SOC ENDOCRINOLOGIA
Dipartimento di Area Oncologica
P.O. Santa Maria della Misericordia di Udine
Direttore dott. Fabio Vescini

ASU FC
Azienda sanitaria universitaria Friuli Centrale
REGIONE AUTONOMA FRIULI VENEZIA GIULIA

NUOVE PROSPETTIVE TERAPEUTICHE DELL'OSTEOPOROSI

Abaloparatide

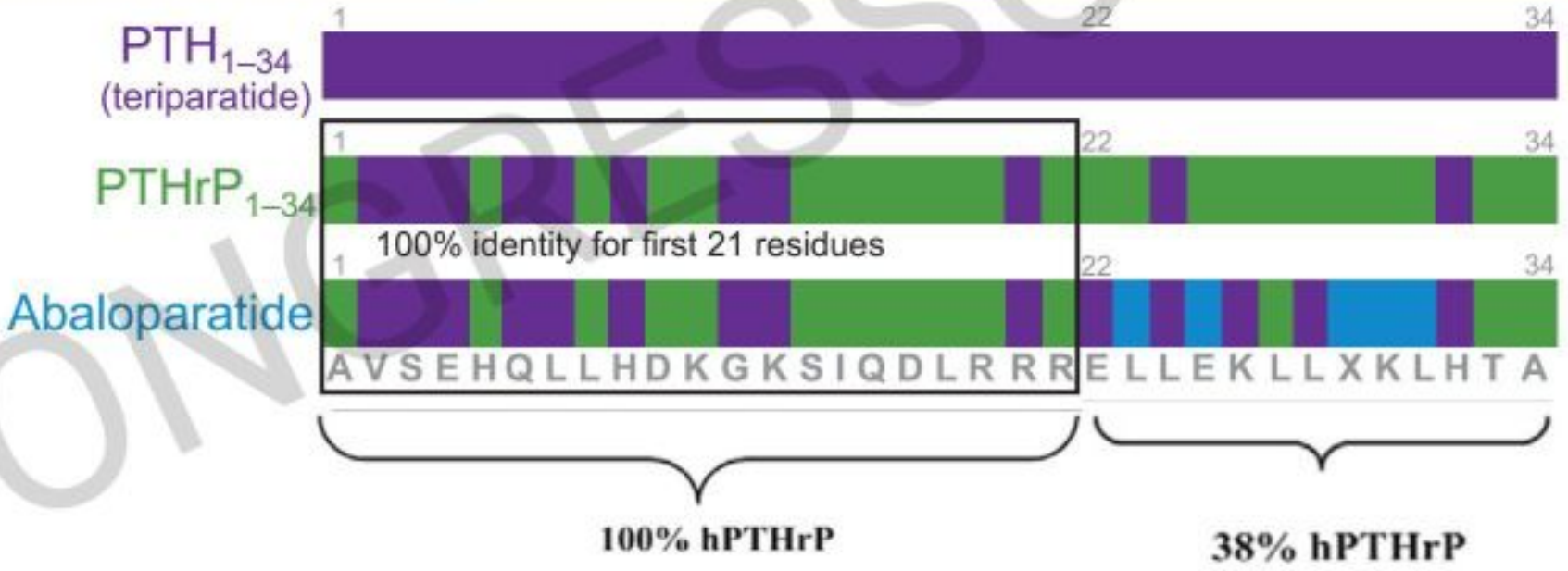
Fabio Vescini

Conflitti di interesse

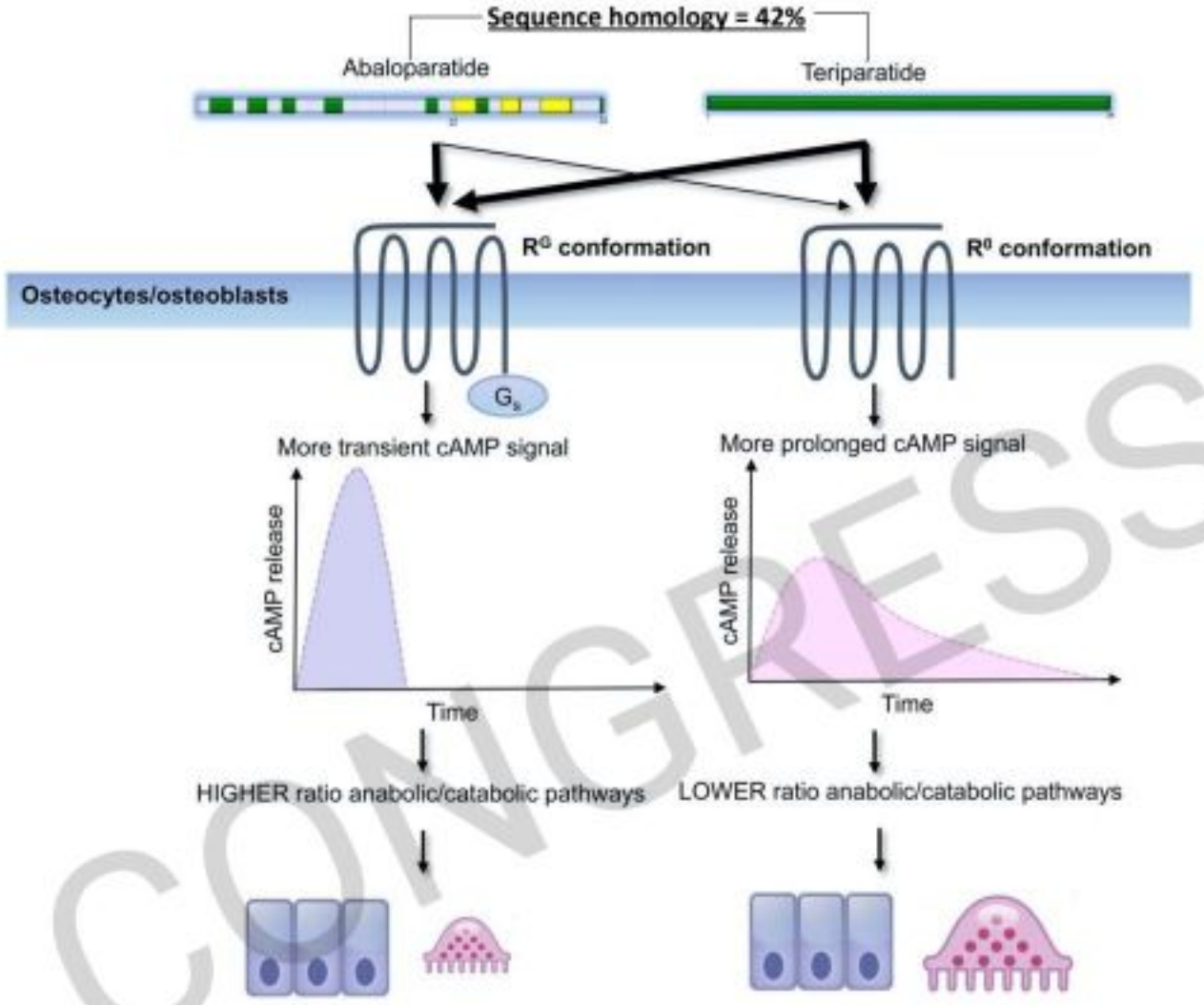
- Ai sensi dell'art. 4.5 su "Docenti e moderatori dell'evento", pag. 8 del Manuale Nazionale di Accreditamento per l'erogazione di eventi ECM del 06/12/2018, dichiaro che negli ultimi 2 anni ho avuto rapporti diretti di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:
  - Amgen
  - Abiogen
  - Bruno Farmaceutici
  - UCB
  - IBSA
  - Theramex
  - Italfarmaco

ANABOLIC COMPOUNDS FOR TREATMENT OF OSTEOPOROSIS

Property	Teriparatide	Abaloparatide
Regulatory approval	2002	2017
Molecule	PTH(1-34)	PTHrP(1-34)
Mechanism	PTH receptor agonist	PTH receptor agonist
Bone formation	Increases	Increases
Bone resorption	Increases	Increases



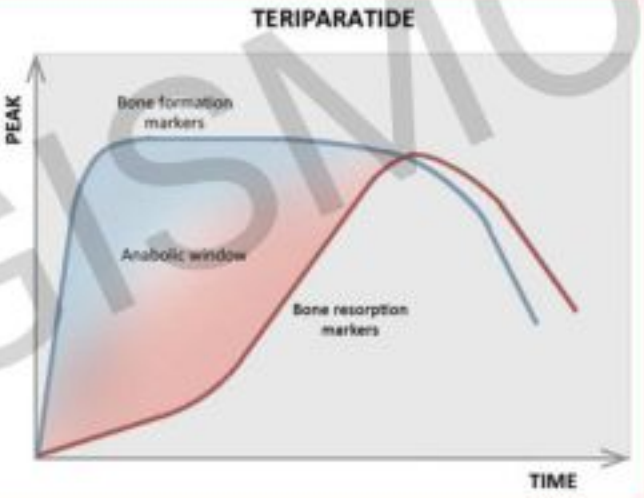
Meccanismo d'azione



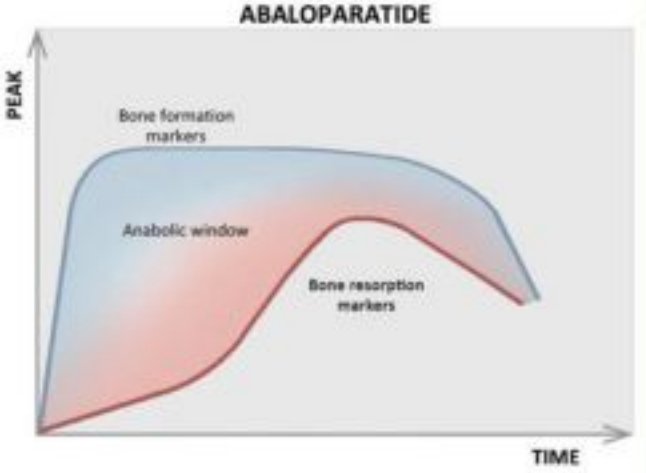
AZIONE ANABOLICA

Tay D, et al. Br J Clin Pharmacol. 2018 Feb;84(2):252-267.

