We noted non-statistically significant improvements from baseline of -0.66 for question 7 and -0.44 for question 8 at the second follow-up post teriparatide therapy ($p = 0.052$ and 0.094 respectively). All other follow-up scores were not statistically significant.

**Leisure:** Questions 9 and 10 (Appendix) address the HRQL domain of leisure. We noted non-statistically significant improvements from baseline of -0.34 for question 9 and -0.5 for question 10 at the second follow-up post teriparatide therapy ($p = 0.165$ and 0.093 respectively). All other follow-up scores were not statistically significant, except for question 9 at the second follow-up during teriparatide therapy, which showed an improvement of -0.38 ($p = 0.05$), question 9 at the first follow-up after teriparatide therapy, which showed an improvement of -0.48 ($p = 0.013$) and question 10 also at the first follow-up after teriparatide therapy, which showed an improvement of -0.56 ($p = 0.023$).

## Discussion

The results of our study support the existing literature in that treatment with teriparatide improves BMD at the lumbar spine, femoral neck and total hip sites regardless of prior treatment with or without antiresorptive agents [15,22]. These improvements were noted to persist at all three sites at the third follow-up post teriparatide therapy. Use of antiresorptive agents prior and after teriparatide therapy showed no statistically significant difference to patients naïve to antiresorptive therapy. With regards to benefits

relating to HRQL, it is well documented in the literature that teriparatide treatment demonstrates significant benefits during the course of an 18 and 24-month treatment regimen, with evidence suggesting that these improvements in HRQL are superior to improvements gained through bisphosphonate treatment alone [18,23,24]. Following teriparatide treatment, literature regarding sustained improvements of HRQL is scarcer and mostly drawing from the European Forteo Observational Study (EFOS). In these studies, HRQL was measured using the EuroQol five dimensions questionnaire (EQ-5D) consisting of the 5 domains mobility, self-care, usual activities, pain/discomfort and anxiety/depression. All domains demonstrated sustained improvements at 18-months post teriparatide treatment [19,20]. In assessing HRQL during and post teriparatide treatment, our study utilized the mini-OQLQ, a shortened version of the OQLQ, which has been shown to be effective clinical tool in evaluating the health-related quality of life in osteoporotic women with back pain due to vertebral fractures [21]. The results of our study indicate significant improvements most notably in the symptoms, emotional functioning and physical functioning domains at the final follow-up post teriparatide therapy. The activities of daily living and leisure domains showed improvements at the final follow-up post teriparatide therapy, although they were not statistically significant. The reduction in the symptoms, emotional functioning and physical functioning domains indicate that patients who have received teriparatide therapy showed a reduction of distress or discomfort, are less fearful of fractures and falling and are able to perform more rigorous activity. Although possibly, partly attributable to alternate pharmacological treatments after completion of teriparatide, these improvements were sustained for up to 2 years following treatment.

Several important limitations of our study must be addressed. This was a retrospective cohort study, and comes with the known limitations of such a study design. Patients were not randomized to teriparatide versus standard therapy, and therefore our findings are susceptible to selection bias regarding patients who were eligible for teriparatide. Patients and physicians were not blinded to therapy, which may influence outcomes; though this is less significant with more objective scores such as BMD, it may play a role in the interpretation of more subjective outcomes such as self-reported HRQL symptoms. Our retrospective review did not have a control group, which would have been beneficial as a comparator for our study. Furthermore, the assumption was made that all patients were compliant with their teriparatide therapy. However, this is likely an over-estimate, and thus the effects of teriparatide therapy may have been understated in our analysis. Despite these limitations, the robust improvement in BMD, particularly at the lumbar spine, as well as in HRQL symptoms, is supportive of teriparatide as an effective anabolic agent for the treatment of osteoporosis.

## Conclusion

Our study is consistent with the literature in the effects of teriparatide treatment in increasing the BMD of patients treated for osteoporosis. BMD improvements were shown to extend for at least up to three follow-up visits or two years post teriparatide therapy. These BMD improvements are accompanied by significant improvements in various domains of the mini-OQLQ demonstrating an improvement in HRQL both during teriparatide treatment and subsequently up to two years post treatment.

## Appendix

### Shortened Osteoporosis Quality of Life Questionnaire

1) How much distress or discomfort have you had because of pain in the last two weeks?

2) How much distress or discomfort you had in last two weeks because it had been painful to stand for a long time

3) How often in the last two weeks have you felt afraid of fractures?

4) How often in the last two weeks have you felt afraid of falling?

5) How difficult has it been for you to lift things in the last two weeks?

6) How difficult has it been for you to carry things in the last two weeks, because of back problems due to osteoporosis?

7) How difficult has it been for you to vacuum in the last two weeks?

8) How difficult has it been for you to housework in the last two weeks?

9) How difficult has it been for you to travel in the last two weeks?

10) How difficult has it been for you to take the type of vacation or holiday you enjoy because of your back

problems due to osteoporosis

## References

1. NIH Consensus Development Panel on Osteoporosis Prevention D, Therapy (2001) Osteoporosis prevention, diagnosis, and therapy. Jama 285: 785-795.

2. Kanis JA, Melton LJ, Christiansen C, Johnston CC, Khaltaev N (1994) The diagnosis of osteoporosis. Journal of Bone and Mineral Research 9: 1137-1141.

3. Blake GM and Fogelman I (2007) Role of dual-energy X-ray absorptiometry in the diagnosis and treatment of osteoporosis. Journal of Clinical Densitometry 10: 102-110.

