Effects of EB613 Tablets [Oral PTH(1-34)] on Trabecular and Cortical Bone Using 3D-DXA: Post-Hoc Results from Phase 2 Study

Gregory Burshtein, Constantin Itin, Hillel Galitzer, Michal Kushnir, Miranda Toledano, Ludovic Humbert, Serge L Ferrari, Rachel B Wagman, Felicia Cosman

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Disclosures

- **Rachel B Wagman – Chief Clinical Advisor, Entera Bio Ltd**
- **Felicia Cosman – Chair, Scientific Advisory Board, Entera Bio Ltd**
- **Serge L Ferrari – Scientific Advisory Board Member, Entera Bio Ltd**
- **Ludovic Humbert – Employee and Stockholder of 3D-Shaper Medical**
- **Gregory Burshtein, Constantin Itin, Hillel Galitzer, Michal Kushnir, and Miranda Toledano – employees of Entera Bio Ltd**
- ***Several co-authors may own stock and/or stock options***

Osteoporosis Treatment Paradigm

Anti-Resorptive

1st Line

Bisphosphonates

RANK-Ligand Inhibitor

EB613

- Osteoporosis at High Risk of Fracture
- Very High Risk who Refuse Injectable Anabolic Therapies
- Intolerant of Other Therapies

EB613
Oral PTH(1-34) Daily Tablets

Injectable Anabolic

1st Line: Very High Risk
2nd Line Suboptimal Response to Other Treatment

PTH Receptor Agonists

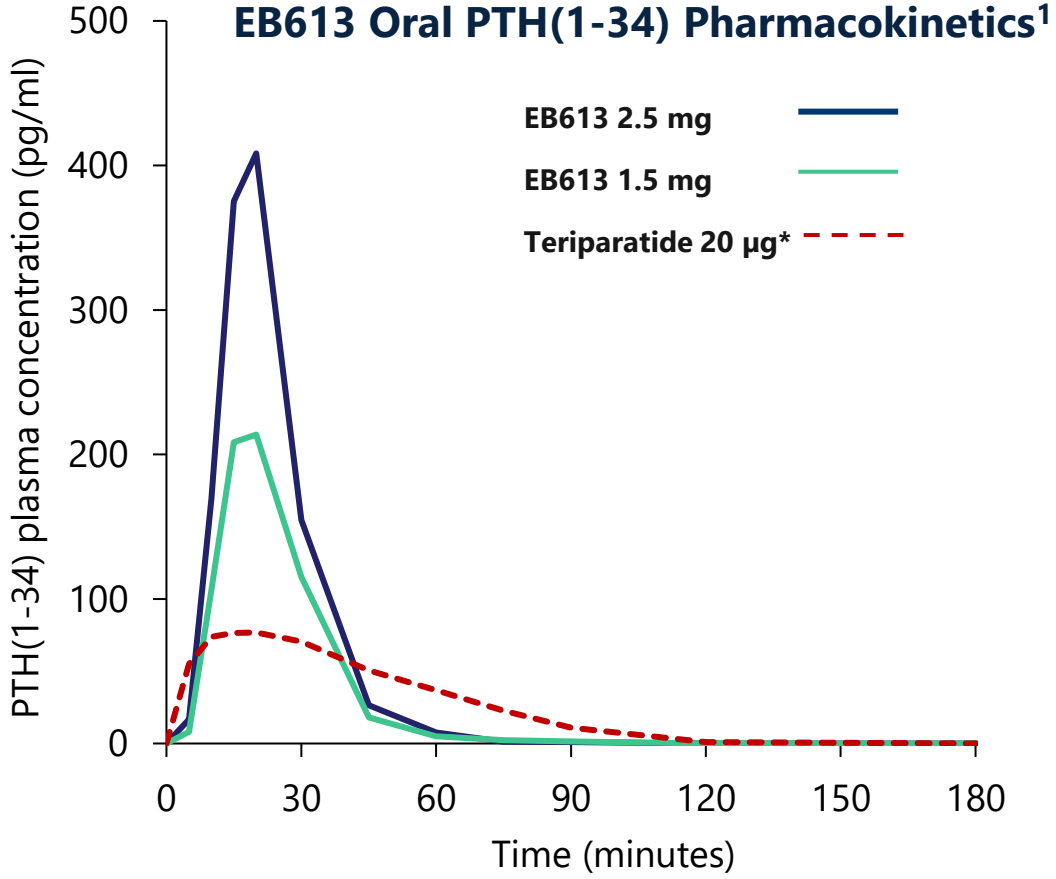
Sclerostin Antibody

High Risk — **Fracture Risk Spectrum** — **Very High**

Camacho et al, 2020; Cosman et al, 2024; Kanis et al, 2019; McClung et al., 2021; Shoback et al., 2020; Veronese et al., 2024

