XXI

CONGRESSO NAZIONALE

GISMO

LE NUOVE FRONTIERE DELLE MALATTIE METABOLICHE DELL'OSSO

Presidente GISMO

Ranuccio Nuti

Presidente Congresso

Fabio Vescini

UDINE

14 | 15 NOVEMBRE 2025

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15/nov/2025

13.00 **Farmaci per l'osteoporosi nelle malattie reumatiche**
Angelo Fassio

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Rheumatology Unit- Verona. Italy

angelo.fassio@aovr.veneto.it

Disclosures

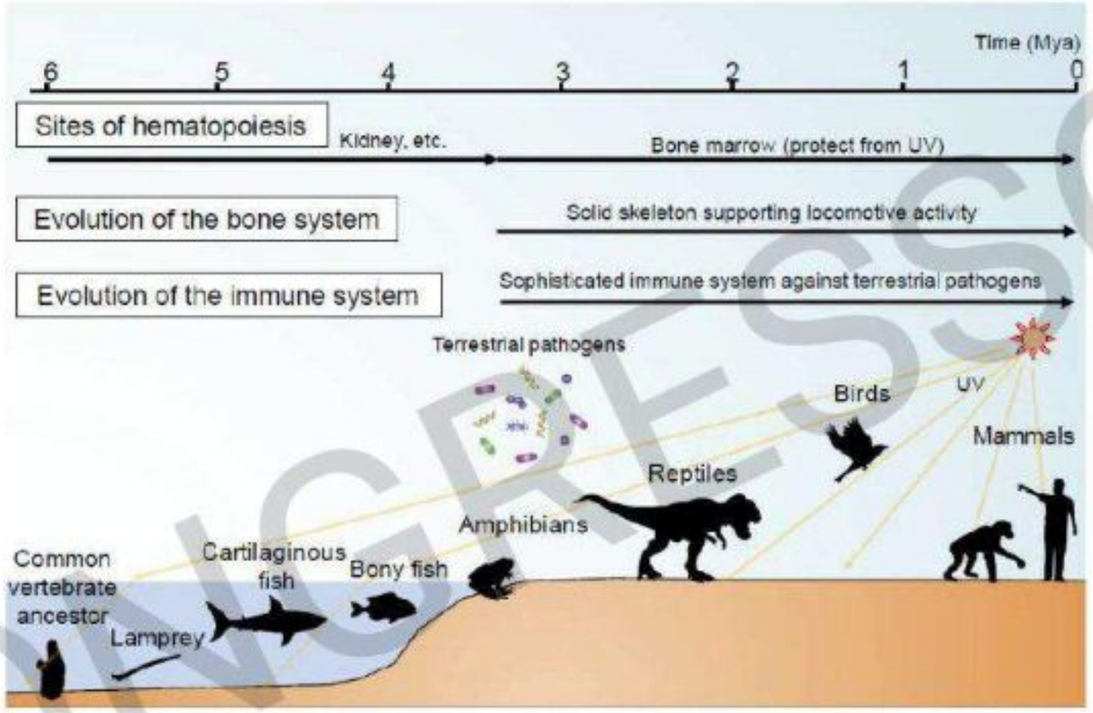
- Boehringer Ingelheim

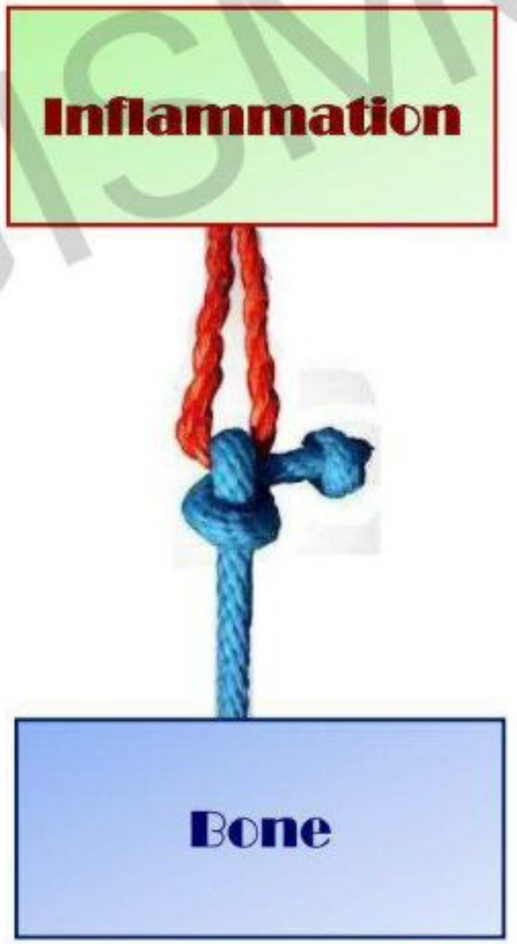
The osteoimmune system

Proc. Jpn. Acad., Ser. B 96 (2020)

Osteoimmunology—Bidirectional dialogue and inevitable union of the fields of bone and immunity—

By Hiroshi TAKAYANAGI*1,†





The **bone** and **immune systems** developed synchronously

Artrite reumatoide

Effects of targeted therapies on bone in rheumatic and musculoskeletal diseases

Boglárka Soós[1], Ágnes Szentpétery[1,2], Hennie G. Raterman[3], Willem F. Lems[4], Harjit P. Bhattoa[5,6] and Zoltán Szekanecz[1,6]

1823

L'**acqua calda** è stata **scoperta** solo nel 1823, da Sara Vellone, al tempo sessantaquattrenne. 1 nov 2021

https://nonciclopedia.org › wiki › Scoperta_dell'acqua_cal...

Scoperta dell'acqua calda - Nonciclopedia

Inflammatory rheumatic and musculoskeletal diseases (RMDs), such as rheumatoid arthritis (RA) and spondyloarthritis (SpA; including ankylosing spondylitis (AS) and psoriatic arthritis (PsA)), as well as other arthritides, have been associated with both generalized osteoporosis and fragility fractures, as well as with localized inflammatory bone resorption (erosions) and/or pathological bone formation[1–7].

Peer review information
Nature Reviews Rheumatology thanks A. Fassio, S. Manske, C. Zerbini and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.

Published: 10 March 2022

AR = fattore di rischio maggiore per OP

FRAX® Fracture Risk Assessment Tool

Home | Calculation Tool | Paper Charts | FAQ | References | CE Mark

Country: US (Caucasian) Name/ID: About the risk factors

Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth
   Age: Date of Birth: Y: M: D:
2. Sex ○ Male ○ Female
3. Weight (kg)
4. Height (cm)
5. Previous Fracture ◉ No ○ Yes
6. Parent Fractured Hip ◉ No ○ Yes
7. Current Smoking ◉ No ○ Yes
8. Glucocorticoids ◉ No ○ Yes
9. Rheumatoid arthritis ◉ No ○ Yes
10. Secondary osteoporosis ◉ No ○ Yes
11. Alcohol 3 or more units/day ◉ No ○ Yes
12. Femoral neck BMD (g/cm^2)

Select BMD

Clear Calculate

The negative bone effects of the disease and of chronic corticosteroid treatment in premenopausal women affected by rheumatoid arthritis