TPTD first stimulates bone formation followed by a later increase in bone resorption



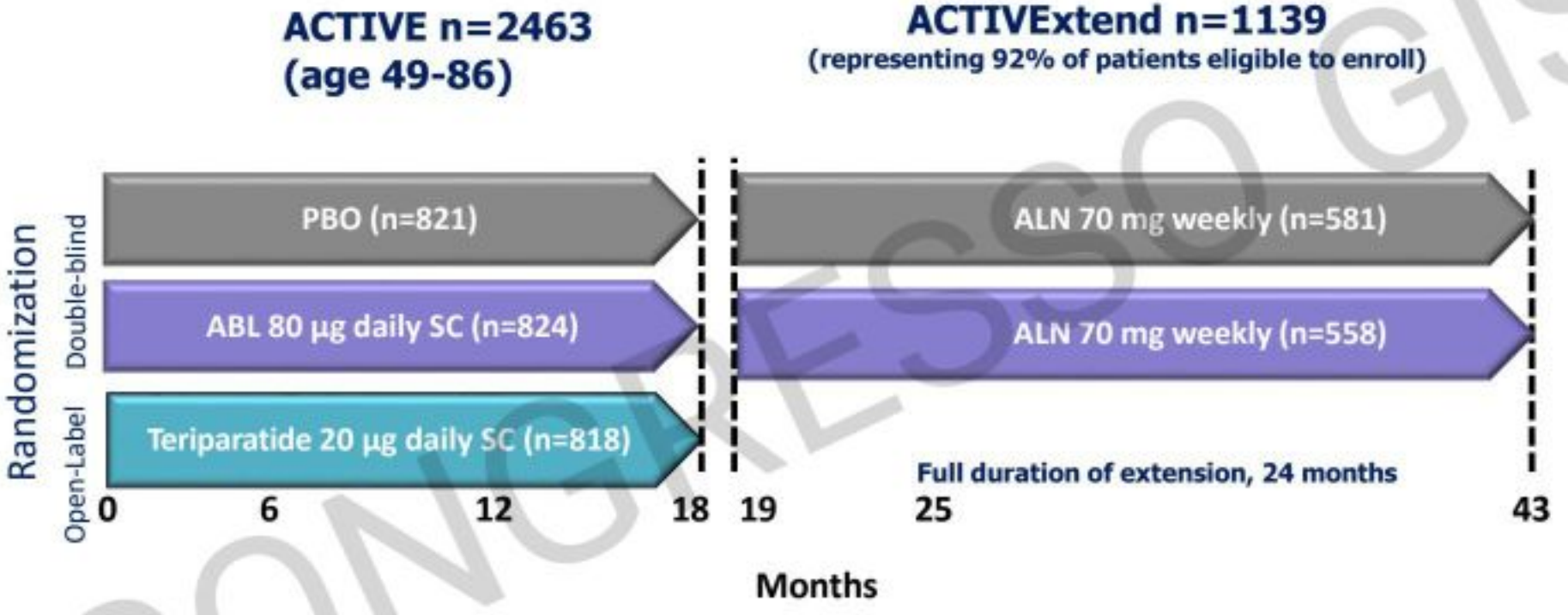
ABL, compared with TPTD, shows lower rates of bone formation and resorption, but a higher net anabolic effect



Adapted from Tabacco G et al. Br J Clin Pharmacol 2019;85:1064-1094

Abaloparatide – Clinical Development

Pivotal phase III trials: ACTIVE[1] and ACTIVExtend[2]



Patient inclusion criteria: Postmenopausal women, aged 49 to 86 years, with BMD ≤ -2.5 and < -5.0 T score at the lumbar spine or femoral neck together with radiologic evidence of at least 2 mild vertebral fractures or at least 1 moderate vertebral fracture

Efficacy Endpoints

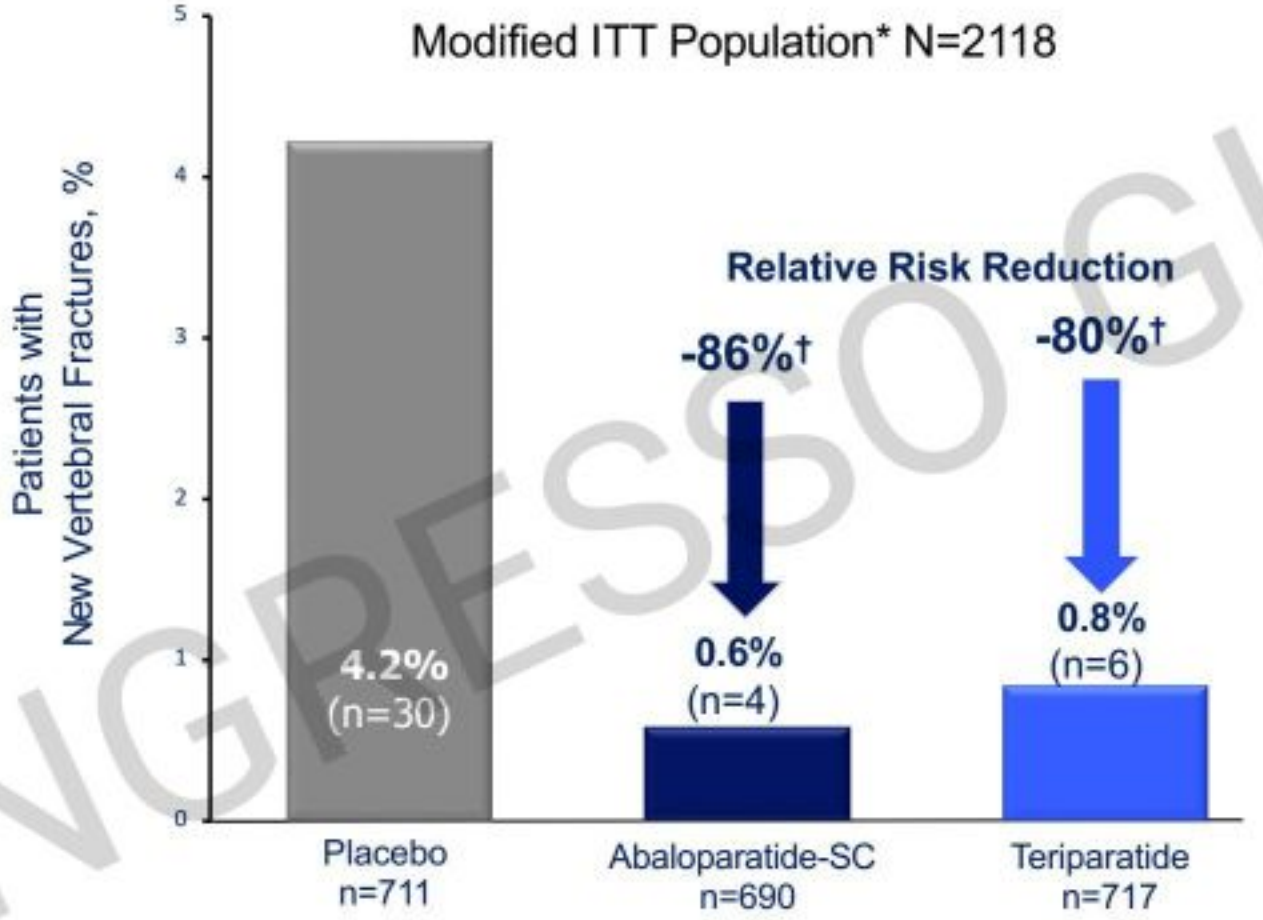
Fracture Outcomes
Vertebral
(primary endpoint)

Nonvertebral
(secondary endpoint)
Clinical
(exploratory endpoint)
Major osteoporotic
(exploratory endpoint)

BMD
Total hip
Femoral neck
Lumbar spine

1. Miller et al. JAMA 2016(7);316:722-733; 2. Bone 18;103(8):2949–2957

ACTIVE Study
Risk Reduction of New Vertebral Fractures (*Primary endpoint*)

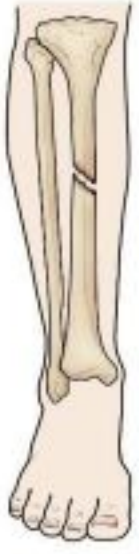


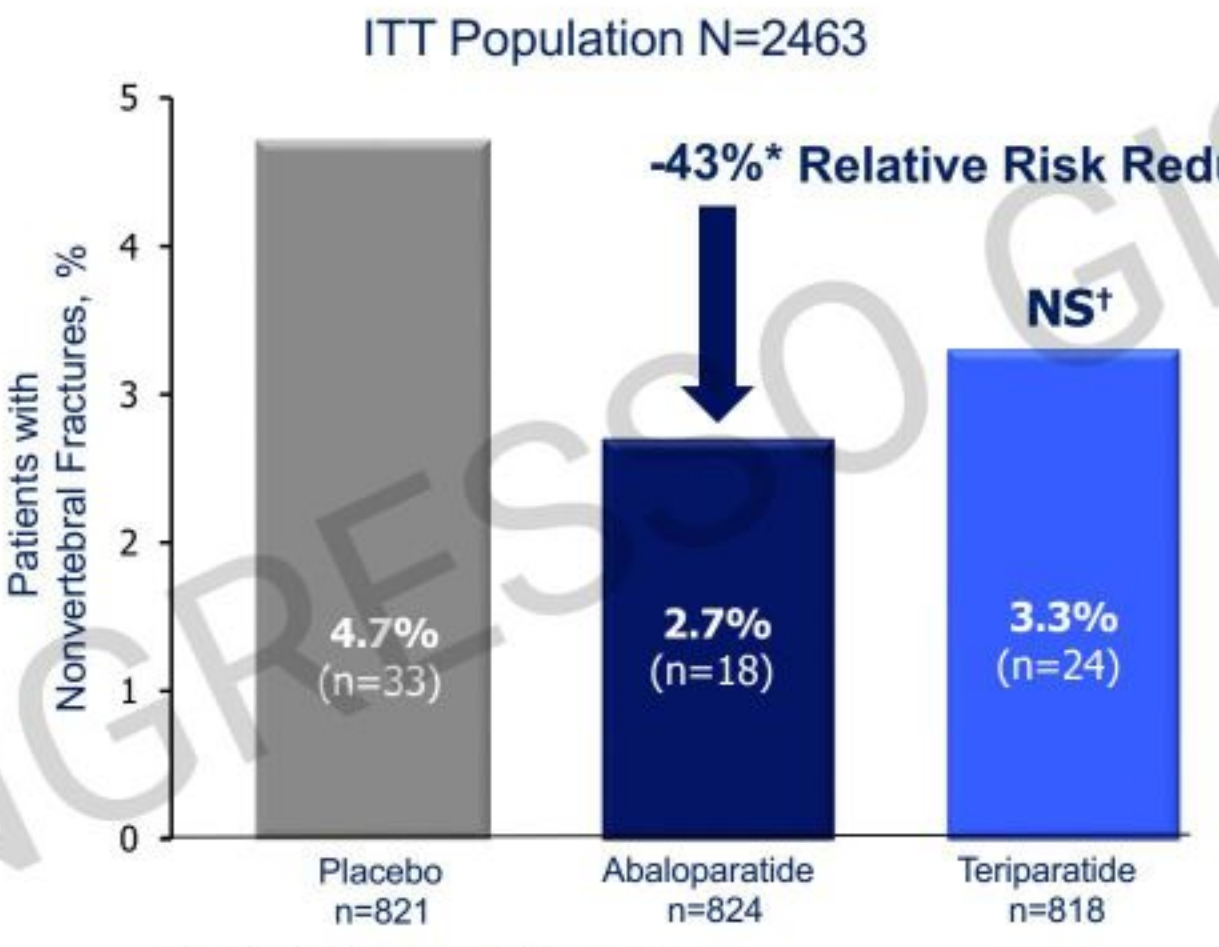
New vertebral fractures:
Morphometric fractures assessed by blinded radiographic review[2]

*Includes all ITT patients who had pretreatment and postbaseline evaluable radiologic assessments.
†$P < 0.001$ vs placebo. *P* values were not adjusted for multiple comparisons.

1. Miller et al. JAMA 2016(7);316:722-733
2. Genant HK et al. J Bone Miner Res. 1995;8:1137-1148. 2. Kanis JA on behalf of the World Health Organization Scientific Group (2007). FRAX WHO Fracture Risk Assessment Tool. World Health Organization Collaborating Centre for Metabolic Bone Diseases, University of Sheffield, UK. Available at: https://www.shef.ac.uk/FRAX/.

