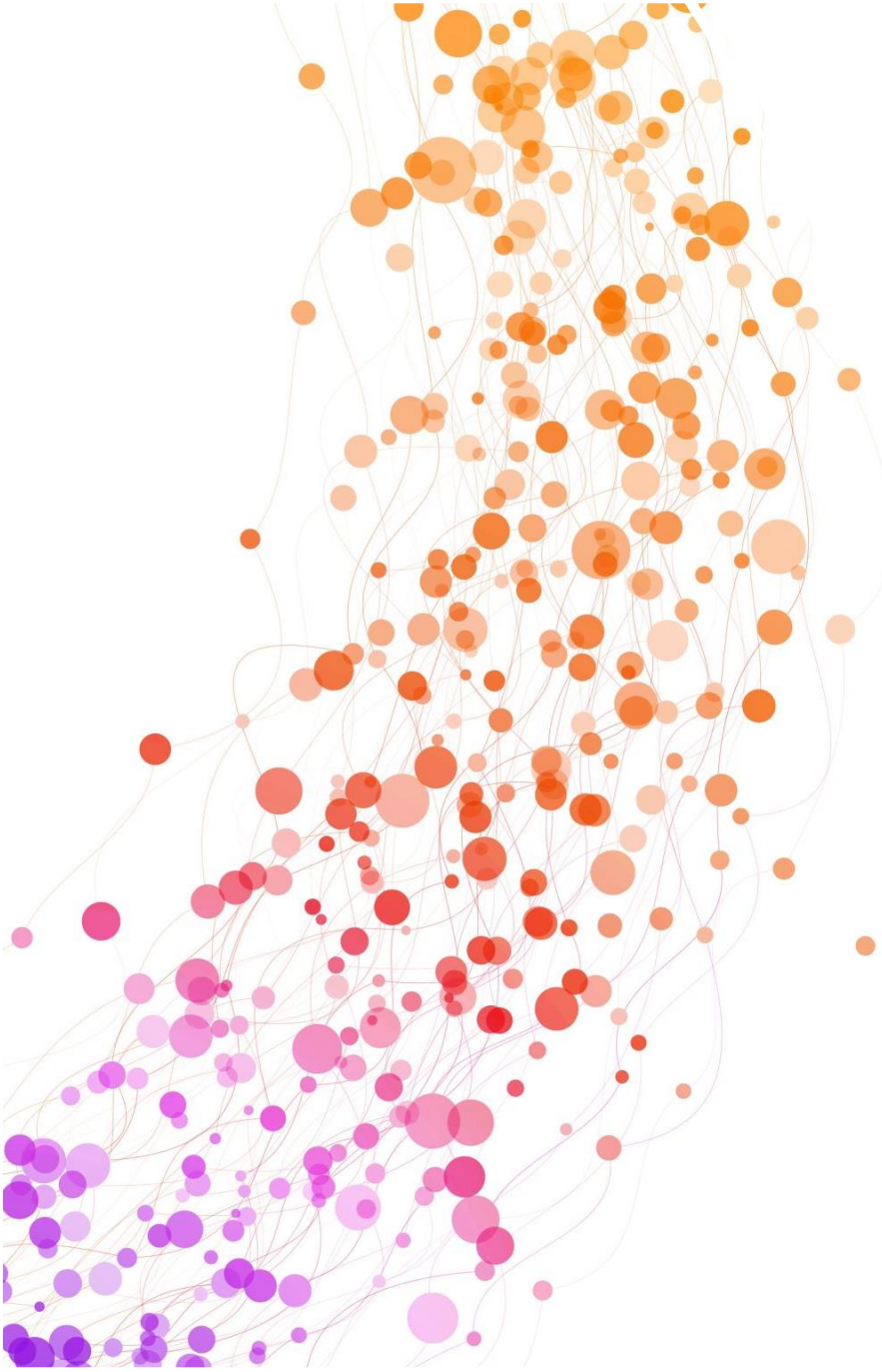


ΑΡΙΣΤΟΤΕΛΕΙΟ
ΠΑΝΕΠΙΣΤΗΜΙΟ
ΘΕΣΣΑΛΟΝΙΚΗΣ

ΕΕΜΜΟ
Ελληνική Εταιρεία
Μελέτης Μεταβολισμού
των Οστών

Επιστημονική Εκδήλωση
Μεταβολικά Νοσήματα των Οστών
Βιβλιογραφική Ενημέρωση

Εκτός ένδειξης (off label) χρήση αντιοστεοπορωτικών φαρμάκων

Στέργιος Α. Πολύζος

Ενδοκρινολόγος – Κλινικός Φαρμακολόγος

Α΄ Εργαστήριο Φαρμακολογίας

Τμήμα Ιατρικής Α.Π.Θ.