A. Fassio, L. Idolazzi, M.A. Jaber, C. Dartizio, O. Viapiana, M. Rossini, D. Gatti

Reumatismo, 2016; 68 (2): 65-71

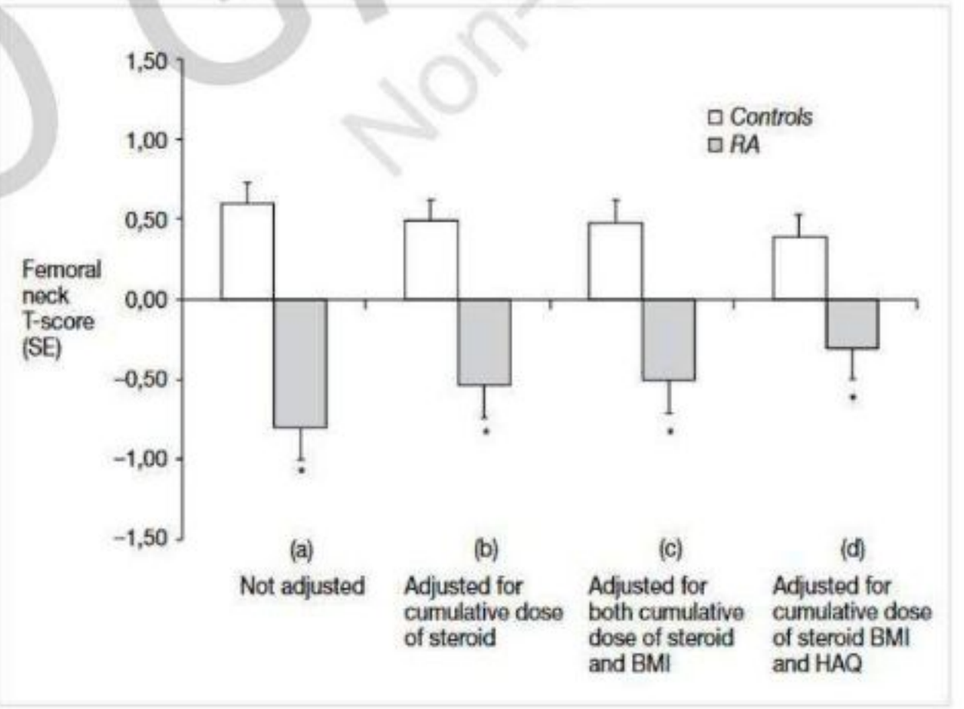
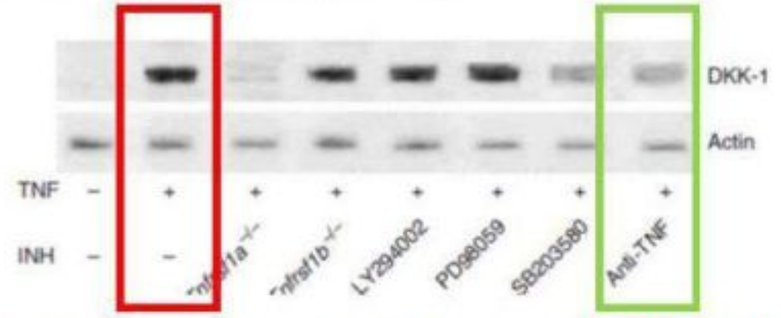


Figure 2 - Mean femoral neck T-score values (±SE) both un-adjusted and adjusted (see figure for adjusting variables) in patients with rheumatoid arthritis and controls. *P<0.05 vs control subjects.

TNFα, Dkk-1 and RANKL in RA

Dickkopf-1 is a master regulator of joint remodeling

Danielle Diarra[1,2,5], Marina Stolina[3,5], Karin Polzer[1], Jochen Zwerina[1], Michael S Ominsky[3], Denise Dwyer[3], Adelheid Korb[2], Josef Smolen[2], Markus Hoffmann[2], Clemens Scheinecker[2], Desiree van der Heide[4], Robert Landewe[4], Dave Lacey[3], William G Richards[3] & Georg Schett[1,2]



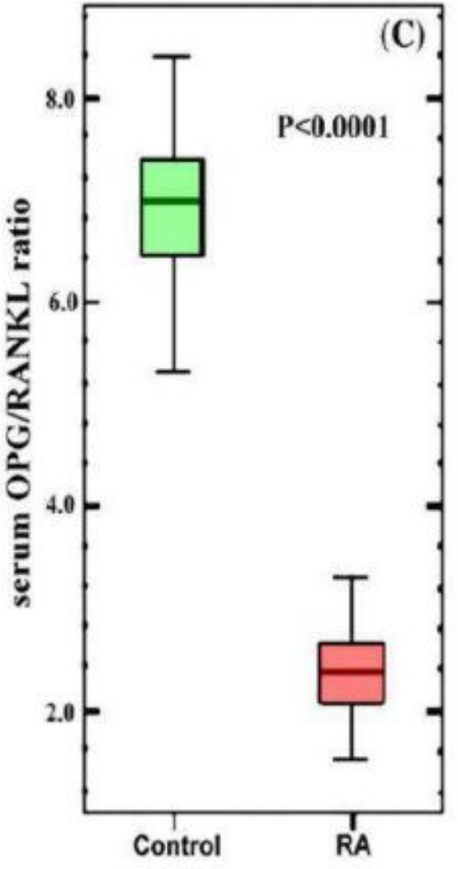
VOLUME 13 | NUMBER 2 | FEBRUARY 2007 NATURE MEDICINE

ORIGINAL ARTICLE

Osteoprotegerin and RANKL in the pathogenesis of rheumatoid arthritis-induced osteoporosis

Shengqian Xu · Yu Wang · Jingqiu Lu · Jianhua Xu

Rheumatol Int (2012) 32:3397–3403



Review

The serum level of Dickkopf-1 in patients with rheumatoid arthritis: A systematic review and meta-analysis

Yubo Ma[a,b,1], Xu Zhang[a,b,1], Mengmeng Wang[a,b], Qing Xia[a,b], Jiajia Yang[a,b], Meng Wu[a,b], Renfang Han[a,b], Mengya Chen[a,b], Xingxing Hu[a,b], Yaping Yuan[a,b], Rui Liu[a,b], Guangming Jiang[a,b], Guixia Pan[a,b], Yanfeng Zou[a,b], Shengqian Xu[c], Faming Pan[a,b,*]

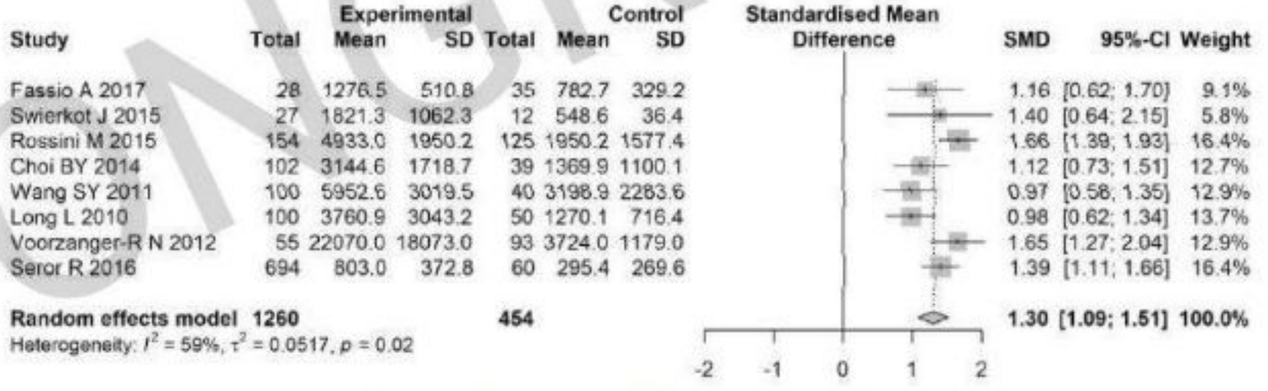


Fig. 2. Forest plots on the difference of serum DKK-1 between RA patients and healthy controls: A) Forest plot including all eligible studies; B) Forest plot after the sensitivity analysis.