ACTIVE Study
Risk Reduction of Nonvertebral Fractures (*Secondary endpoint*)





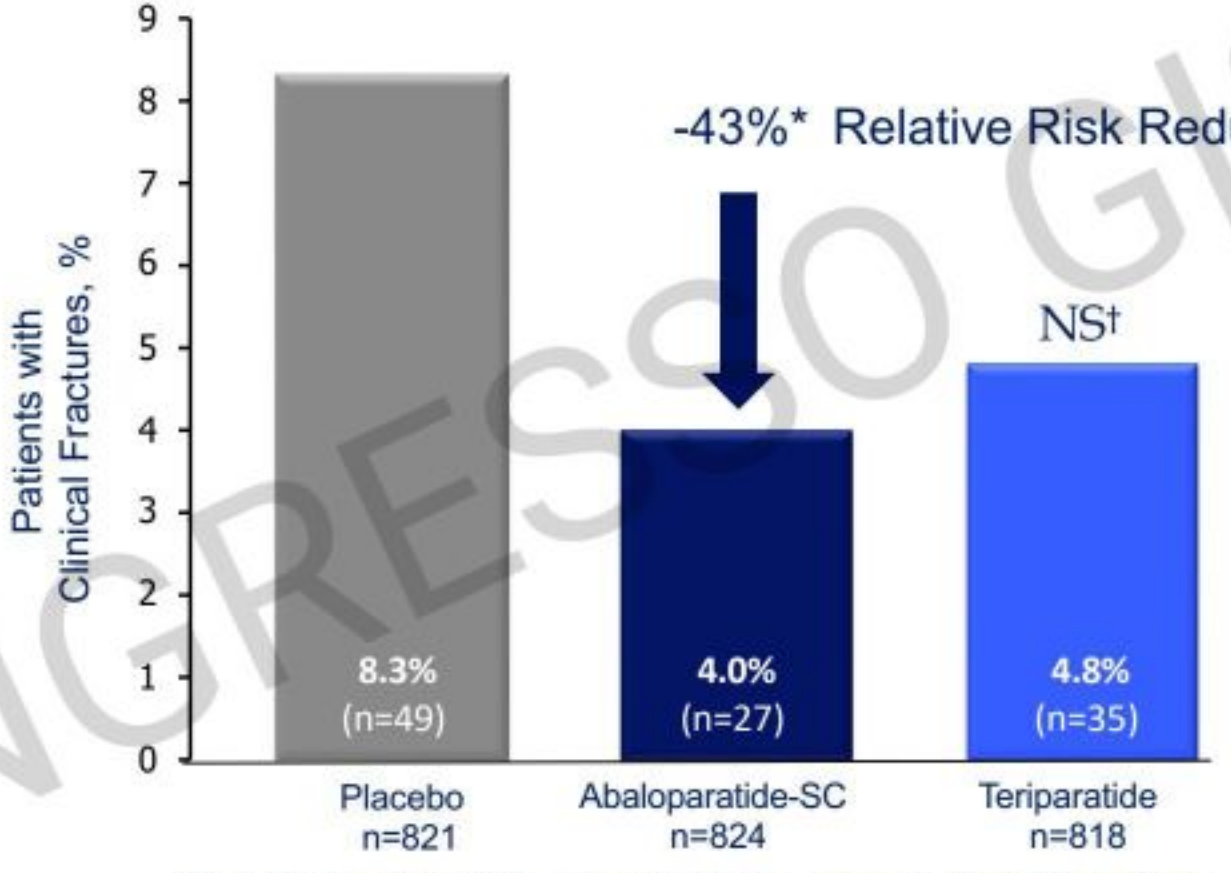
Nonvertebral fractures:
Clinical fractures associated with low trauma, excluding those of the spine, sternum, patella, toes, fingers, skull, and face

*P = 0.049 vs placebo; †NS vs placebo
Based on cumulative Kaplan-Meier estimates ITT at 19 months.

In the EU SmPC nonvertebral fracture risk reduction is not significant

Miller et al. JAMA 2016(7);316:722-733

ACTIVE Study
Risk Reduction of Clinical Fractures (*preplanned exploratory endpoint*)



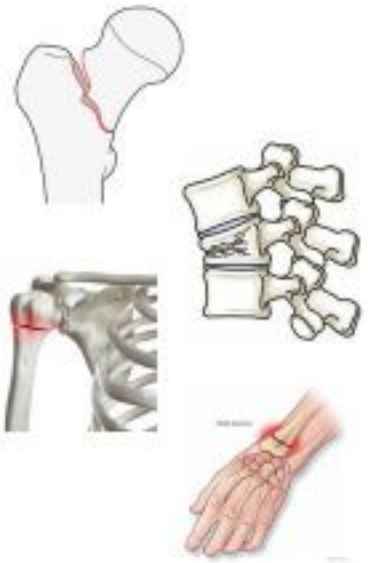
Clinical fractures:
All fractures that would cause a patient to seek medical care, regardless of the level of trauma, including clinical spine

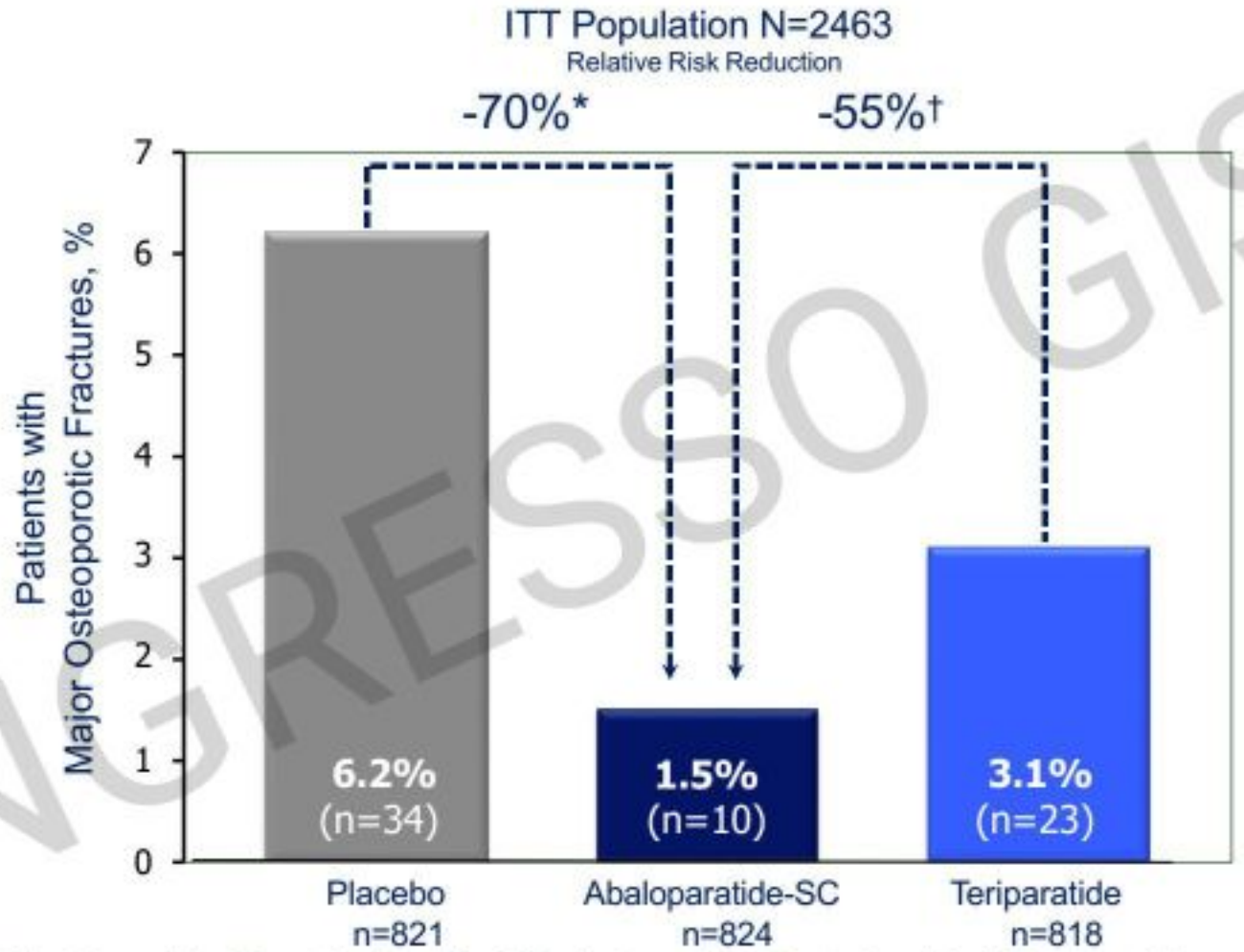
*P = 0.02 vs placebo; †NS vs placebo. P values were not adjusted for multiple comparisons Based on cumulative Kaplan-Meier estimates ITT at 19 months.

Miller et al. JAMA 2016(7);316:722-733

In the EU SmPC clinical fracture risk reduction is not significant

ACTIVE Study
Risk Reduction of Major Osteoporotic Fractures (*preplanned exploratory endpoint*)





Major osteoporotic fractures:
High- or low-trauma fractures of the **upper arm, wrist, hip, or clinical spine**[2]

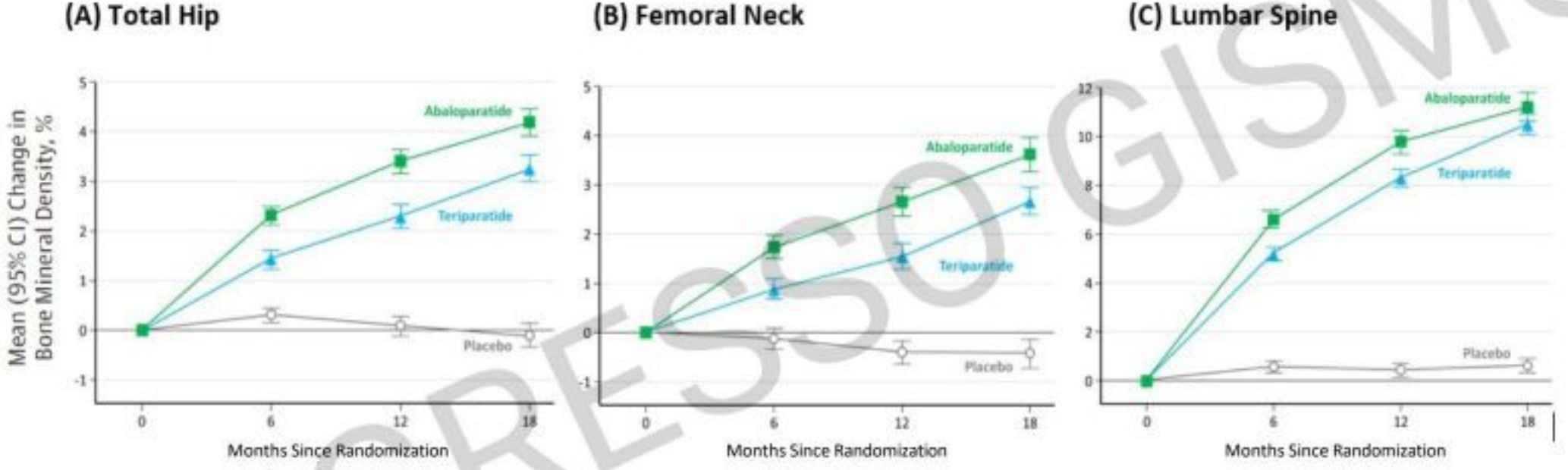
*$P < 0.001$, abaloparatide-SC vs placebo; †$P = 0.03$, abaloparatide-SC vs teriparatide; NS, teriparatide vs placebo.

