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ABSTRACT

# World Congress on Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (WCO-IOF-ESCEO 2020): Oral Communications Abstracts

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## OC1

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

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Objective: To determine if baseline (BL) renal function affects the efficacy and safety of romosozumab (Romo).

Materials and Methods: We performed post hoc analyses of 2 Romo trials in postmenopausal women with osteoporosis. In ARCH, 4,093 patients (pts) were randomized 1:1 to Romo 210 mg monthly or alendronate (ALN) 70 mg weekly for 12 months (mean age, 74.3; 96.1% with prevalent vertebral fractures [VFx]). In FRAME, 7,180 pts were randomized 1:1 to Romo 210 mg or placebo (Pbo) monthly for 12 months (mean age, 70.9; 18.3% with prevalent VFx). For these analyses, pts were categorized by BL eGFR (mL/min/1.73m$^2$): normal renal function (eGFR ≥ 90), mild renal insufficiency (eGFR 60–89), or moderate renal insufficiency (eGFR 30–59). Least squares mean (LSM) % change from BL in 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 BL, most pts had mild/moderate renal insufficiency: 84% in ARCH, 88% in FRAME. In both studies, change from BL in BMD was significantly higher in the Romo group across BL eGFR categories (Figure). There was an interaction between BMD increase and renal function, and although BMD increase was less in women with impaired renal function, differences between Romo and control groups remained significant (Figure). Among pts with eGFR ≥ 90, 60–89, and 30–59, the incidence of new VFx (Romo vs ALN or Pbo) at month 12 was 3.3% vs 7.3%, 3.2% vs 3.9%, and 3.4% vs 6.2% in ARCH and 0.5% vs 3.0%, 0.4% vs 1.5%, and 0.6% vs 2.1% in FRAME. 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 hypocalcemia (investigator reported) occurred in 2 pts (1 Romo [eGFR 60–89], 1 ALN [eGFR ≥ 90]) in ARCH and 1 pt (Romo [eGFR 60–89]) in FRAME. Five pts (0 Romo, 5 ALN) in ARCH and 19 pts (14 Romo, 5 Pbo) in FRAME had decreases in serum Ca levels (albumin adjusted); in the Romo group all were mild (< LLN–8.0 mg/dL) or moderate (< 8.0–7.0 mg/dL). Similar % of pts in each group had changes in renal function over 12 months of treatment.

Conclusion: The efficacy and safety of Romo vs ALN or Pbo was similar among postmenopausal women with osteoporosis and different levels of renal function.

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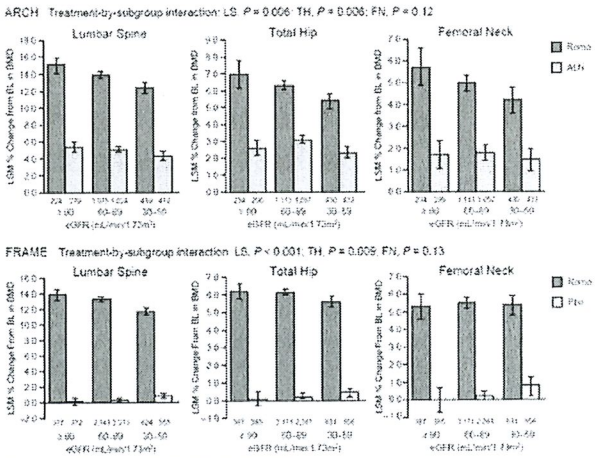
Disclosures: PM reports consultant/advisory activities for Amgen and Radius Health and has received grants from Amgen, Radius Health, and Ultragenyx; JA is a consultant and speaker for Amgen; BHA has received speaking and consultation fees from Eli Lilly and Amgen; AMC has received honoraria/consultation fees from Eli Lilly and Amgen; AC, MO, NRS, WY, and ZY are employees and stockholders of Amgen; EG reports consultant/speaker's bureau/advisory activities for Amgen, Takeda, Sandoz, and UCB Pharma; BL is on advisory boards for Amgen, UCB Pharma, and Eli Lilly and has received research grants from Amgen and Novo Nordisk; AM has received consulting fees from Amgen, Astellas BioPharma K.K., and Teijin Pharma; IRR has received speaking and consultation fees from Eli Lilly and Amgen; MV is an employee of UCB Pharma.