RA, synovial biopsies

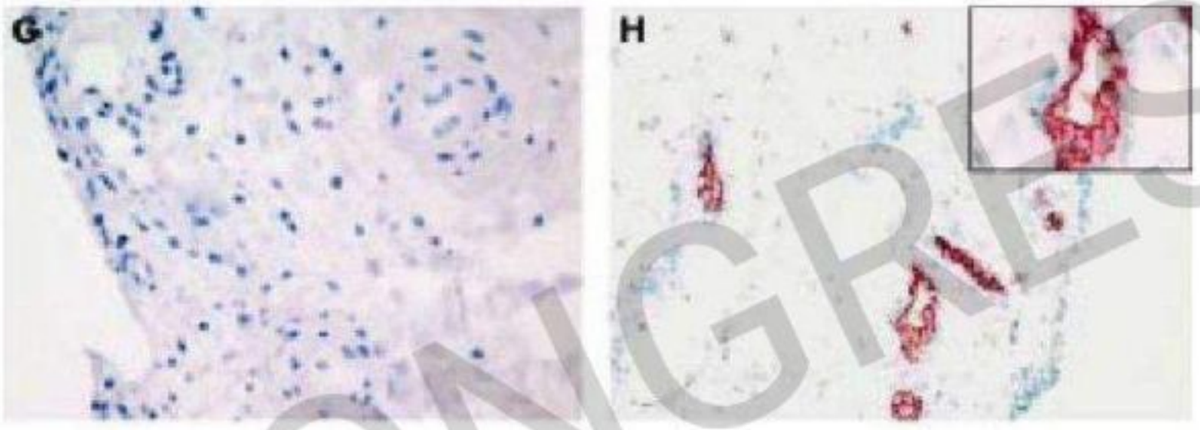
Microarchitecture and protective mechanisms in synovial tissue from clinically and arthroscopically normal knee joints

M D Smith, E Barg, H Weedon, V Papengelis, T Smeets, P P Tak, M Kraan, M Coleman, M J Ahern

Normal synovium

↓RANKL

↑OPG

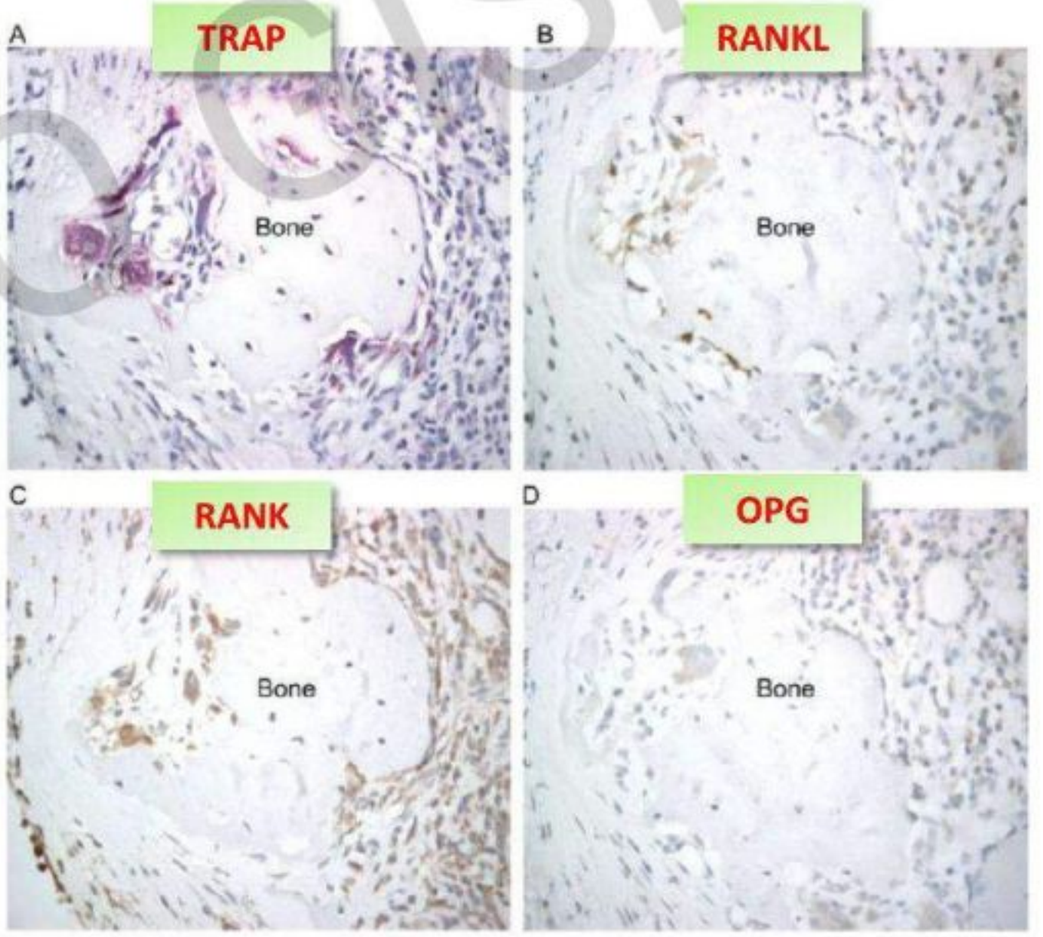


Ann Rheum Dis 2003;**62**:303–307

RANKL protein is expressed at the pannus–bone interface at sites of articular bone erosion in rheumatoid arthritis

