



67° CONGRESSO NAZIONALE
SIGGG

LA LONGEVITÀ DECLINATA AL FEMMINILE

Giovanni Adami

Simposio Gruppo YES (Young Epidemiologists SIGGG)

Un caso inter-societario

SIGGG – SIOMMMS

Questione di Fragilità



SOCIETÀ ITALIANA
DI GERONTOLOGIA
E GERIATRIA

Roma, 30 novembre - 3 dicembre 2022
UNIVERSITÀ CATTOLICA DEL SACRO CUORE



Diclosures

- Eli-lilly
- Theramex
- Galapagos
- UCB
- Amgen
- Fresenius-Kabi
- BMS



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Chi trattare?



NOTA 79 AIFA

- Prevenzione secondaria in soggetti con pregresse fratture osteoporotiche
 - *Fratture vertebrali o di femore*

Condizione	Trattamento I scelta ^a	II scelta	III scelta
1-2 fratture ^b	Alendronato (± vit.D), Risedronato, Zoledronato ^d	Denosumab ^e Ibandronato, Raloxifene, Bazedoxifene	
≥ 3 fratture	Teriparatide ^g	Denosumab ^e Zoledronato ^d	Alendronato (± vit.D) Risedronato, Ibandronato
≥ 1 frattura + T-score colonna o femore ^c ≤ -4			
≥ 1 frattura + trattamento > 12 mesi con prednisone o equivalenti ≥ 5 mg/die			
Nuova frattura vertebrale o femorale nonostante trattamento in Nota 79 da almeno 1 anno			

**FX
OSTEOPOROTICA =
TRAUMA MINORE =
CADUTA DALLA
PROPRIA ALTEZZA**

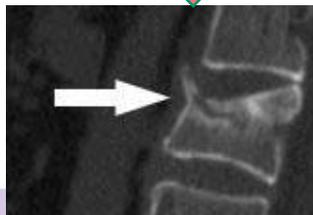
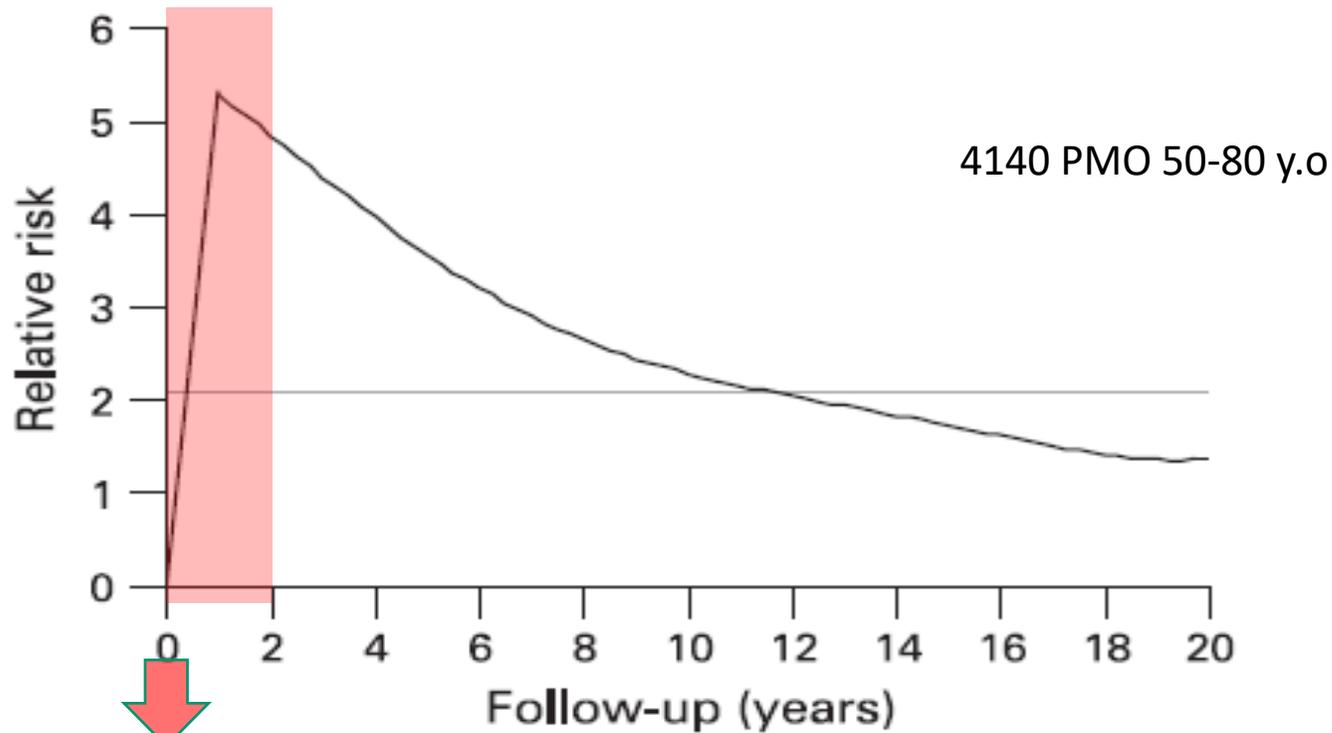