Σύγκρουση συμφερόντων

Καμία σχετική

Bone 129 (2019) 115048

Contents lists available at ScienceDirect

Bone

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

Review Article

Off-label uses of denosumab in metabolic bone diseases

Stergios A. Polyzos[a,*,1], Polyzois Makras[b,1], Symeon Tournis[c,1], Athanasios D. Anastasilakis[d,1]

[a] First Department of Pharmacology, Faculty of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece
[b] Department of Endocrinology and Diabetes and Department of Medical Research, 251 Hellenic Air Force General Hospital, Athens, Greece
[c] Laboratory for Research of the Musculoskeletal System "Th. Garofalidis", National and Kapodistrian University of Athens, KAT Hospital, Athens, Greece
[d] Department of Endocrinology, 424 General Military Hospital, Thessaloniki, Greece

Disease	Suggestion based on preliminary results (Yes; Yes in specific conditions; No; Neither yes or not)[a]
Dmab administered mainly for BMD and/or BTM improvement and/or fracture risk reduction	
Paget's disease of bone	Yes in specific conditions
Juvenile Paget disease	Yes
Fibrous dysplasia	Yes
Thalassemia bone disease	Yes
CKD-associated bone disease	Yes in specific conditions
Organ transplantation-associated bone disease	Yes in specific conditions
Osteogenesis imperfecta	Neither yes or not
Mastocytosis	Neither yes or not
Neurofibromatosis	Neither yes or not
Osteoradionecrosis	Neither yes or not
Multiple system atrophy	Neither yes or not
Duchenne muscular dystrophy	Neither yes or not
Spinal cord injury-associated bone loss	Neither yes or not
Anorexia Nervosa	Neither yes or not
Hypophosphatasia	No
Pregnancy and lactation-associated osteoporosis	No
Dmab administered mainly to manage symptoms and lesions	
Hajdu Cheney syndrome	Yes
Langerhans cell histiocytosis	Yes
Giant cell granuloma	Yes in specific conditions
Aneurysmal bone cysts	Yes in specific conditions
Melorheostosis	Neither yes or not
Diffuse sclerosing osteomyelitis	Neither yes or not
Bone marrow edema syndrome	Neither yes or not
Perthes' disease	Neither yes or not
Low Back Pain and Modic Changes	Neither yes or not
Gorham-Stout disease	Neither yes or not
Charcot neuropathic osteoarthropathy	Neither yes or not
Periprosthetic osteolysis	Human data still unpublished
Dmab administered mainly to manage hypercalcemia	
Hyperparathyroidism	Yes in specific conditions
Immobilization hypercalcemia	Yes
Tuberculosis-associated hypercalcemia	Yes in specific conditions
Myelofibrosis	Neither yes or not

Juvenile Paget disease	Yes
Fibrous dysplasia	Yes
Thalassemia bone disease	Yes

Hajdu Cheney syndrome	Yes
Langerhans cell histiocytosis	Yes

Immobilization hypercalcemia	Yes

Polyzos SA et al. Bone 2019

PICO plus / PICOTT

P.I.C.O. Model for Clinical Questions		
P	**P**atient, Population, or Problem	How would I describe a group of patien ts similar to mine?
I	**I**ntervention, Prognostic Factor, o r Exposure	Which main intervention, prognostic fact or, or exposure am I considering?
C	**C**omparison or Intervention (if a ppropriate)	What is the main alternative to compar e with the intervention?
O	**O**utcome you would like to meas ure or achieve	What can I hope to accomplish, measur e, improve, or affect?
T	What type of question are you asking?	Diagnosis, Etiology/Harm, Therapy, Pro gnosis, Prevention
T	Type of study you want to find	What would be the best study design /methodology?