Based on cumulative Kaplan-Meier estimates ITT at 19 months.

1.Miller et al. JAMA 2016(7);316:722-733
2.FRAX® is a risk assessment instrument, developed by the University of Sheffield, and is a registered trademark of Sheffield

ACTIVE Study
Change from baseline in Bone Mineral Density (BMD)

ITT Population N=2463



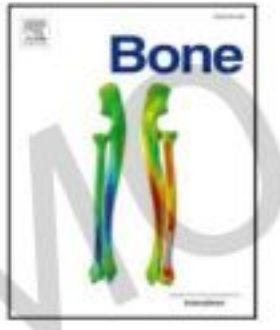
No. of participants evaluated												
Abaloparatide	822	736	651	615	822	736	651	615	823	738	652	617
Placebo	820	762	693	651	820	762	693	651	821	764	694	650
Teriparatide	818	754	705	660	818	754	705	660	818	755	704	665

Improvements with abaloparatide were significantly greater than those with teriparatide at the total hip and femoral neck at all time points ($P < .001$) and at lumbar spine at 6 and 12 months ($P < .001$). Error bars indicate 95% CIs.

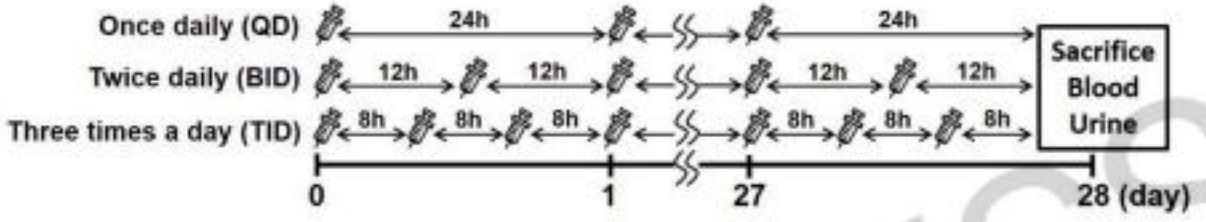
Miller et al. JAMA 2016(7):316:722-733

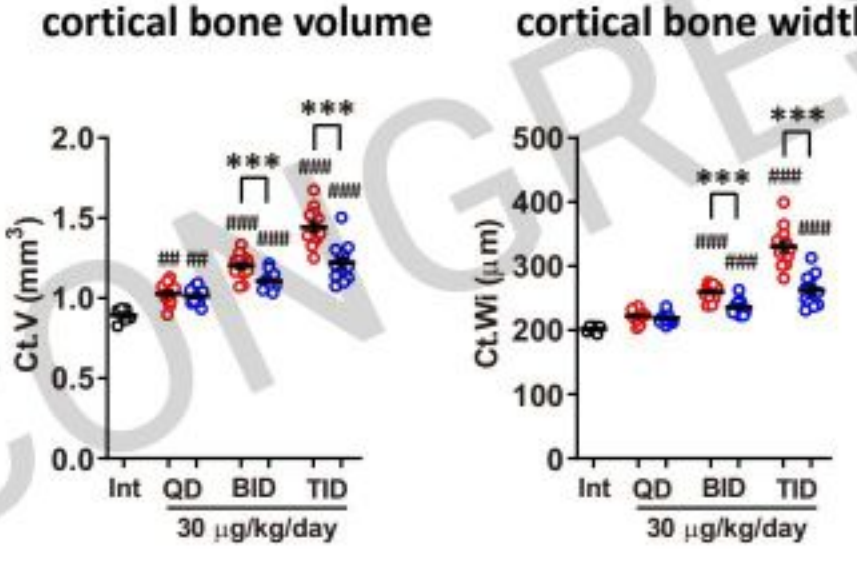
Frequent administration of abaloparatide shows greater gains in bone anabolic window and bone mineral density in mice: A comparison with teriparatide

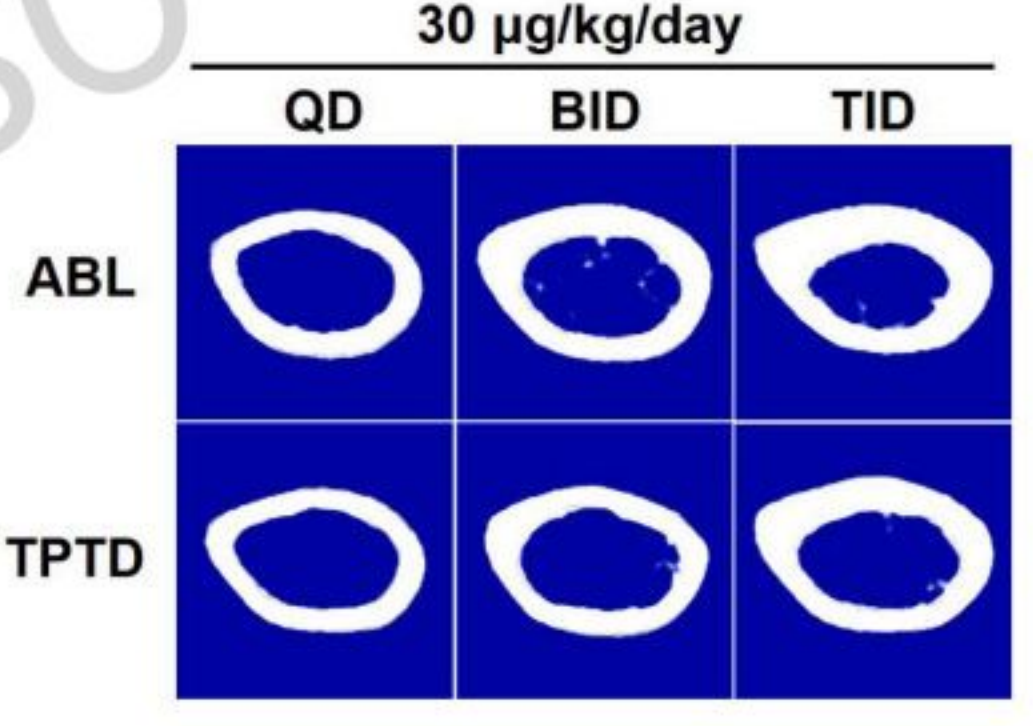
Akito Makino[a,b,*], Tomoka Hasegawa[b], Hideko Takagi[a], Yoshimasa Takahashi[a], Naoki Hase[a], Norio Amizuka[b]



Bone 142 (2021) 115651

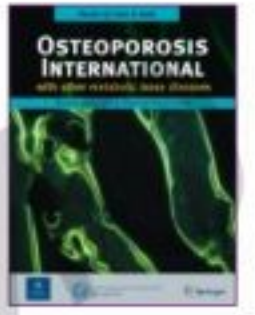




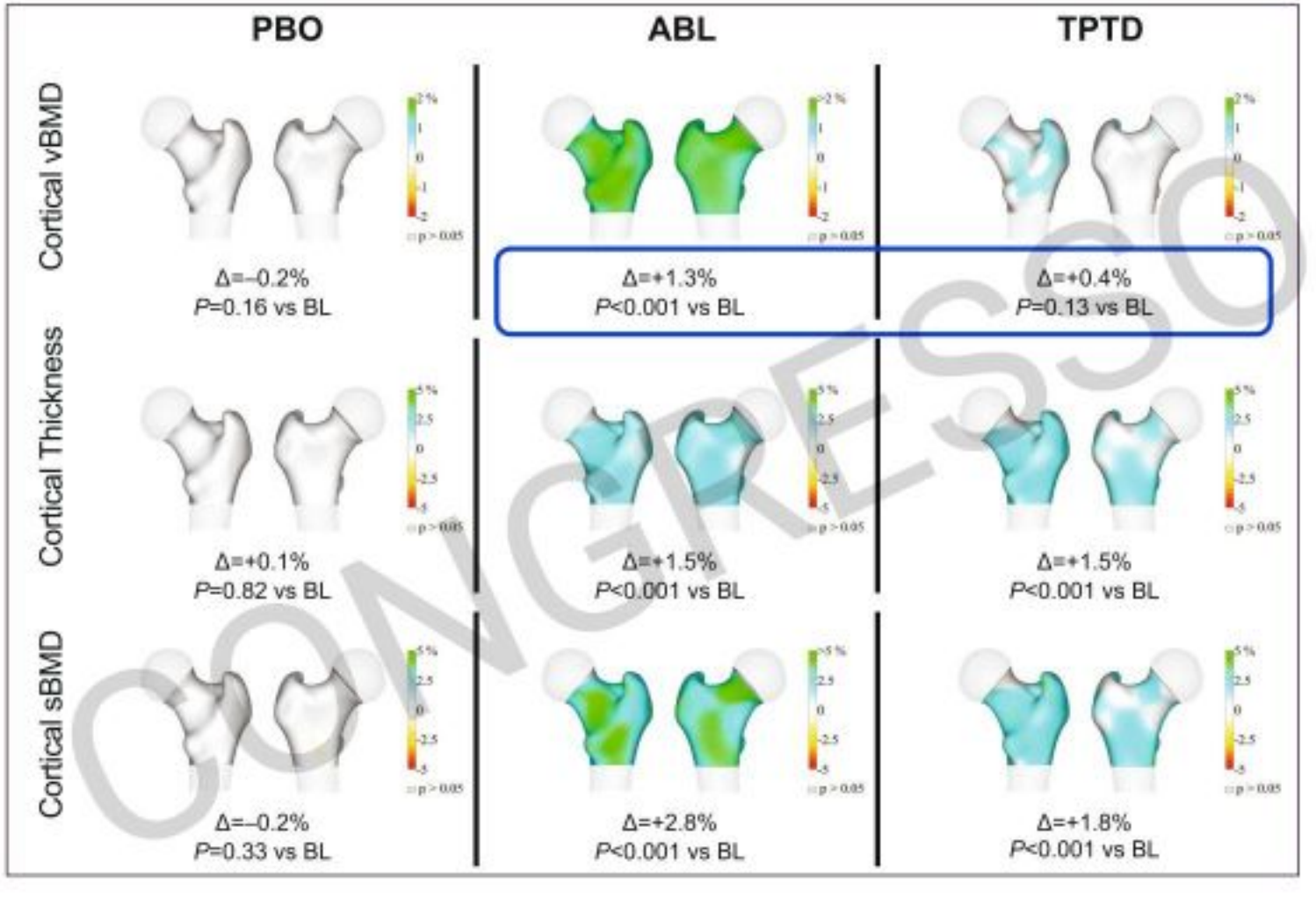


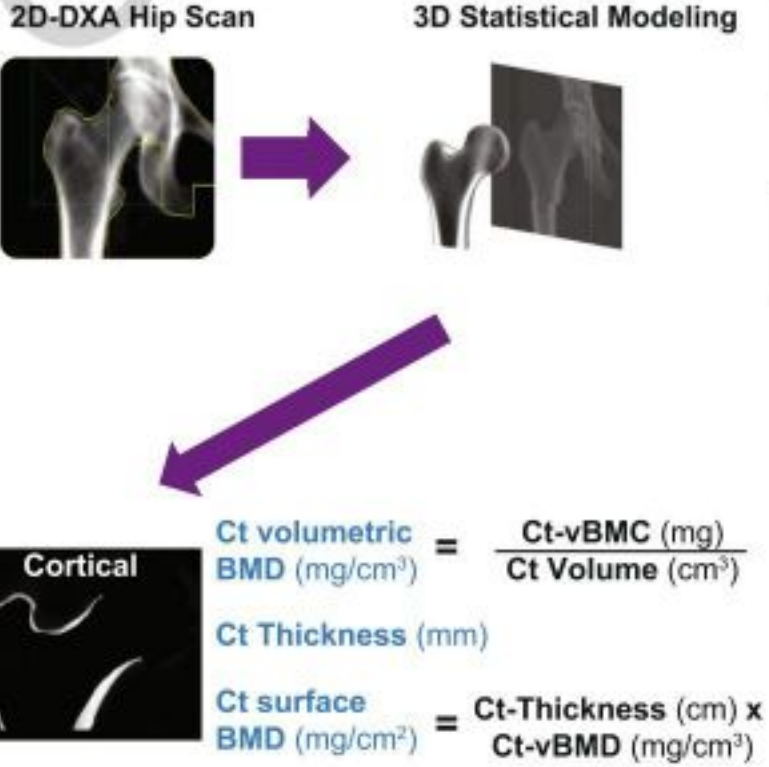
Differential effects of abaloparatide and teriparatide on hip cortical volumetric BMD by DXA-based 3D modeling

