Protecting her future with romosozumab first

A summary of the UCB-sponsored symposium at WCO-IOF-ESCEO 2026

What is holding us back?

Symposium facilitated by Professor Kassim Javaid (University of Oxford, UK)

Subsequent fractures can be devastating for patients − but they are not inevitable if we act fast.[1-3] Yet, despite the availability of advanced anabolic therapies like EVENITY® (romosozumab) and a clearer path to personalised care, too many postmenopausal osteoporosis (PMO) patients at very high fracture risk (VHFR) are still not receiving the treatment they desperately need.[1-3] Together, we must confront what is holding us back from delivering the high-quality care our patients deserve.

The urgent imperative

Presented by Professor Ralf Schmidmaier (Ludwig-Maximilians-Universität, Munich, Germany)

"A significant advantage of [EVENITY] over [alendronate] is already evident after 12 months, and this advantage is maintained during the subsequent alendronate therapy"[4,5]

The impact of a single vertebral fracture can be profound for patients. Seemingly overnight, patients who were once highly active can struggle to perform everyday movements due to the constant and enduring pain that comes with a fracture.[6] As clinicians, this should be our warning sign − the period immediately following a fracture is when PMO patients are at the highest risk of another, which is why we must act fast after a fracture to prevent another.[2,7] However, this imminent risk is too often underestimated in practice, with German real-world evidence (RWE) indicating that 60–85% of patients remain untreated 6 months after a vertebral fracture, even with national guidance advocating for rapid initiation of osteoanabolic therapy, preferably first-line, in VHFR patients.[8,9]

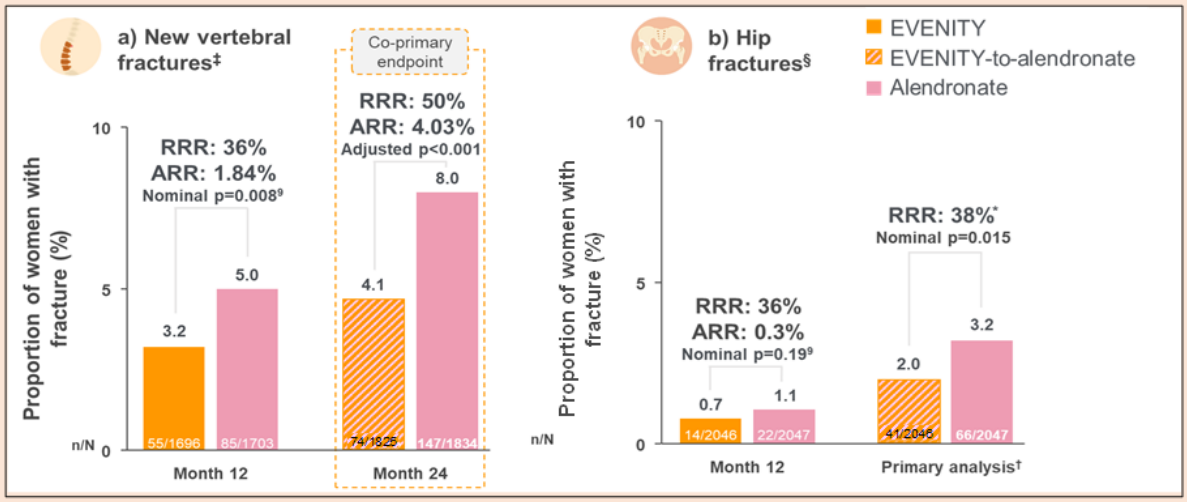

Figure 1. Fracture incidence EVENITY vs alendronate (ARCH).[4,10] a) New vertebral fracture at Months 12 and 24; b) Hip fracture at Month 12 and primary analysis. *Absolute relative risk not available as subjects have various exposure at primary analysis. †Primary analysis after clinical fractures had been confirmed in ≥330 patients (median time on study at primary analysis: ~33 months). ‡Risk ratio based on Mantel-Haenszel method adjusted for age strata, baseline TH BMD T-score (≤−2.5, >−2.5) and presence of severe vertebral fracture at baseline; nominal P-values were based on a logistic regression model adjusting for age strata, baseline TH BMD T-score and presence of severe vertebral fracture at baseline; missing data handled using last-observation-carried-forward. §Hazard ratio and nominal P-values were based on a Cox proportional hazards model adjusting for age strata, baseline TH BMD T-score and presence of severe vertebral fracture at baseline. ARR, absolute risk reduction; BMD, bone mineral density; RRR, relative risk reduction; TH, total hip.