The Journal of Clinical Endocrinology & Metabolism, 2024, **109**, 1873–1882
https://doi.org/10.1210/clinem/dgae012
Advance access publication 5 January 2024
Clinical Research Article

Efficacy and Safety of Denosumab vs Zoledronic Acid in OI Adults: A Prospective, Open-Label, Randomized Study

Xiaoyun Lin,[1] Jing Hu,[1] Bingna Zhou,[1] Xiaojie Wang,[1] Qian Zhang,[1] Yan Jiang,[1] Ou Wang,[1] Weibo Xia,[1] Xiaoping Xing,[1] and Mei Li[1]

[1]Department of Endocrinology, National Health Commission Key Laboratory of Endocrinology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100730, China

J Clin Endocrinol Metab 2024; 109: 1873-1882

Σκοπός

- P: Ενήλικες με ατελή οστεογένεση, Z-score -2.0 (LS ή FN) και ιστορικό 1 τουλάχιστον κατάγματος (n=51)

  Κάποιοι είχαν λάβει προηγουμένως θεραπεία (ΧΩΡΙΣ wash-out)

- I: Denosumab (sub), 60 mg/ 6 μήνες

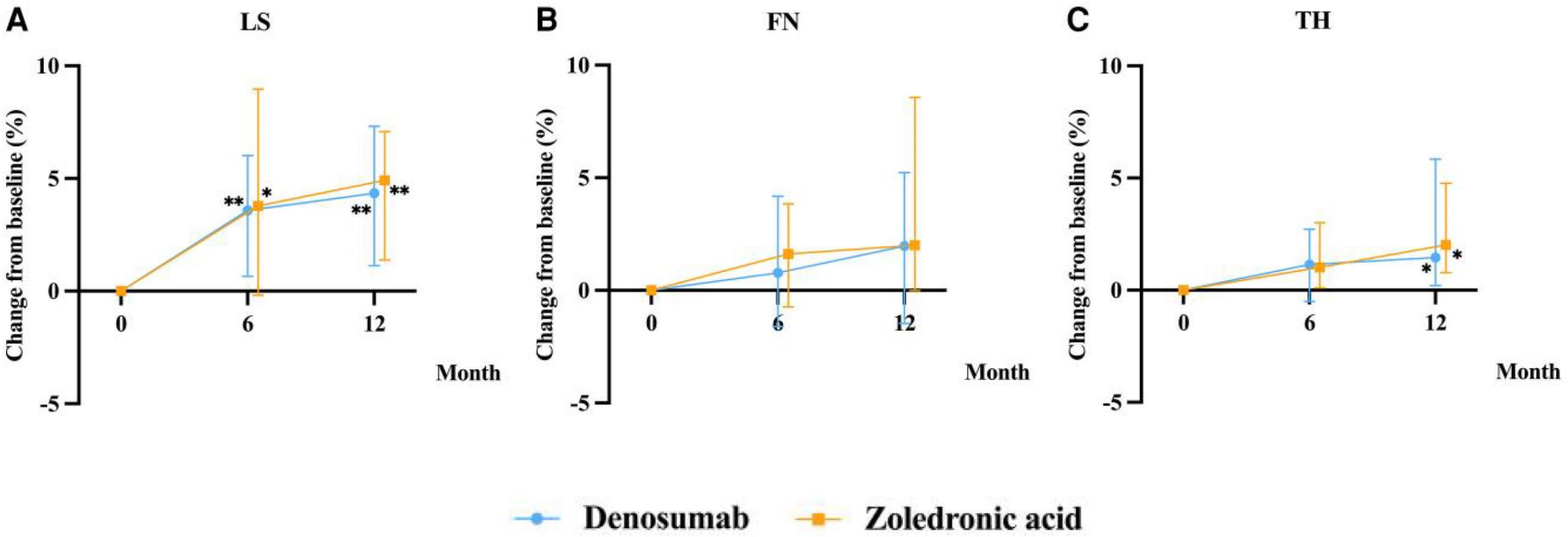
- C: Ζολεδρονικό οξύ (iv), 5 mg/ εφάπαξ

- O: Αλλαγή σε: α) BMD (%), β) TBS (%), γ) CTX, ALP (%)

