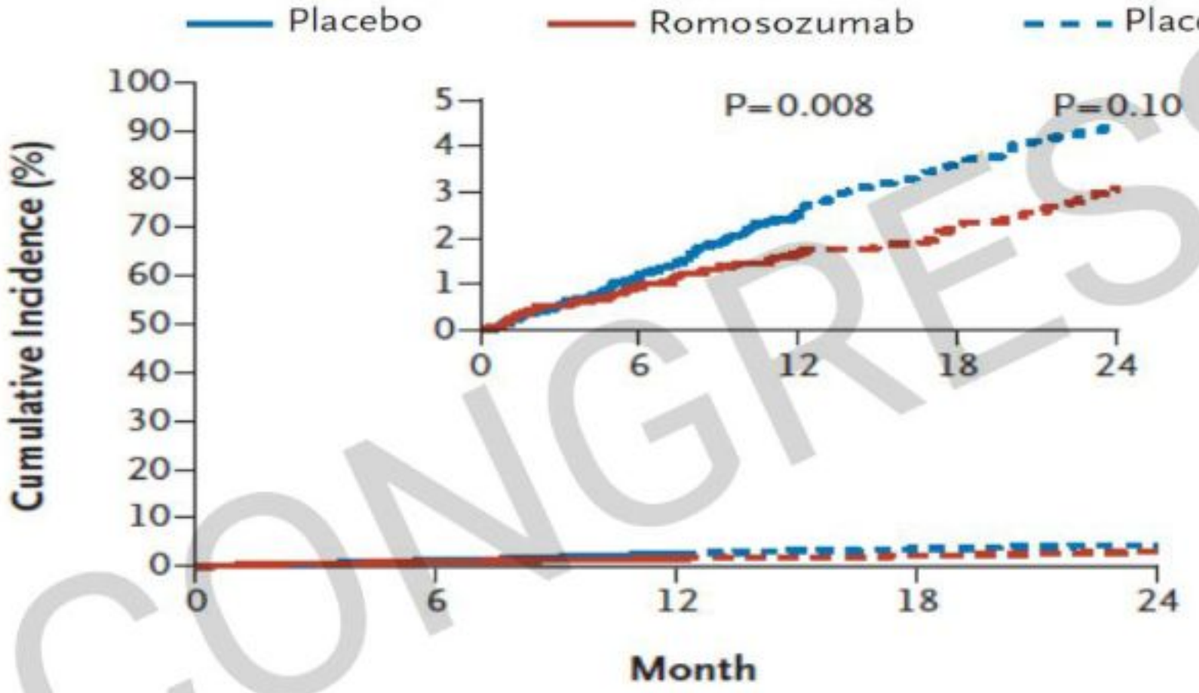
The NEW ENGLAND JOURNAL of MEDICINE

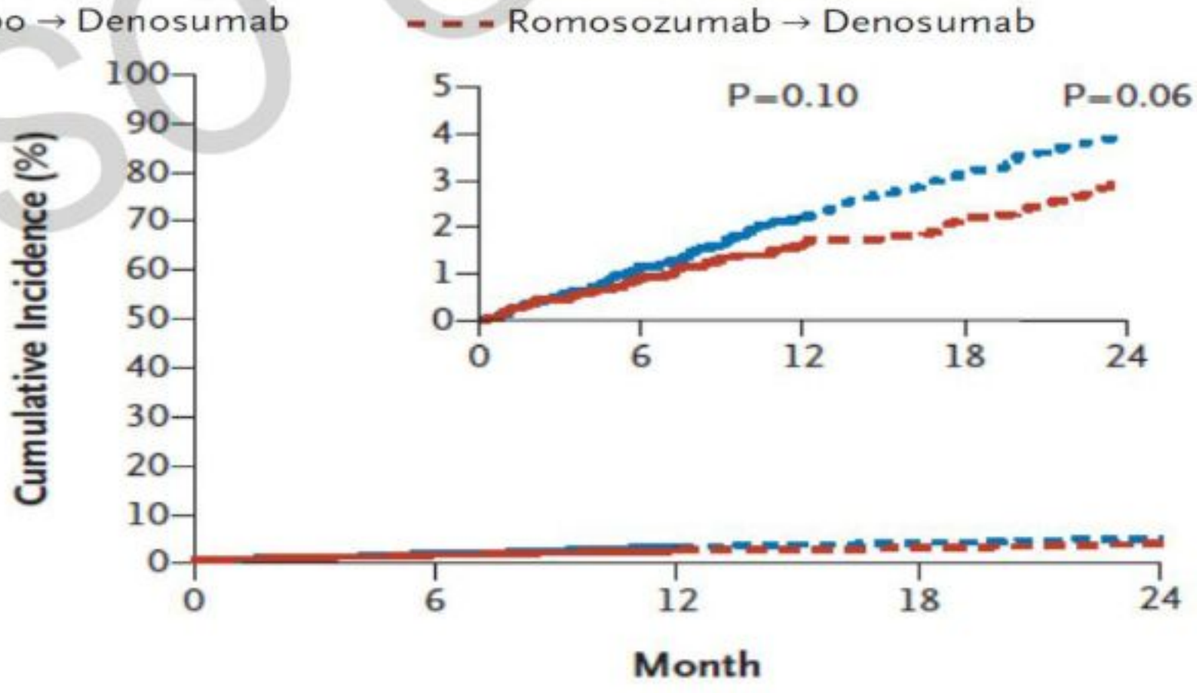
ORIGINAL ARTICLE

Romosozumab Treatment in Postmenopausal Women with Osteoporosis

First Clinical fracture



First Non vertebral fracture



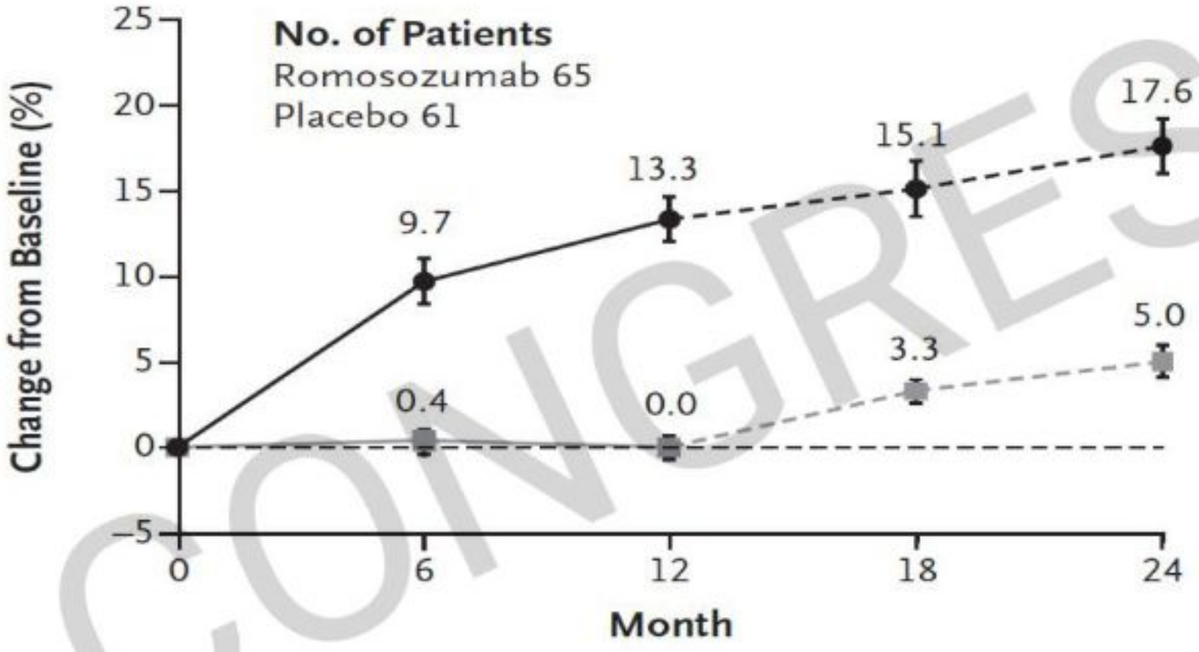
Cosman F et al. N Engl J Med 2016

The NEW ENGLAND JOURNAL of MEDICINE

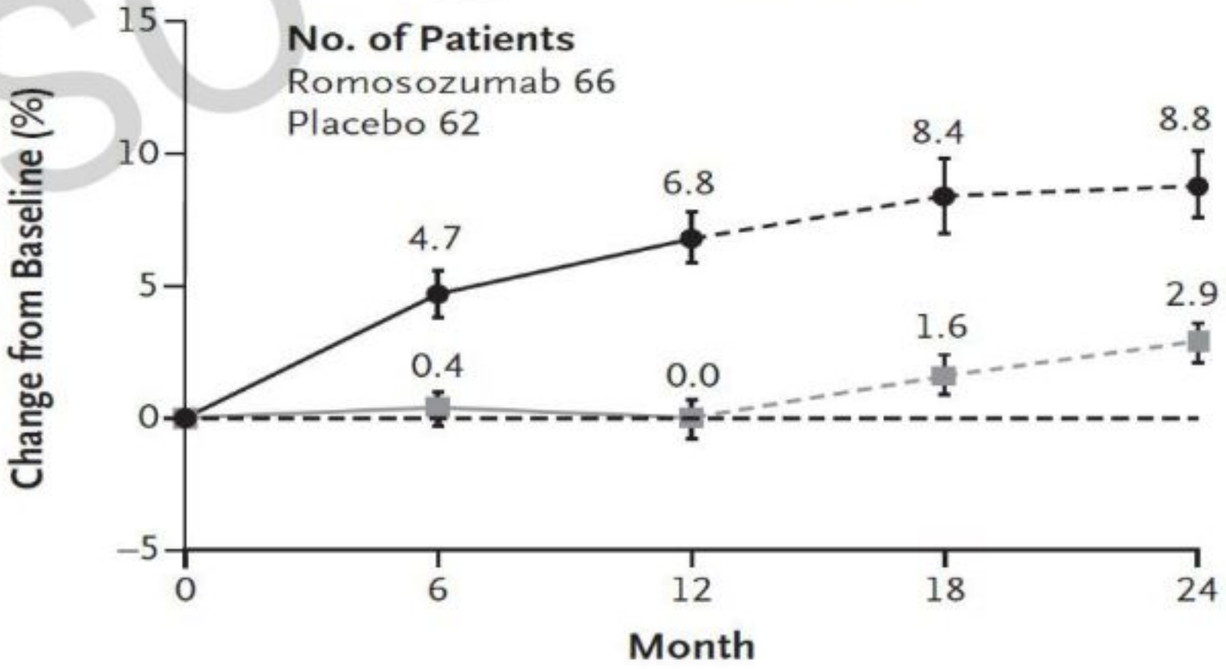
ORIGINAL ARTICLE

Romosozumab Treatment in Postmenopausal Women with Osteoporosis

Change in BMD at lumbar Spine



Change in BMD at Total Hip



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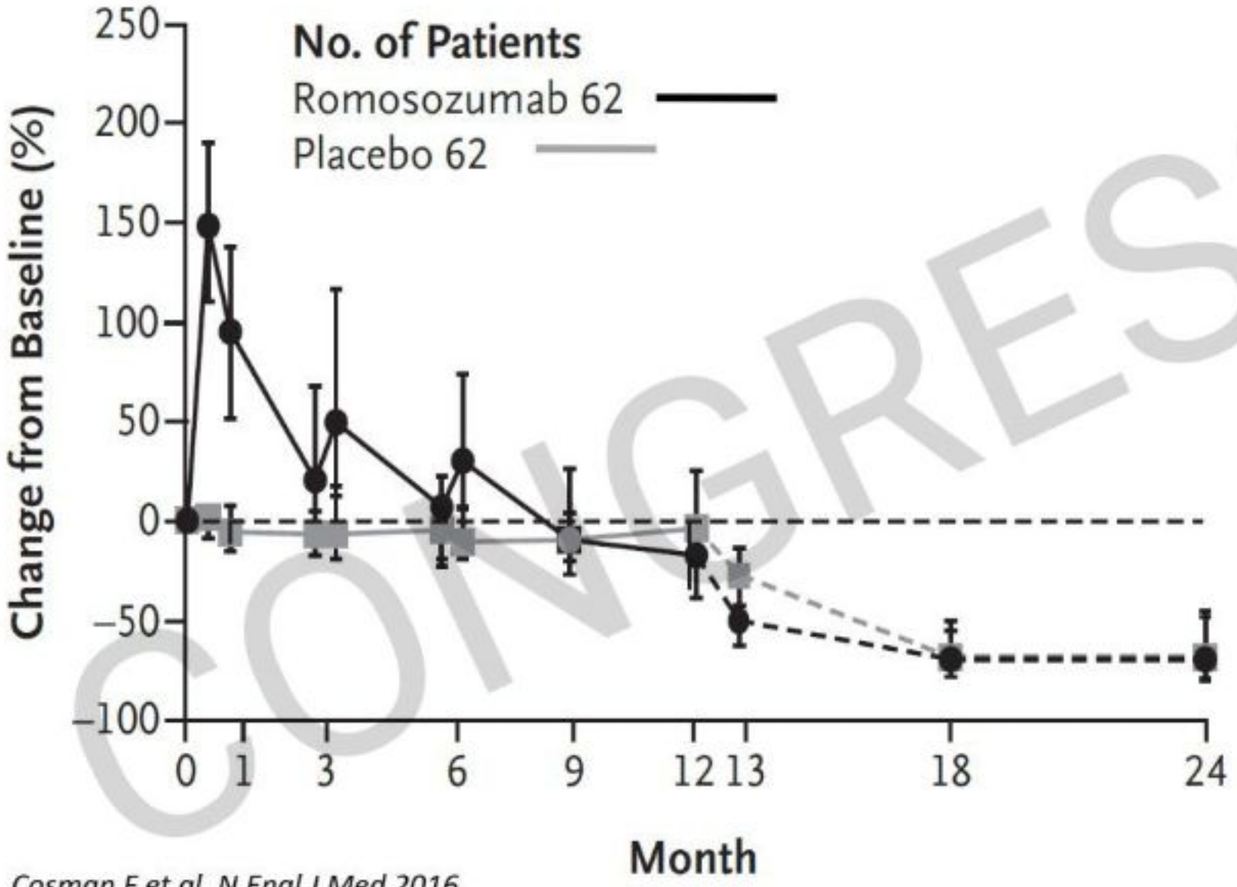
The NEW ENGLAND JOURNAL of MEDICINE