A. R. Pettit, N. C. Walsh[1], C. Manning[1], S. R. Goldring[1] and E. M. Gravallese[1]

RA synovium



Rheumatology 2006;45:1068–1076

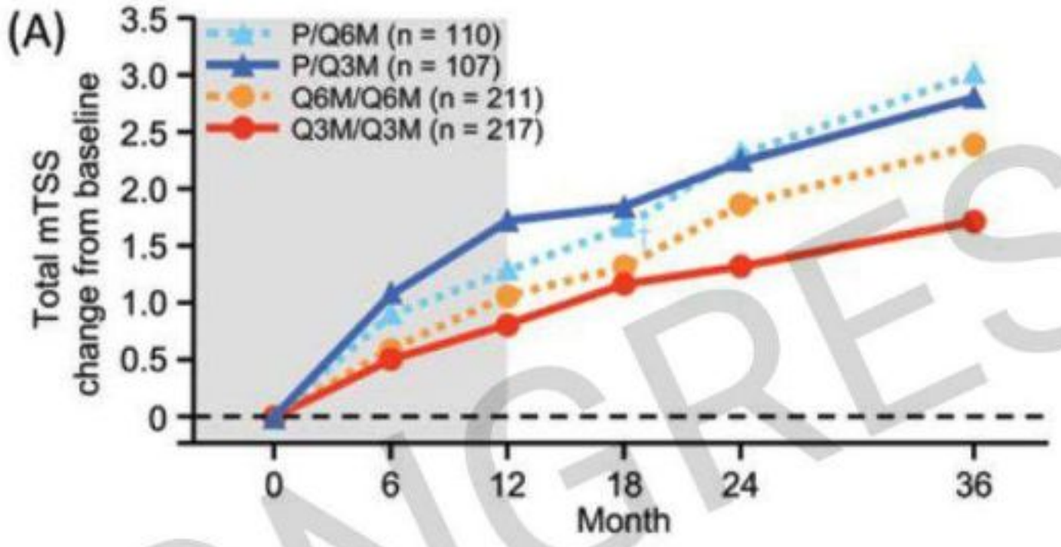
anti-RANKL and Rheumatoid Arthritis

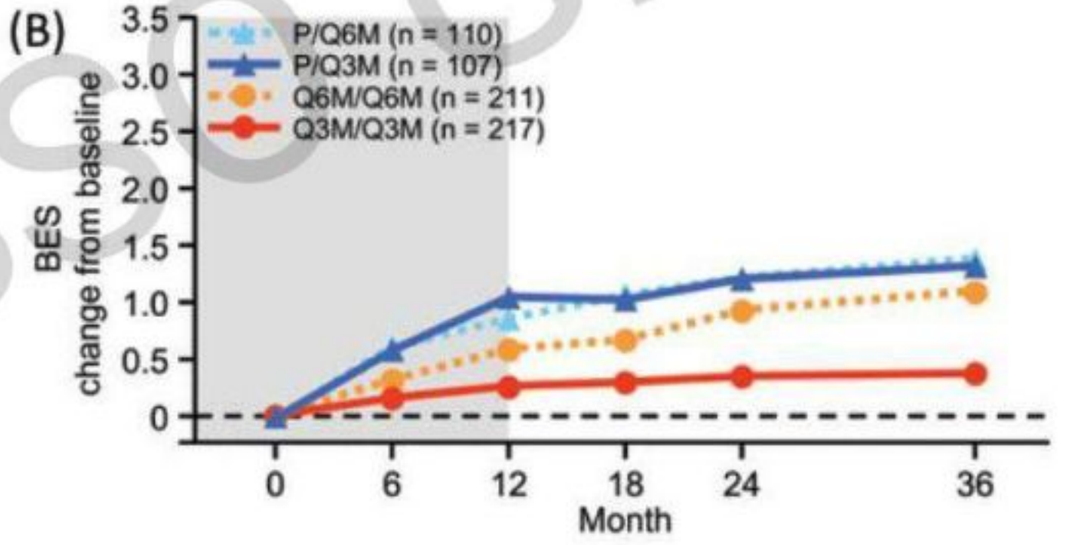
Effects of Denosumab in Japanese Patients With Rheumatoid Arthritis Treated With Conventional Antirheumatic Drugs: 36-month Extension of a Phase III Study

Yoshiya Tanaka[1], Tsutomu Takeuchi[2], Satoshi Soen[3], Hisashi Yamanaka[4], Toshiyuki Yoneda[5], Sakae Tanaka[6], Takaya Nitta[7], Naoki Okubo[7], Harry K. Genant[8], and Désirée van der Heijde[9]

MTX ± GCs

The Journal of Rheumatology





DMAb maintained inhibition of progression of joint destruction up to 36 months

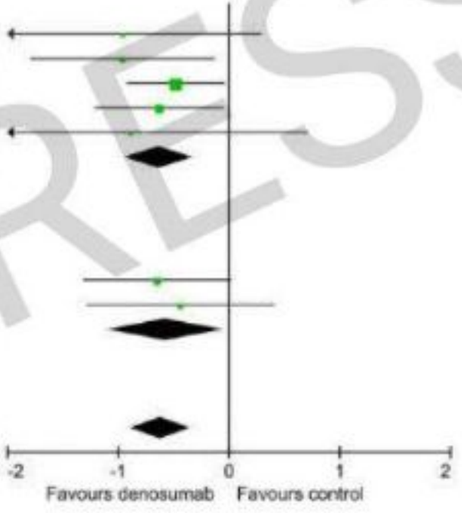
anti-RANKL and Rheumatoid Arthritis

frontiers in Immunology

The Efficacy of Denosumab in Patients With Rheumatoid Arthritis: A Systematic Review and Pooled Analysis of Randomized or Matched Data

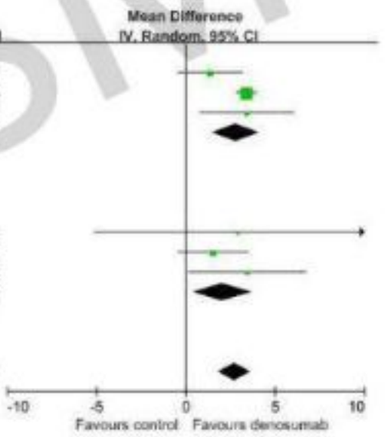
*Qiongwen Hu[†], Xue Zhong[†], Hua Tian[†] and Pu Liao[†]**

The effect of denosumab on the mean change of modified sharp erosion score (B)



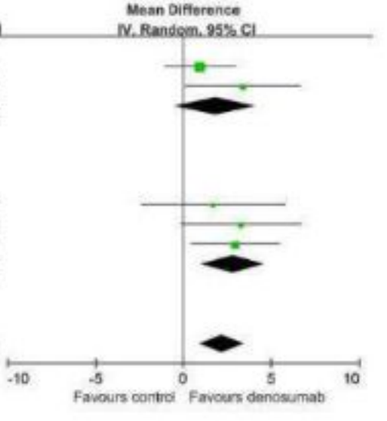
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Denosumab vs placebo/blank								
Cohen et al 2008	0.91	2.59	138	1.87	5.05	71	4.5%	-0.96 [-2.21, 0.29]
Takeuchi et al 2016	0.57	2.32	252	1.53	3.73	88	10.2%	-0.96 [-1.79, -0.13]
Hasegawa et al 2017	0.16	0.47	40	0.64	1.34	40	36.3%	-0.48 [-0.92, -0.04]
Takeuchi et al 2019	0.86	3.15	436	1.49	3.8	218	20.6%	-0.63 [-1.21, -0.05]
So et al 2021	0.82	4.05	55	1.71	4.48	55	2.8%	-0.89 [-2.49, 0.71]
Subtotal (95% CI)			**921**			**472**	**74.4%**	**-0.63 [-0.94, -0.32]**
Heterogeneity: Tau² = 0.00; Chi² = 1.42, df = 4 (P = 0.84); I² = 0%								
Test for overall effect: Z = 4.02 (P < 0.0001)								
Denosumab vs bisphosphonates								
Ebina et al 2018	0.27	0.88	30	0.92	1.64	30	15.9%	-0.65 [-1.32, 0.02]
Mori et al 2021	1.12	2.31	56	1.56	2.15	50	9.8%	-0.44 [-1.29, 0.41]
Subtotal (95% CI)			**86**			**80**	**25.6%**	**-0.57 [-1.09, -0.05]**
Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 1 (P = 0.70); I² = 0%								
Test for overall effect: Z = 2.13 (P = 0.03)								
Total (95% CI)			**1007**			**552**	**100.0%**	**-0.62 [-0.88, -0.35]**
Heterogeneity: Tau² = 0.00; Chi² = 1.61, df = 6 (P = 0.95); I² = 0%								
Test for overall effect: Z = 4.55 (P < 0.00001)								
Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.84), I² = 0%								

The effect of denosumab on the percentage change of total hip BMD (A)



Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Denosumab vs placebo								
Cohen et al 2008	1.65	6.22	143	0.3	6.77	75	17.7%	1.35 [-0.49, 3.19]
Takeuchi et al 2016	2.53	2.37	246	-0.65	2.38	87	48.3%	3.38 [2.80, 3.96]
So et al 2021	2.3	8.31	55	-1.1	5.64	55	10.0%	3.40 [0.75, 6.05]
Subtotal (95% CI)			**444**			**217**	**76.0%**	**2.82 [1.49, 4.14]**
Heterogeneity: Tau² = 0.75; Chi² = 4.27, df = 2 (P = 0.12); I² = 53%								
Test for overall effect: Z = 4.17 (P < 0.0001)								
Denosumab vs bisphosphonates								
Nakamura et al 2017	16.5	13.8	26	13.6	15.8	26	1.3%	2.90 [-5.16, 10.96]
Ebina et al 2018	2.9	0.8	30	1.4	5.48	30	15.9%	1.50 [-0.48, 3.48]
Mori et al 2021	4.03	9.25	56	0.61	8.1	50	6.9%	3.42 [0.12, 6.72]
Subtotal (95% CI)			**112**			**106**	**24.0%**	**2.05 [0.38, 3.71]**
Heterogeneity: Tau² = 0.00; Chi² = 1.00, df = 2 (P = 0.61); I² = 0%								
Test for overall effect: Z = 2.41 (P = 0.02)								
Total (95% CI)			**556**			**323**	**100.0%**	**2.72 [1.80, 3.64]**
Heterogeneity: Tau² = 0.37; Chi² = 6.96, df = 5 (P = 0.22); I² = 28%								
Test for overall effect: Z = 5.79 (P < 0.00001)								
Test for subgroup differences: Chi² = 0.50, df = 1 (P = 0.48), I² = 0%								