R. Winzenrieth[1] · M.S. Ominsky[2] · Y. Wang[2] · L. Humbert[1] · R.J. Weiss[2]

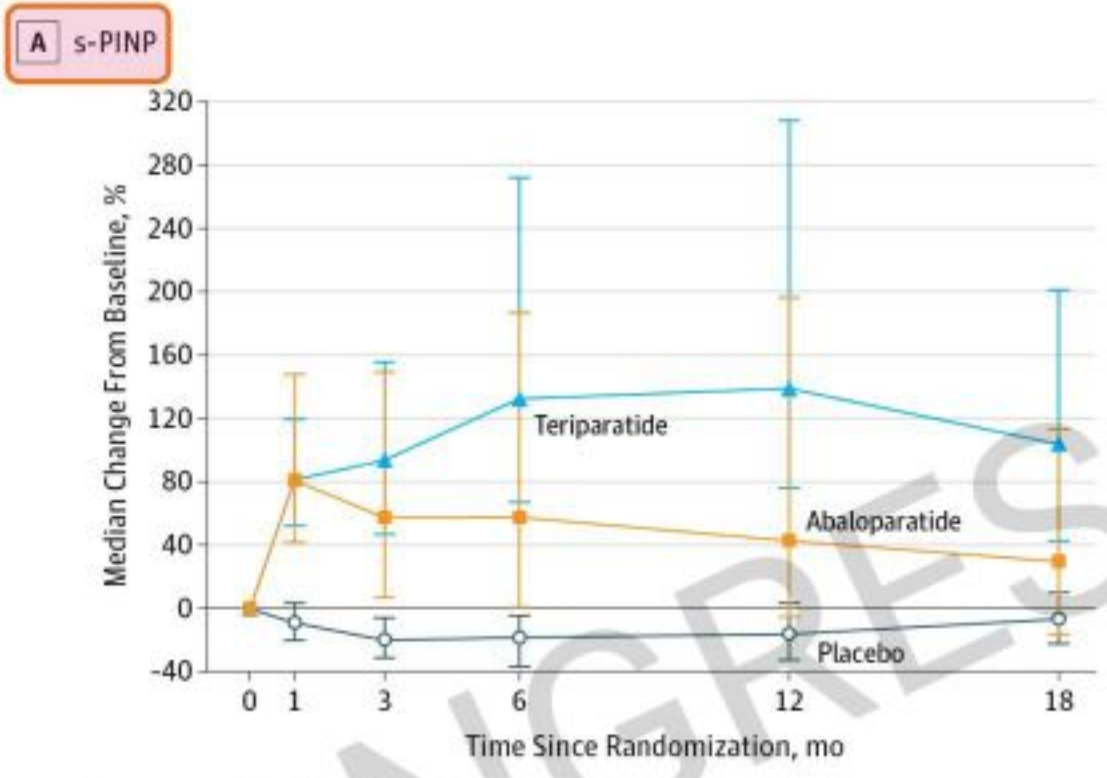


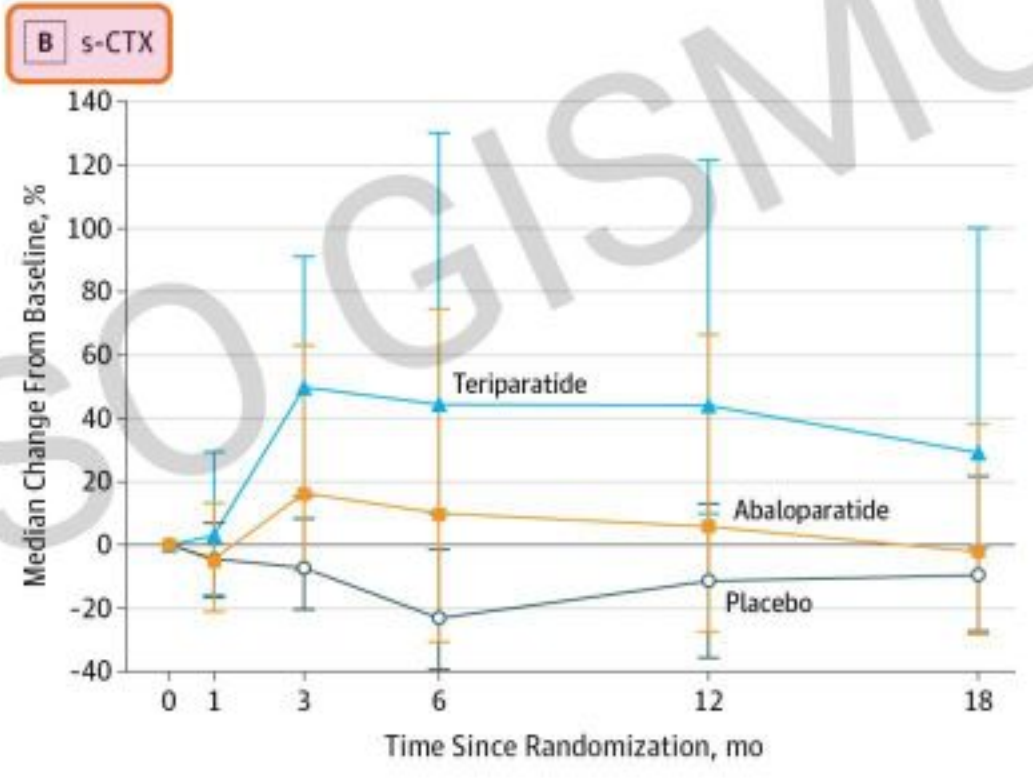
Osteoporos Int
(2021) 32, 575–583





Studio ACTIVE





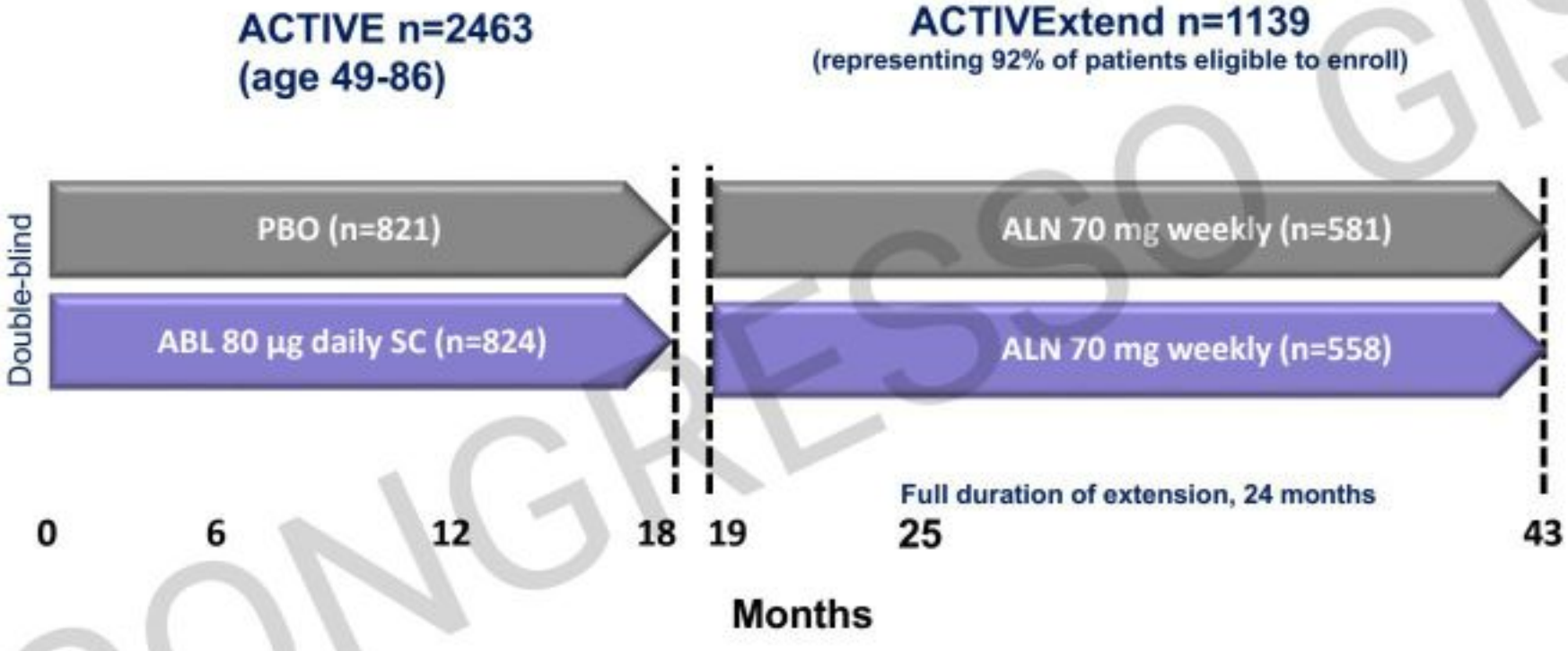
No. of participants evaluated						
Abaloparatide	189	187	187	189	189	189
Placebo	184	183	181	184	184	184
Teriparatide	227	227	227	227	227	227

189	187	187	189	189	189
184	183	181	184	184	184
227	227	227	227	227	227

Miller PD, Hattersley G, Riis BJ, et al. Effect of abaloparatide vs placebo on new vertebral fractures in postmenopausal women with osteoporosis: a randomized clinical trial. JAMA. 2016;316(7):722-733.