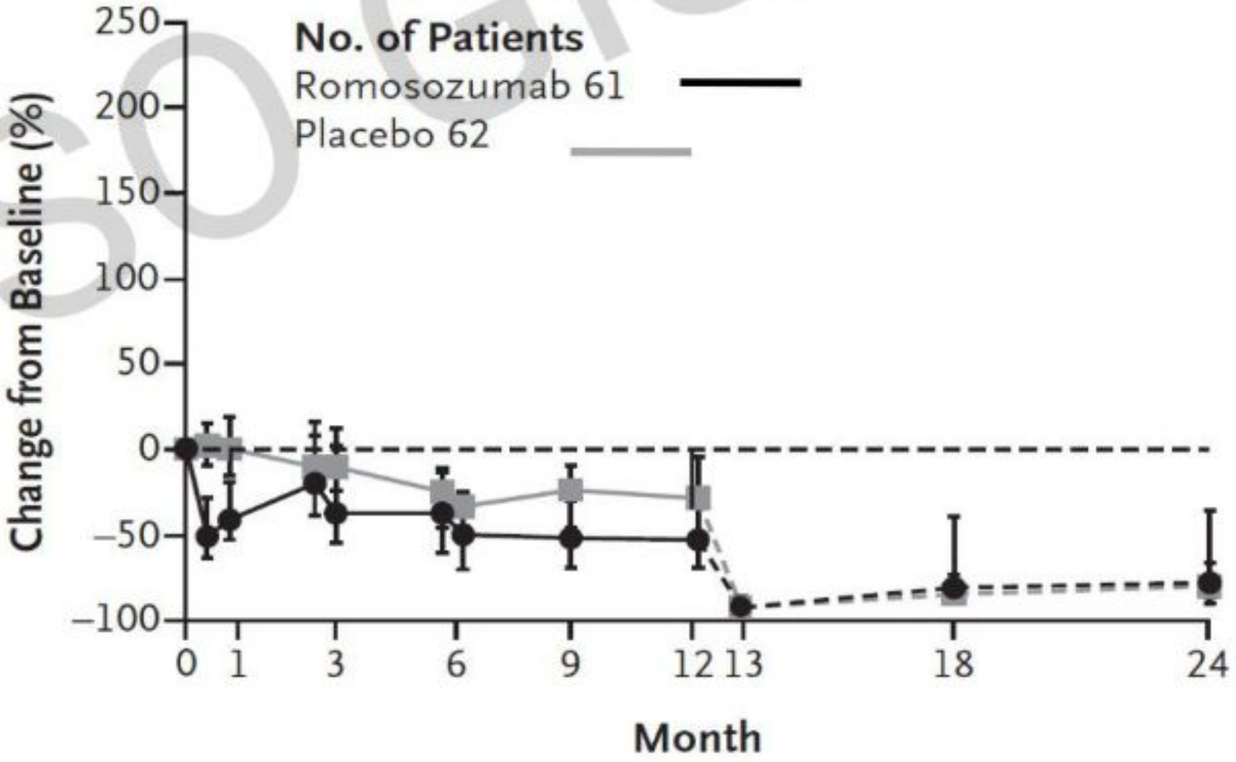
ORIGINAL ARTICLE

Romosozumab Treatment in Postmenopausal Women with Osteoporosis

Change in P1NP level



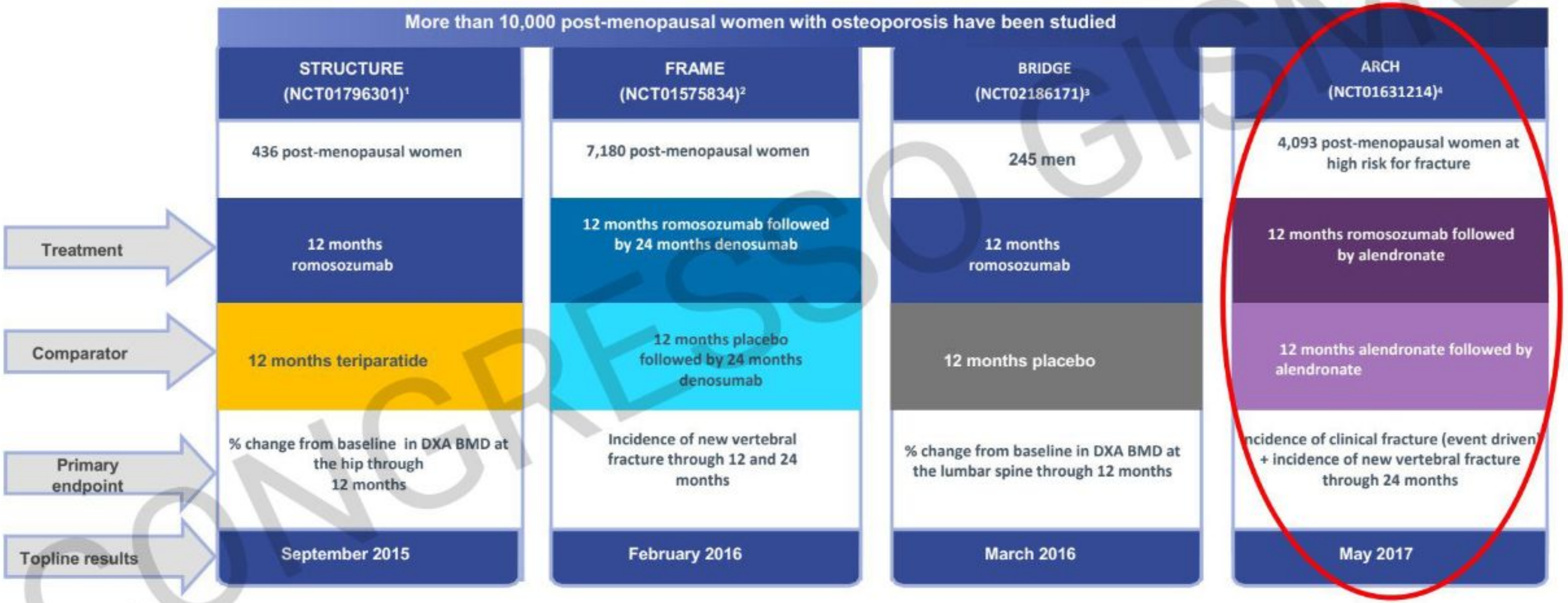
Change in β-CTX level



Cosman F et al. N Engl J Med 2016

PRIMA ANABOLIZZANTE

Overview of the Romosozumab Phase 3 Clinical Programme



PRIMA ANABOLIZZANTE

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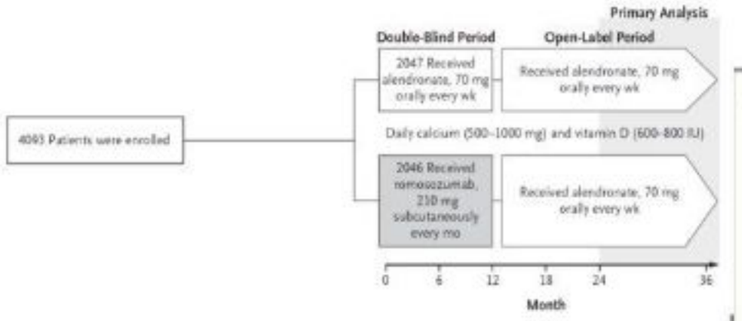
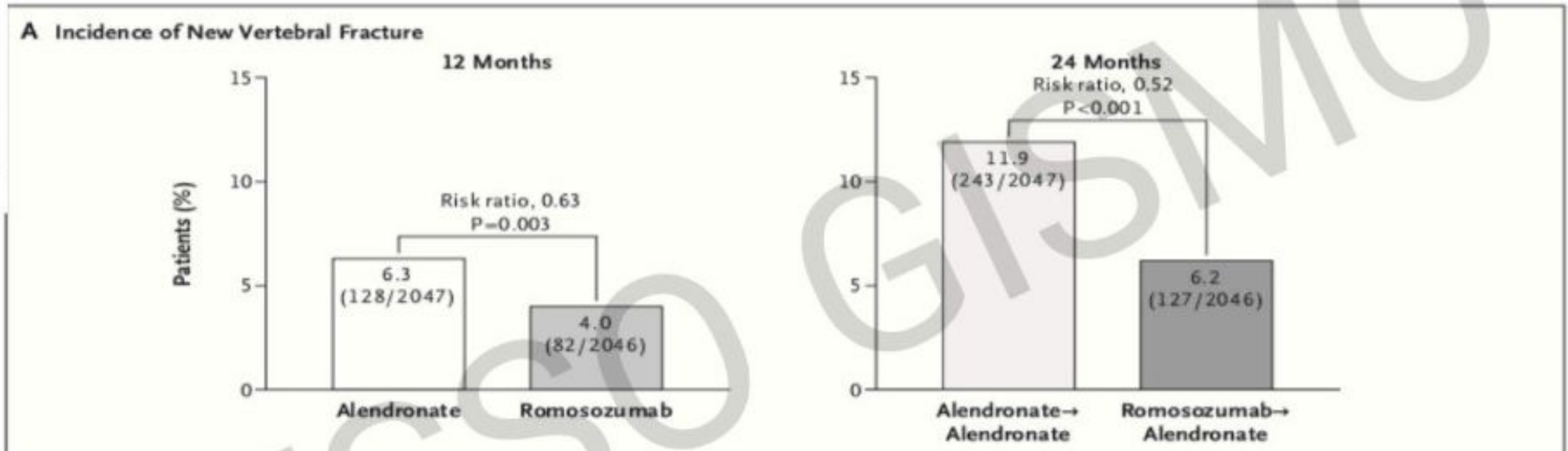
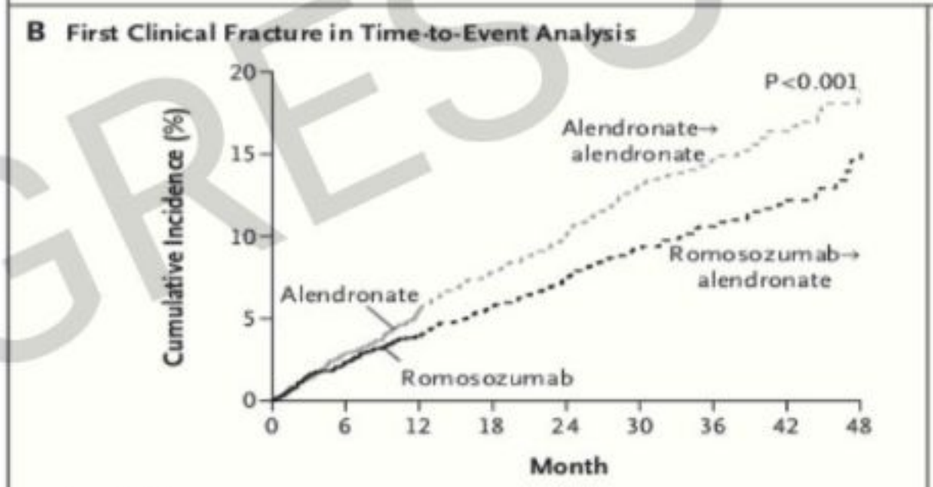
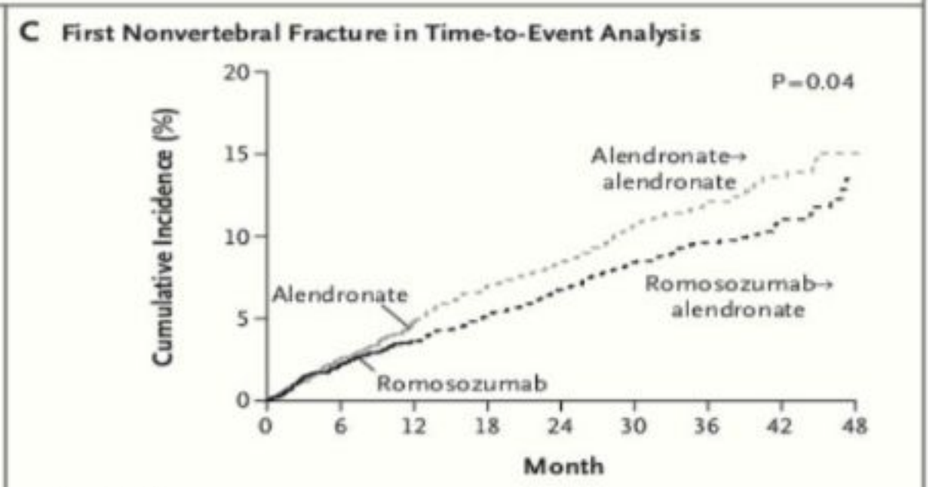






No. at Risk										
Alendronate	2047	1868	1743							
Romosozumab	2046	1865	1770							
Alendronate→ alendronate				1645	1564	1066	680	325	108	
Romosozumab→ alendronate				1683	1615	1103	705	347	109	



No. at Risk										
