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Comparative Effects of Teriparatide, Denosumab, and Combination Therapy on Peripheral Compartmental Bone Density, Microarchitecture, and Estimated Strength: the DATA-HRpQCT Study

JN Tsai¹, AV Uihlein¹, SM Burnett-Bowie¹, RM Neer¹, Y Zhu¹, N Derrico¹, H Lee², ML Boussein^{1,3}, and BZ Leder¹

¹Endocrine Unit, Massachusetts General Hospital, Boston, MA

²Biostatistics Center, Massachusetts General Hospital, Boston, MA

³Orthopedic Surgery, Beth Israel Deaconess Medical Center, Boston, MA

Abstract

Combined teriparatide and denosumab increases spine and hip bone mineral density more than either drug alone. The effect of this combination on skeletal microstructure and microarchitecture, however, is unknown. Because skeletal microstructure and microarchitecture are important components of skeletal integrity, we performed high-resolution peripheral QCT assessments at the distal tibia and radius in postmenopausal osteoporotic women randomized to receive teriparatide 20- μ g daily (n=31), denosumab 60-mg every 6 months (n=33), or both (n=30) for 12 months. In the teriparatide group, total volumetric BMD (vBMD) did not change at either anatomic site but increased in both other groups at both sites. The increase in vBMD at the tibia was greater in the combination group (3.1 \pm 2.2%) than both the denosumab (2.2 \pm 1.9%) and teriparatide groups (-0.3 \pm 1.9%) (p<0.02 for both comparisons). Cortical vBMD decreased by 1.6 \pm 1.9% at the tibia and by 0.9 \pm 2.8% at the radius in the teriparatide group whereas it increased in both other groups at both sites. Tibia cortical vBMD increased more in the combination group (1.5 \pm 1.5%) than both monotherapy groups (p<0.04 for both comparisons). Cortical thickness did not change in the teriparatide group, but increased in both other groups. The increase in cortical thickness at the tibia was greater in the combination group (5.4 \pm 3.9%) than both monotherapy groups (p<0.01 for both comparisons). In the teriparatide group, radial cortical porosity increased by 20.9 \pm 37.6% and by 5.6 \pm 9.9% at the tibia but did not change in the other two groups. Bone stiffness and failure load, as estimated by finite element analysis, did not change in the teriparatide group but increased in the other two groups at both sites. Together, these findings suggest that the use of denosumab and

Corresponding author: Joy Tsai, 50 Blossom St, Thier 1051, Boston, MA 02114, (617) 726-4650, jntsai@partners.org.

Disclosures

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Contributors

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teriparatide in combination improves HR-pQCT measures of bone quality more than either drug alone and may be of significant clinical benefit in the treatment of postmenopausal osteoporosis.

Keywords

osteoporosis; high-resolution peripheral quantitative computed tomography; microarchitecture; denosumab; teriparatide

Introduction

While therapeutic options for osteoporosis have expanded greatly over the past few decades, no single agent is able to restore skeletal integrity in most patients with advanced disease. Despite initial enthusiasm for an approach that would target both bone resorption and formation, studies investigating the efficacy of combined bisphosphonates and parathyroid hormone or teriparatide generally demonstrated minimal or no greater increase in bone mass compared to monotherapy.⁽¹⁻⁴⁾ In the Denosumab and Teriparatide Administration (DATA) study, we demonstrated that 12-months of combined denosumab and teriparatide therapy increases areal bone mineral density at the spine and hip as measured by dual X-ray absorptiometry (DXA) more than either treatment and more than has been reported with any currently approved treatment for postmenopausal osteoporosis.⁽⁵⁾ The effects of combined denosumab and teriparatide on compartment-specific changes in bone density, changes in skeletal microarchitecture, or changes in bone strength, however, are unknown.

Until recently, treatment-induced bone microarchitectural changes could only be assessed by histomorphometric analyses of iliac crest bone biopsies. The development of high-resolution peripheral quantitative computed tomography (HR-pQCT), however, enables non-invasive assessments of cortical and trabecular bone volumetric density, geometry, and microarchitecture at peripheral anatomic sites *in vivo*. Only a few studies have investigated the effects of osteoporosis treatment on bone microarchitecture assessed by HR-pQCT⁽⁶⁻¹⁴⁾ and no published studies have assessed the microarchitectural and compartmental structural changes in response to the combination of antiresorptive and anabolic therapy in humans. Furthermore, recent technical advances now allow for the HR-pQCT measurement of intracortical porosity, a parameter that is independently associated with prevalent hip fracture and is known to independently contribute to the age-related decrease in bone strength.⁽¹⁵⁻¹⁷⁾ HR-pQCT images can also be used to estimate bone strength by micro-finite element analysis (μ FEA), a technique that utilizes accepted engineering principles to estimate fracture resistance at these peripheral sites.⁽¹⁸⁻²¹⁾ To define the effects of combination teriparatide and denosumab on cortical and trabecular bone density, microarchitecture, and predicted bone strength, we obtained HR-pQCT measurements of the distal tibia and radius in postmenopausal women randomized to receive 12 months of teriparatide, denosumab, or both medications in the DATA study. Specifically, we aimed to test the hypotheses that 12 months of combined teriparatide and denosumab would increase cortical and trabecular volumetric BMD, improve trabecular and cortical microstructure and geometry, and increase predicted bone strength more than either drug alone.