EB613 Consistently Demonstrates Rapid Increases in PTH(1-34) Plasma Levels and Robust Bioavailability in Phase 1 Studies

- Brief intermittent exposures (30 to 60 minutes) of high PTH concentrations stimulate bone formation
- Rapid increase in plasma PTH(1-34) levels, with peak concentrations within 20 minutes after dosing and a rapid elimination phase
- Overall duration of systemic exposure is shorter than that of SC injection Forteo®



* Forteo® 20 µg subcutaneous

[1] G Burshtein G et al., EB613 (oral PTH[1-34] tablets) shows differentiated pharmacokinetic profile from Forteo – new results from Phase 1b open-label study. J Bone Miner Res 2024; 39 (Suppl 1): 210.

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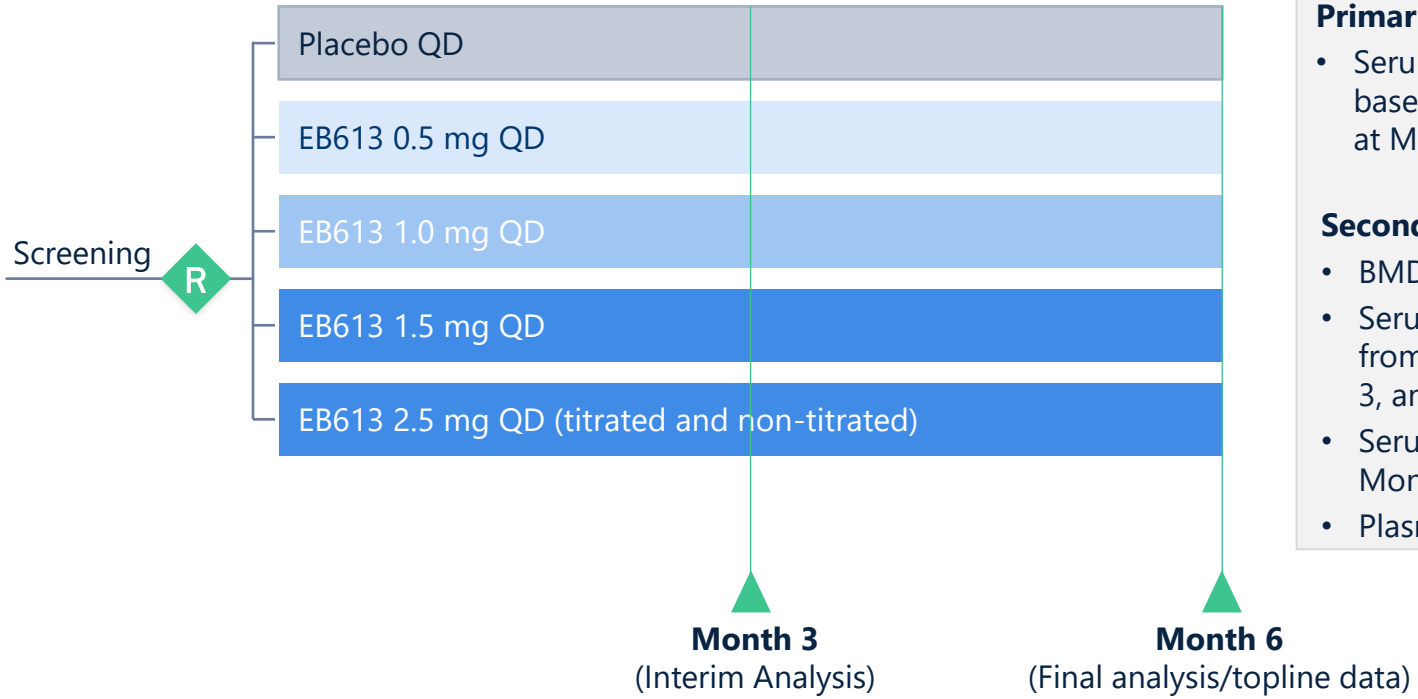
EB613 Phase 2 Clinical Study Design