Alendronate	2047	1873	1755							
Romosozumab	2046	1867	1776							
Alendronate→ alendronate				1661	1590	1097	697	330	110	
Romosozumab→ alendronate				1693	1627	1114	714	350	109	

ORIGINAL ARTICLE

Romosozumab Followed by Antiresorptive Treatment Increases the Probability of Achieving Bone Mineral Density Treatment Goals

Felicia Cosman,[1] Cesar Libanati,[2] Cynthia Deignan,[3] Zhigang Yu,[3] Zhenxun Wang,[3] Serge Ferrari,[4] Jens-Erik Beck Jensen,[5] Pilar Peris,[6] Francesco Bertoldo,[7] Eric Lespessailles,[8] Eric Hesse,[9] and Steven R Cummings[10]

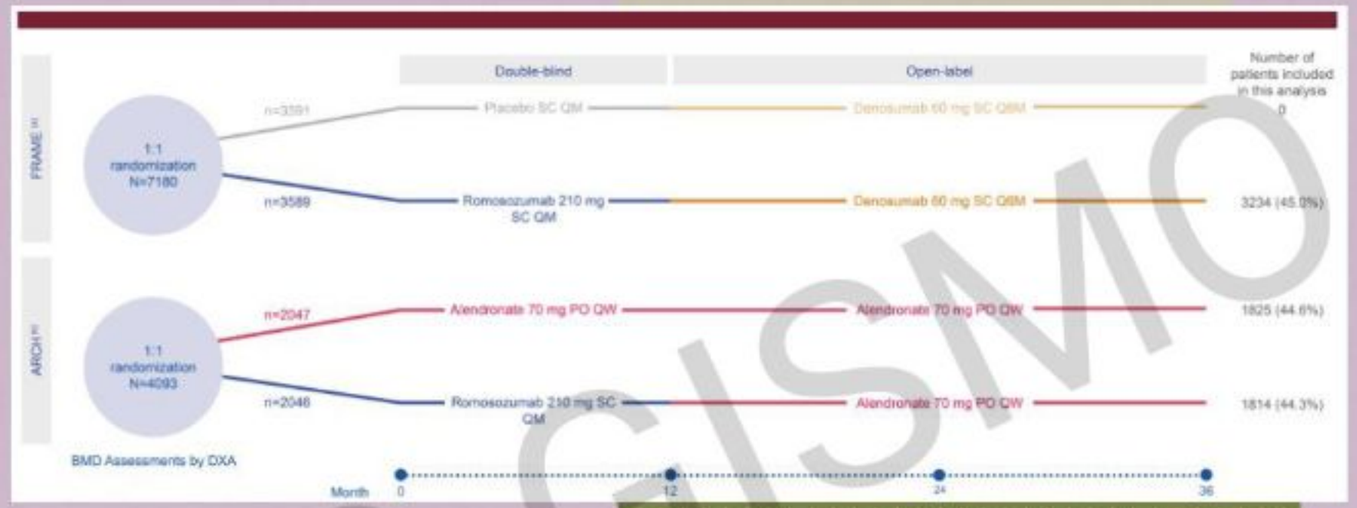


Table 2. Probabilities of Achieving a *T*-Score > −2.5 in the Total Hip and Lumbar Spine at Years 3 and 1 in Patients With Baseline *T*-Scores Equal to −2.7, −3.0, and −3.5