Abaloparatide – Clinical Development

Pivotal phase III trials: ACTIVE[1] and ACTIVExtend[2]



Efficacy Endpoints

Fracture Outcomes

Vertebral
(primary endpoint)

Nonvertebral
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Clinical
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Major osteoporotic
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BMD

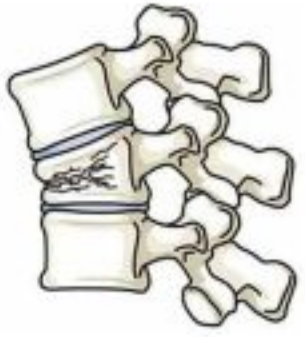
Total hip

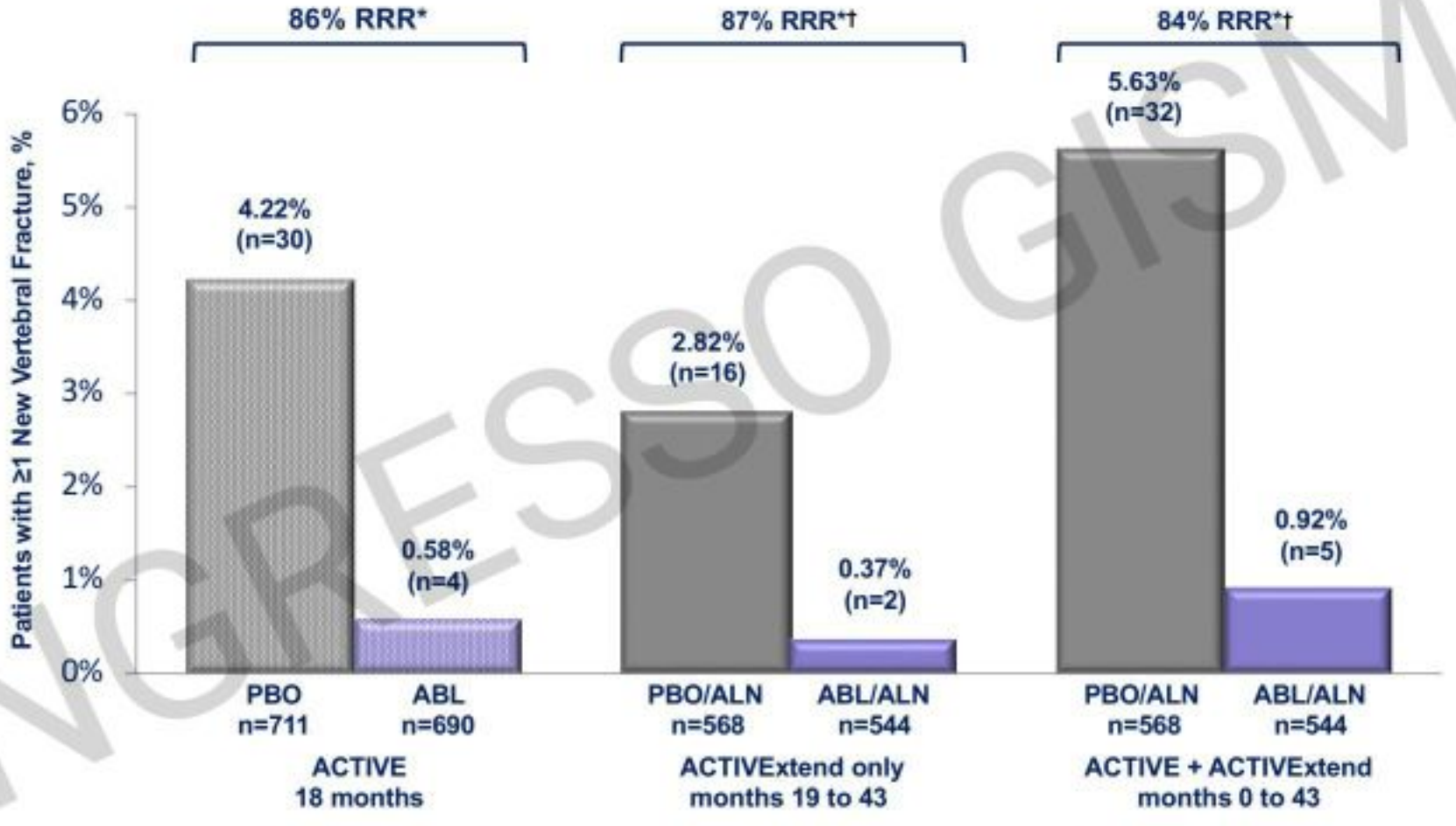
Femoral neck

Lumbar spine

1. Miller et al. JAMA 2016(7);316:722-733; 2. Bone 18;103(8):2949–2957

ACTIVE + ACTIVExtend Studies - New Vertebral Fracture Risk Reduction





*$P \leq 0.001$ for ABL vs PBO and for ABL/ALN vs PBO/ALN

† No statistical adjustments for multiple comparisons were made to additional subsequent analyses for Months 31, 37, and 43

ABL, abaloparatide; **ALN**, alendronate; **mITT**, modified intent to treat; **PBO**, placebo; **RRR**, relative risk reduction

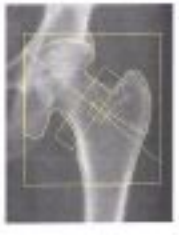
ACTIVE findings were reported by Miller et al JAMA 2016

1. Miller et al. JAMA 2016(7);316:722-733; 2. Bone 18;103(8):2949–2957

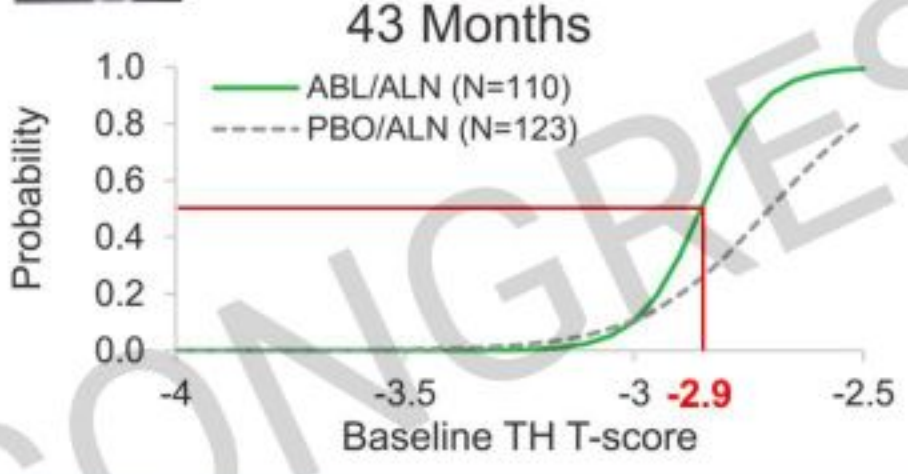
Probability of achieving bone mineral density treatment targets with abaloparatide and teriparatide

Felicia Cosman[1,*], Bruce H. Mitlak[2], Yamei Wang[3], Leny Pearman[4], Carolina A. Moreira[5], E. Michael Lewiecki[6], Steven R. Cummings[7,8]

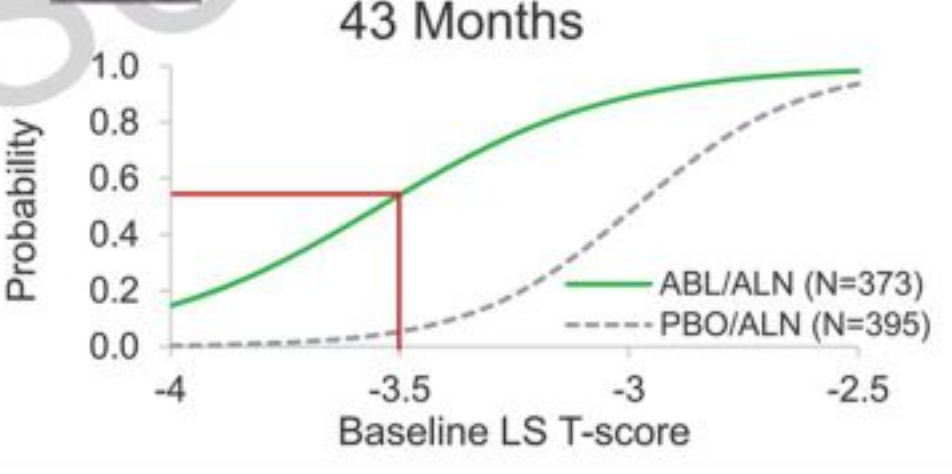
2025, **40**, 773–778



Probability of TH T-score >−2.5



Probability of LS T-score >−2.5



Over 3.5 yr of sequential treatment with abaloparatide/alendronate, >50% of women with baseline THT-scores ≥−2.9 and LST-scores ≥−3.5 were predicted to achieve T-scores >−2.5, respectively.

Endocrine Practice 31 (2025) 159–168

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Original Article

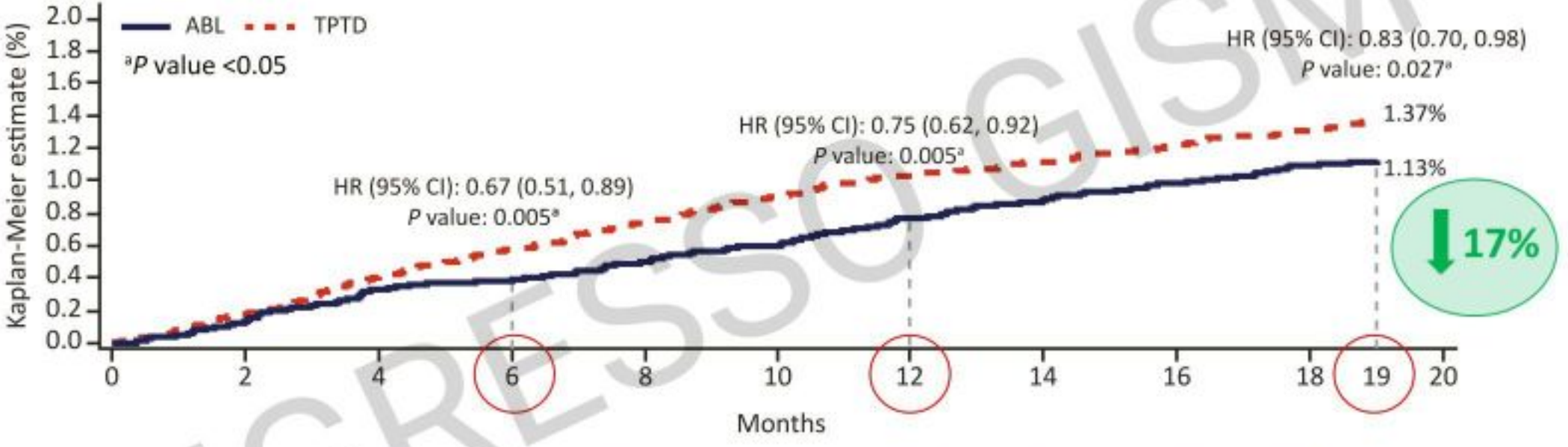
Comparative Effectiveness of Abaloparatide and Teriparatide in Women 50 Years of Age and Older: Update of a Real-World Retrospective Analysis

Laila Tabatabai, MD [1], Felicia Cosman, MD [2], Jeffrey R. Curtis, MD, MS, MPH [3], Kristi T. DeSapri, MD [4], Clayton T. LaBaume, PA-C, MPAS [5], Jean-Yves Reginster, MD, PhD [6], René Rizzoli, MD [7], Bernard Cortet, MD, PhD [8], Yamei Wang, PhD [9], Joseph Chiodo, III, PharmD [10,*], Bruce H. Mitlak, MD [11,†]