Key Inclusion Criteria
- 50+ years old
- 3+ years post-menopause
- Low bone mass
- High risk; no prior fracture

Key Exclusion Criteria
- Osteoporosis treatment within last 2 years
- Severe osteoporosis that precludes placebo



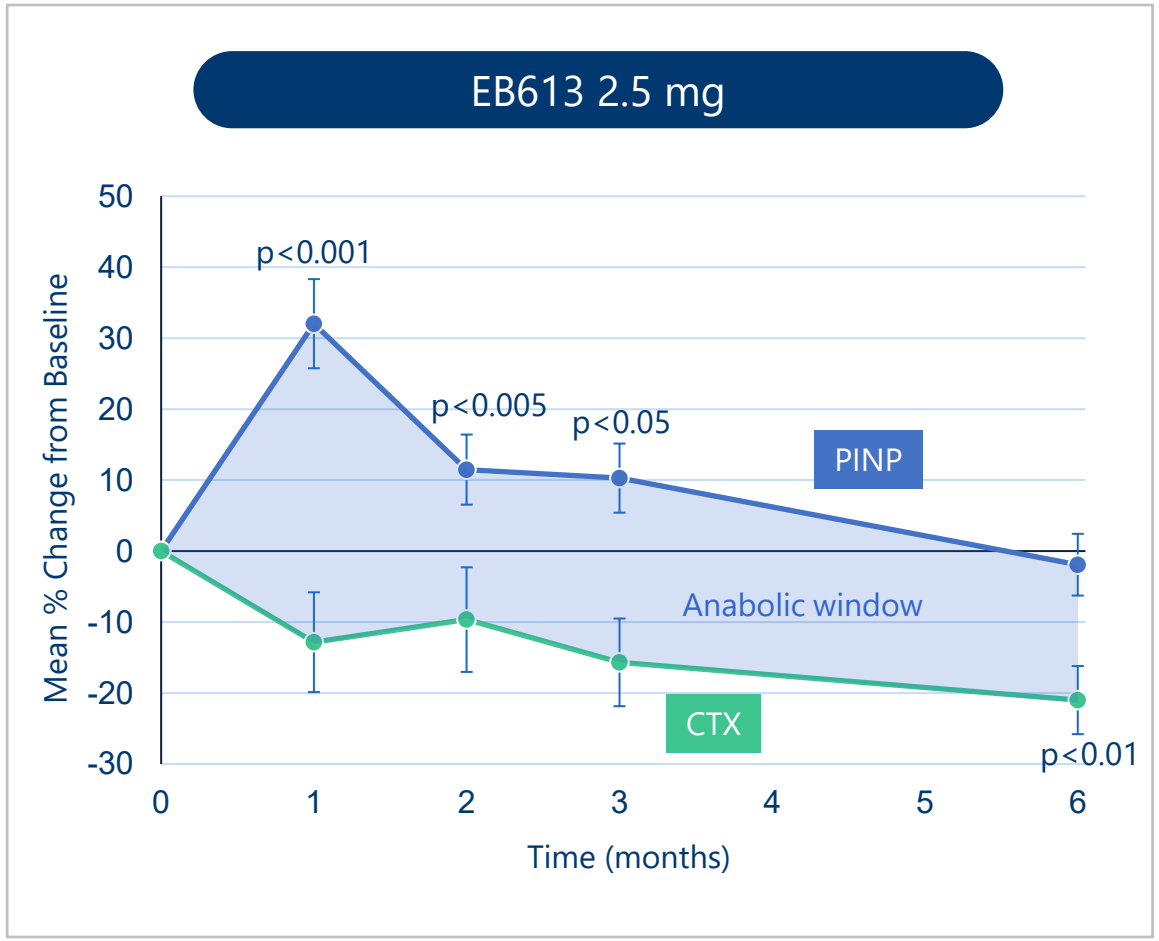
Primary Endpoint
- Serum PINP % change from baseline (placebo-adjusted) at Month 3

Secondary Endpoints
- BMD % change from baseline
- Serum OC and CTX % change from baseline at Months 1, 2, 3, and 6
- Serum PINP % change at Months 1, 2, and 6
- Plasma PTH(1-34) at T15 min