NOTA 79 AIFA 2022 update

<p>Pazienti di sesso femminile con T-score colonna o femore $<-2,5$ ($<-2,0$ se ≥ 2 fratture vertebrali moderate o gravi oppure se frattura femorale nei 2 anni precedenti)</p> <p>+ anamnesi ≥ 1 fratture vertebrali moderate o gravi oppure ≥ 2 fratture vertebrali lievi oppure frattura femorale</p> <p>+ rischio di frattura a 10 anni (determinato con calcolatore validato) elevato $\geq 20\%$</p> <p>+ impossibilità a seguire altri trattamenti efficaci (intolleranza, inefficacia o scadenza del periodo di impiego autorizzato)</p>	<p>Romozosumab^f per max 12 mesi, seguito da farmaci antiriassorbitivi (bisfosfonati o denosumab)</p>		
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Clinical subsequent fractures cluster in time after first fractures





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Quando trattare?
«Fx healing»



Denosumab Treatment in Postmenopausal Women with Osteoporosis Does Not Interfere with Fracture-Healing

Results from the FREEDOM Trial

Silvano Adami, MD, PhD, Cesar Libanati, MD, Steven Boonen, MD, PhD, Steven R. Cummings, MD, Pei-Ran Ho, MD, Andrea Wang, MA, Ethel Siris, MD, Joseph Lane, MD, and the FREEDOM Fracture-Healing Writing Group*

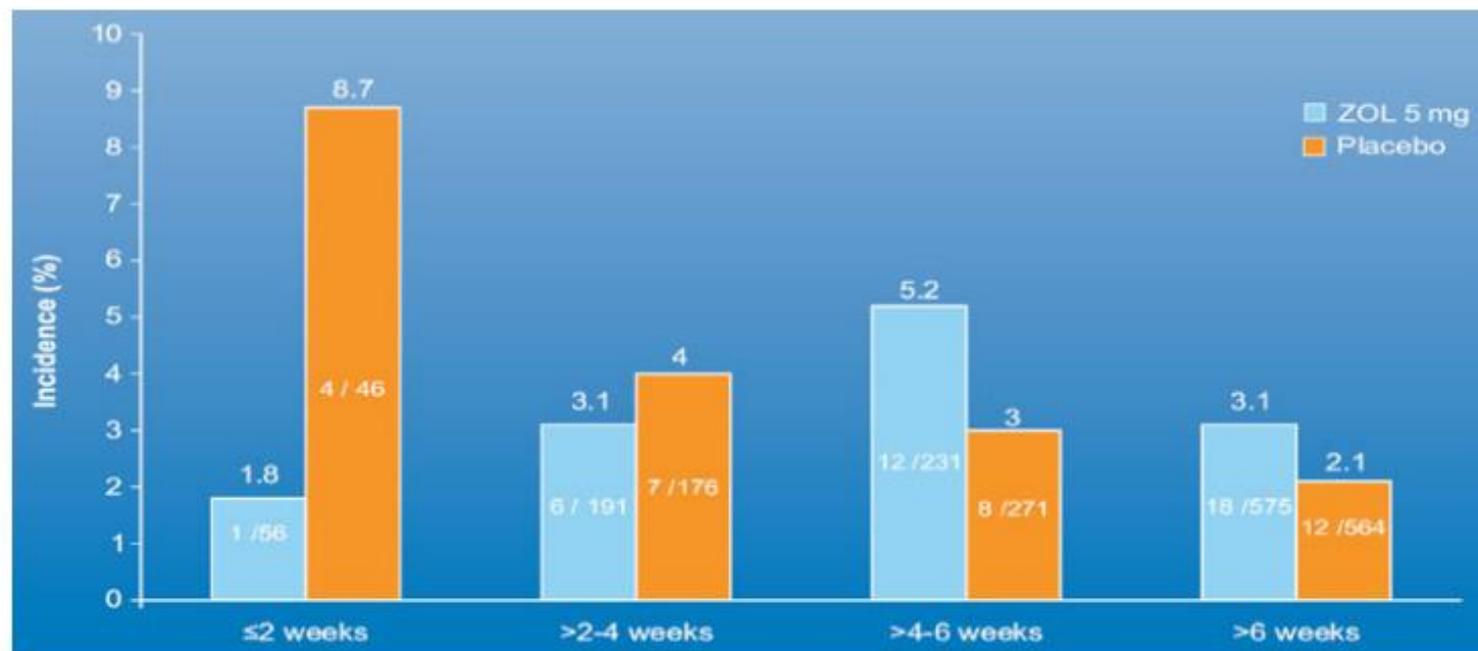
Results: Six hundred and sixty-seven subjects (303 treated with denosumab and 364 who received a placebo) had a total of 851 nonvertebral fractures (386 in the denosumab group and 465 in the placebo group), including 199 fractures (seventy-nine in the denosumab group and 120 in the placebo group) that were treated surgically. Delayed healing was reported in seven subjects (two in the denosumab group and five in the placebo group), including one with subsequent nonunion (in the placebo group). Neither delayed healing nor nonunion was observed in any subject who had received denosumab within six weeks preceding or following the fracture. A complication associated with the fracture or intervention occurred in five subjects (2%) and twenty subjects (5%) in the denosumab and placebo groups, respectively ($p = 0.009$).