PRIMARY EFFICACY ENDPOINT: TIME TO FIRST HIP FRACTURE

PRIMARY EFFICACY ENDPOINT: TIME TO FIRST HIP FRACTURE

A

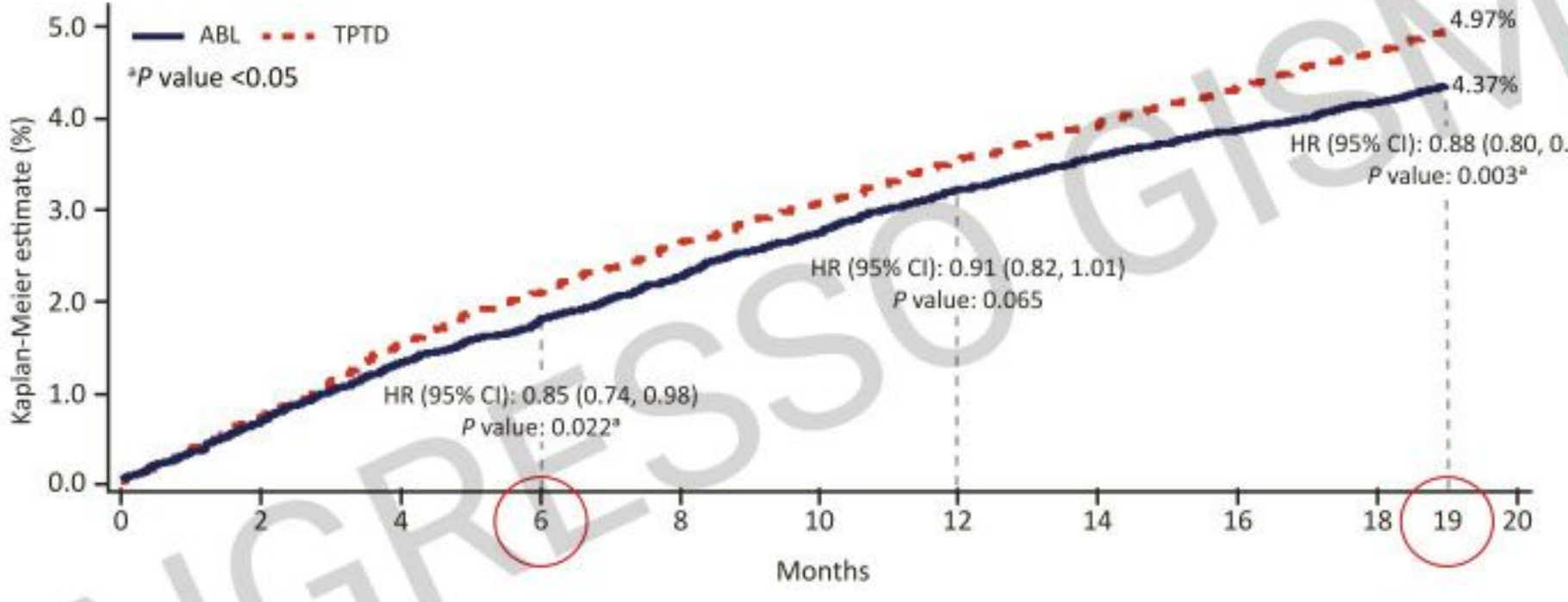


Patients at risk, n	21,676	21,647	21,606	21,593	21,568	21,545	21,508	21,486	21,463	21,437	
	21,676	21,638	21,587	21,550	21,515	21,480	21,453	21,433	21,411	21,393	
Cumulative number of patients with event, n	0	30	70	85	109	131	168	191	213	239	245
	0	39	90	126	162	196	223	244	266	284	296

Tabatabai L et al, Endocrine Practice 2025

TIME TO FIRST NON-VERTEBRAL FRACTURE

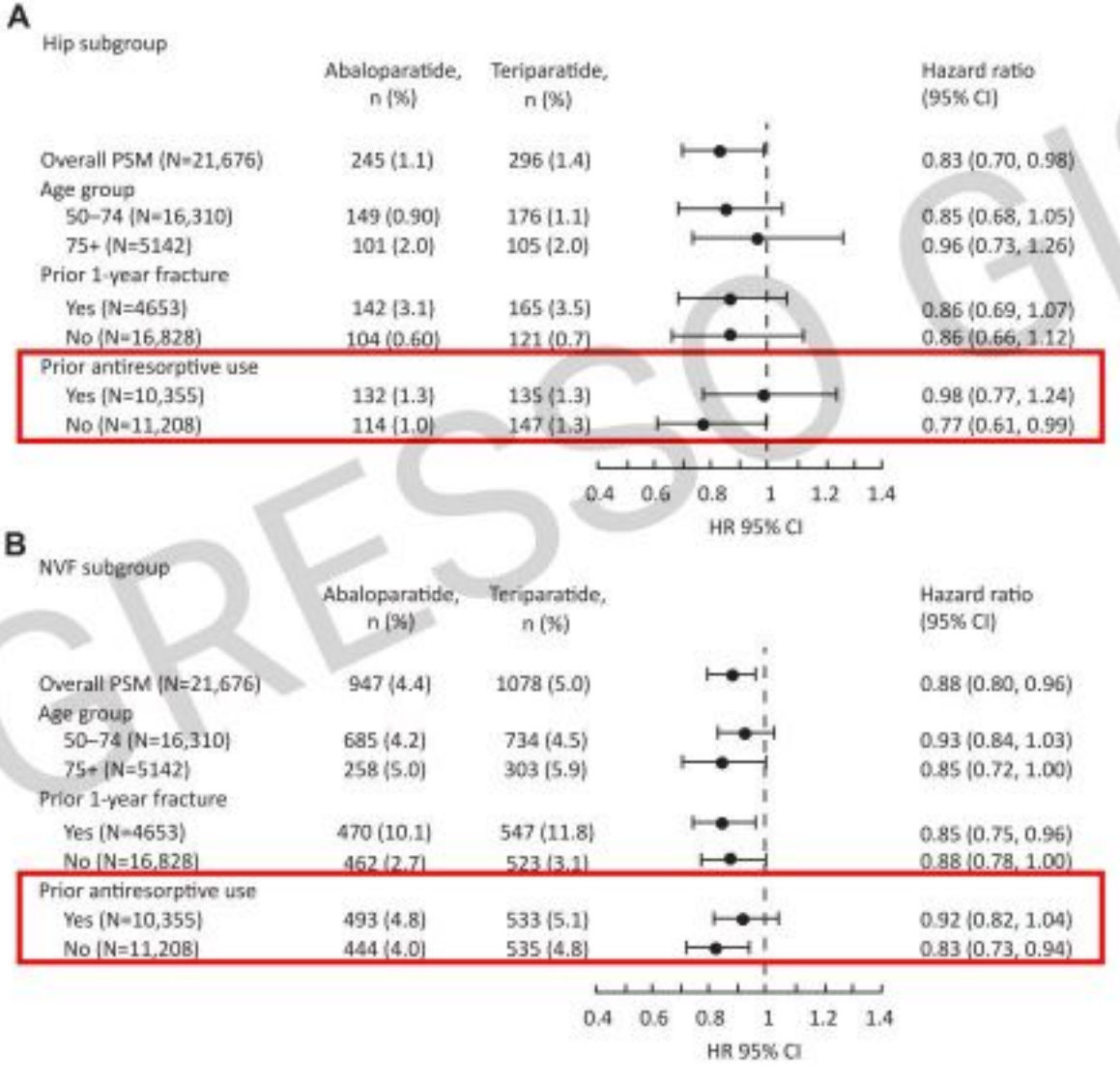
B



Patients at risk, n	21,676	21,536	21,395	21,296	21,188	21,084	20,979	20,900	20,836	20,771	
	21,676	21,526	21,348	21,226	21,109	21,012	20,910	20,825	20,735	20,652	
Cumulative number of patients with event, n	0	143	282	386	489	592	698	778	840	906	947
	0	153	329	452	570	665	767	852	944	1027	1078

Tabatabai L et al, Endocrine Practice 2025

Time to first incidence of hip fracture and nonvertebral fracture by subgroup



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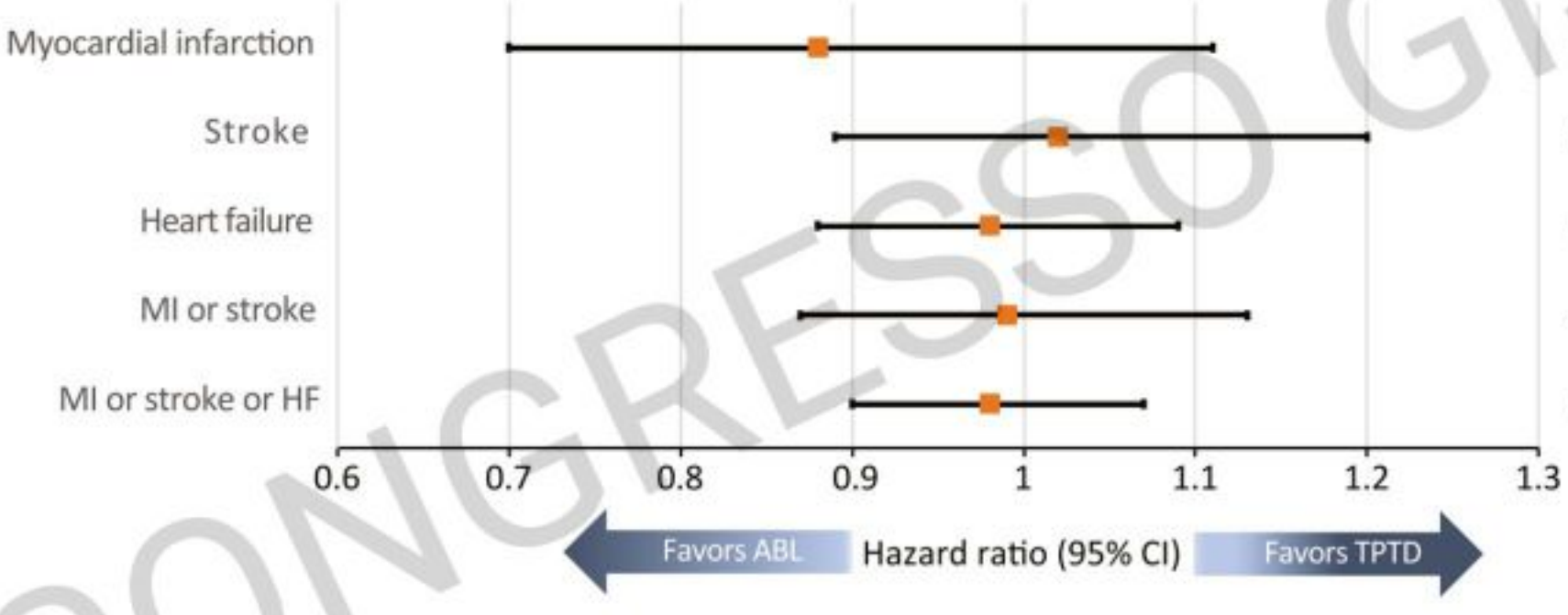
CARDIOVASCULAR OUTCOMES DURING TREATMENT

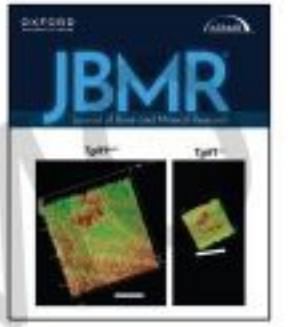


	ABL, n (%)	TPTD, n (%)	*P* value
Myocardial infarction	135 (1.0)	157 (1.1)	0.29
Stroke	288 (2.1)	290 (1.9)	0.81
Heart failure	626 (4.2)	655 (4.5)	0.70
MI or stroke	412 (2.9)	427 (2.9)	0.89
MI or stroke or HF	948 (6.4)	988 (6.6)	0.70