- 6-month, randomized, dose-ranging, placebo-controlled study in postmenopausal women with osteoporosis
- Conducted at 4 sites; Enrollment: 161 patients (118 active, 43 placebo)

PINP, serum N-terminal propeptide of Type 1 collagen; CTX, serum crosslinked C-telopeptide; OC, osteocalcin
Tripto-Shkolnik et al., J Bone Miner Res 2024

EB613 Increased Bone Formation (PINP) and Decreased Bone Resorption (CTX)



- EB613 significantly increased P1NP while also decreasing CTX
- This anabolic profile does not have the typical increase in bone resorption seen with subcutaneous teriparatide

PINP, serum N-terminal propeptide of Type 1 collagen; CTX, serum crosslinked C-telopeptide, p-value as compared to baseline
Tripto-Shkolnik et al., J Bone Miner Res 2024

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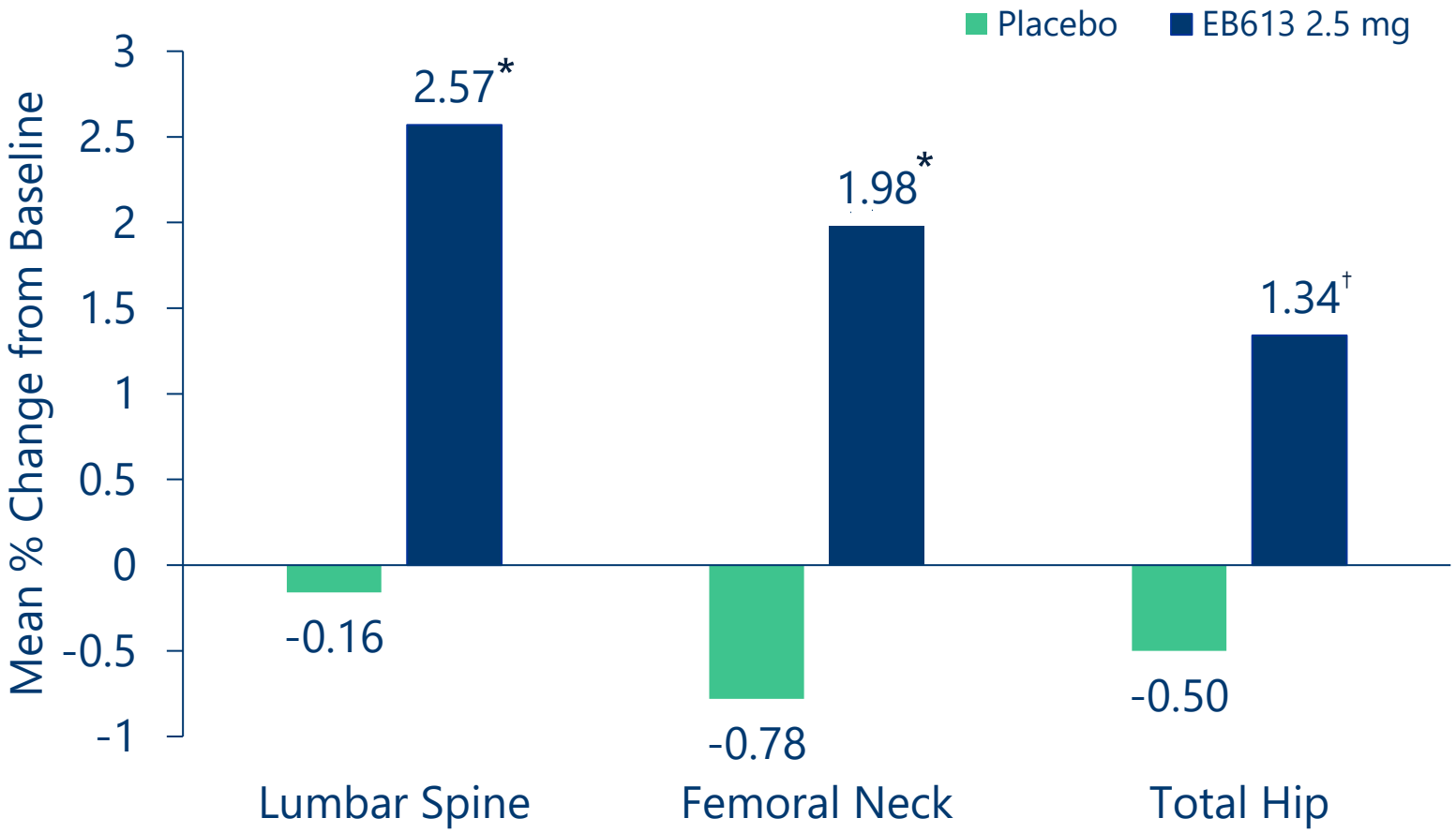
EB613 Increased BMD from Baseline to Month 6 at All Measured Skeletal Sites