Treatment	Baseline *T*-score	Site of BMD measurement at year 3	Probability of *T*-score > −2.5 at 3 years, % (95% CI)	Site of BMD measurement at year 1	Probability of *T*-score > −2.5 at 1 year, % (95% CI)
ALN	−2.7	Total hip ($n = 735$)[a]	53.3 (46.8, 59.7)	Total hip	38.4 (34.1, 42.8)
($N = 1825$)	−3.0		9.3 (6.2, 13.8)	($n = 1778$)[c]	3.5 (2.4, 5.1)
	−3.5		0.2 (0.1, 0.5)		0.0 (0.0, 0.1)
	−2.7	Lumbar spine	82.6 (76.2, 87.5)	Lumbar spine	63.9 (58.8, 68.7)
	−3.0	($n = 719$)[b]	54.8 (47.6, 61.7)	($n = 1714$)[d]	25.1 (21.0, 29.6)
	−3.5		11.0 (7.5, 15.9)		2.0 (1.3, 3.3)
Romo/ALN	−2.7	Total hip ($n = 748$)[a]	72.8 (67.7, 77.4)	Total hip	70.7 (66.8, 74.4)
($N = 1814$)	−3.0		38.0 (32.6, 43.8)	($n = 1773$)[c]	21.5 (18.0, 25.5)
	−3.5		5.0 (3.1, 8.0)		0.7 (0.4, 1.2)
	−2.7	Lumbar spine	91.5 (87.8, 94.2)	Lumbar spine	95.3 (93.5, 96.7)
	−3.0	($n = 730$)[b]	80.6 (75.5, 84.9)	($n = 1715$)[d]	85.0 (81.6, 87.8)
	−3.5		45.9 (40.0, 51.8)		39.9 (35.5, 44.4)
Romo/Dmab	−2.7	Total hip	90.0 (88.3, 91.5)	Total hip	77.6 (75.2, 79.8)
($N = 3234$)	−3.0	($n = 2837$)[a]	61.0 (57.5, 64.5)	($n = 3186$)[c]	23.8 (20.6, 27.3)
	−3.5		7.8 (5.6, 10.9)		0.6 (0.4, 0.9)
	−2.7	Lumbar spine	97.3 (96.4, 98.0)	Lumbar spine	96.5 (95.5, 97.4)
	−3.0	($n = 2791$)[b]	92.5 (90.9, 93.8)	($n = 3140$)[d]	85.8 (83.5, 87.9)
	−3.5		67.2 (64.2, 70.1)		32.3 (28.9, 35.8)

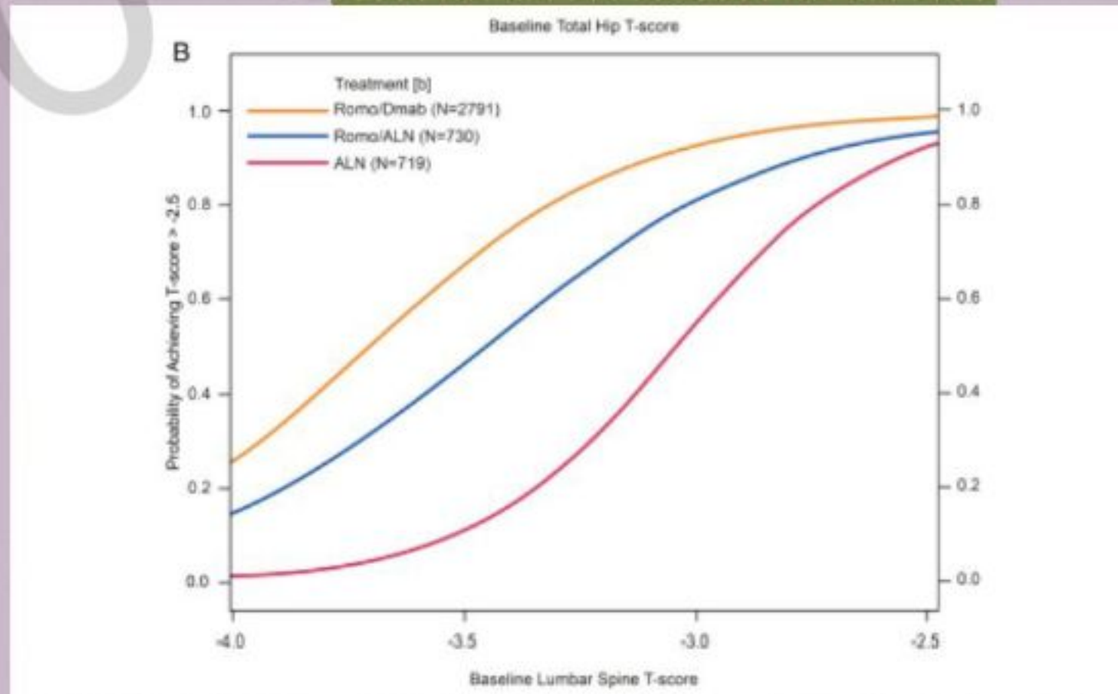


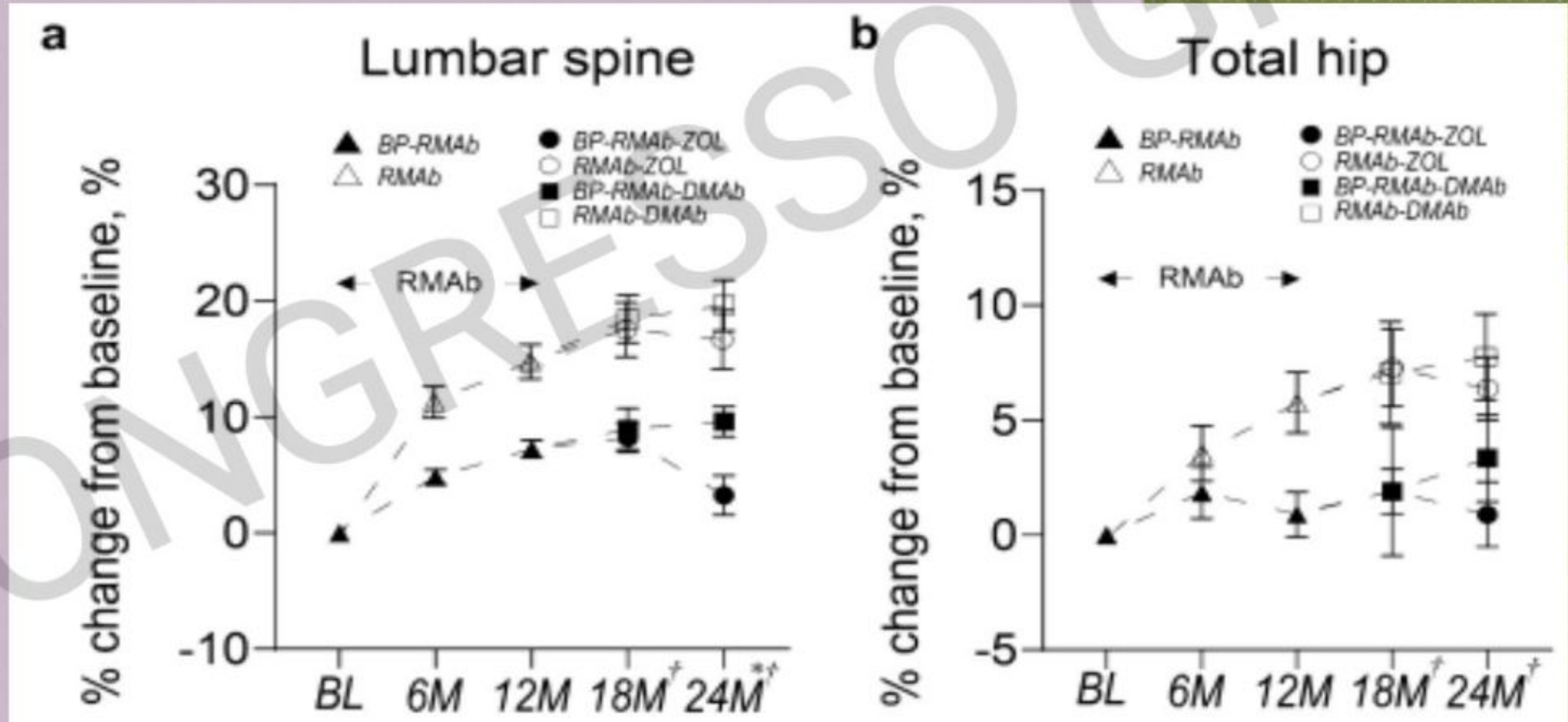
Fig. 2. Probabilities of achieving a *T*-score > −2.5 in the total hip (*A*) and lumbar spine (*B*) after 3 years of treatment with Romo/Dmab, Romo/ALN, or ALN only. (*A*) Number of patients with evaluable total hip bone mineral density (BMD) value at baseline and month 36. (*B*) Number of patients with evaluable lumbar spine BMD value at baseline and month 36. ALN — alendronate; Dmab — denosumab; Romo — romosozumab.

Calcified Tissue International (2023) 112:683–690
https://doi.org/10.1007/s00223-023-01079-y

ORIGINAL RESEARCH

Comparison of the Efficacy of Zoledronate Acid or Denosumab After Switching from Romosozumab in Japanese Postmenopausal Patients

Tetsuro Oue[1] · Tomohiro Shimizu[1] · Tsuyoshi Asano[2] · Shun Shimodan[3] · Hotaka Ishizu[1] · Kosuke Arita[1] · Norimasa Iwasaki[1]



POSSIAMO SOMMINISTRARE ROMOSOZUMAB PRIMA DI TERIPARATIDE?

JBMR Plus, 2024, **8**, ziae131
https://doi.org/10.1093/jbmrpl/ziae131
Advance access publication: November 23, 2024
Research Article

ASBMR The American Society for Bone and Mineral Research

OXFORD

Therapy with transitions from one bone-forming agent to another: a retrospective cohort study on teriparatide and romosozumab

Tomonori Kobayakawa[1], Yasuhide Kanayama[2], Yuji Hirano[3], Toshitaka Yukishima[1], Yukio Nakamura[4,*]

