OP0297

EFFICACY AND SAFETY OF ROMOSUZUMAB AMONG POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS AND MILD-TO-MODERATE CHRONIC KIDNEY DISEASE

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Background: Osteoporosis and renal insufficiency are coexisting disease states in a substantial proportion of postmenopausal women. Since bisphosphonates are generally contraindicated in patients with estimated glomerular filtration rate (eGFR) <35 mL/min, it is important to evaluate other osteoporosis treatments in this setting.

Objectives: To determine if baseline renal function affects the efficacy and safety of romosozumab.

Methods: We performed post hoc analyses of two clinical trials of romosozumab in postmenopausal women with osteoporosis. In ARCH (NCT01631214), 4,093 patients were randomised 1:1 to romosozumab 210 mg monthly or alendronate 70 mg weekly for 12 months (mean age: 74.3 years; 96.1% with prevalent vertebral fractures [Vfx]). In FRAME (NCT01575834), 7,180 patients were randomised 1:1 to romosozumab 210 mg or placebo monthly for 12 months (mean age: 70.9 years; 18.3% with prevalent Vfx). For these analyses, patients were categorised by baseline eGFR (mL/min/1.73m²): normal renal function (eGFR ≥90), mild renal insufficiency (eGFR 60–89), or moderate renal insufficiency (eGFR 30–59). Least squares mean (LSM) percent change from baseline in bone mineral density (BMD) at the lumbar spine, total hip, and femoral neck; incidence of new Vfx and adverse events (AEs); and changes in renal function were assessed for each eGFR category at Month 12 of the double-blind treatment period.

Results: At baseline, most patients had mild/moderate renal insufficiency: 84% in ARCH, 88% in FRAME. In both studies, change from baseline in BMD was significantly higher in the romosozumab group across baseline eGFR categories (Figure). There was an interaction between BMD increase and renal function, and although BMD increase was not as large in women with impaired renal function, differences between romosozumab and control groups remained significant (Figure). In ARCH, among patients with eGFR ≥90, 60–89, and 30–59, the incidence of new Vfx (romosozumab vs alendronate) at Month 12 was 3.3% vs 7.3%, 3.2% vs 3.9%, and 3.4% vs 6.2% in ARCH. In FRAME, the incidence of new Vfx (romosozumab vs placebo) at Month 12 was 0.5% vs 3.0%, 0.4% vs 1.5%, and 0.6% vs 2.1%.

In both studies, the incidences of AEs and serious AEs were similar in both treatment groups within and across eGFR categories. AEs of mild-to-moderate hypocalcaemia (investigator reported) occurred in two patients in ARCH (one romosozumab [eGFR 60–89] and one alendronate [eGFR ≥90]), and one patient in FRAME (romosozumab [eGFR 60–89]). Five patients in ARCH (all in the alendronate group) and 19 patients in FRAME (14 romosozumab, 5 placebo) had decreases in serum Ca levels (albumin adjusted); in the romosozumab group all were mild (<LLN–8.0 mg/dL) or moderate (<8.0–7.0 mg/dL). A similar percentage of patients in each group had changes in renal function over 12 months of treatment.

Conclusion: The efficacy and safety of romosozumab vs alendronate or placebo was similar among postmenopausal women with osteoporosis and different levels of renal function.

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Figure. LSM (95% CI) % Change in BMD From Baseline to Month 12

ARCH Treatment-by-subgroup interaction: LS, $P = 0.006$; TH, $P = 0.006$; FN, $P = 0.12$

Number of pts are shown below each bar. Error bars represent 95% CIs.

In FRAME, change in BMD from baseline for the eGFR 15–29 mL/min/1.73m² subgroup is not reported: there were only 7 patients in the placebo group for each of the measured sites and only 7, 8, and 8 patients in the romosozumab group for LS, TH, and FN, respectively. Abbreviations: ALN, alendronate; BL, baseline; BMD, bone mineral density; CI, confidence interval; eGFR, estimated glomerular filtration rate; FN, femoral neck; LS, lumbar spine; LSM, least squares mean; Pbo, placebo; Romo, romosozumab; TH, total hip.

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OP0298

STUDY OF RISK OF VERTEBRAL FRACTURES AFTER THE WITHDRAWAL OF DENOSUMAB TREATMENT

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Background: The discontinuation of treatment with denosumab (Dmb) has been associated with a reactivation effect of bone metabolism that manifests itself with a loss of bone mass and an increased risk of vertebral fractures (VF). The incidence and risk factors that may lead to such loss are not clearly established.

Objectives: Determine the incidence of VF and bone loss in patients who have withdrawn treatment with Dmb and objectively possible associated risk factors.

Methods: Retrospective review study of patients treated with Dmb and monitored the last two years in monographic osteoporosis consultations. We selected patients who withdrew treatment with Dmb and registered demographic characteristics, risk factors for osteoporosis and densitometries prior to treatment and during the period of suspension. We identified patients who presented fractures during treatment withdrawal period, assessing: number of fractures, time from withdrawal to fracture presence, location and if they had received osteoactive treatment in that period.

Results: Of 415 patients treated with Dmb, 83 discontinued treatment. The average age was 63.91 years, 95.2% of them women. The average duration of treatment prior to withdrawal was 2.73 years. 43.4% of the patients had previous fractures, 47.2% vertebral. The data of the previous bone mineral density and during the follow-up are shown in Table 1. 60 patients presented risk factors for osteoporosis, the most frequent being low calcium intake (36.6%) and 15.6% had disease and osteopenizing treatment. 92.7% of the patients had received prior osteoactive treatment. The most frequent reason for withdrawal of Dmb was for therapeutic vacations (56.6%). 39 patients performed post-withdrawal osteoactive treatment, mostly zoledronate (51.3%). During the two years after the rest, 9 patients had fractures (10.9%), seven of vertebral location (77.7%) and ≥ 2 VF were observed in five of them. 5 patients (71.4%) already had fractures prior to the onset of Dmb. The average time from withdrawal from treatment to fracture presentation was 15 months. None of the fractured patients had received treatment after Dmb withdrawal. Although the mean BMD analyzed by DXA at the end of treatment and that the loss of BMD during rest was higher in patients with fracture compared to those without fracture (-7.8% vs -4.3% in the spine and -8.6% vs -4.4% in total femur), the differences were not significant.

Conclusion: The incidence of VF in patients who interrupted Dmb was 8.43%. Fractured patients had lower BMD gain despite the treatment than non-fractured patients and also the loss of BMD at rest was greater, without significant differences probably due to low number of patients. Neither the presence of previous fractures nor the duration of treatment could be related to the presence of VF at rest.

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