EB613 2.5 mg dose includes titrated and non-titrated groups
EB613 vs baseline: * p-value = 0.01; † p-value = 0.04
EB613 vs placebo: all p-values <0.01
Tripto-Shkolnik et al., J Bone Miner Res 2024

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EB613 Safety Profile Consistent with PTH Agonists

Most Common Treatment Emergent AE (≥5% of participants)	EB613 Treated (N=118) n (%)
Headache	21 (17.8)
Nausea	18 (15.3)
Dizziness	13 (11.0)
Nasopharyngitis	7 (5.9)
Back pain	7 (5.9)
Palpitation	6 (5.1)
Dyspepsia	6 (5.1)
Presyncope	6 (5.1)

- Similar AE profile to that reported with Forteo® and other PTH agonists
- Mechanistic symptoms of orthostatic hypotension
  - Headache, nausea, and dizziness
- EB613 was not associated with serum calcium increases or hypercalcemia adverse events
- 2.5 mg dose with titration (1.5 mg for 1 month, 2.0 mg for the next month and 2.5 mg during months 3 to 6) well tolerated
- No serious AEs related to EB613

Tripto-Shkolnik et al., J Bone Miner Res 2024

Objective of Current Study

Characterize effects of EB613 on trabecular & cortical bone of the proximal femur using 3D-DXA modeling at 6 months

Methods

- All Phase 2 study subjects from the EB613 2.5 mg (n=21) and placebo (n=38) groups who had DXA scans of the proximal femur at baseline and 6 months were included
- 3D-DXA analyses were performed using 3D-Shaper® software to assess trabecular and cortical compartments
- For each parameter, % change from baseline for each subject and mean (SD) for each group were calculated
- Data were analyzed within groups vs baseline and between groups using t-tests
- Average 3D-DXA models were developed to show anatomical distribution of structural changes in each group

Demographics and Baseline Characteristics

Parameter (Mean, SD)	EB613 2.5 mg (N = 21)	Placebo (N= 38)
Age	62.2 (4.5)	61.2 (5.4)
Body mass index	26.6 (4.3)	25.3 (5.1)
Baseline T-score		
Lumbar spine	-2.2 (0.8)	-2.3 (0.7)
Total hip	-1.9 (0.7)	-2.0 (0.6)
Femoral neck	-2.2 (0.5)	-2.1 (0.6)

Subgroup analysis based on data presented in Tripto-Shkolnik et al., J Bone Miner Res 2024

Percentage Change from Baseline to Month 6 in aBMD by DXA and vBMD by 3D-Shaper

Parameter (Mean % Change, SD)	EB613 (N = 21)	Placebo (N = 38)	Placebo-adjusted % change	Group Difference p-value
Areal BMD				
Total hip	1.4 (2.7)	-0.5 (2.8)	1.8	<0.01
Femoral neck	1.9 (2.5)	-0.7 (3.9)	2.6	<0.01
Integral vBMD				
Total hip	1.1 (4.4)	-0.6 (4.4)	1.7	<0.08
Femoral neck	2.1 (4.7)	-0.5 (5.1)	2.6	<0.03
Trabecular vBMD				
Total hip	2.8 (6.8)	-0.2 (10.0)	3.0	0.14†
Femoral neck	4.3 (6.3)	-0.1 (8.3)	4.4	<0.03

vBMD, volumetric BMD
Areal BMD (g/cm^2); Integral vBMD (mg/cm^3); Trabecular vBMD (mg/cm^3)
All p-values are placebo-adjusted, † Group difference not significant, though increase with EB613 vs baseline p = 0.05