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EVENITY has demonstrated rapid and significant reduction in vertebral fracture incidence at 12 months in both placebo-controlled (FRAME: 0.5% [n=16/3321]; p<0.001 vs placebo [1.8%, n=59/3322]) and alendronate-controlled studies (ARCH: nominal p=0.008, fig. 1a), which was sustained when followed with antiresorptive (AR) treatment at Month 24 (FRAME: 0.6% [n=21/3325]; p<0.001 vs placebo [2.5%, n=84/3327]) (ARCH: adjusted p<0.001, fig. 1a).[4,5,11] A reduction in hip fracture incidence was also observed in the ARCH study at Month 12 with romosozumab, which, when followed by alendronate, showed significance compared with alendronate alone at primary analysis (nominal p=0.015; fig. 1b)[4,10] (study design details on page 5).

Recent German RWE also observed 64.3% patient persistence with EVENITY (N=8876) at 12 months, which was the highest among the other anti-osteoporosis medications (AOMs) evaluated (teriparatide [52.4%; N=7853], abaloparatide [47.1%; N=576] and alendronate [31.9%; N=229,058]),[12] further supporting its use in eligible patients.

Breaking the cycle

Presented by Professor Nicola Napoli (Fondazione Policlinico Universitario Campus Bio-Medico di Roma, Italy)

"[EVENITY] remains an effective therapy in patients previously treated with anti-osteoporosis medication"[13,14]

The more fractures a PMO patient experiences, the more their independence and mobility are threatened.[6] Hip fractures can have an especially devastating effect on quality of life, often leaving patients dependent on others and socially isolated.[15] Therefore, a fracture whilst on treatment without sufficient improvements in bone mass may signal the need for a more potent therapy to prevent further fractures.[14] Whilst EVENITY reportedly achieves larger bone mineral density (BMD) gains in treatment-naïve patients,[14,16] the clinical reality is that many patients have received a prior AOM;[17] indeed, this is generally the case in Italy, where reimbursement is often limited to second- or later-line use.[18]

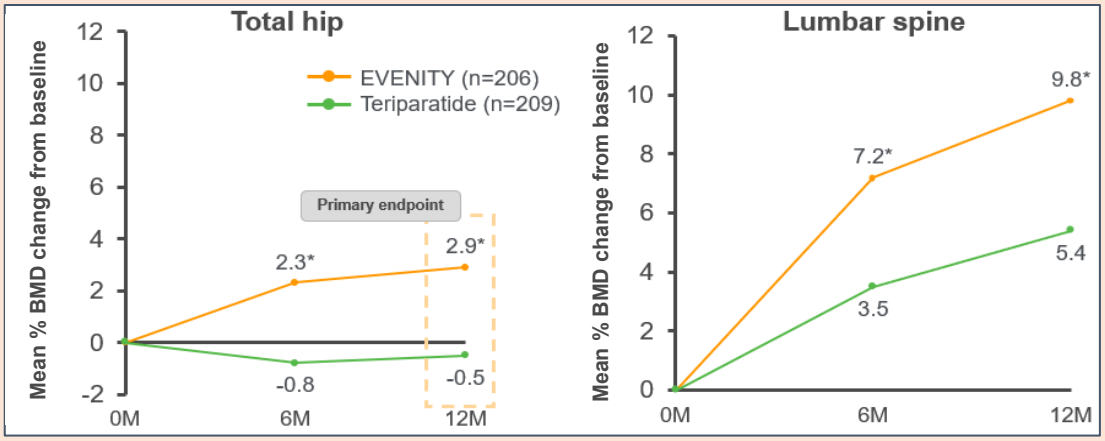

Figure 2. Mean change in BMD from baseline at the total hip and lumbar spine with EVENITY vs teriparatide (STRUCTURE). Figures adapted from Langdahl BL, et al. (2017).[13]
*p<0.0001 vs baseline and teriparatide.