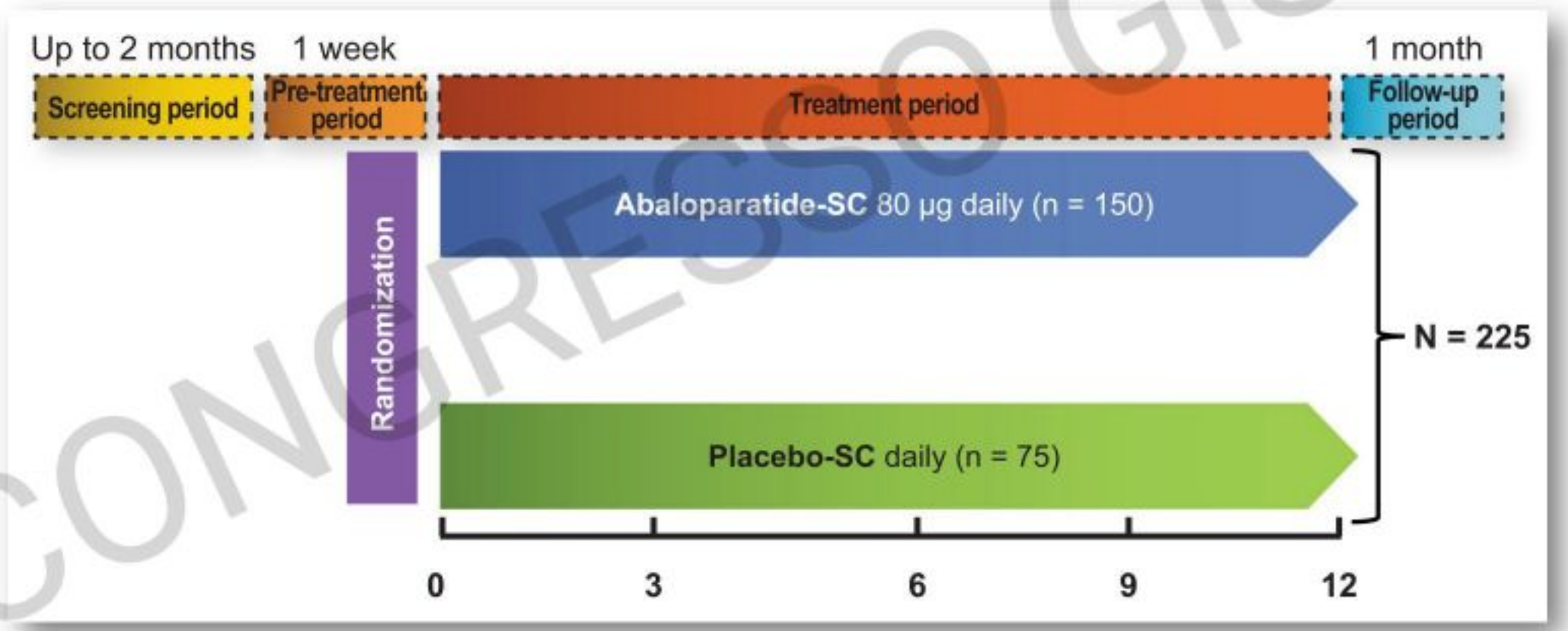
Tabatabai L et al, Endocrine Practice 2025

The Efficacy and Safety of Abaloparatide-SC in Men With Osteoporosis: A Randomized Clinical Trial

Edward Czerwinski,[1] Jose Cardona,[2] Rafal Plebanski,[3] Chris Recknor,[4] Tamara Vokes,[5] Kenneth G Saag,[6] Neil Binkley,[7] E Michael Lewiecki,[8] Jonathan Adachi,[9] Dorota Knychas,[10] David Kendler,[11] Eric Orwoll,[12] Yinzhong Chen,[13] Leny Pearman,[13] Y Heather Li,[13] and Bruce Mitlak[13]



2022, **37**, 2435–2442



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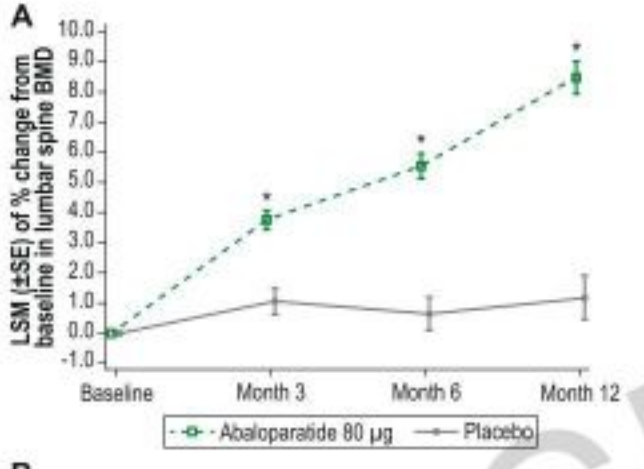
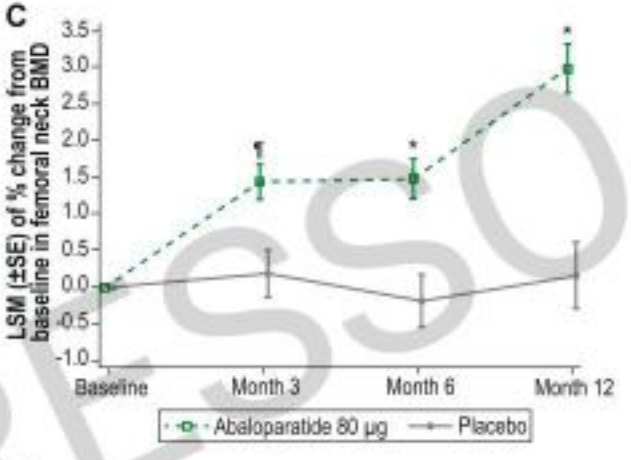
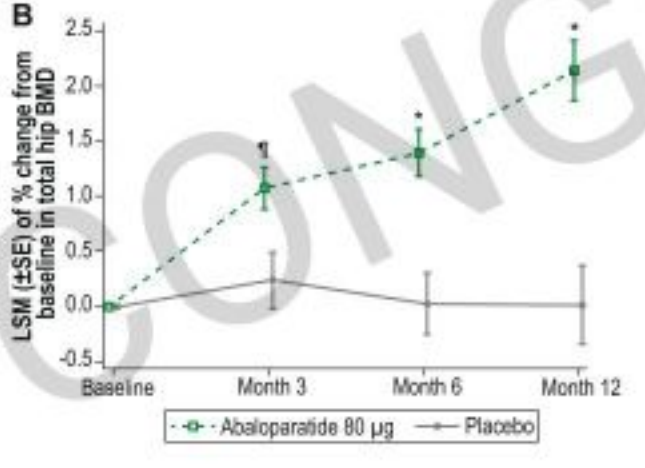
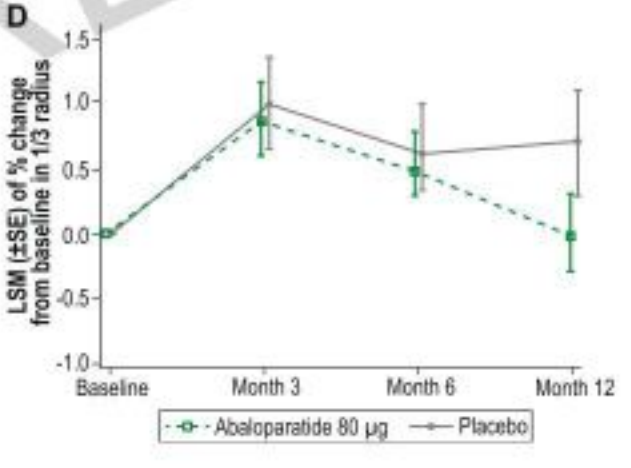
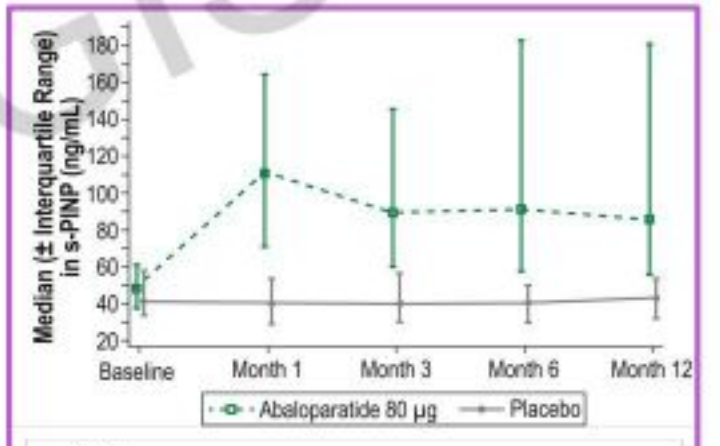
2022, **37**, 2435–2442

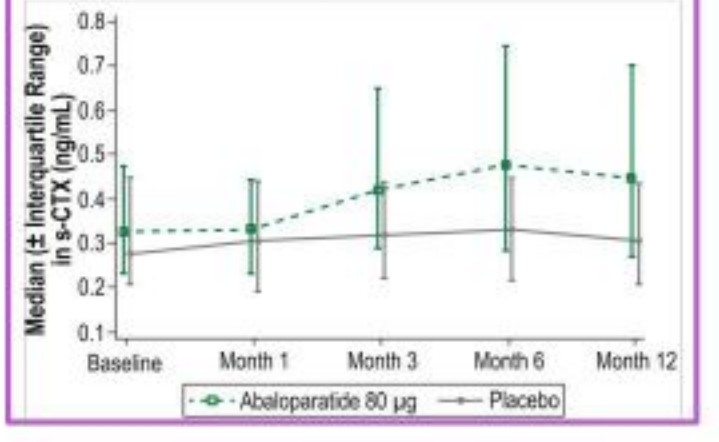












Indicazioni

Table 1. Summary of selected properties of interest for three approved anabolic compounds for treatment of osteoporosis

Property	Teriparatide	Abaloparatide	Romosozumab
Indications	Postmenopausal osteoporosis Male osteoporosis GIO	Postmenopausal osteoporosis	Postmenopausal osteoporosis

AIFA
AGENZIA ITALIANA DEL FARMACO

UFFICIO PROCEDURE CENTRALIZZATE

CLASSIFICAZIONE DI MEDICINALI PER USO UMANO AI SENSI DELL'ART. 12 COMMA 5 DEL DECRETO-LEGGE 13 SETTEMBRE 2012 N. 158 CONVERTITO NELLA LEGGE 8 NOVEMBRE 2012 N. 189

Regime di fornitura: Medicinale soggetto a prescrizione medica limitativa, vendibile al pubblico su prescrizione di centri ospedalieri o di specialisti - internista, reumatologo, endocrinologo, ginecologo, geriatra, ortopedico, fisiatra, nefrologo (RRL).

Al termine del periodo massimo (18 mesi) deve seguire un **trattamento antiriassorbitivo** per mantenere i risultati sulla BMD.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Grazie per l'attenzione