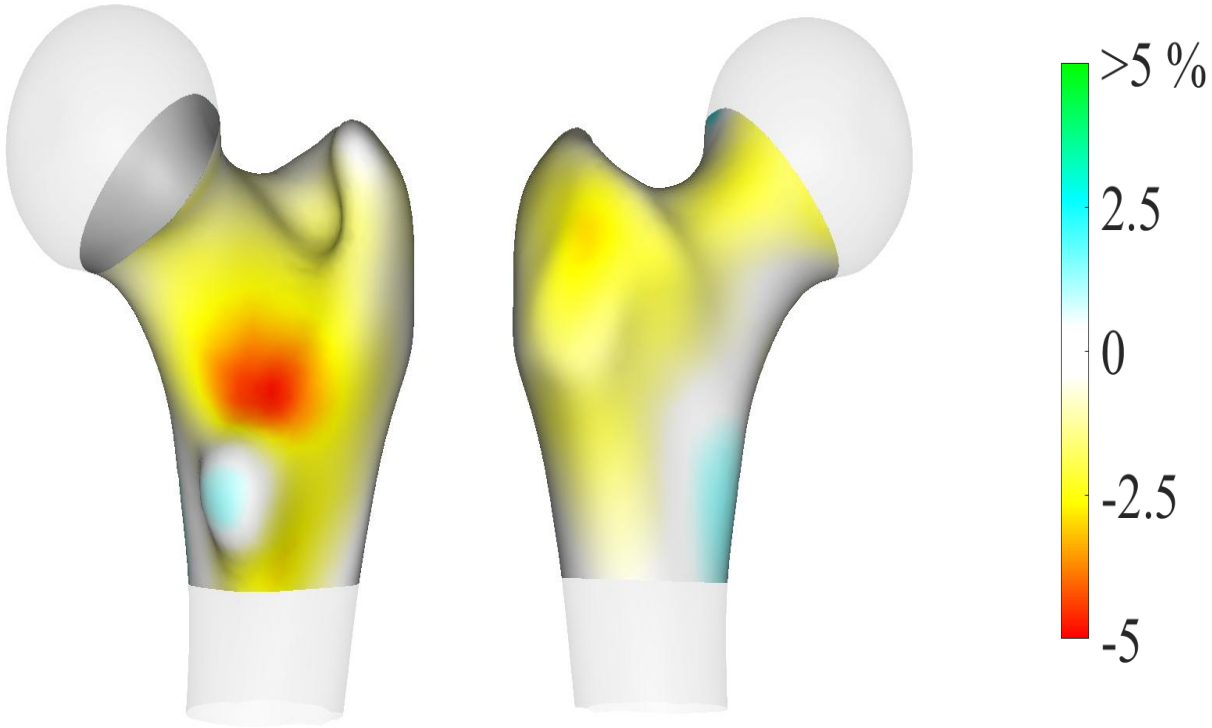
Percentage Change from Baseline to Month 6 in Selected Cortical Parameters by 3D-Shaper

Parameter (Mean % Change, SD)	EB613 (N = 21)	Placebo (N = 38)	Placebo-adjusted % change	Group Difference p-value
Cortical vBMD				
Total hip	0.4 (4.3)	0.0 (3.4)	0.4	0.36
Femoral neck	0.6 (3.7)	-0.1 (3.2)	0.7	0.21
Cortical thickness				
Total hip	0.4 (2.8)	-0.9 (2.6)	1.3	0.04
Femoral neck	0.5 (3.8)	-1.2 (3.7)	1.7	0.06
Cortical sBMD				
Total hip	0.7 (3.4)	-0.8 (3.0)	1.5	<0.05
Femoral neck	0.9 (4.0)	-1.3 (4.2)	2.1	<0.05

vBMD, volumetric BMD; sBMD, surface BMD
Cortical vBMD (mg/cm^3); cortical thickness (mm); cortical sBMD (mg/cm^2), calculated as the multiplication of the cortical thickness and the cortical volumetric BMD
All p-values are placebo-adjusted