EVENITY's dual-effect mechanism rapidly increases bone formation and decreases bone resorption after just 2 months, improving bone mass, structure and strength by Month 12 without altering bone microarchitecture.[4] This is reflected in the results of the STRUCTURE study, where EVENITY demonstrated superior BMD gains compared with teriparatide in PMO women with severe osteoporosis transitioning from bisphosphonates (BPs) through Month 12 at all measured sites (p<0.0001; fig. 2).[4,13] EVENITY also led to early improvements in total hip BMD and estimated hip strength at Month 6, whereas teriparatide showed declines in these endpoints[4,13] (study design details on page 5).

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Italian RWE revealed that whilst significantly more patients with minimal prior exposure to BPs* (n=91) achieved the BMD surrogate threshold effect (BMD-STE) for minimal fracture risk reduction for all fractures than pre-treated patients† (n=42) following 6 months of EVENITY treatment ($p<0.05$), this was not seen at 12 months, where an almost equal proportion of patients achieved BMD-STE regardless of prior BP exposure.[19]

*Patients with <3 months of continuous exposure to BPs in the last 2 years prior to EVENITY initiation.[19] †Patients with >3 months of continuous oral bisphosphonates in the last 2 years prior to EVENITY initiation or ever treated with IV bisphosphonates.[19]

Rebuilding foundations in VHFR

Presented by Professor Bente Langdahl (Aarhus University Hospital, Denmark)

"If we have patients at high risk, where we think that it is important to increase BMD very rapidly, there's a clear benefit of going for [EVENITY] and then follow on with an antiresorptive"[5,14]

The fear of a second fracture can be all-encompassing, preventing patients from doing activities they love and leading to an unwanted sedentary life overshadowed by anxiety.[6,20] Prioritising anabolic therapy as an initial treatment for PMO patients at VHFR – followed by an AR – is widely agreed upon as the optimal treatment sequence to rapidly attain BMD gains,[14] supporting patients to have an improved quality of life.[20] Despite EVENITY's effectiveness in patients previously treated with AR therapy, osteoanabolic therapies should be considered as initial therapy (followed by AR treatment) in patients with very low BMD as this approach is associated with greater and faster BMD increases at the hip and spine than the reverse sequence.[4,14]

Post hoc analyses have suggested that EVENITY first in sequence leads to more rapid gains in BMD than AR treatment alone.[21,22] One such analysis reported the mean T-score changes from baseline over the 2-year course of the FRAME study and contrasted them with long-term BMD changes seen with up to 10 years of denosumab treatment, as characterised in the FREEDOM and FREEDOM extension studies.[21] Results of this analysis observed that T-score gains at the total hip and lumbar spine with the 2-year sequence of EVENITY for 1 year followed by denosumab for 1 year were comparable to approximately 7 years of treatment with denosumab alone (fig. 3)[21] (study design details on page 5). Another analysis estimated that patients were more likely to achieve a non-osteoporotic T-score (>−2.5) at 3 years when starting with EVENITY as opposed to continuous AR treatment, particularly in patients with low baseline BMD.[22]