The effect of denosumab on percentage change of femoral neck BMD (B)



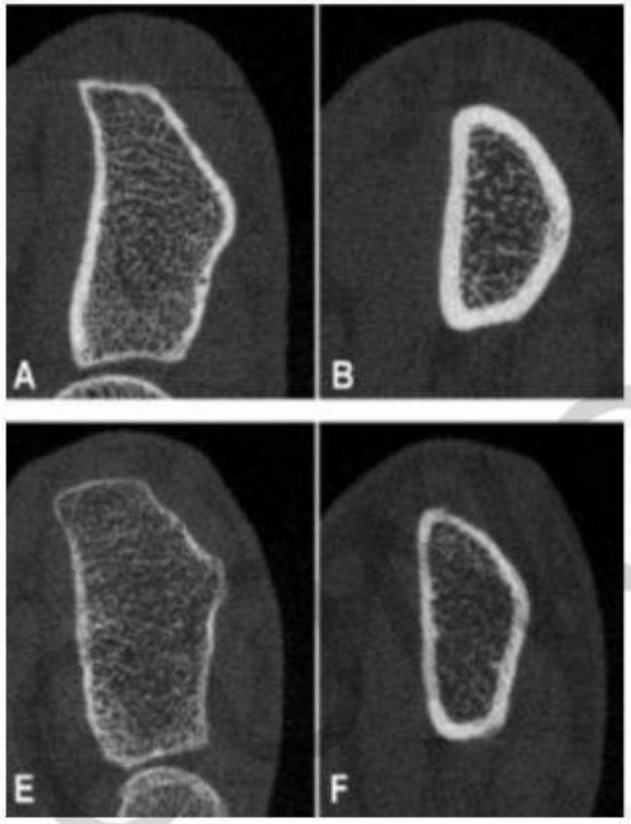
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Denosumab vs placebo								
Cohen et al 2008	1.45	7.17	143	0.5	7.43	75	37.6%	0.95 [-1.10, 3.00]
So et al 2021	2.8	5.37	55	-0.6	11.12	55	14.8%	3.40 [0.14, 6.66]
Subtotal (95% CI)			**198**			**130**	**52.4%**	**1.83 [-0.47, 4.14]**
Heterogeneity: Tau² = 1.07; Chi² = 1.55, df = 1 (P = 0.21); I² = 36%								
Test for overall effect: Z = 1.56 (P = 0.12)								
Denosumab vs bisphosphonates								
Kinoshita et al 2017	4.2	11.1	49	2.5	9.8	49	9.2%	1.70 [-2.45, 5.85]
Ebina et al 2018	4.5	8.22	30	1.2	4.93	30	13.4%	3.30 [-0.13, 6.73]
Mori et al 2021	3.75	7.5	56	0.78	5.69	50	24.9%	2.97 [0.45, 5.49]
Subtotal (95% CI)			**135**			**129**	**47.6%**	**2.82 [0.99, 4.64]**
Heterogeneity: Tau² = 0.00; Chi² = 0.37, df = 2 (P = 0.83); I² = 0%								
Test for overall effect: Z = 3.03 (P = 0.002)								
Total (95% CI)			**333**			**259**	**100.0%**	**2.20 [0.94, 3.46]**
Heterogeneity: Tau² = 0.00; Chi² = 2.76, df = 4 (P = 0.60); I² = 0%								
Test for overall effect: Z = 3.43 (P = 0.0006)								
Test for subgroup differences: Chi² = 0.43, df = 1 (P = 0.51), I² = 0%								

BMD and microstructure impairment in RA

RA = corticale più sottile e più (micro)porosa

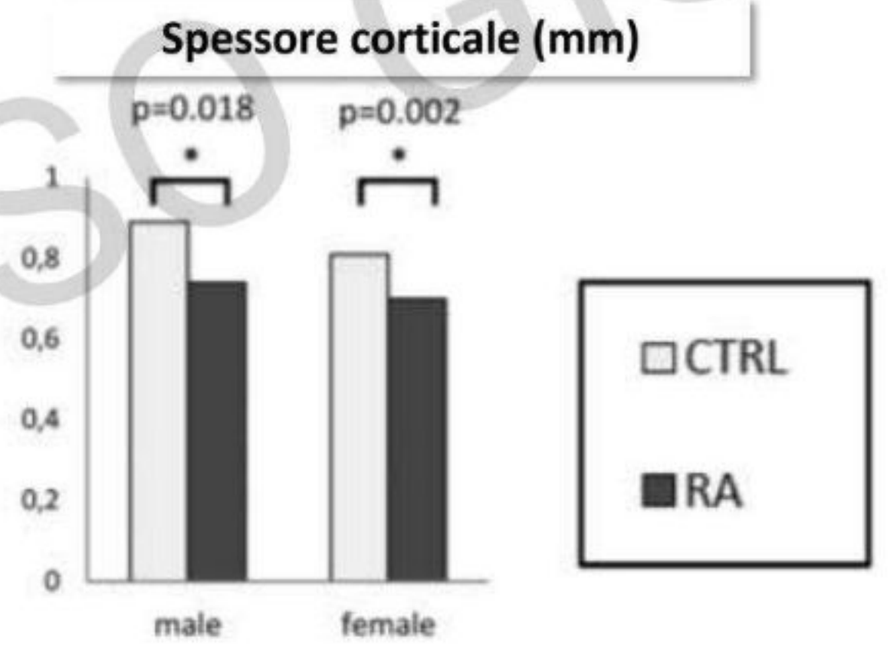
Alterations of Bone Density, Microstructure, and Strength of the Distal Radius in Male Patients With Rheumatoid Arthritis: A Case-Control Study With HR-pQCT

Tracy Y Zhu,[1] James F Griffith,[2] Ling Qin,[3] Vivian W Hung,[3] Tsz-Ning Fong,[3] Sze-Ki Au,[4] Martin Li,[1]