- T: Θεραπεία

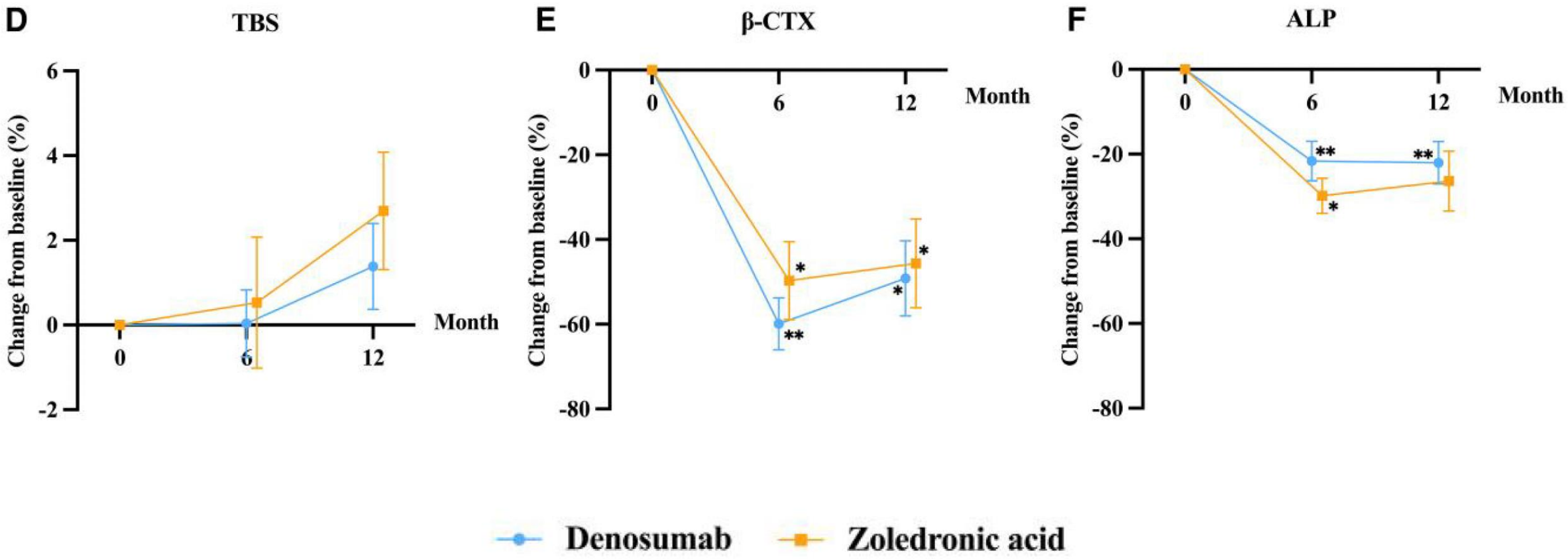
- T: RCT, open label, head-to-head, χωρίς placebo, ενός κέντρου, 12 μηνών

Κύρια έκβαση 1



Median %

Κύρια έκβαση 2



Mean %

Ανεπιθύμητες ενέργειες

Table 2. AEs during denosumab and zoledronic acid treatment

	Denosumab (n = 25)	Zoledronic acid (n = 26)	*P* value
Injection site reaction, n (%)	1 (4.0)	2 (7.7)	1.000
New fracture, n (%)	2 (8.0)	1 (3.8)	.610
Acute-phase reaction, n (%)	0 (0.0)	9 (34.6)	**.002**
Pyrexia	0 (0.0)	7 (26.9)	**.010**
Myalgia	0 (0.0)	2 (7.7)	.490
Headache	0 (0.0)	0 (0.0)	—
Other events of interest, n (%)			
Hypercalcemia	0 (0.0)	0 (0.0)	—
Hypocalcemia	0 (0.0)	0 (0.0)	—
Bone pain	3 (12.0)	5 (19.2)	.703
Fatigue	1 (4.0)	0 (0.0)	.490
Osteonecrosis of the jaw	0 (0.0)	0 (0.0)	—
Atypical fracture	0 (0.0)	0 (0.0)	—
Soft tissue infections	0 (0.0)	0 (0.0)	—
Serious AEs, n (%)	0 (0.0)	0 (0.0)	—
All AEs, n (%)	5 (20.0)	14 (53.8)	**.012**

Bold numbers represent $P < .05$.
Abbreviations: AEs, adverse events.

The Journal of Clinical Endocrinology & Metabolism, 2024, **109**, 1827–1836
https://doi.org/10.1210/clinem/dgad732
Advance access publication 10 January 2024
Clinical Research Article