Distribution of Average Cortical Surface BMD % Change from Baseline to Month 6

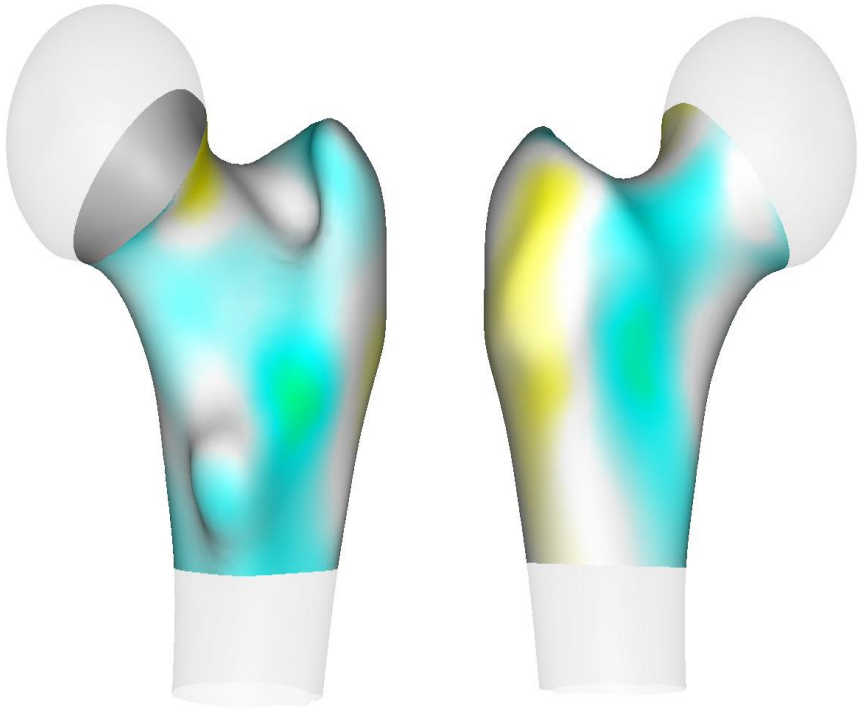
Placebo (N = 38)



Posterior View **Anterior View**

Total Hip, mean (SD): -0.8 (3.0)

EB613 (N = 21)



Posterior View **Anterior View**

Total Hip, mean (SD): 0.7 (3.4)

Cortical sBMD (mg/cm^2) is calculated as the multiplication of the cortical thickness and the cortical volumetric BMD

Evaluation of Subcutaneous Teriparatide and Abaloparatide on 3D-DXA Modeling

Indices of Cortical Bone for Total Hip at 6 Months in Cross-Study Comparison

Parameter (Mean % Change)	EB613 (N = 21)	Placebo (N = 38)	Teriparatide (N = 250)	Abaloparatide (N = 250)	Placebo (N = 250)
	Phase 2 Study		Phase 3 Study (ACTIVE)*		
Cortical vBMD	0.4	0.0	0.2	0.4	0.2
Cortical thickness	0.4	-0.9	0.7	0.6	0.0
Cortical sBMD	0.7	-0.8	1.0	1.0	0.1

*Percent changes estimated from Figure 2, Winzenrieth R et al., Osteoporos Int 2021; 32: 575-583
Cortical vBMD (mg/cm^3); cortical thickness (mm); cortical sBMD (mg/cm^2), calculated as the multiplication of the cortical thickness and the cortical volumetric BMD