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




## OC2

### ROMOSOZUMAB AFTER DENOSUMAB IMPROVES LUMBAR SPINE AND MAINTAINS TOTAL HIP BONE MINERAL DENSITY IN POSTMENOPAUSAL WOMEN WITH LOW BONE MASS

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**Objective:** Romosozumab (Romo), an anti-sclerostin antibody that increases bone formation while decreasing bone resorption, reduces fracture risk within 12 months. Here we evaluate the effects of transitioning from denosumab (DMAb) to Romo in treatment-naïve patients.

**Materials and Methods:** This phase 2 trial (NCT00896532) enrolled postmenopausal women with a lumbar spine (LS), total hip (TH), or femoral neck T-score ≤–2.0 and ≥–3.5. Patients were randomized to placebo (Pbo) or various doses of Romo monthly or every 3 months from baseline (BL) to month (M) 24, were rerandomized to 12 months of DMAb or Pbo (M24-36), and then all were to receive Romo 210mg monthly for 12 months (M36-48). Results for the overall population have been previously published (1,2). Here we present data from a subset of patients who were randomized to Pbo for 24 months, DMAb (n=16) or Pbo (n=12) for 12 months, and then Romo for 12 months.

**Results:** In patients who were randomized to Pbo followed by DMAb, Romo treatment for 12 months maintained bone mineral density (BMD) gained during DMAb treatment at the TH (mean change from end of DMAb treatment, 0.9%) and further increased BMD gains at the LS (mean change from end of DMAb treatment, 5.3%) (Table). As expected, P1NP and β-CTX levels decreased with DMAb. Upon transition to Romo (M36-48), P1NP levels initially increased and gradually returned to BL by M48 while β-CTX gradually increased to BL levels.

In patients who transitioned to Romo after 36 months of Pbo, BMD increased at the LS and TH (Table). P1NP levels initially increased with Romo and gradually returned to BL by M48 while median β-CTX level remained below BL with Romo treatment.

**Conclusions:** BMD response in the Pbo to Romo group was similar to that observed in other studies. Transitioning to Romo after 12 months of DMAb further improves LS BMD and maintains TH BMD.

**References:** 1) McClung MR, J Bone Miner Res 2018;33:1397-1406. 2) Kendler DL, Osteoporos Int 2019;30:2437-2448.

**Table**

| Treatment from M0–24 | Pbo | Pbo |
|---|---|---|
| Treatment from M24–36 | Pbo | DMAb 60 mg Q6M |
| Treatment from M36–48 | Romo 210 mg QM | Romo 210 mg QM |
| | N = 12 | N = 16 |
| BMD, mean % change (95% CI) | | |
| Lumbar spine | | |
| M0–24 | 2.7 (0.2, 5.1) | 0.6 (–2.8, 1.1) |
| M24–36 | –0.4 (–2.1, 1.4) | 5.8 (3.6, 7.4) |
| M36–48 | 9.1 (6.1, 12.1) | 5.3 (3.2, 7.4) |
| M24–48 | 8.9 (6.5, 12.4) | 11.5 (8.8, 14.3) |
| Total hip | | |
| M0–24 | –2.2 (–3.6, –0.8) | –1.0 (–2.7, +0.5) |
| M24–36 | –0.3 (–1.4, 0.8) | 2.8 (2.1, 3.6) |
| M36–48 | 4.6 (2.7, 6.4) | 0.9 (–0.1, 1.8) |
| M24–48 | 4.7 (2.7, 6.7) | 3.8 (2.6, 5.0) |
| BTM, median (Q1, Q3) | | |
| P1NP, ng/L | | |
| M0 | 37.0 (33.3, 41.0) | 52.4 (44.9, 59.2) |
| M24 | 38.2 (30.5, 55.6) | 50.0 (40.0, 56.0) |
| M36 | 36.9 (30.3, 55.5) | 17.4 (11.2, 21.4) |
| M39 | 49.5 (36.3, 79.9) | 43.1 (31.9, 55.6) |
| M48 | 36.2 (29.2, 49.2) | 54.6 (54.2, 72.5) |
| β-CTX, ng/L | | |
| M0 | 372.0 (306.0, 416.5) | 503.5 (392.5, 638.5) |
| M24 | 334.0 (432.5, 692.0) | 826.0 (466.0, 833.0) |
| M36 | 376.0 (326.0, 533.5) | 162.5 (95.5, 268.0) |
| M39 | 346.0 (282.0, 436.5) | 311.0 (238.0, 385.0) |
| M48 | 321.5 (276.5, 487.0) | 532.0 (378.0, 661.0) |