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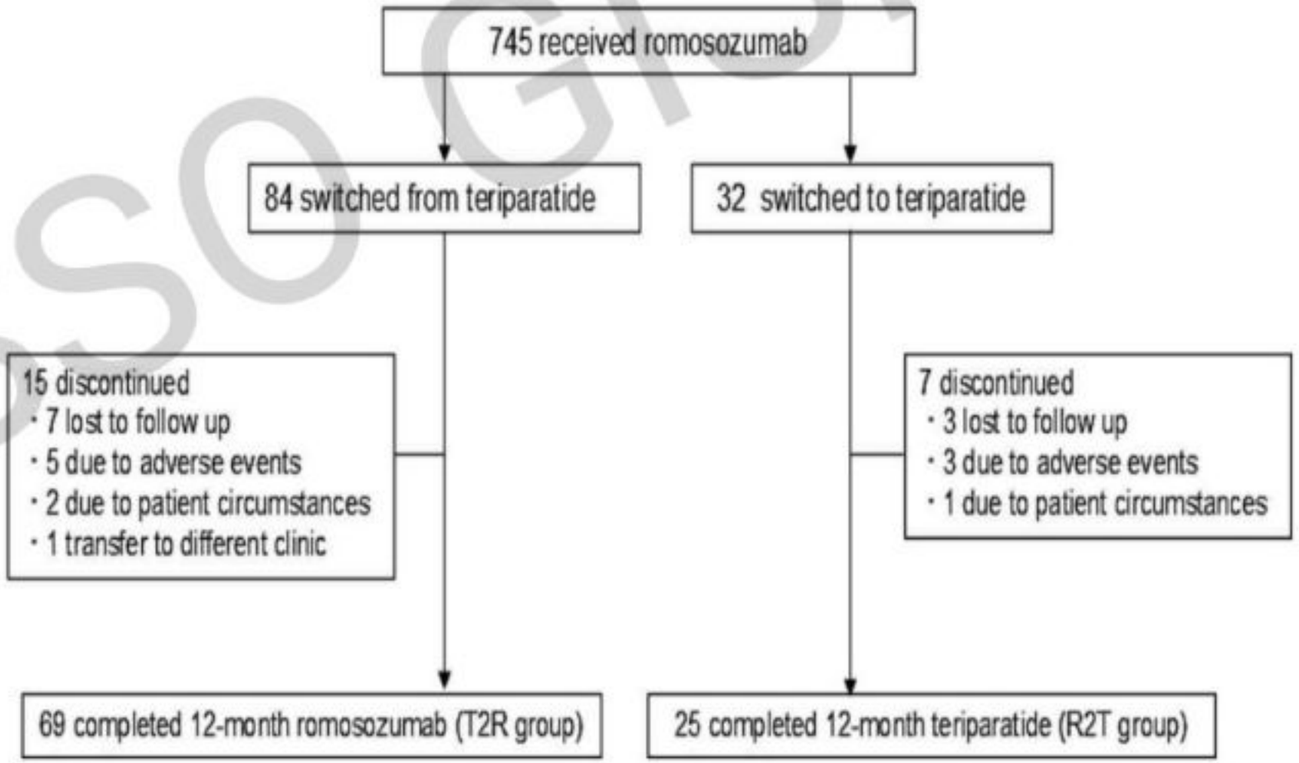
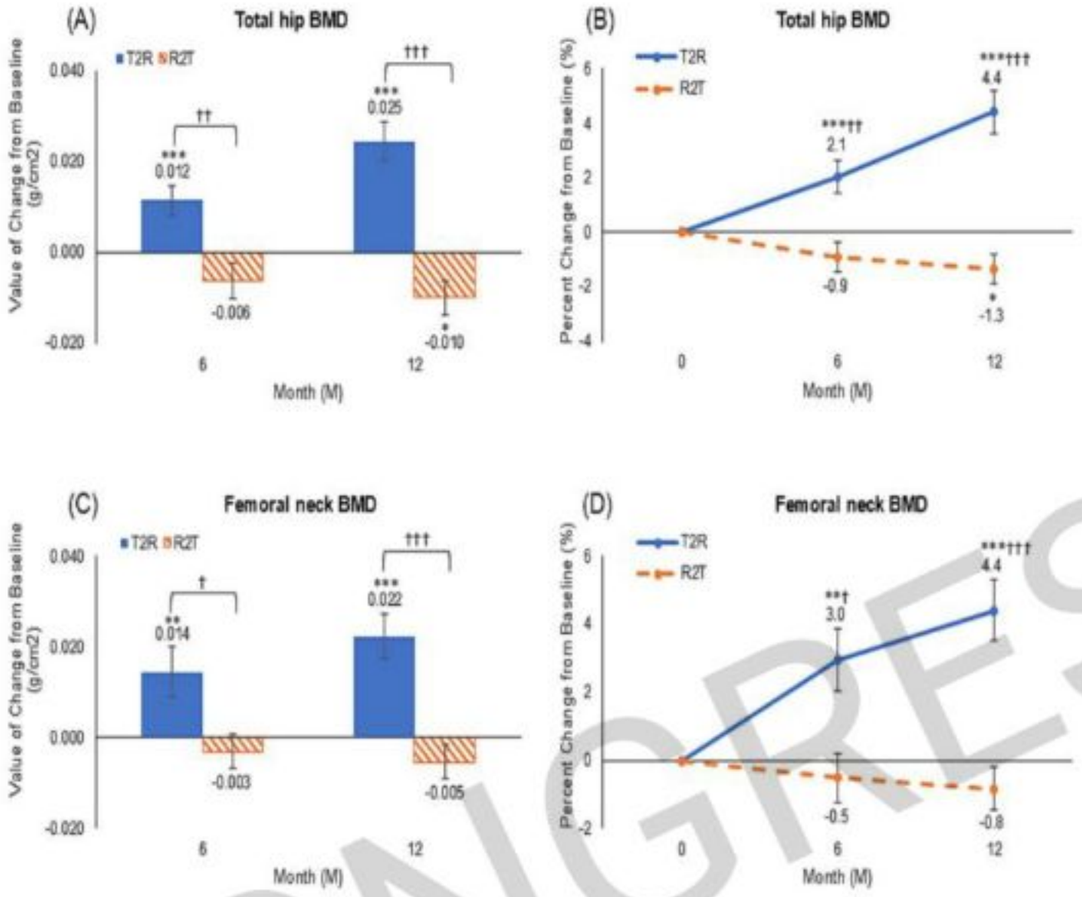
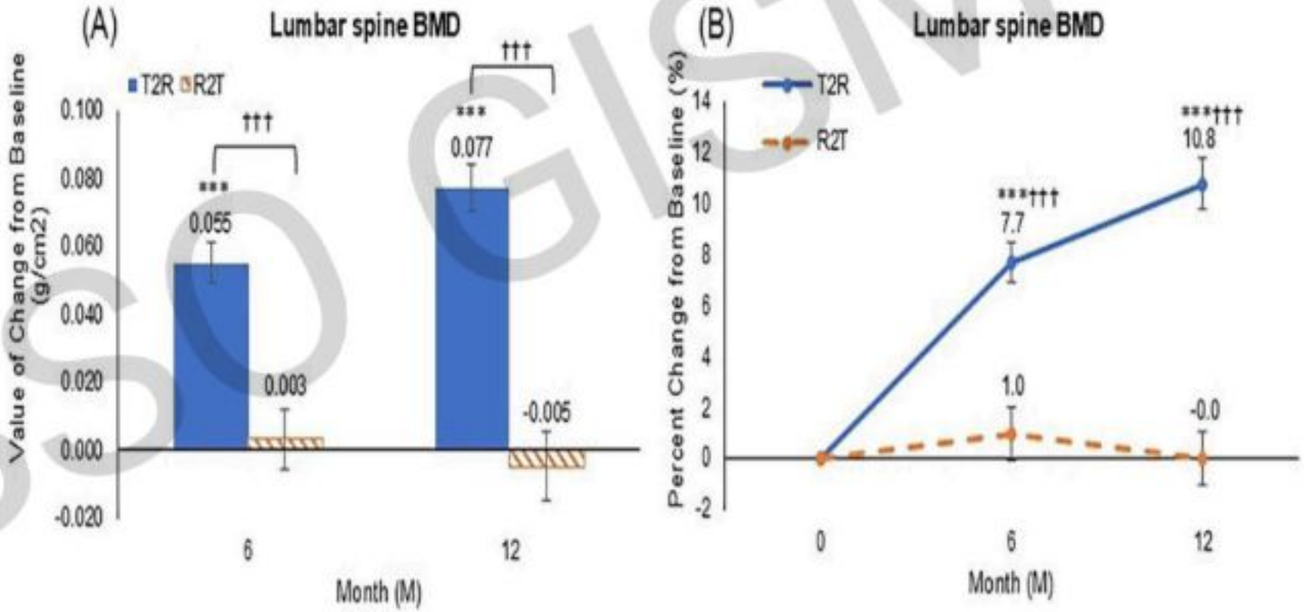






Nei pazienti già trattati con romosozumab, la somministrazione successiva di teriparatide non determina alcun incremento nella BMD, che anzi peggiora leggermente.

TERIPARATIDE PRIMA DI ROMOSOZUMAB

Bone 193 (2025) 117389

Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Full Length Article

Impact of prior teriparatide treatment on the effectiveness of romosozumab in patients with postmenopausal osteoporosis: A case-control study

Kosuke Ebina [a,b,*], Tomonori Kobayakawa [c], Yuki Etani [b], Takaaki Noguchi [a], Masafumi Kashii [d], Gensuke Okamura [d], Yoshio Nagayama [e], Hideki Tsuboi [f], Akira Miyama [g], Makoto Hirao [d], Yuji Fukuda [a], Takuya Kurihara [a], Atsushi Sugimoto [a], Ken Nakata [b], Seiji Okada [a]

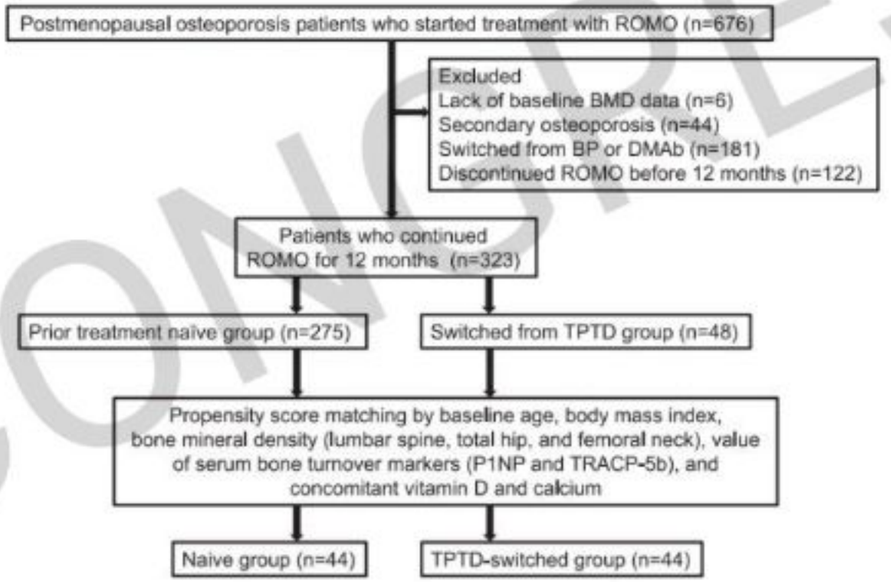


Table 1
Initial clinical characteristics of patients following propensity score matching.

