FRI0470

EFFECT OF DISCONTINUATION OF DENOSUMAB IN SUBJECTS WITH RHEUMATOID ARTHRITIS TREATED WITH GLUCOCORTICOIDS

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Background: Denosumab, a monoclonal antibody against RANKL, is approved for the treatment of glucocorticoid (GC) induced osteoporosis (GiOP). In postmenopausal women with osteoporosis, denosumab discontinuation leads to a transient increase in bone turnover above baseline, peaking at 12 months from the last dose, and a corresponding decline in bone mineral density (BMD). To better understand the effects of denosumab discontinuation in GC-treated patients, we analyzed a subgroup receiving GCs at baseline from a phase 2 study of denosumab in subjects with rheumatoid arthritis (RA), followed for 12 months after denosumab discontinuation.

Objectives: To evaluate changes in bone turnover and BMD in subjects with RA on GCs treated with denosumab, after discontinuing denosumab for 12 months.

Methods: This double-blind, placebo-controlled study enrolled subjects with RA who were randomized to receive denosumab 60 mg, denosumab 180 mg, or placebo subcutaneously for 12 months, and followed for progression of structural damage. Subjects were followed for an additional 12 months after denosumab discontinuation. Outcome measures in this subgroup analysis of subjects treated with GCs at study baseline included percent change from baseline in serum C-terminal telopeptide of type I collagen (CTX) and lumbar spine (LS) and total hip (TH) BMD on- and off-treatment. Baseline mean (SD) prednisone equivalent dose (mg/day) was 6.1 (2.4), 5.2 (2.1), and 6.1 (3.2) in the placebo, denosumab 60 mg, and denosumab 180 mg groups, respectively. Data on CTX are reported as median and interquartile range. Percent changes in LS and TH BMD at each time point were assessed based on a repeated-measures model adjusting for treatment, baseline use of steroids, previous use of biologics, and baseline BMD value.

Results: Among 218 subjects in the phase 2 study, 82 (26 placebo, 27 denosumab 60 mg, and 29 denosumab 180 mg) were included in this analysis. After 12 months of denosumab treatment, CTX decreased from baseline in both groups (Figure); in the off-treatment period, CTX returned to baseline by 18 months and was overall similar to placebo at 24 months. BMD increased at the LS and TH at 12 months with denosumab treatment (Figure) and returned to baseline levels after 12 months of discontinuation.

Conclusion: Like all non-bisphosphonate medications for osteoporosis, denosumab is reversible with discontinuation. In this small subgroup of GC-treated subjects with RA, BMD gains achieved with denosumab were lost upon discontinuation, consistent with observations in postmenopausal women receiving denosumab for osteoporosis. In this analysis of short-term denosumab use in subjects with RA receiving GCs, bone turnover was reduced with denosumab and gradually returned to baseline upon discontinuation, without a clear increase to above-baseline levels in the off-treatment period.

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BONE QUALITY ASSESSMENT IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Background: Type 2 diabetes mellitus (T2DM) is a risk factor for osteoporotic fractures although bone mineral density is normal or even increased. Thus, diabetes may be associated with a reduction of bone strength that is not reflected in the measurement of bone mineral density (BMD).

Objectives: The aim of this study was to compare BMD with a non invasive assessment of trabecular microarchitecture, (Trabecular bone score) TBS, in patients with T2DM

Methods: In a prospective cross-sectional study, trabecular microarchitecture was examined in patients with T2DM and non diabetic control subjects. The exclusion criteria were diseases (hyperthyroidism, Cushing's syndrome, primary hyperparathyroidism, renal failure, malabsorption), rheumatic diseases and/or medications that might affect bone and mineral metabolism, post menopausal women. Lumbar spine BMD was measured by dual-emission x-ray absorptiometry (DXA), and TBS was calculated by examining pixel variations within the DXA images using TBS iNsight

Results: 205 patients (108 male, 97 female), aged 25 to 60 years with T2DM and 205 non diabetic control subjects ((105 male, 100 female) Mean TBS was lower in T2DM (1.256±0.103 vs. 1.291±0.101, p=0.001). Mean BMD was higher in T2DM Z score (0.516±1.346 vs. -0.8151 ±1.153, p= 0.016).

Conclusion: In T2DM, TBS is lower than control subjects. Abnormal trabecular microarchitecture may help explain the paradox of increased fractures at a higher BMD in T2DM

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FRI0472 **COMPARISON OF THE THERAPEUTIC EFFICACY OF DAILY VERSUS WEEKLY DOSE OF TERIPARATIDE FOR PREVENTING BONE FRACTURE IN PATIENTS WITH OSTEOPOROSIS – A SINGLE CENTRE, PROSPECTIVE OPEN-LABEL STUDY**

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Background: In Japan, teriparatide (20 µg) and teriparatide acetate (56.5 µg) have been approved for treatment of osteoporosis. Teriparatide is a recombinant human parathyroid hormone (PTH) administered as daily subcutaneous injections, whereas teriparatide acetate is a biologically active fragment containing the N-terminal 34 amino acids of human PTH administered as weekly subcutaneous injections. To the best of our knowledge, a study comparing the therapeutic effects of these two teriparatide preparations does not exist.

Objectives: We aimed to compare the therapeutic effects of the two teriparatide preparations that varied in dose interval.