Association between timing of zoledronic acid infusion and hip fracture healing

C. Colón-Emeric · L. Nordsletten · S. Olson · N. Major ·
S. Boonen · P. Haentjens · P. Mesenbrink ·
J. Magaziner · J. Adachi · K. W. Lyles · L. Hyldstrup ·
C. Bucci-Rechtweg · C. Recknor ·
for the HORIZON Recurrent Fracture Trial

Fig. 2 Delayed hip fracture healing by time between hip fracture surgery and first study drug infusion



Odds ratio 0.19 (0.01, 1.35) 0.78 (0.25, 2.40) 1.80 (0.73, 4.67) 1.48 (0.72, 3.20)

(95% CI)

P-value 0.10 0.67 0.20 0.29



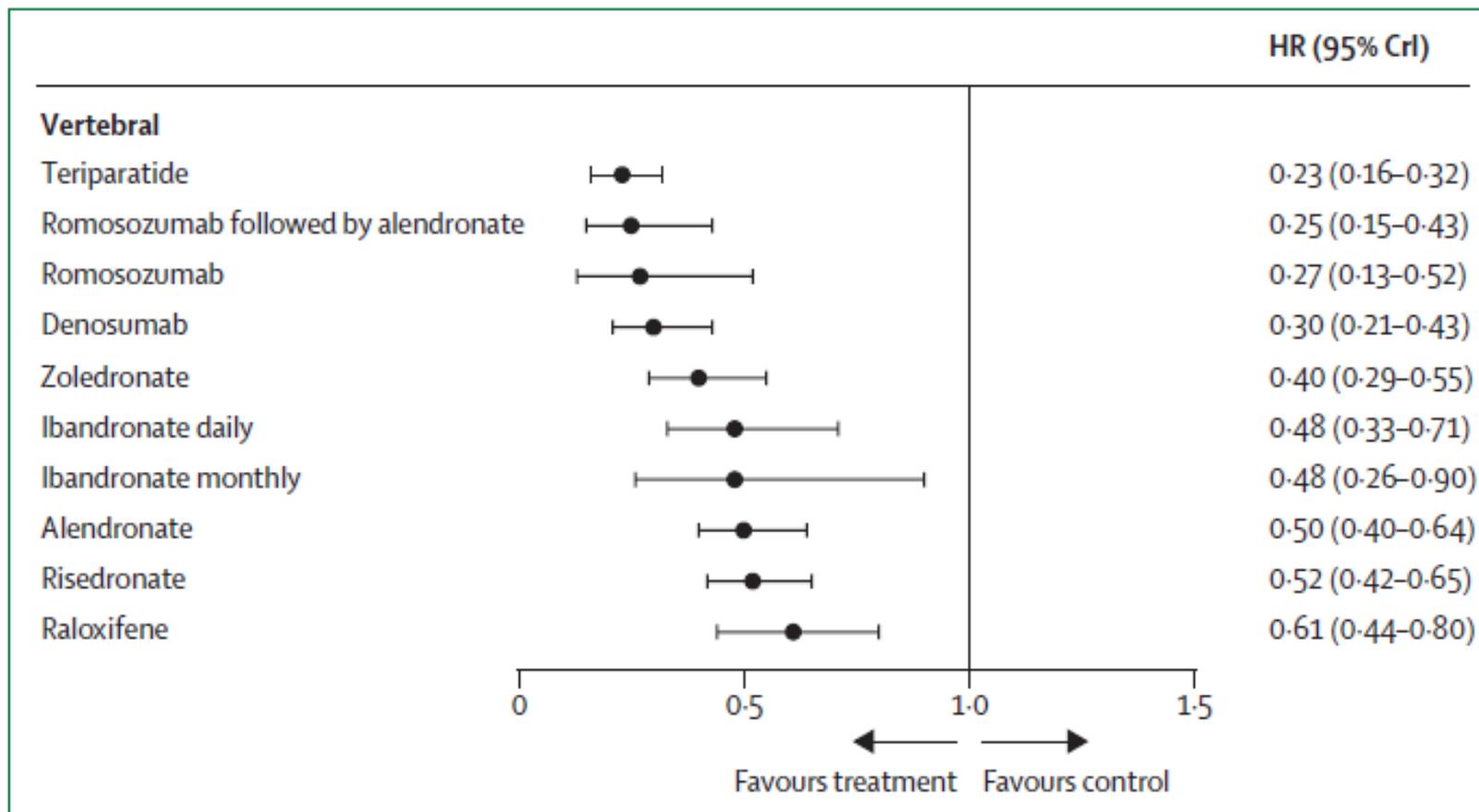
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Come trattare?