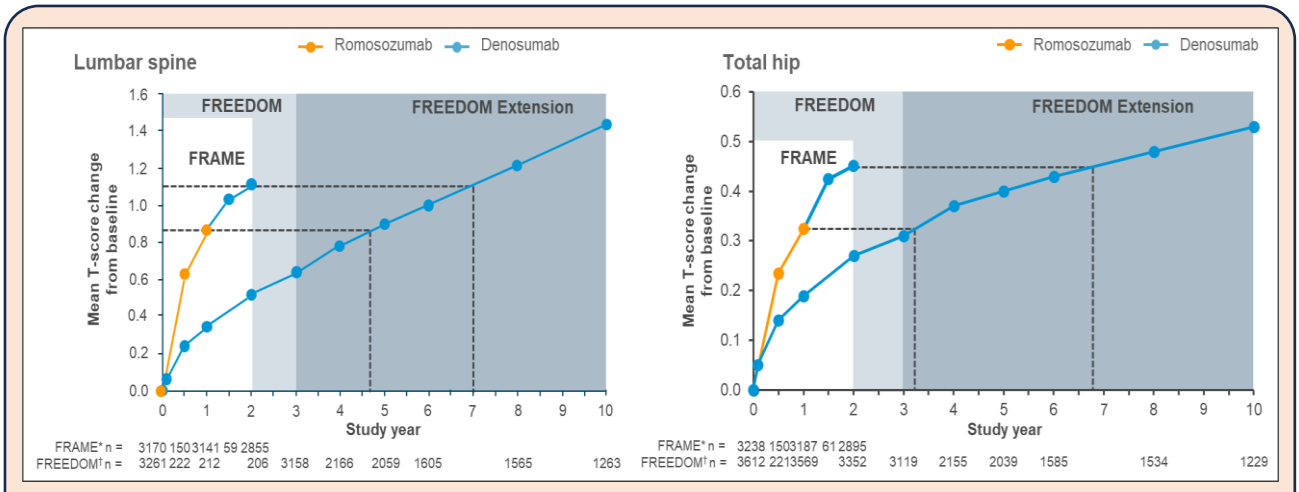

Figure 3. *Post hoc* analysis: BMD T-score increases at the lumbar spine and total hip in FRAME relative to FREEDOM and FREEDOM Extension. Figures adapted from Cosman F, et al. (2018).[21] Data shown are not from a head-to-head study. Results should be interpreted with caution due to differing study populations and methodology (study design details on page 5).

*BMD was measured more frequently (Months 6 and 18) in a subset of patients from FRAME who participated in a DXA substudy; additionally, BMD was measured at Month 6 in women from Argentina. †BMD was measured more frequently in a subset of patients from FREEDOM who participated in a DXA substudy. DXA, dual-energy X-ray absorptiometry.

Real-world insights from a Danish cohort mirrored clinical trial data, showing significant BMD gains with EVENITY at Month 12 that were superior to teriparatide at all sites (fig. 4).[23] Notably, TH BMD – a crucial indicator of fracture risk reduction[14,24] – significantly improved from baseline by Month 6 (+4.0%), with subgroup analysis revealing a significantly greater increase in treatment-naïve vs previously treated patients (4.9% vs 3.0%, respectively [p=0.02]).[23]