Methods: We prospectively enrolled 55 osteoporotic patients with vertebral fracture who needed bone-strengthening therapy in a single-centre cohort. The patients randomly selected either daily injection of teriparatide for 2 years or weekly injection of teriparatide acetate for 72 weeks. The primary endpoint was comparison of the new fracture onset ratio at 18 months, based on the approval for use of teriparatide and teriparatide acetate for up to 2 years and 72 weeks, respectively at the time of the trial. However, since May 2017, teriparatide acetate use for osteoporosis treatment has been approved for up to 24 months in Japan. We evaluated their background data (age, sex, bisphosphonate use, basal disease, glucocorticoid use, vertebral and femoral bone marrow density (BMD), number of thoracic and lumbar vertebral fractures, levels of tartrate-resistant acid phosphatase 5b (TRACP-5b), total procollagen type 1 amino-terminal propeptide (total P1NP), 1,25(OH)2-vitamin D3(1,25(OH)2D3), total serum calcium corrected for albumin level (cCa), inorganic phosphorus(IP), homocysteine, whole PTH and estimated glomerular filtration rate, ankle-brachial index(ABI), and brachial-ankle pulse wave velocity (baPWV)). IP levels were observed until month 1, while levels of TRACP-5b, total P1NP, cCa, 1,25(OH)2D3, BMD, number of fractured vertebrae, ABI, and baPWV were observed until month 18.

Results: The background factors were not significantly different between the groups. The onset rates of new vertebral fractures until 18 months were 50% and 52% for teriparatide and teriparatide acetate, respectively. However, we did not observe the onset of new non-vertebral fracture in the two groups for 18 months. Survival rates in new bone fracture onset (teriparatide vs teriparatide acetate) were 71.4% vs. 60.0% at month 6, 57.1% vs. 52.2% at month 12, and 46.4% vs. 52.2% at month 18. The survival curve showed no significant difference in new bone fracture onset between the groups using the log rank test ($p=.976$) with a hazard ratio (teriparatide vs. teriparatide acetate) of 0.867 (95% confidential interval; 0.291-2.582) ($p=.797$) (see Fig.1). No significant differences were seen in the continuation rates for 18 months for teriparatide (93.3%) and teriparatide acetate (96.0%) ($p=.669$). Statistically significant differences in Δ vertebral BMD at month 6 and baseline ($p<.01$); TRACP-5b at months 12 and 18 ($p<.05$); total P1NP at months 1,6,12, and 18 ($p<.01$); and cCa at month 6($p<.01$) were seen between the groups. Moreover, levels of 1,25(OH)2D3 at months 6, 12, and 18 were lower with teriparatide acetate than those of teriparatide ($p<.01$).

Conclusion: The protective efficacy of the teriparatide preparations to prevent bone fracture showed no difference. In osteoporosis treatment with vertebral fracture, teriparatide preparation daily or weekly may be selected based on the patient's choice.

[UMIN000024503]

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Figure. 1 Survival curve in new bone fracture onset of teriparatide and teriparatide acetate.

FRI0473 **ASSESSING THE CLINICAL RELEVANCE OF BONE DENSITOMETRY SCREENING IN PATIENTS UNDER 40 YEARS OF AGE: INDICATIONS AND RESULTS**

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Background: Guidelines for the diagnosis and treatment of osteoporosis in patients under the age of 40 years are lacking. The International Osteoporosis Foundation (IOF) working group has recommended dual-energy X-ray absorption (DXA) screening should only be performed in this age group if patients have an associated chronic disease such as inflammatory bowel disease (IBD) in conjunction with a vertebral fracture or multiple fractures elsewhere.¹ For these patients, a T-score of <-2.5 can be used to diagnosis low BMD but the term osteoporosis may not be appropriate and there is minimal evidence supporting the use of bisphosphonates (BPs).

Objectives: In patients under 40 years of age undergoing DXA screening, to determine (1) the indication and (2) the DXA results (age adjusted Z score and standard T score), in order to conclude whether DXA screening in this group was appropriate and relevant for making meaningful treatment decisions.

Methods: Clinical details for all DXA scans requested for patients less than 40 years of age were obtained from the Mid Cheshire Hospital NHS Trust radiology department for a 6 month period from July to December 2018 inclusive. Descriptive data was produced regarding basic patient demographics, DXA indication and DXA results in the form of Z- and T-scores at the neck of femur (NOF) and spine.

Results: In total, 35 patients under the age of 40 years underwent DXA screening in the defined time period. The mean age of patients was 30.5 years (s.d. 6.0) and 24 patients (69%) were female. The youngest patients were 19 years. Regarding indications, only two patients (6%) were appropriate for DXA screening according to the IOF suggested guidelines, both of whom had vertebral fractures. Twenty seven patients (77%) had an established diagnosis of a disease known to cause OP but no history of fracture. Regarding results, at the NOF and spine respectively mean Z-scores were -0.77 (s.d. 1.19) and -0.96 (s.d. 0.97), and mean T-scores were -0.88 (s.d. 1.19) and -0.945 (0.93). Only three patients (9%) had Z- or T-score of <-2.5 ; two patients who had a history of thoracic vertebral fracture, and a patient with high steroid use for IBD but no fracture history.

Conclusion: The majority of patients aged less than 40 years referred for DXA screening are being referred due to associated diagnoses with no history of fracture, not in keeping with IOF recommendations. Of the 33 patients with no history of fracture, only one patient (3%) had a T-score consistent with low BMD. There is little evidence to support bisphosphonate use in this group. We therefore conclude that DXA screening in patients less than 40 years should be reserved for those with a history of fracture.

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