Farmaci!





JAMA Internal Medicine | Original Investigation

Time to Benefit of Bisphosphonate Therapy for the Prevention of Fractures Among Postmenopausal Women With Osteoporosis A Meta-analysis of Randomized Clinical Trials

William James Deardorff, MD; Irena Cenger, PhD; Brian Nguyen, BA; Sei J. Lee, MD, MAS

THERAPEUTIC ADVANCES in
Musculoskeletal Disease

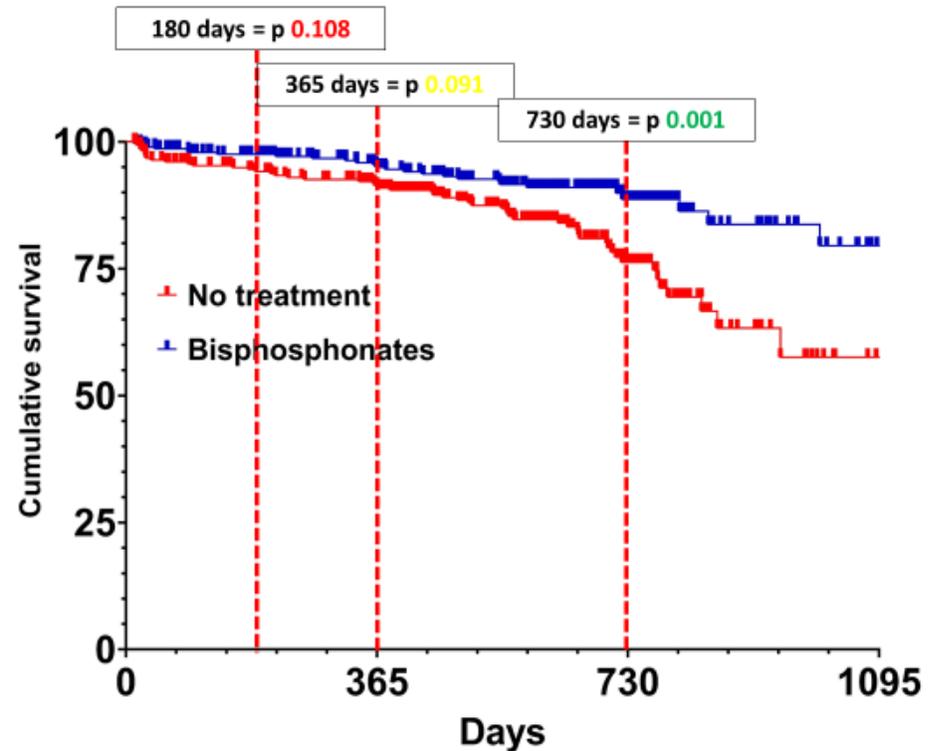
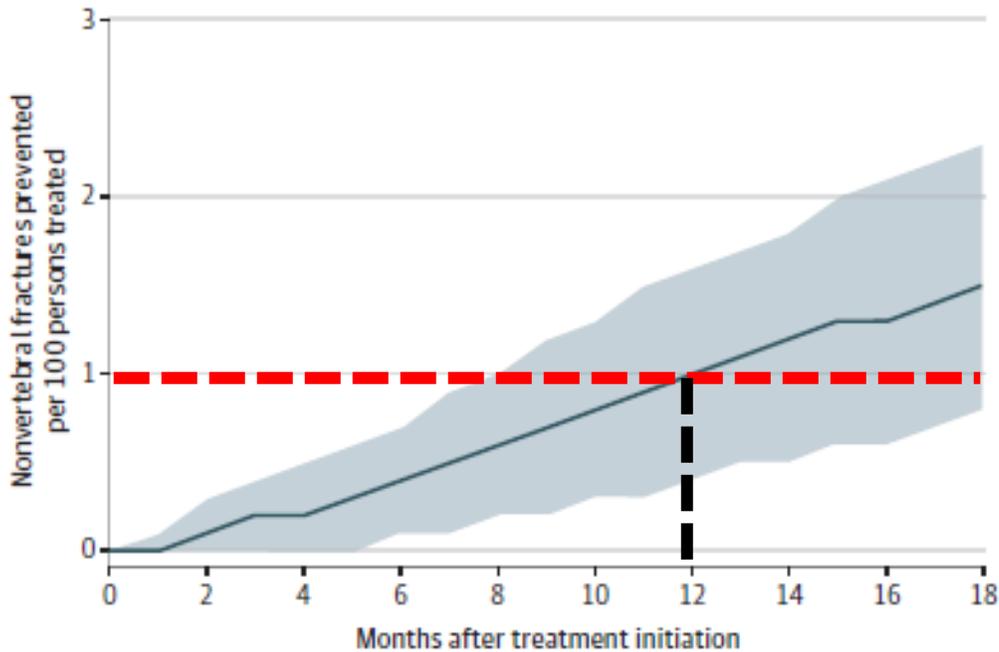
Original Research