Variable	Naive group (n = 44)	TPTD-switched group (n = 44)	*P* value
Age (years)	79.5 ± 7.6	76.6 ± 7.3	0.068
Body Mass Index (kg/m^2)	20.11 ± 3.0	19.7 ± 2.7	0.54
Prior vertebral fracture (%)	34.1	56.8	0.053
Prior nonvertebral fracture (%)	22.7	25.0	1.0
Lumbar spine BMD (g/cm^2)	0.66 ± 0.10	0.67 ± 0.12	0.53
Lumbar spine BMD (T-score)	−3.6 ± 0.8	−3.5 ± 0.9	0.67
Total hip BMD (g/cm^2)	0.59 ± 0.10	0.59 ± 0.10	0.84
Total hip BMD (T-score)	−2.8 ± 0.8	−2.8 ± 0.8	0.93
Femoral neck BMD (g/cm^2)	0.55 ± 0.10	0.55 ± 0.10	0.92
Femoral neck BMD (T-score)	−3.4 ± 0.8	−3.3 ± 0.9	0.49
Corrected serum calcium (mg/dl)	9.1 ± 0.4	9.4 ± 0.4	0.005
eGFR (ml/min/1.73 m^2)	71.0 ± 23.7	72.3 ± 17.9	0.78
PINP (μg/l)	87.4 ± 47.5	90.7 ± 57.5	0.77
TRACP-5b (mU/dl)	569.1 ± 217.9	587.6 ± 314.6	0.75
25(OH)D (ng/ml)	16.4 ± 6.2	18.4 ± 10.6	0.28
Prior osteoporosis treatment			
Daily TPTD (20 μg) (%)	N.A.	65.9	N.A.
Weekly TPTD (56.5 μg) (%)	N.A.	22.7	N.A.
Twice-weekly TPTD (28.2 μg) (%)	N.A.	11.4	N.A.
Treatment duration (months)	N.A.	14.0 ± 6.7	N.A.
Combined vitamin D (%)	72.7	75.0	1.0
Combined calcium (%)	38.6	52.3	0.28

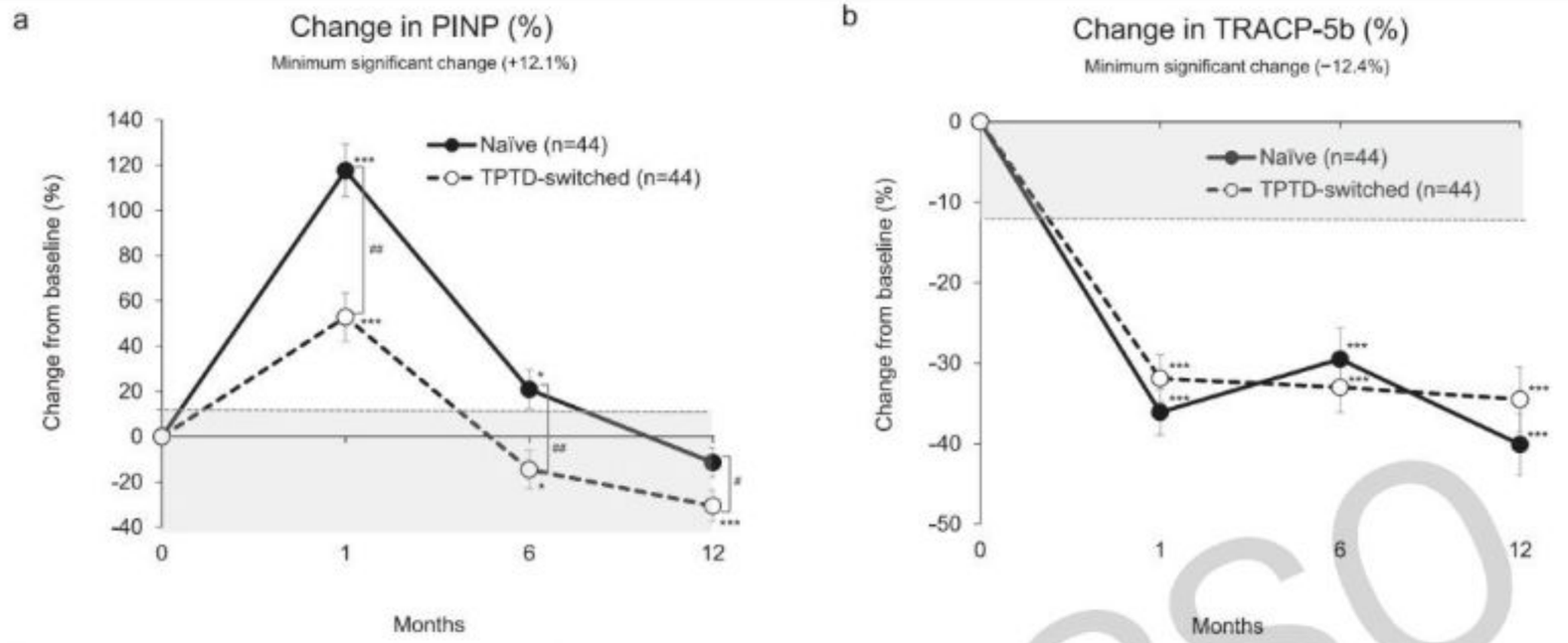
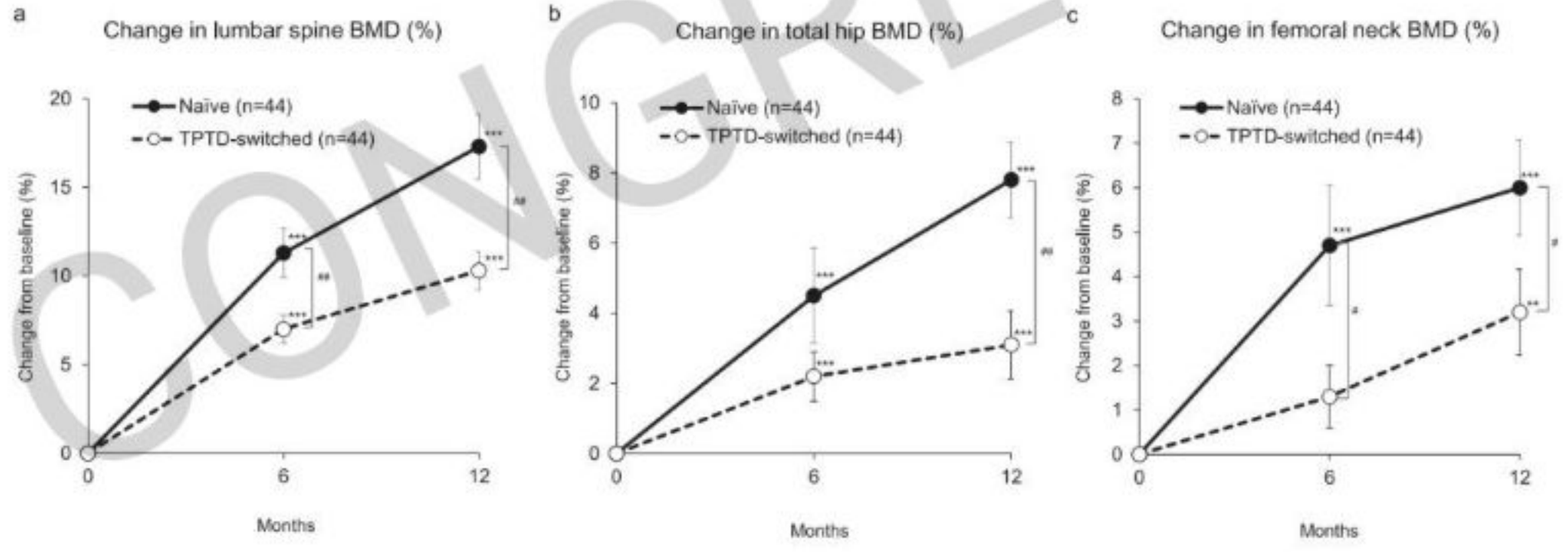


Fig. 2. Percentage change of serum PINP level (a) and TRACP-5b level (b).
PINP, N-terminal type I procollagen propeptide; TRACP-5b, isoform 5b of tartrate-resistant acid phosphatase; TPTD, teriparatide.
Bars indicate mean ± standard error. $^{*}P < 0.05$, $^{***}P < 0.001$; change within each treatment group compared with baseline. $^{\#}P < 0.05$, $^{\#\#}P < 0.01$; difference between the two indicated groups.



Il P1NP aumenta significativamente nel gruppo naïve rispetto a quello già trattato con teriparatide.

All'opposto, la riduzione di TRACP-5b è sovrapponibile.

Quanto al BMD, l'aumento è nettamente superiore nel gruppo naïve, per cui si può supporre che **la precedente terapia con teriparatide riduca parzialmente l'effetto benefico del romosozumab**, verosimilmente per una sorta di «esaurimento» della finestra anabolica.

E’ POSSIBILE RI-SOMMINISTRARE IL ROMOSOZUMAB?

JOURNAL ARTICLE ACCEPTED MANUSCRIPT

Verifying the effectiveness of romosozumab re-administration on bone mineral density

Tomonori Kobayakawa, Yukio Nakamura ✉

Journal of Bone and Mineral Research, zjae196, https://doi.org/10.1093/jbmr/zjae196

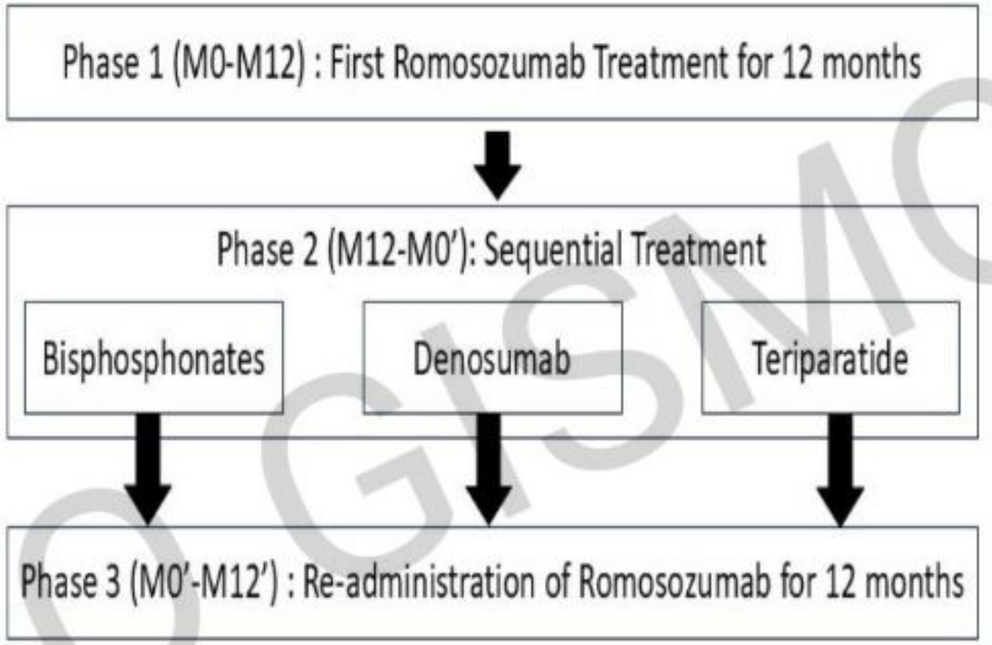
Published: 06 December 2024 **Article history** ▾

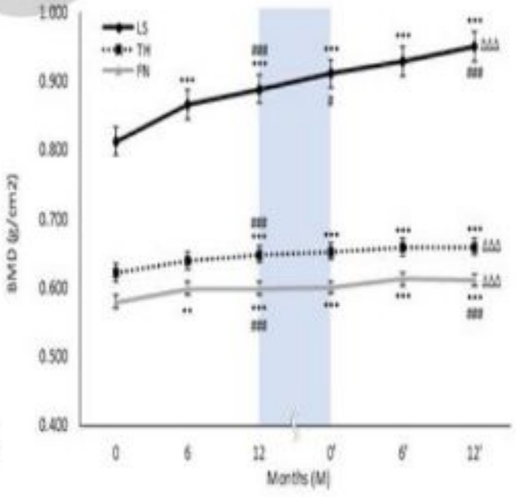
IL **BMD è incrementato significativamente durante la fase di risomministrazione** (P<0,001), con un netto aumento della percentuale di pazienti che hanno raggiunto un T-score >-2,5 sia a livello lombare che femorale rispetto alla precedente terapia, ivi compreso il primo ciclo di romosozumab.