Methods

Subjects

Details of the DATA study subjects have been reported previously.⁽⁵⁾ Briefly, we recruited postmenopausal women over age 45 at high risk of fracture from a single clinical site (Massachusetts General Hospital, Boston, MA). We defined high risk of fracture as T score -2.5 or lower at the spine, total hip, or femoral neck; a T score -2.0 or less with at least one BMD-independent risk factor (fracture after age 50 years, parental hip fracture after age 50 years, previous hyperthyroidism, inability to get up from a chair with arms raised, or current smoking);⁽²²⁾ or a T score -1.0 or less with history of fragility fracture. Women were excluded for use of glucocorticoids or oral bisphosphonates within 6 months of enrollment; use of estrogen, selective estrogen-receptor modulators, or calcitonin within 3 months of enrollment; or any prior use of intravenous bisphosphonates, parathyroid hormone, or strontium ranelate.

Protocol

Prior to randomization, women were stratified by age (younger than 65 years vs 65 years or older) and by previous bisphosphonate use. Subjects were then randomly assigned to open-label treatment of teriparatide 20 mcg subcutaneously once daily, denosumab 60 mg subcutaneously every six months, or both medications. Calcium and vitamin D were prescribed to achieve total daily intakes of 1,200 mg calcium and 25-hydroxyvitamin D concentrations greater than 20 ng/mL. The study was approved by the Partners Healthcare Institutional Review Board and registered on ClinicalTrials.gov, number NCT00926380.

HR-pQCT

Trabecular and cortical density and microarchitecture of the distal radius and tibia were assessed at 0, 3, 6, and 12 months using HR-pQCT (XtremeCT, Scanco Medical AG, Brüttisellen, Switzerland). Scans consisting of 110 CT slices over a 9.02 mm region of interest were acquired with an isotropic voxel size of 82 microns. The non-dominant arm and corresponding leg were scanned unless there was a prior fracture at that region, whereupon the dominant side was scanned. The volume of interest (VOI) shared by a participant's 0, 3, 6, and 12 month scans was identified using the manufacturer's 2D region-matching software which relied on the periosteal contours. In this shared VOI, we used semi-automated software to segment cortical and trabecular regions based on a threshold-based algorithm. Total, trabecular, and cortical bone density (Tot.vBMD, Tb.vBMD, Ct.vBMD, mg HA/cm³) were determined in addition to microarchitecture parameters of cortical thickness (Ct.Th, mm), trabecular thickness (Tb.Th, mm), trabecular number (Tb.N, mm⁻¹), and trabecular separation (Tb. Sp, mm).

The cortical bone compartment in this shared VOI was then further segmented via an autocontouring process that generated periosteal and endosteal contours.⁽²³⁾ All automatically generated contours were inspected, and if the contour deviated from the visually apparent periosteal or endosteal margin, semi-manual adjustment was made. Using this extended cortical analysis, cortical tissue mineral density (Ct.TMD, mgHA/cm³) and cortical porosity (Ct.Po, %) were assessed at months 0 and 12. Ct.TMD is the density of the

cortical bone excluding the resolved Haversian canals and pores. Cortical porosity is the volume of the resolved Haversian canals and intracortical pore space normalized by the sum of their volume plus the cortical solid tissue volume.

Micro-FEA was performed to estimate the biomechanical properties of the bone, as previously described.^(18–20) Following image segmentation (described above), each bone voxel of the HR-pQCT distal radius and tibia images was converted to hexahedral finite elements having linear-elastic and isotropic material behavior, with a Young's modulus and Poisson's ratio of 10 GPa and 0.3, respectively. The μ FEA model was subjected to uniaxial compression, and stiffness (kN/mm) and failure load (kN) were estimated at months 0 and 12. Failure load was estimated by scaling the resultant load from a 1% apparent compressive strain until 2% of all elements reached an effective strain $> 7000 \mu\text{strain}$.⁽²⁴⁾

Two operators performed the endosteal contouring (assigning the same operator for all scans for each subject) and a third operator reviewed all periosteal and endosteal contouring for quality assurance. Images were graded as 1 (excellent), 2 (good), or 3 (poor) for motion artifact and scans with a quality score of 3 were excluded from analysis. Scans with a fracture in the region of interest were excluded from analysis. Same-day reproducibility for repeated measurements is 0.2 to 1.4% for density values, 0.3 to 8.6% for trabecular microarchitecture parameters, 0.6 to 2.4% for cortical microarchitecture parameters, 7.3 to 20.2% for cortical porosity measurements, and 2.1 to 3.0% for μ FEA measures. These ranges are consistent with prior reports.^(18, 25)

Statistical analysis

We performed a modified intention-to-treat analysis, which includes all data from women completing at least one post-baseline study visit. To compare the between-group changes in each parameter, we used repeated measures analysis of variance (ANOVA). Within group changes were assessed by paired t-test. The 0–12 month changes in each variable in subjects with previous bisphosphonate use, no previous use, and the entire cohort were compared by one-way ANOVA. Statistical analyses were performed with SAS for Windows (version 9.3). Data are presented as mean (SD) unless otherwise specified. Two sided p-values of 0.05 or less are considered significant.