Real-life short-term effectiveness of anti-osteoporotic treatments: a longitudinal cohort study

Giovanni Adami, Irene Gavioli, Maurizio Rossini, Ombretta Viapiana, Giovanni Orsolini, Camilla Benini, Eugenia Bertoldo, Elena Fracassi, Davide Gatti and Angelo Fassio

Ther Adv Musculoskelet Dis
2022, Vol. 14: 1-10
DOI: 10.1177/
1759720221105009
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Figure 2. Difference in Nonvertebral Fractures With Bisphosphonate Therapy Over Time

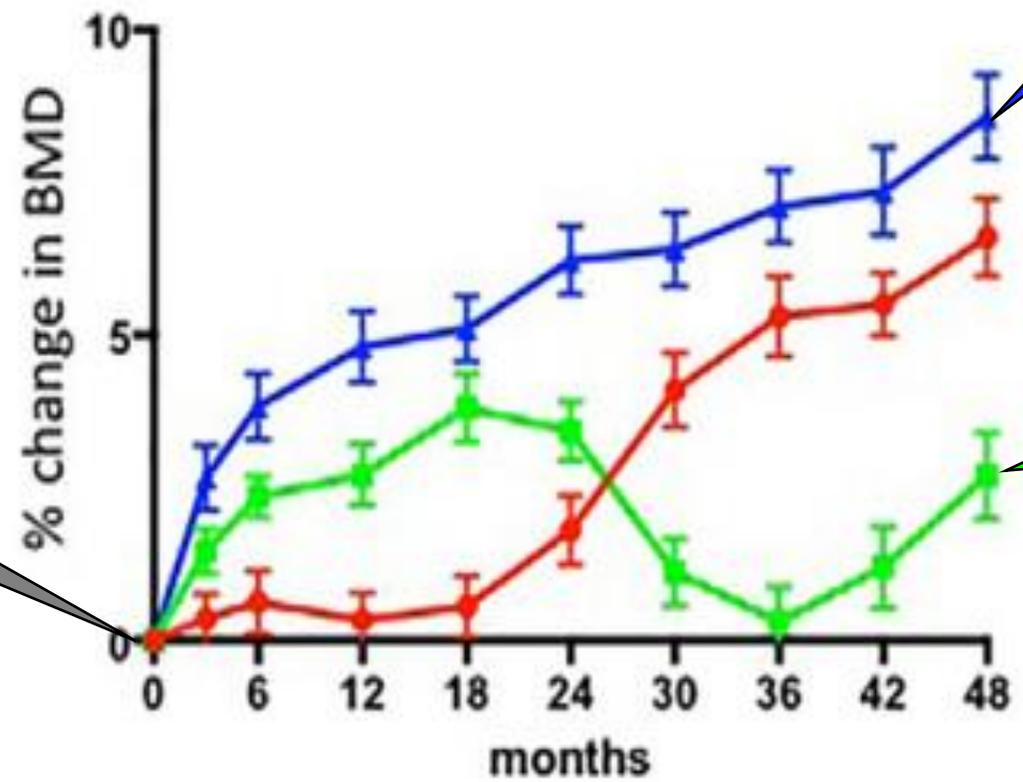




DENOSUMAB – TERIPARATIDE – COMBO

total hip

- TPTD → DMAB
- DMAB → TPTD
- COMBO → DMAB



T-score -3.0

T-score -2.3

T-score -2,8

Leder BZ et al.
 Two years of Denosumab and teriparatide administration in postmenopausal women with osteoporosis
 ([The DATA Extension Study](#)): a randomized controlled trial.
J Clin Endocrinol Metab. 2014 May;99(5):1694-700