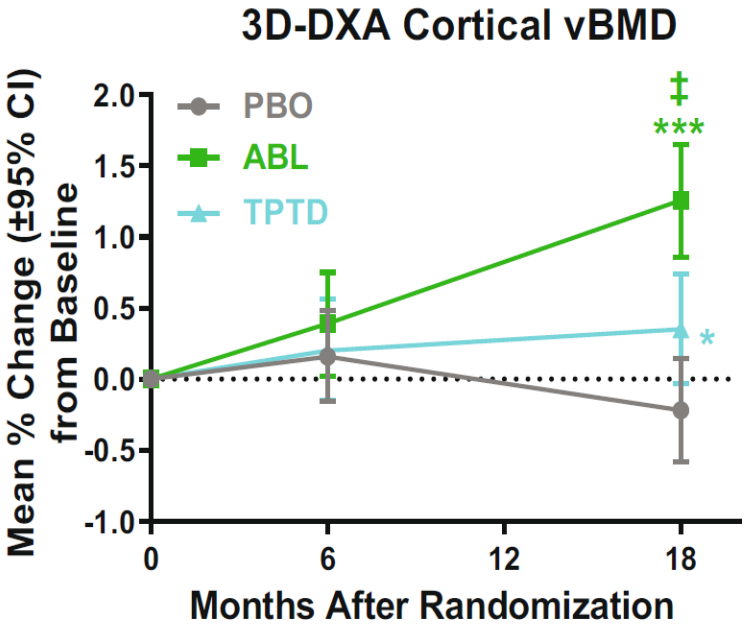
Summary

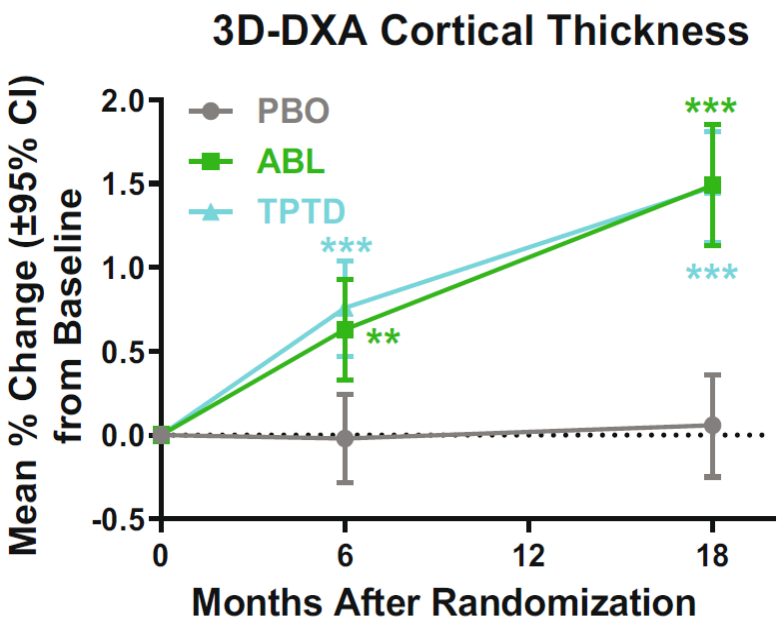
- 6 months of treatment with EB613 showed evidence of an early effect on both trabecular and cortical bone of the proximal femur
- Findings are consistent with the dual mechanism of increased bone formation and decreased resorption
- Safety and efficacy of EB613 will be further evaluated in the planned Phase 3 trial

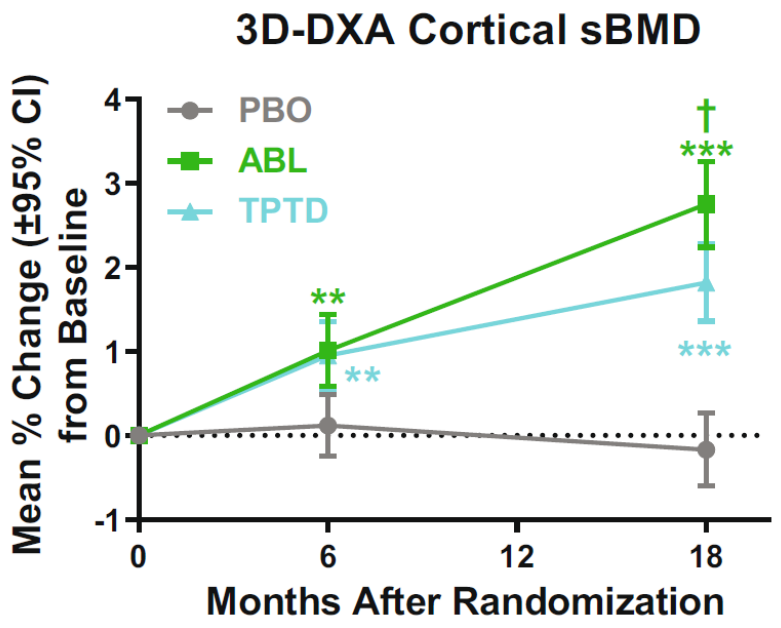
We thank the investigators and study subjects for their participation

Evaluation of Subcutaneous Teriparatide and Abaloparatide on 3D-DXA Modeling

Indices of Cortical Bone







PBO, placebo; ABL, abaloparatide; TPTD, teriparatide; vBMD, volumetric BMD; sBMD, surface BMD
Cortical vBMD (mg/cm^3); cortical thickness (mm); cortical sBMD (mg/cm^2), calculated as the multiplication of the cortical thickness and the cortical volumetric BMD
Winzenrieth R et al., Osteoporos Int 2021; 32: 575-583

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