I **marcatori di formazione ossea sono aumentati significativamente (P<0,001) durante la risomministrazione**, mentre **i marcatori di riassorbimento osseo non hanno mostrato cambiamenti significativi (P=0,408).**

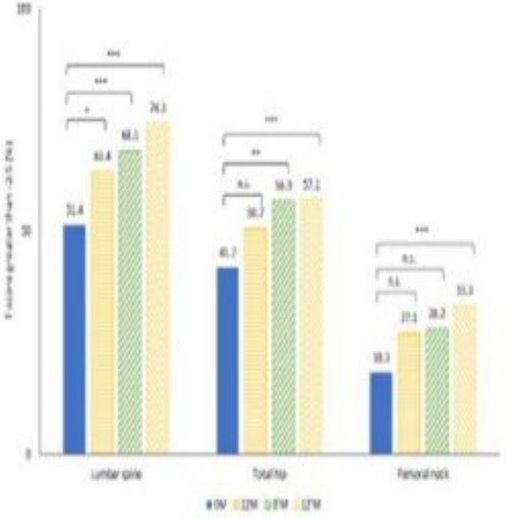
La densità minerale ossea è aumentata significativamente in tutti i siti per i pazienti che hanno ricevuto **bisfosfonati** come terapia sequenziale (P<0,05). Dopo la terapia con **denosumab**, sono stati osservati aumenti significativi della densità minerale ossea solo nella colonna lombare (P<0,01).

Dopo la terapia con **teriparatide**, la densità minerale ossea è temporaneamente diminuita durante il periodo sequenziale ma è ri-aumentata significativamente dopo la risomministrazione di romosozumab, soprattutto nella colonna lombare e nel collo del femore (entrambi P<0,001).





Changes of Bone Mineral Density throughout the observation



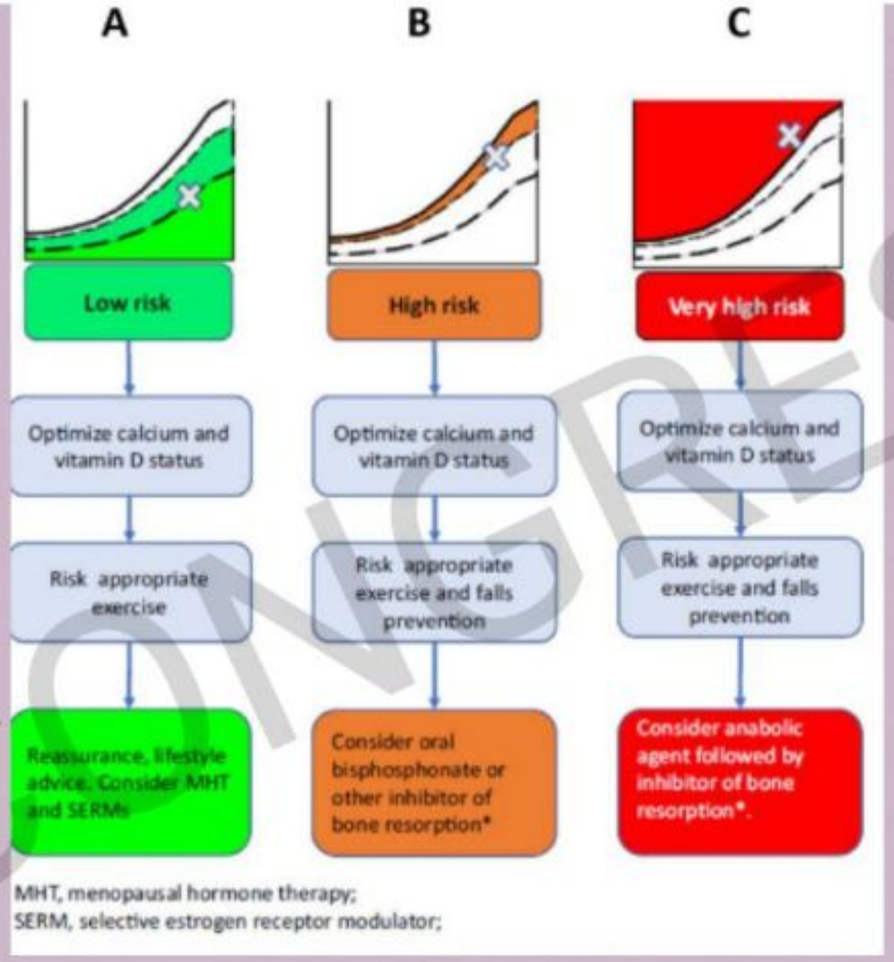
Proportion of patients with T-score greater than -2.5