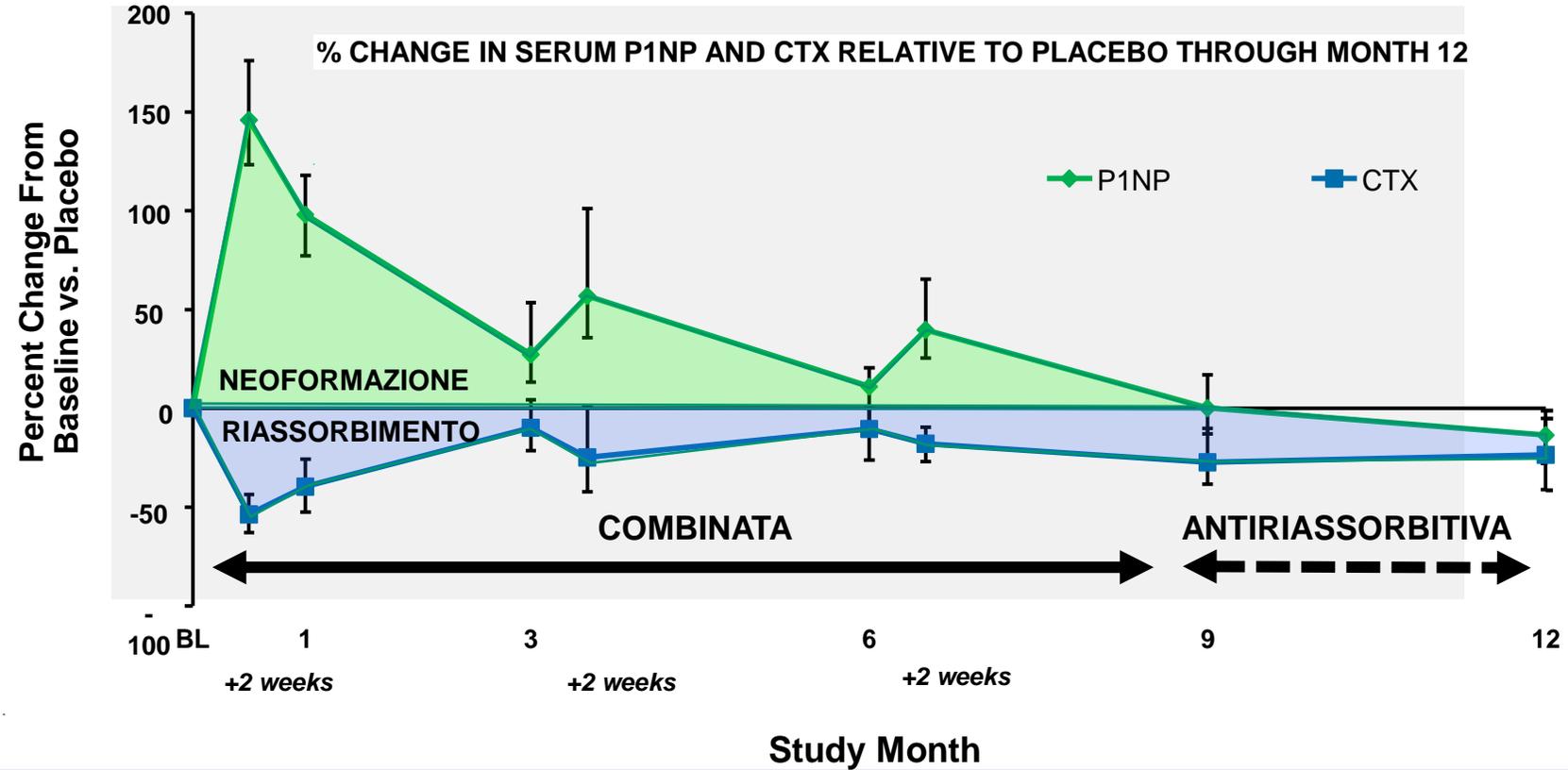
Leder BZ et al.
 Denosumab and teriparatide transitions in postmenopausal osteoporosis ([the DATA-Switch study](#)):
 extension of a randomised controlled trial.
Lancet. 2015 Sep 19;386(9999):1147-55