β-CTX, β-isomer of the C-terminal telopeptide of type I collagen; BMD, bone mineral density; BTM, bone turnover marker; CI, confidence interval; DMAb, denosumab; M, month; P1NP, procollagen type 1 N-terminal propeptide; Pbo, placebo; Q1, quartile 1; Q3, quartile 3; QM, monthly; Q6M, every 6 months; Romo, romosozumab

**Disclosures:** This study was sponsored by Amgen, Astellas, and UCB Pharma. MR McClung received consulting fees and honorarium from Amgen. MA Bolognese received contract fees from Amgen and was a speaker for Amgen. JP Brown received research support from Mereo, Radius, and Servier; received consulting fees from Amgen, Eli Lilly, and Servier; and was on the speakers' bureau for Amgen and Eli Lilly. J-Y Reginster received research funding from IBSA-Genevrier, Mylan, CNIEL, and Radius Health; received lecture fees from IBSA-Genevrier, Mylan, CNIEL, and Dairy Research Council; and received consulting fees or participated in paid advisory boards for IBSA-Genevrier, Mylan, Radius Health, and Pierre Fabre. BL Langdahl received research support from Amgen and Novo Nordisk and was on the speakers' bureau for UCB, Amgen, and Eli Lilly. N Ruiz-Santiago, Y Shi, M Rojeski, H Kassahun, and M Oates are employees of and own stock in Amgen. J Timoshanko and C Libanati are employees of and own stock in UCB.

## OC3

## VERTEBRAL FRACTURES BEFORE, DURING AND AFTER DENOSUMAB. A RETROSPECTIVE STUDY OF 858 CASES

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OBJECTIVE: Evaluate subject characteristics and risk factors associated with the occurrence of vertebral fractures (VF) after treatment with Denosumab (DMAB).

METHODS: Among a network of 22 bone consultants from different parts of Switzerland, we collected the clinical history of 858 randomly chosen women, in whom treatment with DMAB was interrupted, 172 of them having breast cancer. Our questionnaire documented age, BMI, Bone Mineral Density (BMD), life style, family history, bone related diseases and treatments, fractures, bone resorption markers, and treatments for breast cancer. Data for these variables were recorded for the periods before, during and after DMAB treatment.

RESULTS: The mean age was 65 years [range 27 – 92]. Bisphosphonates had been administered before DMAB in 46%, and after in 64.5% (76.4% of them with Zoledronate). The mean duration of DMAB treatment was 35 months [6-96]. Follow-up, starting 6 months after the last dose, was 28 months (1 -107). In 96.5% the follow-up lasted > 6 months. The mean T-score of lumbar spine BMD was -2.55 (SD 0.97) before, -1.90 (1.11) during, and -2.15 (1.16) after treatment. The T-score at femoral neck was -2.06 (SD 0.78) before, -1.45 (0.83) during, and -1.93 (0.76) after treatment. Trabecular Bone Score (TBS) was measured among 95 patients in each period, and was 1.22 before, 1.27 during, and 1.29 after DMAB treatment; with significant increases ($p<0.001$ for trend). The percent of patients with osteoporotic fractures was 36.1% before, 5.2% during and 12.5 % after DMAB treatment; and that of patients with vertebral fractures (VF) was 20.4 % before ( 2.9 % with multiple VF), in 2.1% during (0.5 % with multiple VF), and in 11.0 % after treatment (6.4 % with multiple VF, with a mean of 2.9 VF per fractured patient). Hip fractures were observed in 3.5 % before, 0.7% during and 0.6% after treatment. The numbers of humerus, pelvis and rib fractures were similar.

The influence of each parameter mentioned above on the occurrence of fractures will be evaluated.

CONCLUSION: Treatment with Denosumab in 858 women led to an increase in BMD and TBS, and to a decrease in fractures. In the ± 28 months following treatment cessation, vertebral fractures increased. The occurrence of fractures will be analyzed in respect to case history, clinical characteristics, risk factors as well as evolution of BMD and resorption markers.