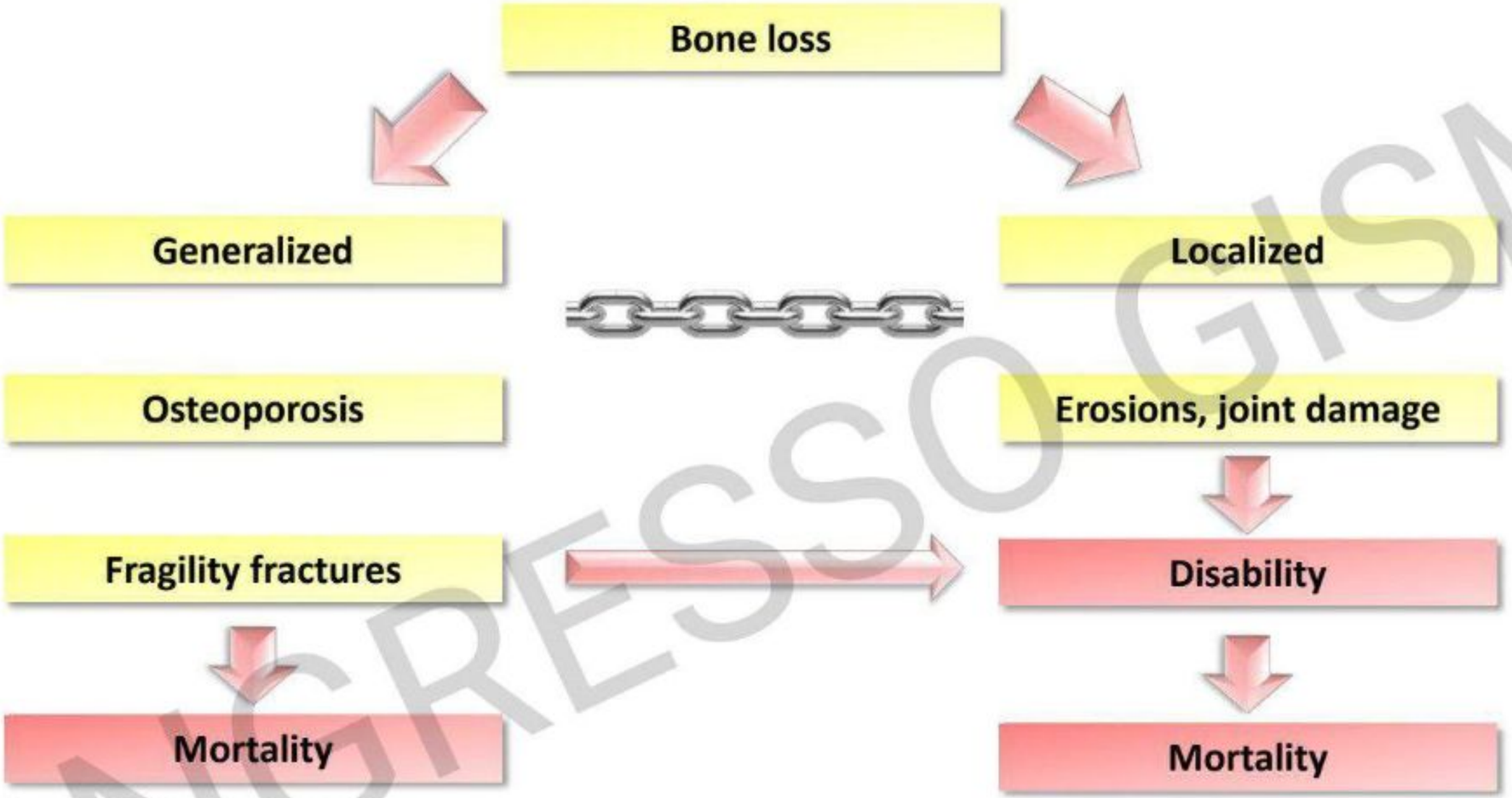
Sano

AR



Zhu TY et al. JBMR 2014

Artrite reumatoide



Denosumab, cortical bone and bone erosions in rheumatoid arthritis

Non-responders to the DMARDs in terms of progression of bone erosions could be indeed the consequences of a concomitant osteoporosis.

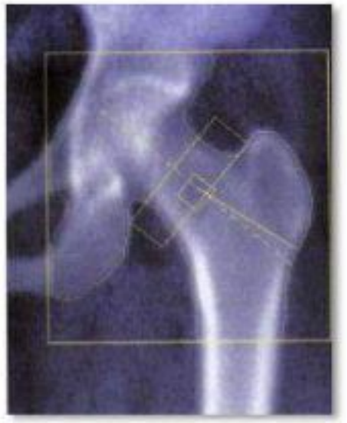
To cite Rossini M, Adami G, Viapiana O, *et al*. *Ann Rheum Dis* 2016;**75**:e70.

AR. BMD ed erosioni

Relationship of Focal Erosions, Bone Mineral Density, and Parathyroid Hormone in Rheumatoid Arthritis

MAURIZIO ROSSINI, GIANFILIPPO BAGNATO, BRUNO FREDIANI, ANNAMARIA IAGNOCCO, GIOVANNI LA MONTAGNA, GIOVANNI MINISOLA, MAURIZIO CAMINITI, MASSIMO VARENNA, and SILVANO ADAMI

	Bone Erosions		
	yes	no	p
Spine BMD (T score)	-1.67 ±1.21	-1.60 ±1.43	ns
Hip BMD (T score)	-1.55 ±1.04	-1.18 ±1.05	0.005
PTH (pg/ml)	25.7 ±13.1	23.2 ±11.0	0.025



Rossini M et al. J Rheumatol. 2011

TPTD and bone erosions in RA RCT (12 m)

DOI 10.1002/art.40385

Lack of effect of teriparatide on joint erosions in rheumatoid arthritis is an expected result: comment on the article by Solomon et al

To the Editor:

We read with great interest the report by Solomon and colleagues describing their randomized controlled trial of teriparatide therapy in tumor necrosis factor inhibitor–treated patients with rheumatoid arthritis (RA) (1). Their study did not demonstrate any significant effect of teriparatide on bone erosions in these patients. In our opinion, it is not surprising that teriparatide did not produce the expected result. A few considerations can explain the lack of effect.

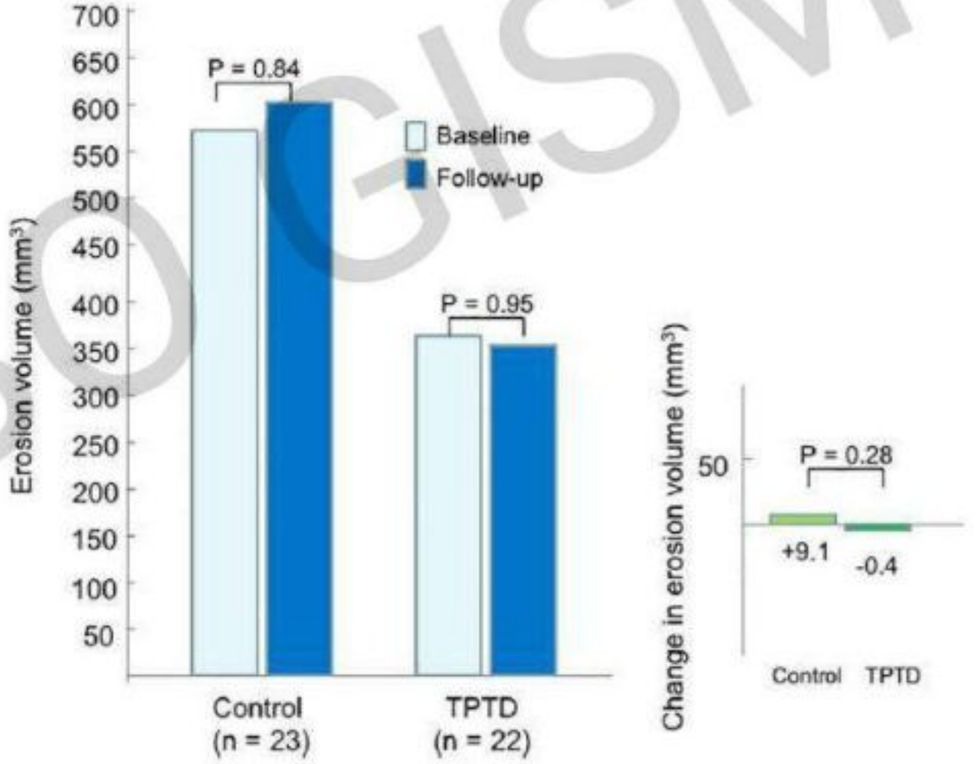
First, bone erosions affect mainly cortical bone (2,3), and it is well known that teriparatide does not exert a positive therapeutic effect on cortical sites in the short term: in particular, during the first 6 months of treatment. Studies, including one with an RA patient group (4), have shown that it had no significant effect on bone mineral density (BMD) at cortical sites such as the femoral neck or third distal radius (5,6). Solomon and colleagues did not observe this lack of effect after 6 months of treatment because changes in BMD were explored only at the 12-month time point. Moreover, when administered as a daily subcutaneous injection, teriparatide has been found to increase cortical porosity in the short term (7–9). Increased cortical porosity, predisposing to bone erosions, has been recently described in RA (10).