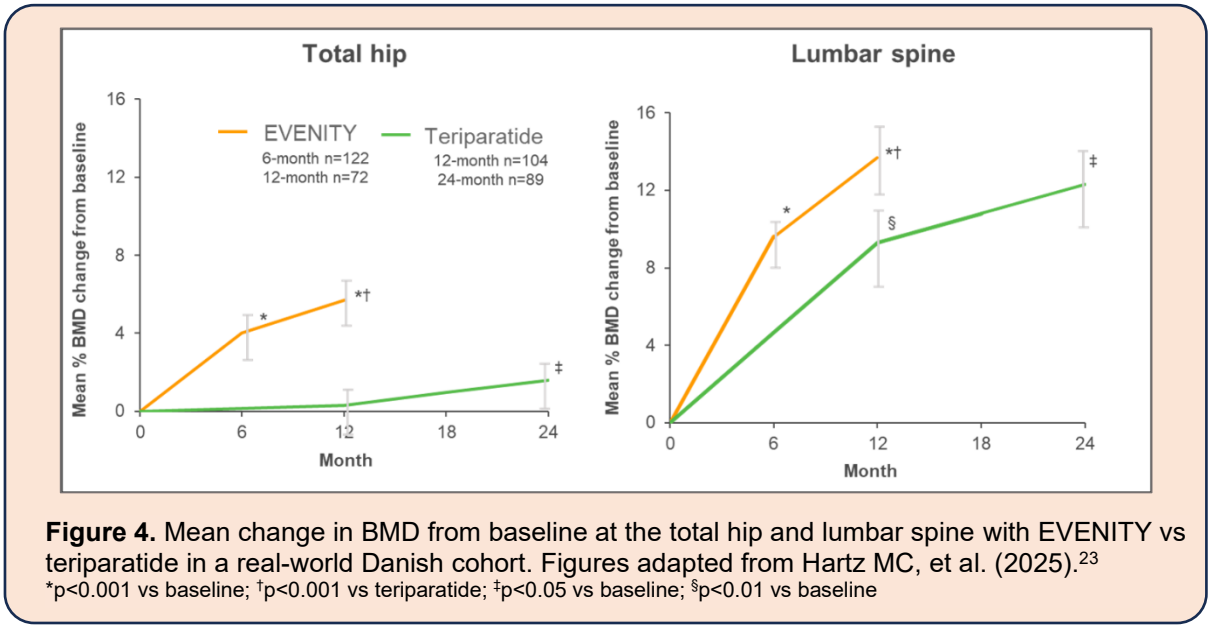

Figure 4. Mean change in BMD from baseline at the total hip and lumbar spine with EVENITY vs teriparatide in a real-world Danish cohort. Figures adapted from Hartz MC, et al. (2025).[23]
*p<0.001 vs baseline; †p<0.001 vs teriparatide; ‡p<0.05 vs baseline; §p<0.01 vs baseline

The most common adverse events observed in patients treated with EVENITY across studies were nasopharyngitis (13.6%) and arthralgia (12.4%). Hypersensitivity-related reactions occurred in 6.7% of patients; hypocalcaemia was reported uncommonly (0.4%). In ARCH, an imbalance was observed in the incidence of major adverse cardiac events (composite of cardiovascular death, myocardial infarction [MI] or stroke) between EVENITY vs alendronate during the 12-month double-blind treatment period, which was not seen in the placebo-controlled study, FRAME.[4] The benefit–risk profile of EVENITY, which is contraindicated in patients with a history of MI or stroke in the EU,[4] has remained unchanged following treatment of more than 1.3 million patients at high fracture risk worldwide since launch in 2019.[25]

From evidence to action: Embedding romosozumab first into routine care

"We need more than data to change practice"[26]

Challenges persist in delivering optimal care for PMO patients at VHFR; globally, the treatment gap remains a considerable problem, with a significant proportion of patients at high risk of fracture still not receiving guideline-recommended therapy.[3,8,27] For those that do receive EVENITY, RWE from Denmark observed that ~50% (n=277/622) have had previous treatment[17] and German RWE revealed many are lost during follow-up.[12] A systematic, single-minded approach is needed to drive the structural changes in healthcare systems to deliver anabolic-first to eligible patients at VHFR.[14,26]

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Study designs

ARCH was a multicentre, multinational, randomised, double-blind, alendronate-controlled, superiority study of 4093 postmenopausal women aged 55–90 years with previous fragility fractures. The primary efficacy endpoints were the incidence of new vertebral fracture through Month 24 and the incidence of clinical fracture (nonvertebral fracture and clinical vertebral fracture) at primary analysis.[4]

FRAME was a multicentre, multinational, randomised, double-blind, placebo-controlled, parallel-group study of 7180 postmenopausal women aged 55–90 years. 40.8% had severe osteoporosis with a prior fracture at baseline; 59.2% had less severe osteoporosis. The co-primary efficacy endpoints were the incidence of new vertebral fractures through Month 12 and through Month 24.[4]

STRUCTURE was a multicentre, randomised, open-label study of 436 postmenopausal women with severe osteoporosis aged 56–90 years transitioning from bisphosphonate therapy to either romosozumab or teriparatide. The primary efficacy endpoint was percent change in total hip BMD from baseline at Month 12.[4]

FREEDOM was a 3-year, randomised, double-blind, placebo-controlled, phase III trial comparing denosumab with placebo in women with PMO (n=7808), followed by a 7-year open-label denosumab **extension** for all participants who missed ≤1 dose of investigational product (n=4550).[28,29] The primary outcome of the controlled study was number of new vertebral fractures at Month 36, with the open-label extension's being comprehensive safety monitoring.[28,29]

The *post hoc* analysis of FRAME and FREEDOM extension aimed to characterise the effects of a 2-year treatment sequence of romosozumab followed by denosumab compared with placebo followed by denosumab by quantifying the percentages of patients who responded at varying magnitudes; mean T-score changes from baseline in FRAME were reported and contrasted with the long-term BMD gains seen with continuous denosumab.[21]

In the EU and the UK, EVENITY is indicated in treatment of severe osteoporosis in postmenopausal women at high risk of fracture.[4,30]

Licenses may vary by country. Please refer to your local Prescribing Information or Summary of Product Characteristics for more information. EU, UK and Irish Prescribing Information can be found on page 6.