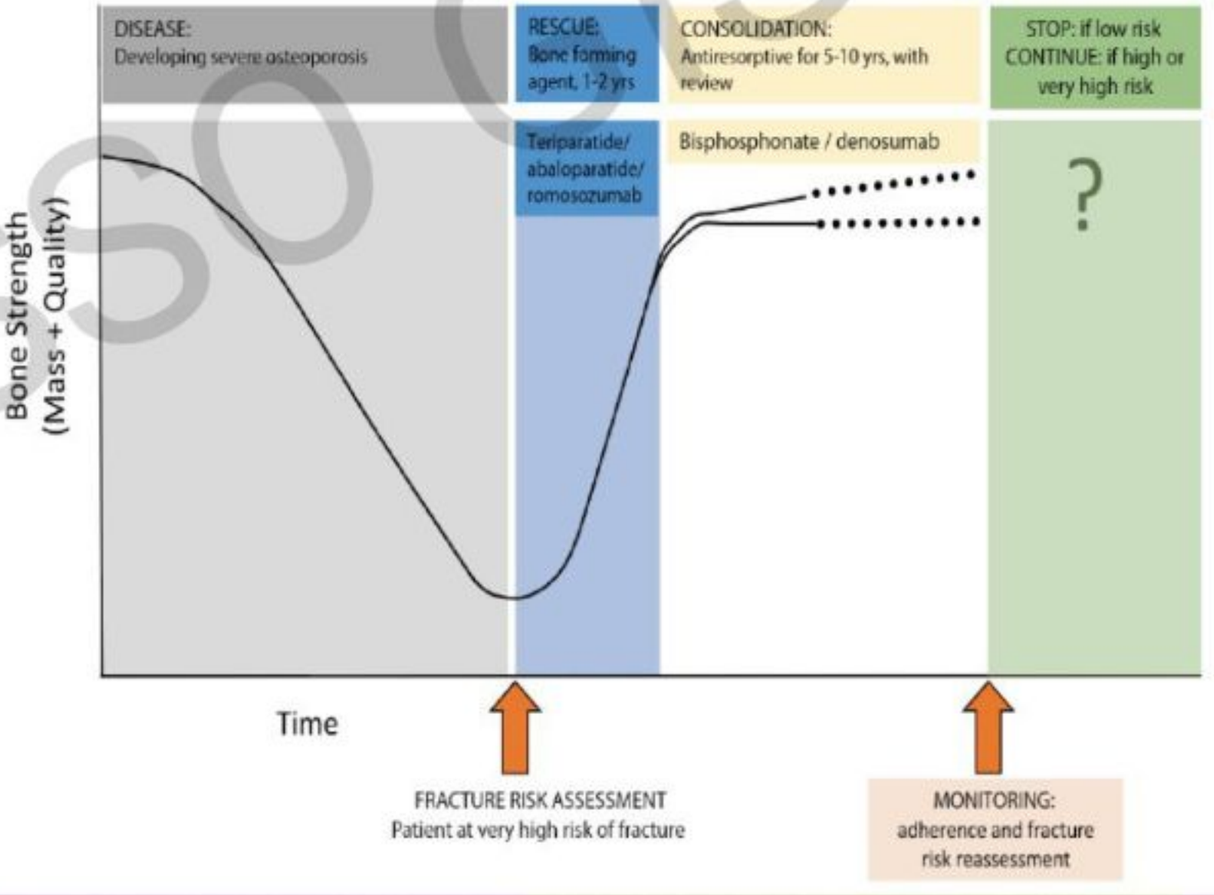
REVIEW ARTICLE

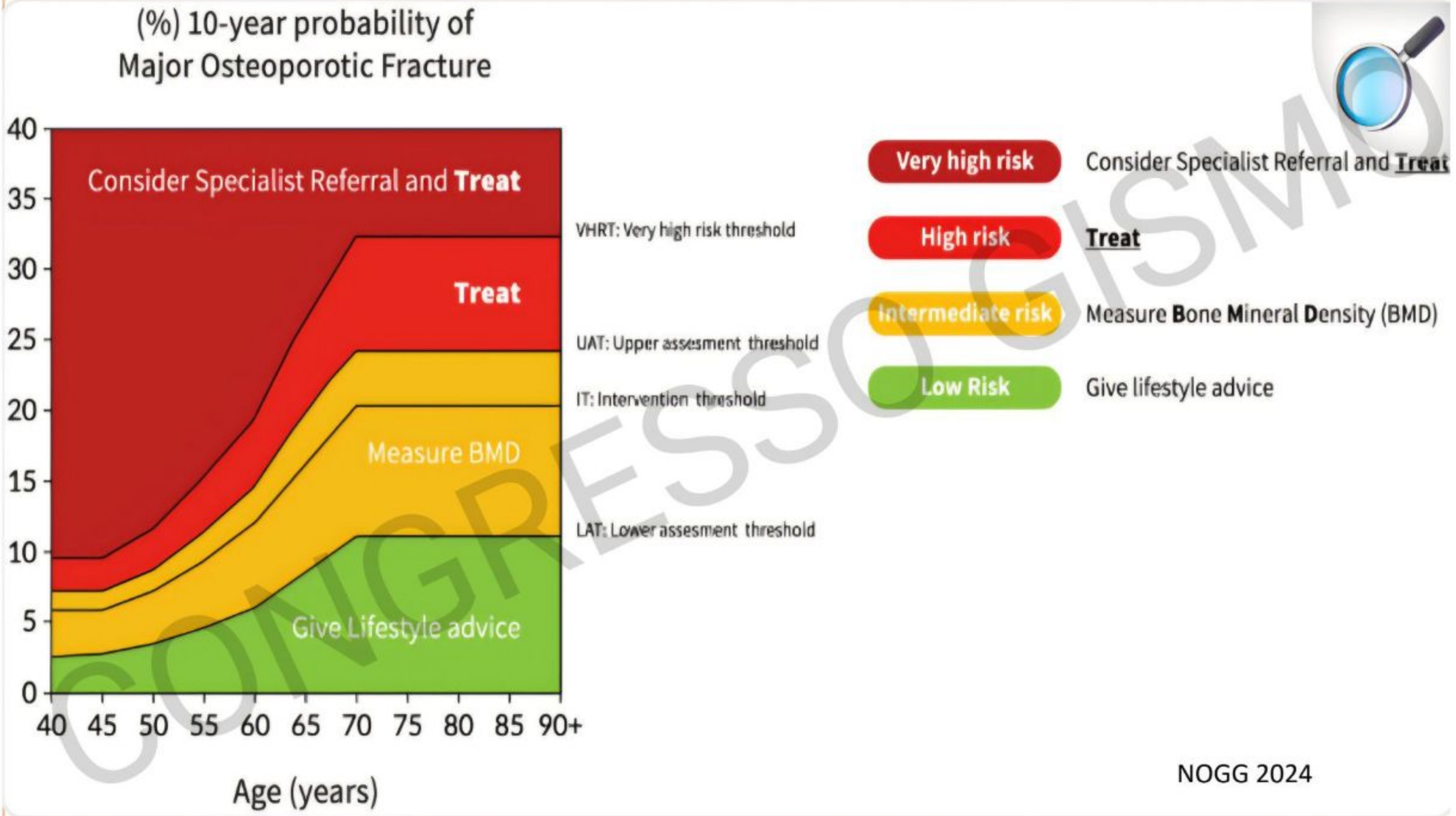
Management of patients at very high risk of osteoporotic fractures through sequential treatments

Elizabeth M. Curtis[1] · Jean-Yves Reginster[2,3] · Nasser Al-Daghri[4] · Emmanuel Biver[5] · Maria Luisa Brandi[6] · Etienne Cavalier[7] · Peyman Hadji[8,9] · Philippe Halbout[10] · Nicholas C. Harvey[1,11] · Mickaël Hiligsmann[12] · M. Kassim Javaid[13] · John A. Kanis[14,15] · Jean-Marc Kaufman[16] · Olivier Lamy[17] · Radmila Matijevic[18,19] · Adolfo Diez Perez[20] · Régis Pierre Radermecker[21] · Mário Miguel Rosa[22] · Thierry Thomas[23,24] · Friederike Thomasius[8] · Mila Vlaskovska[25] · René Rizzoli[5] · Cyrus Cooper[1,11,26]

Received: 11 February 2022 / Accepted: 18 February 2022

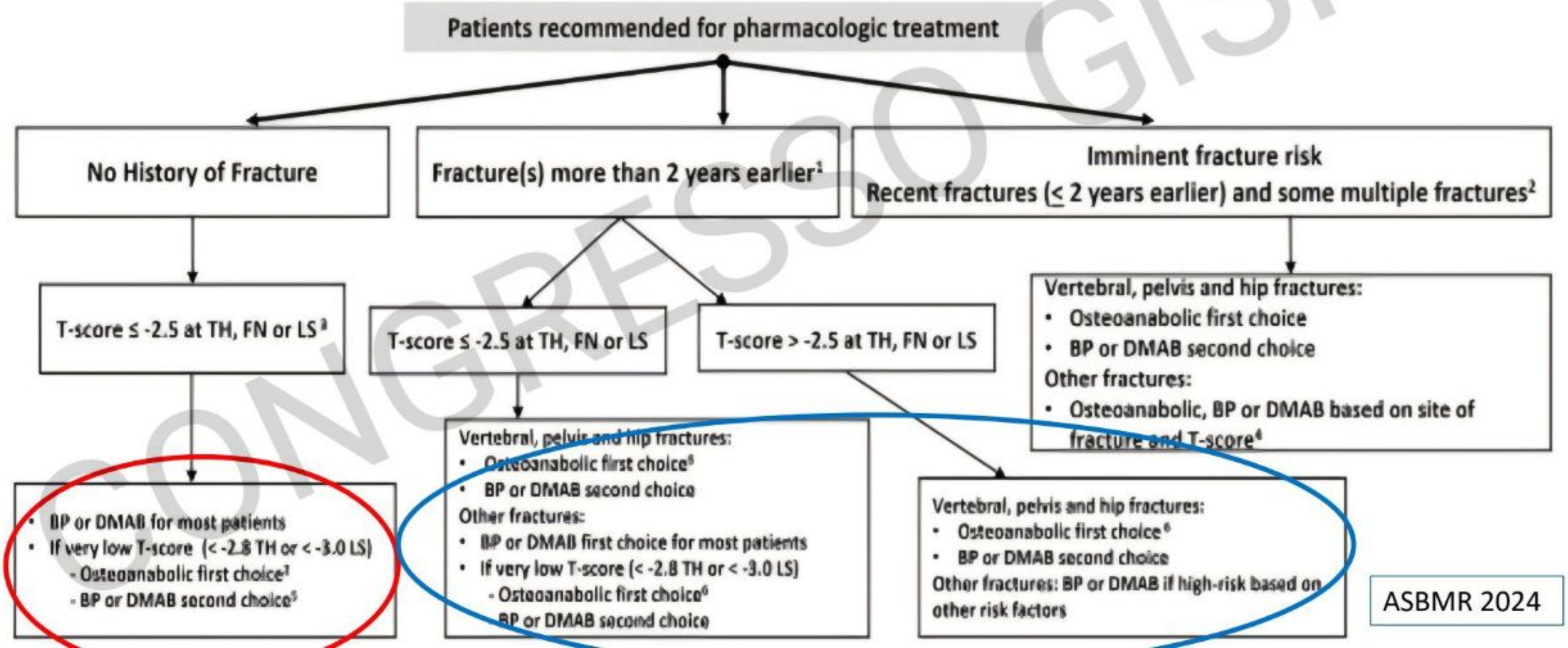






Treatment Targets:

- For imminent risk patients, maximal rapid reduction in fracture risk
- For patients with T-score ≤ -2.5, minimal target is to increase T-score to > -2.5, higher for patients with fracture histo other major risk factors
- For patients with T-score > -2.5, increase TH T-score by 0.2 (3%) and LS by 0.5 (6%)



ASBMR 2024

CONCLUSIONI

1) L'avvento degli Anabolizzanti ha consentito di pianificare una vera terapia sequenziale

2) L'utilizzo degli Anabolizzanti prima degli Antiriassorbitori consente piena espressione della efficacia di entrambi (vale soprattutto per DMAB e TER)

3) Romosozumab ha una potenza superiore che si esprime anche dopo gli Antiriassorbitori (anche dopo DMAB seppur in modo più attenuato) nochè dopo TER (mentre il passaggio ROMO-TER non è efficace), in virtù della sua azione sia sul Remodeling che sul Modeling Questo anche se si valuta l'impatto globale della sequenza terapeutica e non solo dopo lo switch (cosa che andrebbe sempre fatta per valutare l'efficacia della terapia sequenziale)

4) L'utilizzo di Romosozumab, in sequenza o non, consente ad una percentuale di pazienti superiore (il doppio) di raggiungere il Target densitometrico

5) Pertanto in un' ottica di rapporto costo/beneficio , nei pazienti ad Alto Rischio (da 20% a 30%), si potrebbe proporre una sequenza TER-ROMO-DMAB o TER-ROMO-BF ed in quelli ad Altissimo Rischio (>30%) ROMO-DMAB-ROMO

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
1.3.1 switching treatment to anti-resorptive drugs vs switching to placebo									
Black 2005	4.9	4.2	59	-1.7	4.4	60	31.4%	6.60 [5.05, 8.15]	2005
Adami 2008	-1	3.6	143	-4	3.8	158	35.5%	3.00 [2.16, 3.84]	2008
Eastell 2009	-0.2	4.4	90	-2.7	4.4	92	33.1%	2.50 [1.22, 3.78]	2009
Subtotal (95% CI)			**292**			**310**	**100.0%**	**3.96 [1.82, 6.11]**	
Heterogeneity: $Tau^2 = 3.18$; $Chi^2 = 19.18$, df = 2 (P < 0.0001); $I^2 = 90\%$									
Test for overall effect: Z = 3.63 (P = 0.0003)									
1.3.2 switching treatment to anabolic drugs vs continue the anti-resorptive drugs									
Gonnelli 2006	7.1	5.9	27	1.5	4.3	28	100.0%	5.60 [2.86, 8.34]	2006
Subtotal (95% CI)			**27**			**28**	**100.0%**	**5.60 [2.86, 8.34]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 4.01 (P < 0.0001)									
1.3.3 switching treatmentcombination drugs vs continue the anabolic drugs									
Cosman 2009-2	9.2	5.6	39	8.1	5.5	38	38.9%	1.10 [-1.38, 3.58]	2009
Cosman 2009-1	8.4	6	45	4.8	6	45	38.9%	3.60 [1.12, 6.08]	2009
Christian 2013-2	6	5.2	31	2.8	9.3	19	11.5%	3.20 [-1.36, 7.76]	2013
Christian 2013-1	5	6.3	39	2.8	9.3	18	10.7%	2.20 [-2.53, 6.93]	2013
Subtotal (95% CI)			**154**			**120**	**100.0%**	**2.43 [0.89, 3.98]**	
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.08$, df = 3 (P = 0.56); $I^2 = 0\%$									
Test for overall effect: Z = 3.08 (P = 0.002)