Results

Of the 100 women enrolled, 94 women completed at least one post-baseline visit and are included in the modified intention-to-treat analysis (figure one). Six percent of radius scans and 3% of tibia scans were excluded due to motion artifact. When comparing the baseline and 12-month visit only, the shared VOI averaged 93% at the radius and 95% at the tibia. When comparing all four visits, the shared VOI averaged 86% at the radius and 91% at the tibia. Baseline clinical characteristics were similar among the three groups (table 1). Baseline HR-pQCT variables were similar among the three groups with exception of tibial cortical thickness, which was greater in the combination therapy group than in the denosumab group (table 2). It should be noted that there was no difference in overall treatment response in any HR-pQCT variable among subjects with or without a history of bisphosphonate exposure and the entire cohort (Supplemental Table).

Volumetric Density

Tibia—The mean changes in HR-pQCT volumetric density are shown in Figure 2. At the tibia, 12 months of teriparatide treatment did not change total vBMD, whereas denosumab increased total volumetric BMD by $2.2 \pm 1.9\%$ ($p < 0.001$ versus baseline) and combination therapy increased total vBMD by $3.1 \pm 2.2\%$ ($p < 0.001$ versus baseline). The combination of both drugs increased total volumetric BMD more than teriparatide or denosumab ($p < 0.001$, combination versus teriparatide and $p = 0.014$, combination versus denosumab). Similarly, trabecular vBMD did not change in the teriparatide group and increased in both the denosumab and combination groups, although no significant between-group differences were observed. Cortical vBMD decreased by $1.6 \pm 1.9\%$ in the teriparatide group, increased by $0.9 \pm 1.2\%$ in the denosumab group, and increased by $1.5 \pm 1.5\%$ in the combination group ($p < 0.001$ versus baseline for all comparisons). Combination therapy increased cortical vBMD more than teriparatide and denosumab ($p < 0.001$, combination versus teriparatide and $p = 0.035$, combination versus denosumab). Cortical tissue mineral density decreased with teriparatide, remained stable with denosumab, and increased with combination therapy and the change in the combination therapy group differed significantly from the teriparatide group ($p < 0.001$, combination versus teriparatide).

Radius—At the radius, total vBMD did not change in the teriparatide group but increased in both the denosumab ($1.6 \pm 2.1\%$) and combination therapy groups ($2.2 \pm 3.0\%$, $p < 0.01$ for both within group comparisons). The increase in total vBMD was greater in the combination therapy group than in the teriparatide group only ($p < 0.001$). Similarly, trabecular vBMD did not change in the teriparatide group but increased in the denosumab ($1.3 \pm 2.8\%$) and combination therapy ($3.1 \pm 3.3\%$) groups ($p = 0.05$ for both within group comparisons). The increase in total vBMD was greater in the combination therapy group than the teriparatide group only ($p = 0.012$). Cortical vBMD decreased by $1.9 \pm 2.8\%$ in the teriparatide group, increased by $0.7 \pm 1.4\%$ in the denosumab group, and increased by $1.0 \pm 1.6\%$ in the combination groups ($p < 0.02$ for all within group comparisons). Combination therapy increased cortical vBMD more than teriparatide ($p < 0.001$, combination versus teriparatide). Cortical tissue mineral density decreased with teriparatide, remained stable with denosumab, and increased with combination ($p < 0.001$, combination versus teriparatide).

Microarchitecture: geometry and structure

Tibia—At the tibia, 12 months of teriparatide did not change cortical thickness whereas cortical thickness increased by $3.7 \pm 3.3\%$ in the denosumab group and by $5.4 \pm 3.9\%$ in the combination therapy group ($p < 0.001$ versus baseline for the latter 2 groups) (figure 3). Combination therapy increased cortical thickness more than both teriparatide ($p < 0.001$) and denosumab ($p = 0.009$). Also at the tibia, cortical porosity increased by $5.6 \pm 9.9\%$ in the teriparatide group ($p = 0.006$ versus baseline) but did not change in the other two groups.

Radius—At the radius, cortical thickness did not change in the teriparatide group whereas it increased by $2.3 \pm 4.8\%$ in the denosumab group ($p = 0.016$ versus baseline) and by $2.3 \pm 4.8\%$ in the combination therapy group ($p = 0.022$ versus baseline). The increase in cortical thickness was greater in the combination group than the teriparatide group ($p = 0.014$). Also

at the radius, teriparatide increased cortical porosity by $20.9 \pm 37.6\%$ ($p=0.009$ versus baseline) whereas cortical porosity did not change in the other two groups. Note that while the percent changes in porosity appear to be large, the absolute changes are relatively modest. For example, while cortical porosity at the radius increased by 20.9% in the teriparatide group, this represents a change from 2.7% at baseline to 3.1% after 1 year of therapy.

At both the tibia and radius, changes in trabecular architecture were generally small and did not reach statistical significance (table 3).