Adverse events should be reported. Reporting forms and information can be obtained from your local regulatory authority. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ for the UK and https://www.hpra.ie/homepage/about-us/report-an-issue for Republic of Ireland. Adverse events should also be reported to UCB. For UK and Irish healthcare professionals, adverse events should also be reported to ucbcares.uk@ucb.com or 0800 2793177 for the UK and UCB (Pharma) Ireland Ltd at ucbcares.ie@ucb.com or 1800 930075 for Republic of Ireland.

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EVENITY EU Summary of Product Characteristics

EVENITY UK Prescribing Information

Irish Prescribing Information can be found below:

EVENITY® (romosozumab)
Active Ingredient: Romosozumab – solution for injection: 105 mg of romosozumab in 1.17 mL of solution (90 mg/mL).
Indications: Severe osteoporosis in postmenopausal women at high risk of fracture.
Dosage and Administration: Treatment should be initiated and supervised by specialist physicians experienced in the management of osteoporosis. *Dosage:* 210 mg administered as two equal subcutaneous injections of 105 mg each once monthly for 12 months. Patients to be adequately supplemented with calcium and vitamin D before and during treatment. Following completion of therapy, transition to antiresorptive therapy is recommended. *Renal impairment:* No dose adjustment needed. Serum calcium to be monitored in patients with severe renal impairment or receiving dialysis. *Elderly:* No dose adjustment needed. *Discontinuation:* see SmPC for guidance.
Contraindications, Warnings, Precautions for use: Contraindications: Hypersensitivity to romosozumab or to any of the excipients listed in the SmPC; Hypocalcaemia; History of myocardial infarction or stroke. **Warnings and Precautions:** *Myocardial infarction and stroke:* An increase in serious cases of cardiovascular events has been observed in romosozumab treated patients compared to controls. Consideration should be given to fracture risk over the next year and cardiovascular risk factors. If a patient experiences a myocardial infarction or stroke during therapy, treatment should be discontinued. *Hypocalcaemia:* Transient hypocalcaemia has been observed. Hypocalcaemia should be corrected prior to initiating romosozumab. Limited safety data in patients with severe renal impairment or receiving dialysis – calcium levels should be monitored in these patients. *Hypersensitivity:* Erythema multiforme, angioedema and urticaria have been reported. *Osteonecrosis of the jaw (ONJ):* Consider risk factors when evaluating risk of developing ONJ. *Atypical femoral fractures:* Atypical low-energy or low trauma fracture of the femoral shaft have been reported rarely. Consider interruption of romosozumab in patients presenting with an atypical femur fracture, based on an individual benefit-risk assessment. **Refer to SmPC for full information.** Interactions: No data available.
Fertility, pregnancy and lactation: Not to be used in child-bearing potential, pregnant or breastfeeding women. Risk for malformations of developing digits in the human foetus in the first trimester, a period when placental transfer of immunoglobulins is limited. No data available on human fertility.
Driving and use of machines: No or negligible influence on ability to drive and use machines.
Adverse Effects: *Very Common (≥ 1/10):* Nasopharyngitis, arthralgia. *Common (≥ 1/100 to < 1/10):* Sinusitis, hypersensitivity, rash, dermatitis, headache, neck pain, muscle spasms, injection site reactions. *Uncommon (≥ 1/1,000 to < 1/100):* Urticaria, hypocalcaemia, stroke, cataract, myocardial infarction. *Rare (≥ 1/10,000 to < 1/1,000):* angioedema, erythema multiforme. See SmPC for further details.
Pharmaceutical Precautions: Store in a refrigerator (2°C – 8°C) in original container, do not freeze. Keep pre-filled pen in the outer carton in order to protect from light. Do not return to refrigerator after use; EVENITY can be kept at up to 25°C for up to 30 days in original container. Product should be discarded after this period.
Legal Category: POM
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