N ENGL J MED 375;16 NEJM.ORG OCTOBER 20, 2016

Romozozumab Treatment in Postmenopausal Women with Osteoporosis

F. Cosman, D.B. Crittenden, J.D. Adachi, N. Binkley, E. Czerwinski, S. Ferrari,
 L.C. Hofbauer, E. Lau, E.M. Lewiecki, A. Miyauchi, C.A.F. Zerbini, C.E. Milmont,
 L. Chen, J. Maddox, P.D. Meisner, C. Libanati, and A. Grauer



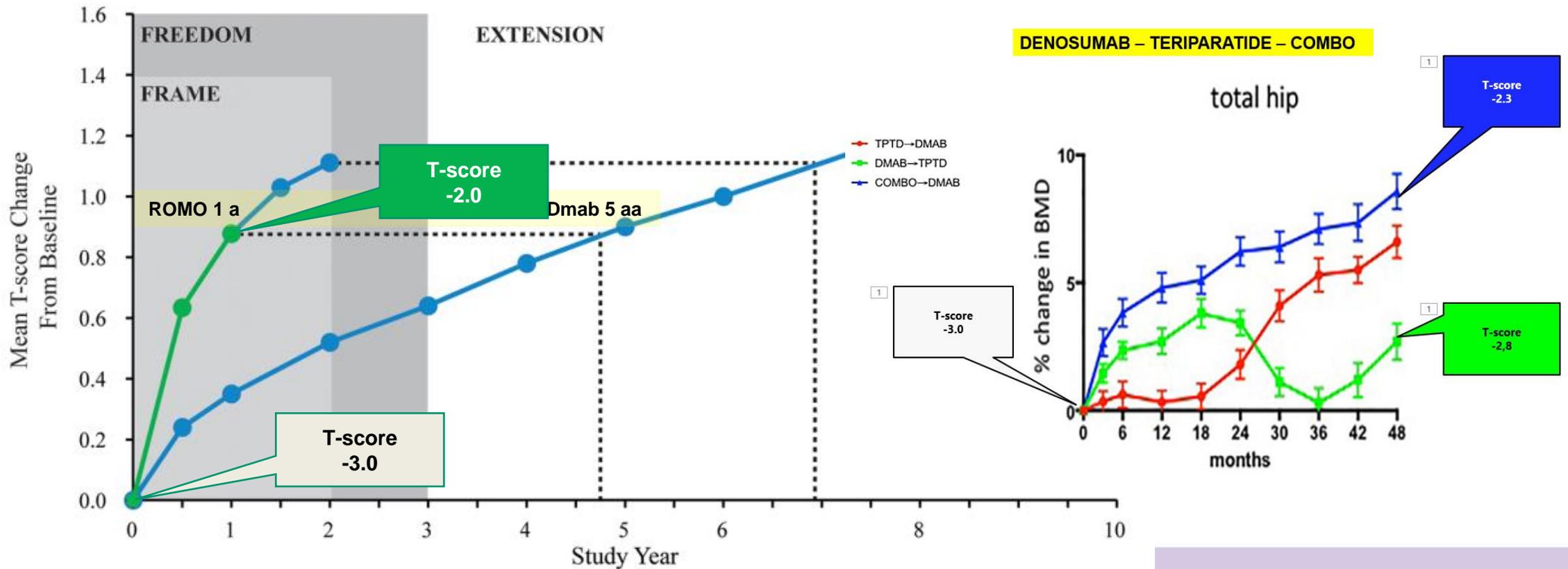


ORIGINAL ARTICLE

Journal of Bone and Mineral Research, Vol. 33, No. 7, July 2018,

FRAME Study: The Foundation Effect of Building Bone With 1 Year of Romosozumab Leads to Continued Lower Fracture Risk After Transition to Denosumab

Felicia Cosman,^{1,2} Daria B Crittenden,³ Serge Ferrari,⁴ Aliya Khan,⁵ Nancy E Lane,⁶ Kurt Lippuner,⁷ Toshio Matsumoto,⁸ Cassandra E Milmont,³ Cesar Libanati,⁹ and Andreas Grauer³





Change in Bone Density and Reduction in Fracture Risk: A Meta-Regression of Published Trials

Estimated Fracture Risk Reduction Associated With BMD Improvement

	Vertebral fracture	Hip fracture	Nonvertebral fracture
Δ Total hip BMD			
2%	28%	16%	10%
4%	51%	29%	16%
6%	66%	40%	21%
Δ Femoral neck BMD			
2%	28%	15%	11%
4%	55%	32%	19%
6%	72%	46%	27%
Δ Lumbar spine BMD			
2%	28%	22%	11%
8%	62%	38%	21%
14%	79%	51%	30%