It should also be noted that, in patients with RA, serum levels of Dkk-1 (a natural inhibitor of Wnt signaling) are significantly increased, correlating with parathyroid hormone levels, and are associated with increased risk of bone erosions and osteoporosis (11). Teriparatide treatment has been shown to increase serum Dkk-1 levels (12); this could be another possible explanation for the inability of teriparatide to heal erosions.

In contrast, better results in preventing bone erosions have been achieved with denosumab, an anti-RANKL antibody (13–15). Denosumab has been associated with a rapid decrease in cortical porosity (16), prevention of metacarpal bone loss (17), and reduction in serum Dkk-1 levels (18). These latter findings are likely the reasons for its better efficacy than teriparatide in preventing and even healing bone erosions, at least in the short term.

ARTHRITIS & RHEUMATOLOGY
Vol. 70, No. 3, March 2018, pp 475–476

Giovanni Adami, MD
Maurizio Rossini, MD
Ombretta Viapiana, MD
Angelo Fassio, MD
Luca Idolazzi, MD
Giovanni Orsolini, MD
Davide Gatti, MD
University of Verona
Verona, Italy

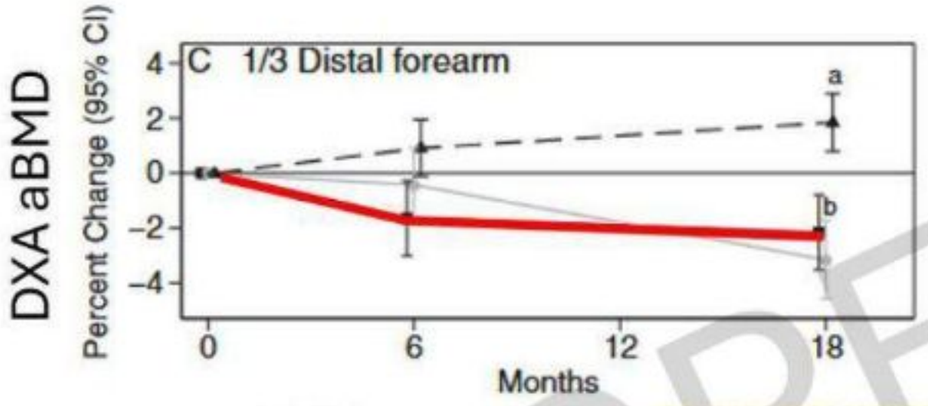


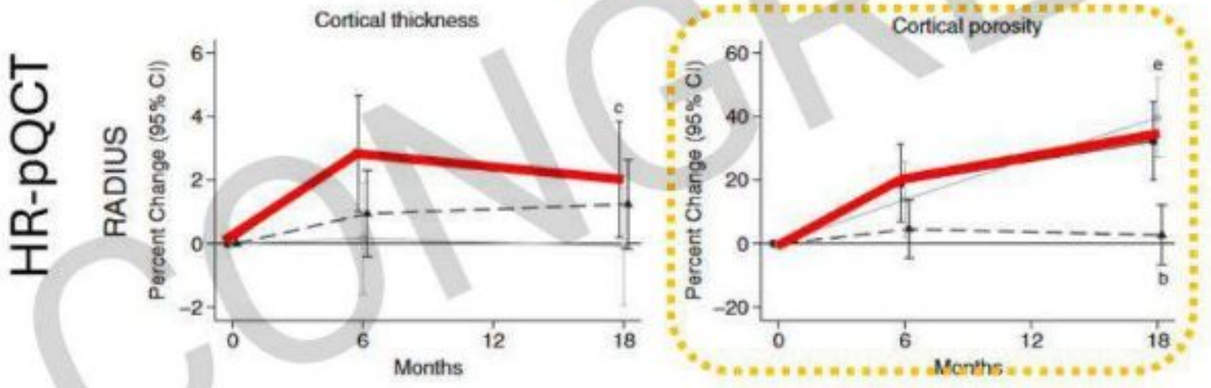
Conclusion. **Our findings indicate that teriparatide treatment for 1 year does not significantly reduce erosion volume in the hands or wrists of patients with established RA with disease activity controlled by TNFi treatment.**

TPTD and cortical effects

Differing Effects of PTH 1–34, PTH 1–84, and Zoledronic Acid on Bone Microarchitecture and Estimated Strength in Postmenopausal Women With Osteoporosis: An 18-Month Open-Labeled Observational Study Using HR-pQCT

Stinus Hansen,[1,2] Ellen M Hauge,[3] Jens-Erik Beck Jensen,[4] and Kim Brixen[1,2]





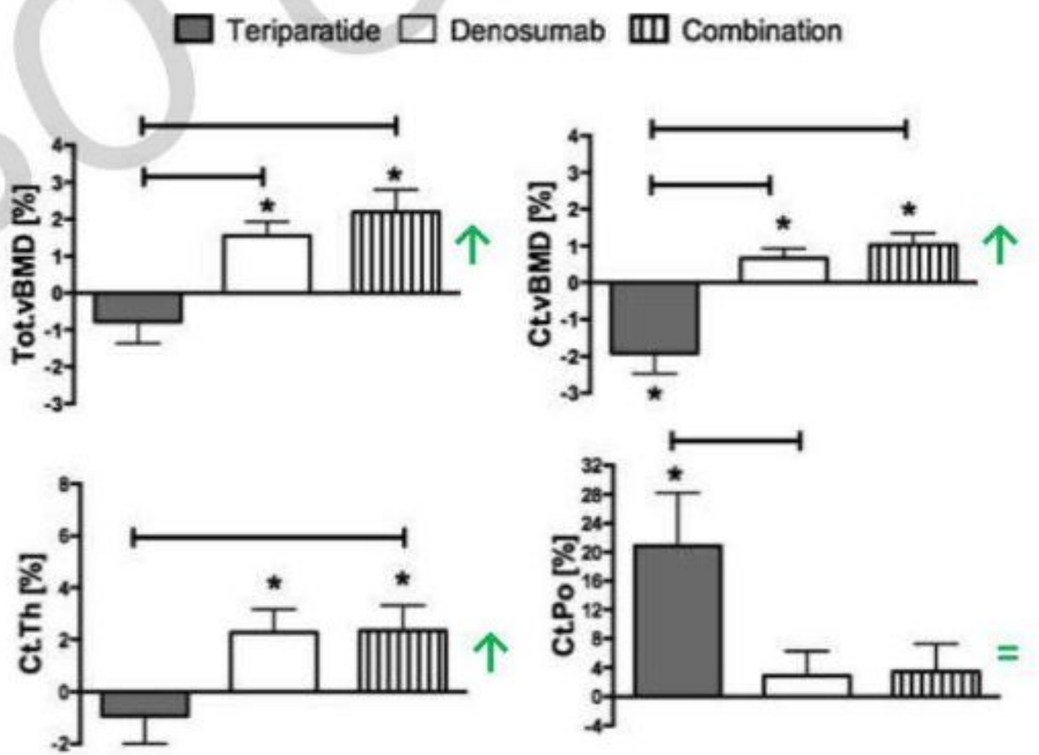
Journal of Bone and Mineral Research, Vol. 28, No. 4, April 2013, pp 736–745

ORIGINAL ARTICLE JBMR®

Comparative Effects of Teriparatide, Denosumab, and Combination Therapy on Peripheral Compartmental Bone Density, Microarchitecture, and Estimated Strength: the DATA-HRpQCT Study

Joy N Tsai,[1] Alexander V Uihlein,[1] Sherri-Ann M Burnett-Bowie,[1] Robert M Neer,[1] Yuli Zhu,[1] Nicholas Derrico,[1] Hang Lee,[2] Mary L Bouxsein,[1,3] and Benjamin Z Leder[1]

Distal radius, 12m



ROMO in RA?