Estimated bone strength

Tibia—At the tibia, FEA-estimates of bone stiffness did not change in the teriparatide group but increased by $2.3 \pm 5.3\%$ in the denosumab group ($p=0.027$ versus baseline) and by $5.3 \pm 5.5\%$ in the combination therapy group ($p<0.001$ versus baseline) (figure 4). The increase in stiffness was greater in the combination therapy group than in the teriparatide group ($p=0.005$). Similarly, failure load did not change in the teriparatide group but increased by $1.9 \pm 4.0\%$ in the denosumab group ($p=0.015$ versus baseline) and by $4.5 \pm 4.6\%$ in the combination group ($p<0.001$ versus baseline). The increase in tibial failure load was greater in the combination group than in both other groups ($p=0.005$, combination versus teriparatide and $p=0.041$, combination versus denosumab).

Radius—Similar patterns in estimated bone strength were observed at the radius, though not all between-group comparisons were statistically significant.

Discussion

The results of this study demonstrate that 12 months of combined denosumab and teriparatide therapy improves peripheral cortical and total bone density, cortical microarchitecture, and estimated bone strength more than either drug alone. While superior efficacy is noted at both the tibia and the radius in the combination group, the advantage of the combined treatment is numerically greater at the tibia than at the radius. The mechanism underlying the differential effects at these two peripheral anatomic sites is uncertain but might reflect an ability of weight-bearing to amplify the skeletal benefits of TPTD in humans, as previously documented in experimental animals.⁽²⁶⁾ There was also greater effect with alendronate in humans as measured with HR-pQCT in the distal tibia compared with the distal radius.⁽⁶⁾

The significant increase in cortical thickness and cortical area along with the concomitant decrease in trabecular area (data not shown) at the radius and tibia in the denosumab and combination therapy groups suggests that resorptive cavities at the endocortical surface are potentially being filled in response to therapy. Alternatively, the apparent increase in cortical thickness may be secondary to increases in the mineralization of cortical bone, which can influence edge detection by threshold-based segmentation algorithms. The relative contributions of these mechanisms to the observed increase in cortical thickness cannot be determined with current methods.

The observed decrease in cortical density and increase in cortical porosity among teriparatide treated women are consistent with HR-pQCT changes observed in prior studies of postmenopausal osteoporosis in which teriparatide monotherapy was shown to either decrease peripheral cortical BMD, increase cortical porosity, or both.^(9, 12) Moreover, numerous rodent and primate animal models show increases in cortical porosity with parathyroid hormone treatment.^(27–29) Importantly, however, teriparatide-induced increases in cortical porosity do not appear to have deleterious effect on μ FEA estimated failure load or stiffness as measured by HR-pQCT.⁽¹²⁾ The explanation for the maintained skeletal integrity may relate to beneficial changes in trabecular microarchitecture not detected in a sample of this size. It is possible that these relatively small absolute changes in cortical porosity do not substantially impact μ FEA strength predictions, as previously reported.⁽²³⁾ Additionally, assessment of cortical porosity that utilize a threshold-based analysis to differentiate cortical and trabecular bone may overestimate if there is substantial undermineralized bone. Methods of assessing cortical porosity that do not rely on a threshold-based analysis, such as a recently reported automated method of segmenting bone into its compact-appearing cortex, transitional zone, and trabecular compartment provide an alternate approach for assessing porosity.^(30, 31)

It is important to note that the improvements in the cortical bone parameters observed in the combination group in the present study do not represent a mixture of the teriparatide and denosumab-associated effects, but rather they represent an advantage over both monotherapies. The HR-pQCT changes described in the denosumab monotherapy group are also similar to those described in prior studies. For example, in a recent study of 83 women with osteoporosis treated with denosumab for 12 months, total vBMD, cortical vBMD, and cortical thickness all increased significantly.⁽⁷⁾ A notable finding of the present study is that in both the tibia and radius, denosumab completely inhibits the commonly observed teriparatide-induced increase in cortical porosity.

Several limitations of our study deserve mention. First, it should be noted that the lack of a placebo control group limits the interpretation of within-group changes. Given that many of the effects of are large magnitude, however, we feel that the within group changes, particularly in cortical parameters, are likely to be related to the specific treatment. Second, HR-pQCT is limited to measurements at the appendicular skeleton, and may not be consistent with changes in the axial skeletal. Additionally, motion artifact is a limitation of HR-pQCT and differences in the quality of serial scans could add to the error associated with these measurements. As suggested by Pialat et al in a report examining impact of scan quality on HR-pQCT measures, developing standardized quality control criteria will be important for HR-pQCT studies in the future.⁽³²⁾ We minimized this effect by censoring scans with severe motion artifact. Another potential limitation is that changes in bone size would not be detectable by HR-pQCT because matching of serial VOI was performed by assuming constant periosteal contours and cross-sectional areas among a participant's serial measurements. This technical limitation makes it impossible to assess if an increase in cortical porosity in the teriparatide group is offset by changes in bone size through periosteal expansion. Lastly, the clinical implications of the μ FEA estimates of bone strength are not yet fully established as there are no prospective longitudinal studies assessing the relationship between changes in μ FEA-estimated bone strength and fracture. Moreover, our

μ FEA analysis assumed fixed, homogeneous material properties although we observed that cortical TMD increased with combination therapy. Prior work has shown that bone tissue mineral density is related directly to the intrinsic material properties of bone (e.g. the elastic modulus), thus the μ FEA-measured stiffness and failure load in the combination group may have been underestimated.⁽³³⁾