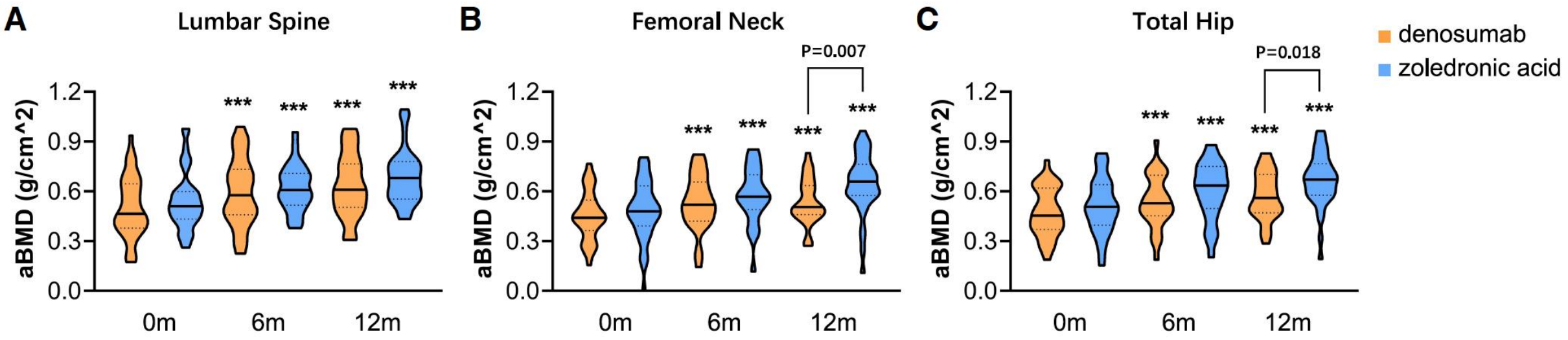
Safety and Efficacy of Denosumab in Children With Osteogenesis Imperfecta—the First Prospective Comparative Study

Jiayi Liu,[1] Xiaoyun Lin,[1] Lei Sun,[1] Qian Zhang,[1] Yan Jiang,[1] Ou Wang,[1] Xiaoping Xing,[1] Weibo Xia,[1] and Mei Li[1]

[1]Department of Endocrinology, Key Laboratory of Endocrinology, National Health and Family Planning Commission, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100730, China

J Clin Endocrinol Metab 2024; 109: 1827-1836

Κύρια έκβαση



Νέα κατάγματα: 9 (Dmab) vs. 7 (ZOL)
Συνολικά: 19% σε 1 έτος υπό αγωγή

Median (IQR)
N=84

Osteoporosis International (2024) 35:1303–1304
https://doi.org/10.1007/s00198-024-07089-2

LETTER TO THE EDITOR

Beneficial effects of romosozumab on bone mineral density and trabecular bone score assessed by dual-energy X-ray absorptiometry in a family with osteogenesis imperfecta

Toru Kusakabe[1] · Yuki Ishihara[1,2] · Takuya Kitamura[1,2] · Akihiro Yasoda[3] · Kazutaka Nanba[1,2] · Mika Tsuiki[2,3] · Noriko Satoh-Asahara[1] · Tetsuya Tagami[1,2]

[1] Department of Endocrinology, Metabolism, and Hypertension Research, Clinical Research Institute, National Hospital Organization (NHO) Kyoto Medical Center, Kyoto, Japan

[2] Department of Endocrinology and Metabolism, National Hospital Organization (NHO) Kyoto Medical Center, Kyoto, Japan

[3] Clinical Research Institute, National Hospital Organization (NHO) Kyoto Medical Center, Kyoto, Japan

Osteoporos Int 2024; 35: 1303-1304

Σκοπός

- P: Ασθενείς της ίδιας οικογένειας με OI (c.757C > T, p.Arg253Ter στο *COL1A1*) και μπλε σκληρούς (**ν=3**)
- I: Romosozumab (sub), 210 mg/μήνα
- C: Όχι
- O: Αλλαγή σε: α) BMD, β) TBS
- T: Θεραπεία
- T: Case series, 1 έτος

Κύρια έκβαση

Table 1 BMD and TBS in patients before and during romosozumab treatment

Patient Age/sex	Time course	BMD (g/cm^2)	TBS	TBS T-score	TBS Z-score
Proband 48 y.o/male	Before	0.496	1.179	− 2.3	− 1.5
	6 M	0.521	1.175	− 2.3	− 1.5
	12 M	0.578	1.224	− 1.9	− 1.1
Mother 72 y.o/female	Before	0.824	1.260	− 3.3	0.6
	12 M	0.957	1.355	− 1.9	2.0
Sister 44 y.o/female	Before	0.713	1.286	− 2.9	− 2.4