An investigation of the differential therapeutic effects of romosozumab on postmenopausal osteoporosis patients with or without rheumatoid arthritis complications: a case–control study

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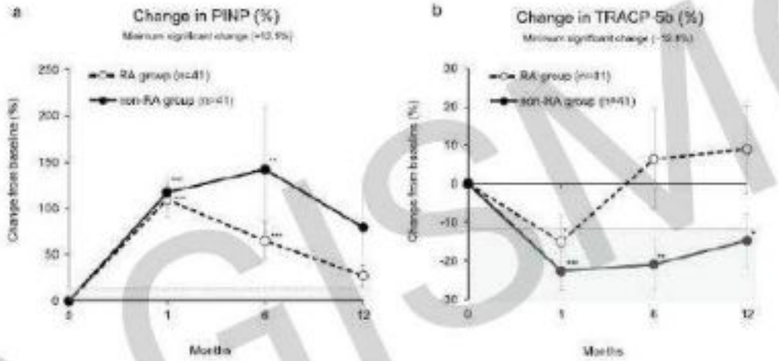
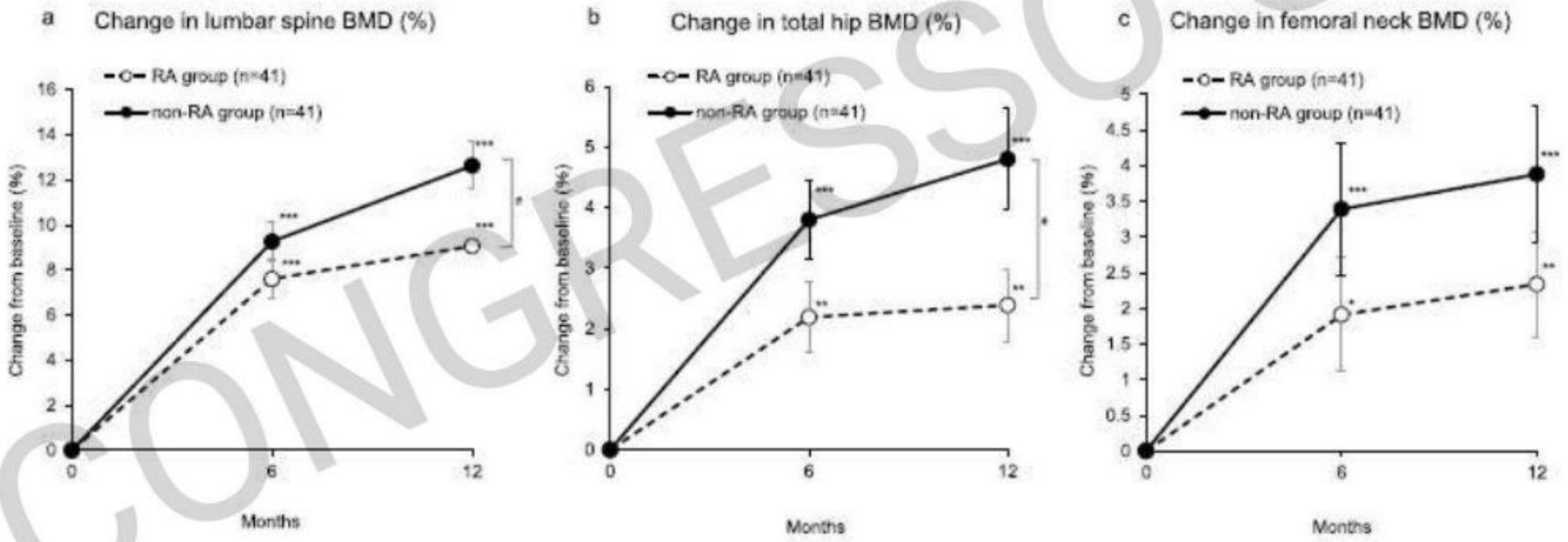
GCs = ???





ROMO in RA might be impaired… but still excellent! +8% in 1 year

Osteoporosis International (2024)

GIOP: who's to blame?

Risk of fracture in women with glucocorticoid requiring diseases is independent from glucocorticoid use: An analysis on a nation-wide database

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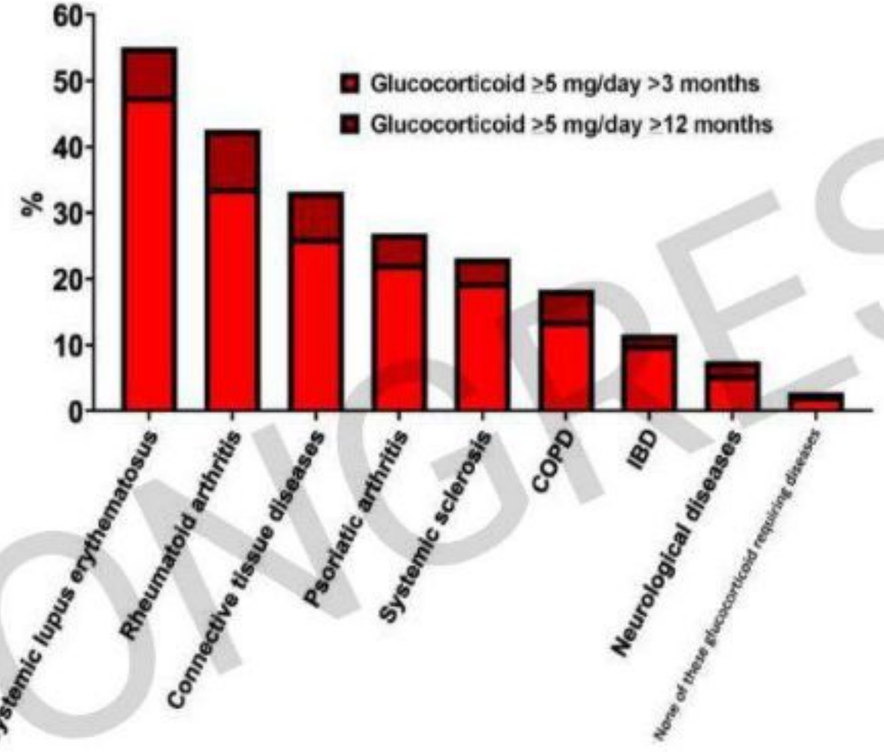

Bone 179 (2024) 116958

BMJ Open Prevalence and prescription patterns of oral glucocorticoids in adults: a retrospective cross-sectional and cohort analysis in France

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Table 1 Characteristics of oral glucocorticoid (GC) initiators, overall and according to the number of oral GC reimbursements over the year following treatment initiation (figures are percentages)

	All GC initiators	Short-term users*	Mid-term users*	Long-term users*
	n=206 759	n=139 703	n=63 267	n=3789
Identified GC recognised indications†	27.3	23.7	33.4	61.1
Obstructive pulmonary diseases	21.3	19.1	26.0	26.2
Cancer	6.4	4.9	8.2	31.9
Rheumatic diseases	1.0	0.6	1.1	12.1
Rheumatoid arthritis	0.4	0.2	0.5	5.7
Polymyalgia rheumatica/giant cell arteritis	0.1	0.0	0.1	3.9
Inflammatory bowel diseases	0.6	0.4	0.9	3.3
Multiple sclerosis	0.2	0.2	0.2	0.2

~22% rheumatic conditions

Bénard-Laribière A, *et al. BMJ Open* 2017;**7**:e015905. doi:10.1136/bmjopen-2017-015905

GCs and fractures

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American College of Rheumatology

Bone Loss in Inflammatory Rheumatic Musculoskeletal Disease Patients Treated With Low-Dose Glucocorticoids and Prevention by Anti-Osteoporosis Medications

Giovanni Adami, Angelo Fassio, Maurizio Rossini, Camilla Benini, Francesca Pistillo, Ombretta Viapiana, Davide Bertelle, and Davide Gatti

1. There is no «safe» GCs dosage
2. BMD loss is (partially) preventable with adequate preventive treatment