In summary, the combination of denosumab and teriparatide appears to result in the most favorable changes in peripheral bone compartmental vBMD, microstructure and estimated strength as compared to either drug alone. Along with the previously reported superior efficacy of increases in DXA-derived BMD at the hip and spine, these changes may translate to greater fracture resistance and support the consideration of combination therapy in patients with severe osteoporosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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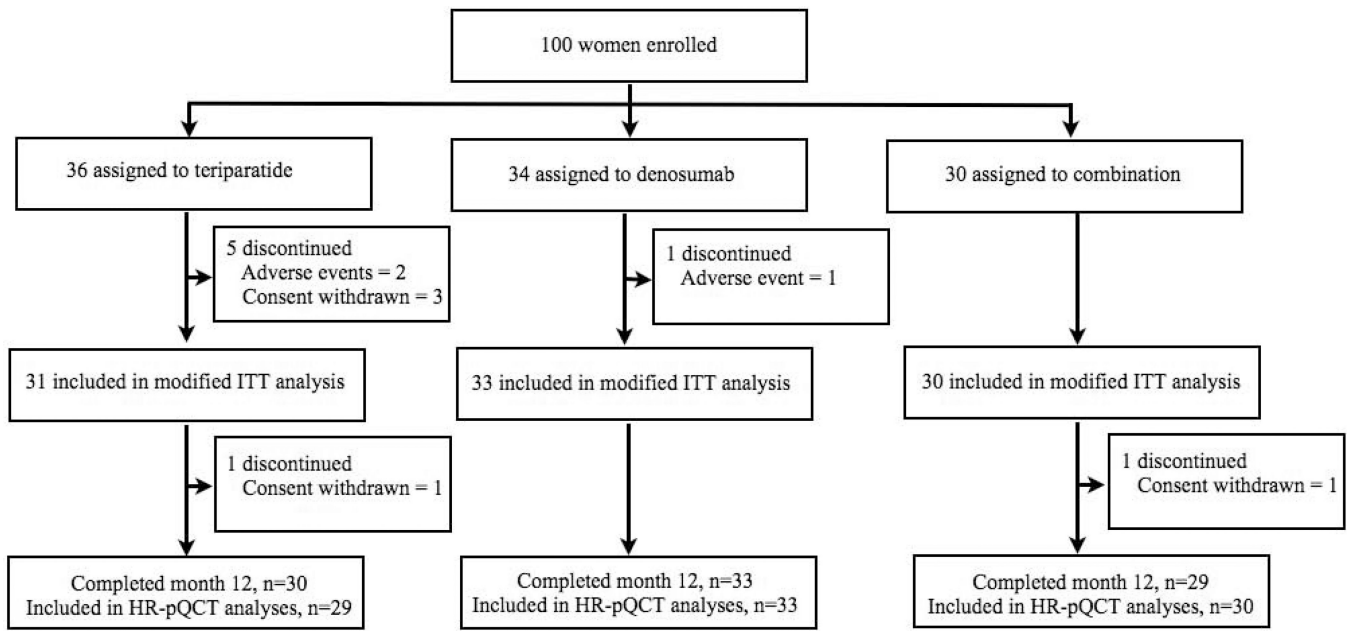


Figure 1.
Subject disposition.