4. Hallberg I, Rosenqvist A, Kartous L, Löfman O, Wahlström O, et al. (2004) Health-related quality of life after osteoporotic fractures. Osteoporosis International 15: 834-841.

5. Adachi J, Ioannidis G, Berger C, Joseph L, Papaioannou A, et al. (2001) The influence of osteoporotic fractures on health-related quality of life in community-dwelling men and women across Canada. Osteoporosis International 12: 903-908.

6. Burge R, Dawson□Hughes B, Solomon DH, Wong JB, King A, et al. (2007) Incidence and economic burden of osteoporosis□related fractures in the United States, 2005-2025. Journal of bone and mineral research 22: 465-475.

7. Benhamou CL (2007) Effects of osteoporosis medications on bone quality. Joint Bone Spine 74: 39-47.

8. Chen JS and Sambrook PN (2012) Antiresorptive therapies for osteoporosis: a clinical overview. Nature Reviews Endocrinology 8: 81-91.

9. Cole Z, Dennison E, Cooper C (2008) Update on the treatment of postmenopausal osteoporosis. British medical bulletin 86: 129-143.

10. Neer RM, Arnaud CD, Zanchetta JR, Prince R, Gaich GA, et al. (2001) Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. New England Journal of Medicine 344: 1434-1441.

11. Jiang Y, Zhao JJ, Mitlak BH, Wang O, Genant HK, et al. (2003) Recombinant human parathyroid hormone (1-34) [teriparatide] improves both cortical and cancellous bone structure. Journal of Bone and Mineral Research 18: 1932-1941.

12. Kaufman JM, Orwoll E, Goemaere S, San Martin J, Hossain A, et al. (2005) Teriparatide effects on vertebral fractures and bone mineral density in men with osteoporosis: treatment and discontinuation of therapy. Osteoporosis International 16: 510-516.

13. Dobnig H and Turner RT (1995) Evidence that intermittent treatment with parathyroid hormone increases bone formation in adult rats by activation of bone lining cells. Endocrinology 136: 3632-3638.

14. Jilka RL, Weinstein RS, Bellido T, Roberson P, Parfitt AM, et al. (1999) Increased bone formation by prevention of osteoblast apoptosis with parathyroid hormone. Journal of Clinical Investigation 104: 439.

15. Obermayer□Pietsch BM, Marin F, McCloskey EV, Hadji P, Farrerons J, et al. (2008) Effects of two years of daily teriparatide treatment on BMD in postmenopausal women with severe osteoporosis with and without prior antiresorptive treatment. Journal of Bone and Mineral Research 23: 1591-1600.

16. Body JJ, Gaich GA, Scheele WH, Kulkarni PM, Miller PD, et al. (2002) A randomized double-blind trial to compare the efficacy of teriparatide [recombinant human parathyroid hormone (1-34)] with alendronate in postmenopausal women with osteoporosis. The Journal of Clinical Endocrinology & Metabolism 87: 4528-4535.

17. Lau AN, Ali SH, Sawka AM, Thabane L, Papaioannou A, et al. (2008) Improvement in health-related quality of life in osteoporosis patients treated with teriparatide. BMC musculoskeletal disorders 9: 151.

18. Langdahl BL, Rajzbaum G, Jakob F, Karras D, Ljunggren O, et al. (2009) Reduction in fracture rate and back pain and increased quality of life in postmenopausal women treated with teriparatide: 18-month data from the European Forsteo Observational Study (EFOS). Calcified tissue international 85: 484-493.

19. Rajzbaum, G, Grados, F, Evans, Liu-Leage S, Petto H, et al. (2014) Treatment persistence and changes in fracture risk, back pain, and quality of life amongst patients treated with teriparatide in routine clinical care in France: Results from the European Forsteo Observational Study. Joint Bone Spine 81: 9-75.

20. Ljunggren Ö, Barrett A, Stoykov I, Langdahl BL, Lems WF, et al. (2013) Effective osteoporosis treatment with teriparatide is associated with enhanced quality of life in postmenopausal women with osteoporosis: the European Forsteo Observational Study. BMC Musculoskeletal Disorders 14: 447.

21. Cook D, Guyatt G, Adachi J, Epstein RS, Juniper EF, et al. (1999) Development and validation of the mini-osteoporosis quality of life questionnaire (OQLQ) in osteoporotic women with back pain due to vertebral fractures. Osteoporosis Quality of Life Study Group. Osteoporosis international 10: 207-213.

22. Boonen S, Marin F, Obermayer-Pietsch B, Simões ME, Barker C, et al. (2008) Effects of previous antiresorptive therapy on the bone mineral density response to two years of teriparatide treatment in postmenopausal women with osteoporosis. The Journal of Clinical Endocrinology & Metabolism 93: 852-860.

23. Langdahl BL, Ljunggren Ö, Benhamou CL, Marin F, Kapetanos G, et al. (2016) Fracture Rate, Quality of Life and Back Pain in Patients with Osteoporosis Treated with Teriparatide: 24-Month Results from the Extended Forsteo Observational Study (ExFOS). Calcified Tissue International 99: 259-271.

24. Panico A, Lupoli GA, Marciello F, Lupoli R, Cacciapuoti M, et al. (2011) Teriparatide vs. Alendronate as a treatment for osteoporosis: Changes in biochemical markers of bone turnover, BMD and quality of life. Medical Science Monitor 17: CR442-CR448.