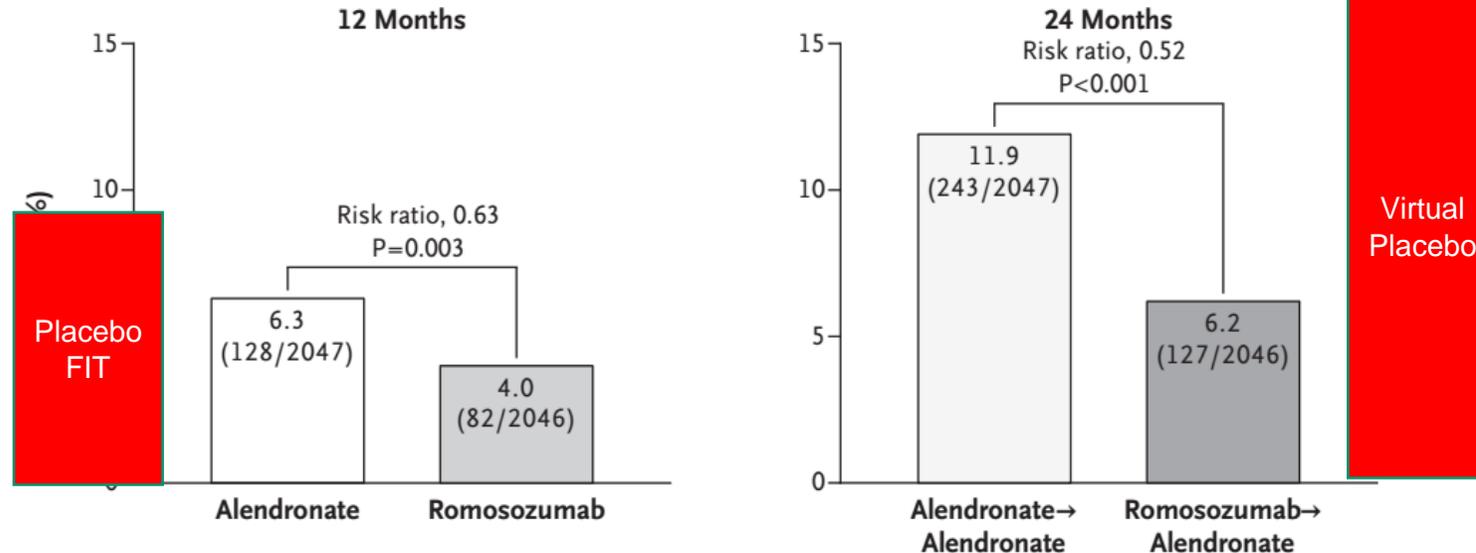


N ENGL J MED 377;15 NEJM.ORG OCTOBER 12, 2017

Romozosumab or Alendronate for Fracture Prevention in Women with Osteoporosis

Kenneth G. Saag, M.D., Jeffrey Petersen, M.D., Maria Luisa Brandi, M.D., Andrew C. Karaplis, M.D., Ph.D., Mattias Lorentzon, M.D., Ph.D., Thierry Thomas, M.D., Ph.D., Judy Maddox, D.O., Michelle Fan, Ph.D., Paul D. Meisner, Pharm.D., and Andreas Grauer, M.D.

A Incidence of New Vertebral Fracture





- **Prevenzione secondaria in soggetti con pregresse fratture osteoporotiche**
 - **Fratture vertebrali o di femore**

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Pazienti di sesso femminile con T-score colonna o femore <-2,5 (<-2,0 se ≥2 fratture vertebrali moderate o gravi oppure se frattura femorale nei 2 anni precedenti)

+ anamnesi ≥1 fratture vertebrali moderate o gravi oppure ≥2 fratture vertebrali lievi oppure frattura femorale

+ rischio di frattura a 10 anni (determinato con calcolatore validato) elevato ≥20%

+ impossibilità a seguire altri trattamenti efficaci (intolleranza, inefficacia o scadenza del periodo di impiego autorizzato)

Romosozumab^f per max 12 mesi, seguito da farmaci antiriassorbitivi (bisfosfonati o denosumab)



Si propone alla paziente follow-up ambulatoriale a distanza di 3 mesi, che la stessa rifiuta chiedendo l'opportunità di una visita domiciliare.

La paziente viene dimessa pertanto con la seguente terapia:

- Ramipril 5 mg
- Beclometasone 87 mcg/formoterolo 5 mcg/glicopirronio 9 mcg 2 inalaz. bid
- **Paracetamolo al bisogno** – *preferisce rinviare avvio terapia cronica dolore una volta rientrata a domicilio*
- **Denosumab 60 mg**
- **Calcio carbonato 500 mg bid**
- **Colecalciferolo 2000 UI die (dopo aver ultimato la dose da carico)**