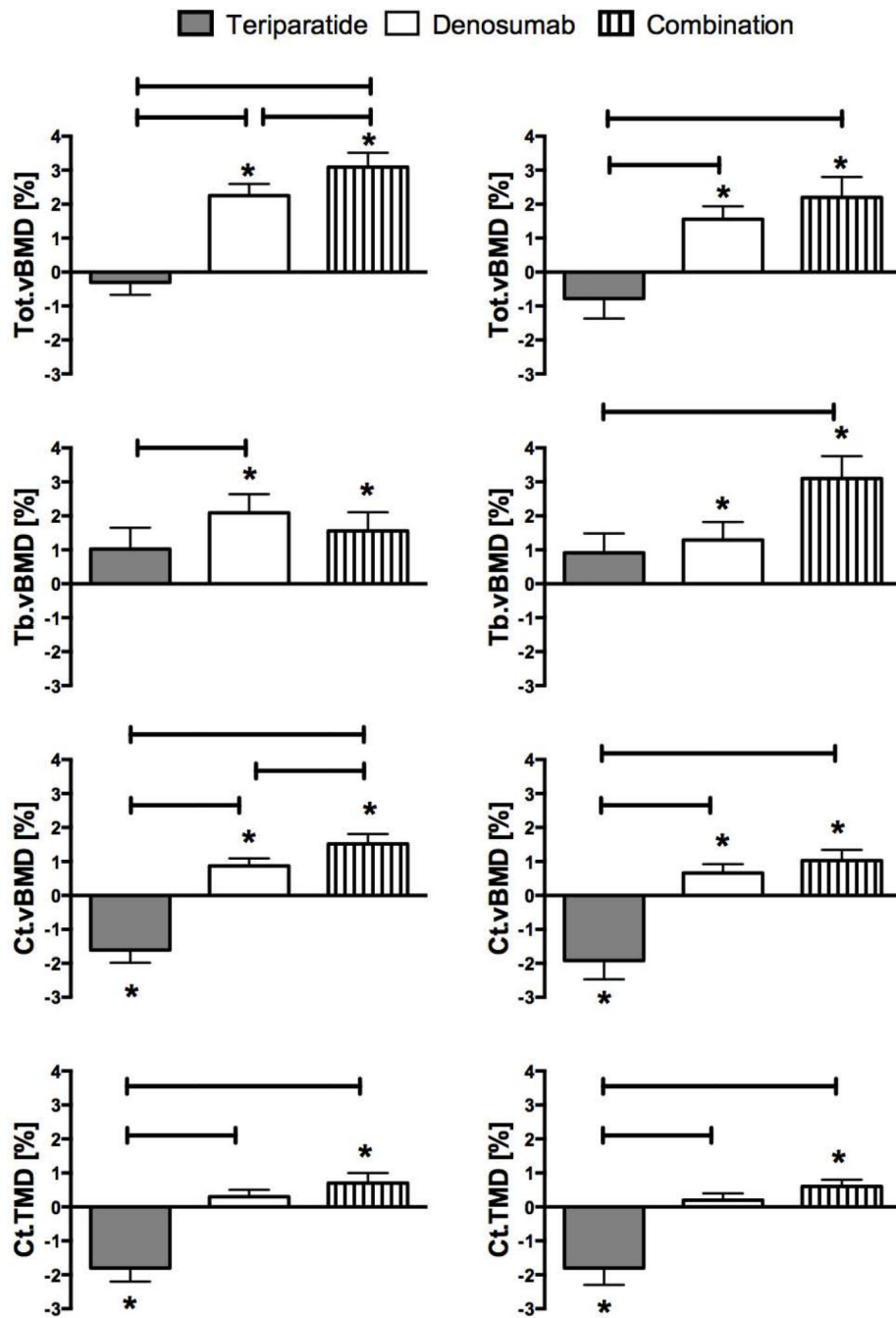


Figure 2. Mean percent change (SEM) from baseline at distal tibia (left column) and distal radius (right column) in bone densities at 12 months. *p value <0.05 versus baseline, bars represent p value <0.05 between groups.

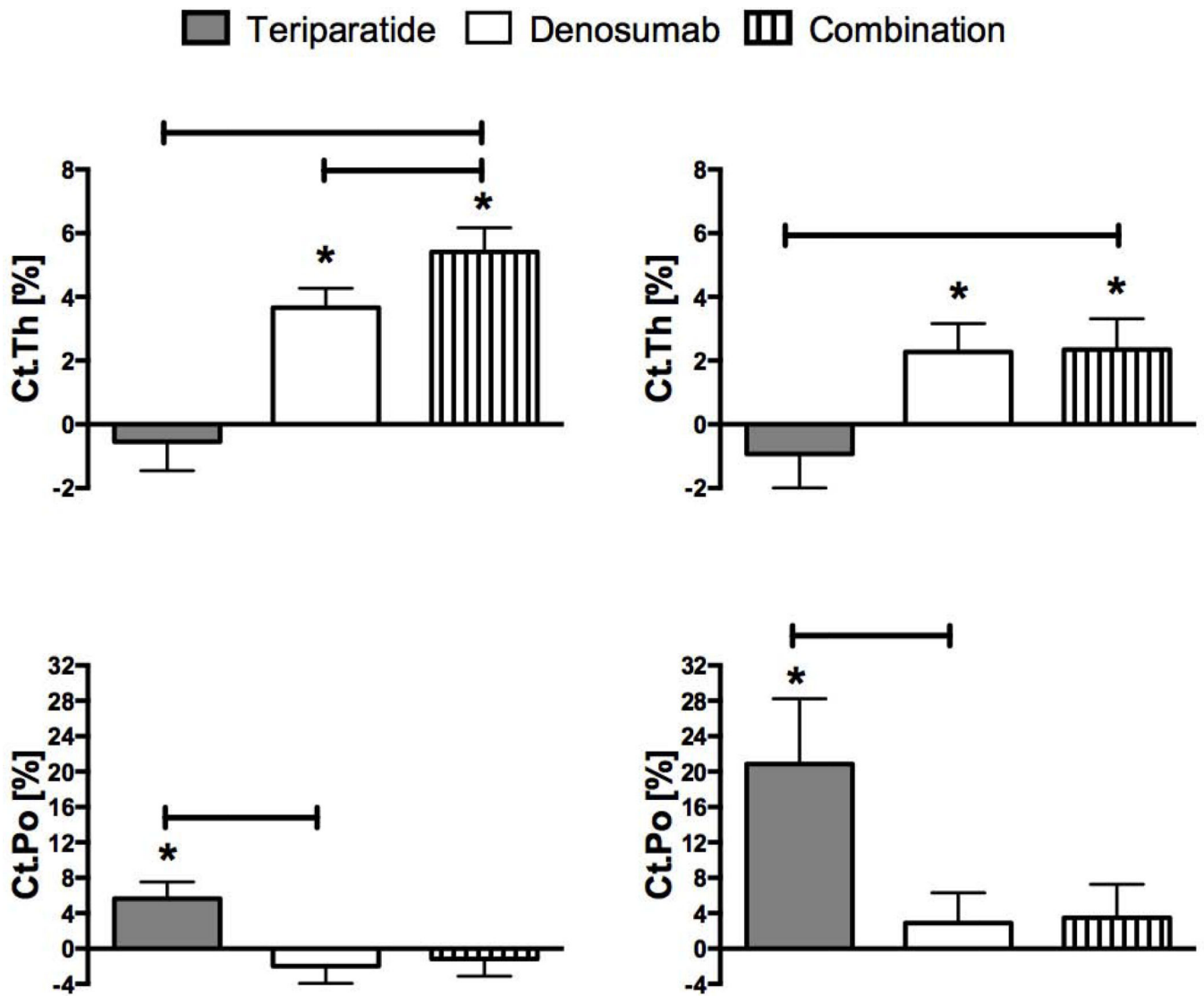


Figure 3. Mean percent change (SEM) from baseline at distal tibia (left) and distal radius (right) in cortical thickness and cortical porosity at 12 months. *p value <0.05 versus baseline, bars represent p value <0.05 between groups.

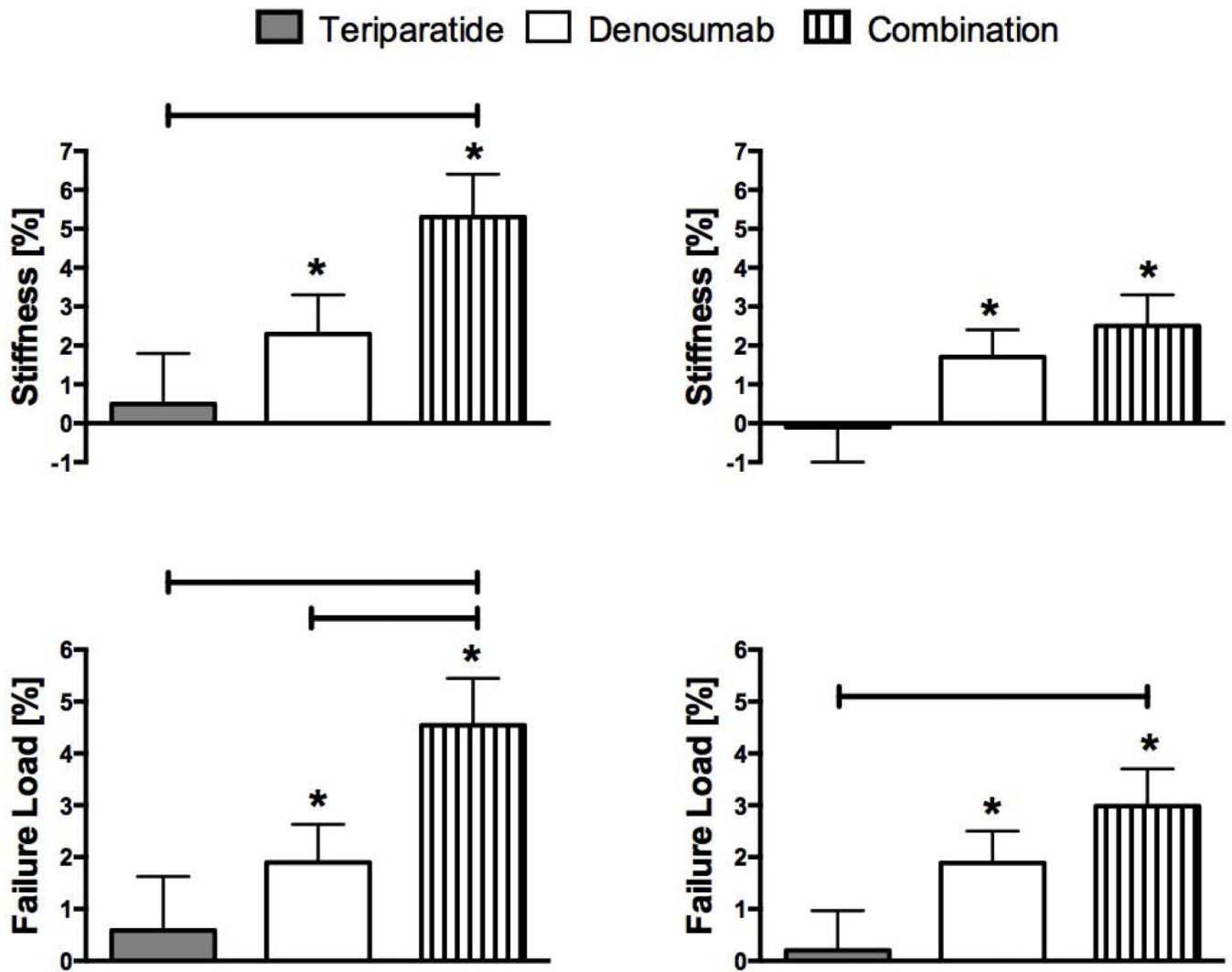


Figure 4. Mean percent change (SEM) from baseline at distal tibia (left) and distal radius (right) in stiffness and failure load at 12 months. *p value <0.05 versus baseline, bars represent p value <0.05 between groups.

Table 1

Baseline clinical characteristics of subjects included in the modified intention-to-treat analysis.

Characteristic	Teriparatide group (N=31)	Denosumab group (N=33)	Combination group (N=30)
Age (year)	66 ± 8	66 ± 8	66 ± 9
Body mass index (kg/m ²)	25.5 ± 3.8	24.1 ± 3.9	25.4 ± 4.9
Percent White, non-Hispanic	31 (100%)	30 (91%)	27 (90%)
History of fragility fracture (no, %)	16 (52%)	12 (36%)	10 (33%)
Previous oral bisphosphonate (BP) use (no, %)	13 (42%)	12 (36%)	10 (33%)
Duration of oral BP use (months)	40 ± 25	43 ± 27	28 ± 21
Time since discontinuation of BP use (months)	27 ± 20	36 ± 23	42 ± 17
Serum 25-hydroxyvitamin D level (ng/mL)	31 ± 9	35 ± 11	34 ± 12
Serum alkaline phosphatase level (U/L)	76 ± 17	79 ± 17	84 ± 21
OC (ng/mL)	49.0 ± 28.8	42.9 ± 19.4	52.2 ± 29.9
P1NP (µg/L)	46.0 ± 19.5	45.7 ± 16.7	49.3 ± 20.9
CTX (ng/mL)	0.36 ± 0.15	0.39 ± 0.21	0.43 ± 0.17
Posterior-anterior spine BMD (g/cm ²)	0.823 ± 0.111	0.866 ± 0.088	0.856 ± 0.131
Femoral neck BMD (g/cm ²)	0.643 ± 0.061	0.641 ± 0.086	0.642 ± 0.067
Total hip BMD (g/cm ²)	0.757 ± 0.068	0.766 ± 0.100	0.759 ± 0.073
One third radius BMD (g/cm ²)	0.612 ± 0.069	0.602 ± 0.082	0.613 ± 0.070

Table 2

Baseline HR-pQCT characteristics of subjects included in the modified intention-to-treat analysis.

	Radius							
	TPTD	DMAB	Both	P-value	TPTD	DMAB	Both	P-value
Tot.vBMD, mg HA /cm ³	236.4 (44.3)	224.7 (53.4)	249.2 (43.8)	ns	268.9 (55.4)	257.1 (60.3)	267.7 (56.8)	ns
Tb.vBMD, mg HA /cm ³	133.3 (31.1)	139.0 (37.4)	142.3 (34.8)	ns	122.9 (26.1)	122.4 (33.9)	122.5 (25.7)	ns
Ct.vBMD, mg HA /cm ³	774.8 (59.4)	756.6 (69.4)	780.2 (65.4)	ns	807.2 (80.4)	802.6 (74.3)	814.6 (69.4)	ns
Ct.Th, mm	0.88 (0.25)	0.77 (0.23)	0.93 (0.20)	0.02	0.63 (0.20)	0.61 (0.18)	0.63 (0.17)	ns
Tb.N, mm ⁻¹	1.59 (0.35)	1.64 (0.47)	1.60 (0.38)	ns	1.65 (0.32)	1.61 (0.42)	1.57 (0.29)	ns
Tb.Sp, mm	0.59 (0.18)	0.61 (0.29)	0.59 (0.17)	ns	0.56 (0.14)	0.62 (0.26)	0.60 (0.13)	ns
Tb.Th, mm	0.071 (0.013)	0.072 (0.013)	0.075 (0.016)	ns	0.062 (0.007)	0.064 (0.008)	0.066 (0.012)	ns
Ct.Po, %	8.7 (3.2)	8.5 (2.7)	9.1 (3.7)	ns	2.8 (1.5)	2.7 (1.2)	2.6 (1.4)	ns
Stiffness, kN/mm	166.3 (29.1)	167.0 (31.9)	167.4 (25.6)	ns	64.4 (15.2)	66.6 (15.7)	61.8 (16.6)	ns
Failure Load, kN	7.68 (1.04)	7.74 (1.31)	7.77 (1.05)	ns	2.76 (5.32)	2.83 (5.41)	2.66 (4.48)	ns

Values are mean (SD). Tot.vBMD = total vBMD; Tb.vBMD = trabecular vBMD; Ct.vBMD = cortical vBMD; Ct.Th = cortical thickness; Tb.N = trabecular number; Tb.Sp = trabecular separation; Tb.Th = trabecular thickness; Ct.Po = cortical porosity.

Table 3

Mean percent change (SD) from baseline in trabecular microarchitecture at 12 months.

	Tibia: % change (SD)			Radius: % change (SD)		
	Teriparatide	Denosumab	Combination	Teriparatide	Denosumab	Combination
Tb.Th	1.8 (7.9)	2.2 (7.0)	3.8 (8.5) *	2.5 (11.3)	4.4 (10.7) *	3.1 (11.5)
Tb.Sp	0.9 (8.5)	0.8 (7.7)	0.4 (8.2)	1.6 (12.0)	2.2 (11.0)	1.6 (12.6)
Tb.N	-0.3 (8.9)	-0.3 (7.3)	-0.1 (8.3)	-0.5 (11.7)	-1.3 (9.5)	-0.2 (13.1)

Tb.Th = trabecular thickness; Tb.Sp = trabecular separation; Tb.N = trabecular number.

* p value <0.05 versus baseline