BMD: Αύξηση 16,5 & 16,1%

TBS: Αύξηση 3,8 & 7,5%

Ατελής οστεογένεση: «θεραπευτική» προσέγγιση και τρέχουσες μελέτες

Drug	Comments
Bisphosphonates	First line therapy; increase bone density; facture reduction and pain relief evidence inconsistent
Anti RANKL antibody	Denosumab: Evidence of benefit inconclusive; trials terminated due to calcium derangements; may be useful for Type VI; no ongoing trials at this time
Teriparatide	Increased BMD (especially Type 1); phase 4 study of teriparatide followed by zoledronate ongoing
Anti-sclerostin antibodies	Setrusumab: phase 2/3 ongoing with promising preliminary data; romosozumab: phase 3 trial ongoing
Anti-TGFβ antibodies	Phase 2 study promising, phase 1 with similar drug underway

Lewiecki EM et al. J Clin Densitom 2025

The Journal of Clinical Endocrinology & Metabolism, 2024, **00**, 1–8
https://doi.org/10.1210/clinem/dgae867
Advance access publication 13 December 2024
Clinical Research Article

Safety and Efficacy of Moderate-dose Denosumab in Fibrous Dysplasia: Observational Results From a Phase 2 Clinical Trial

Vivian Szymczuk,[1] Ibrahim I. Elbashir,[1] Ramzy Ahmed,[1,2] Luis F. de Castro,[1] Kelly Milligan,[1] Xiaobai Li,[3] Babak Saboury,[1,4,5] and Alison M. Boyce[1]

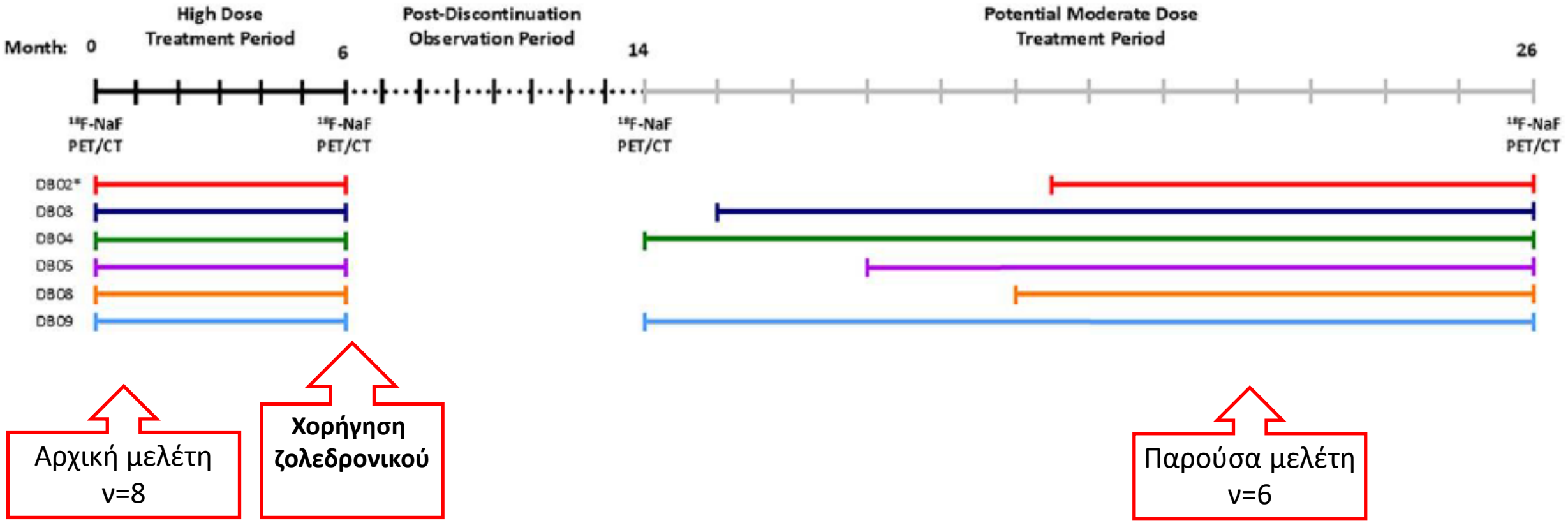
[1]Metabolic Bone Disorders Unit, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, MD 20892, USA
[2]School of Medicine, Eastern Virginia Medical School, Norfolk, VA 23507, USA
[3]Biostatistics and Clinical Epidemiology, Mark O. Hatfield Clinical Research Center, National Institutes of Health, Bethesda, MD 20892, USA
[4]Department of Radiology, University of Pennsylvania, Philadelphia, PA 19103, USA
[5]Institute of Nuclear Medicine, Radiology and Imaging Sciences, Bethesda, MD 20892, USA

J Clin Endocrinol Metab 2024; Epub

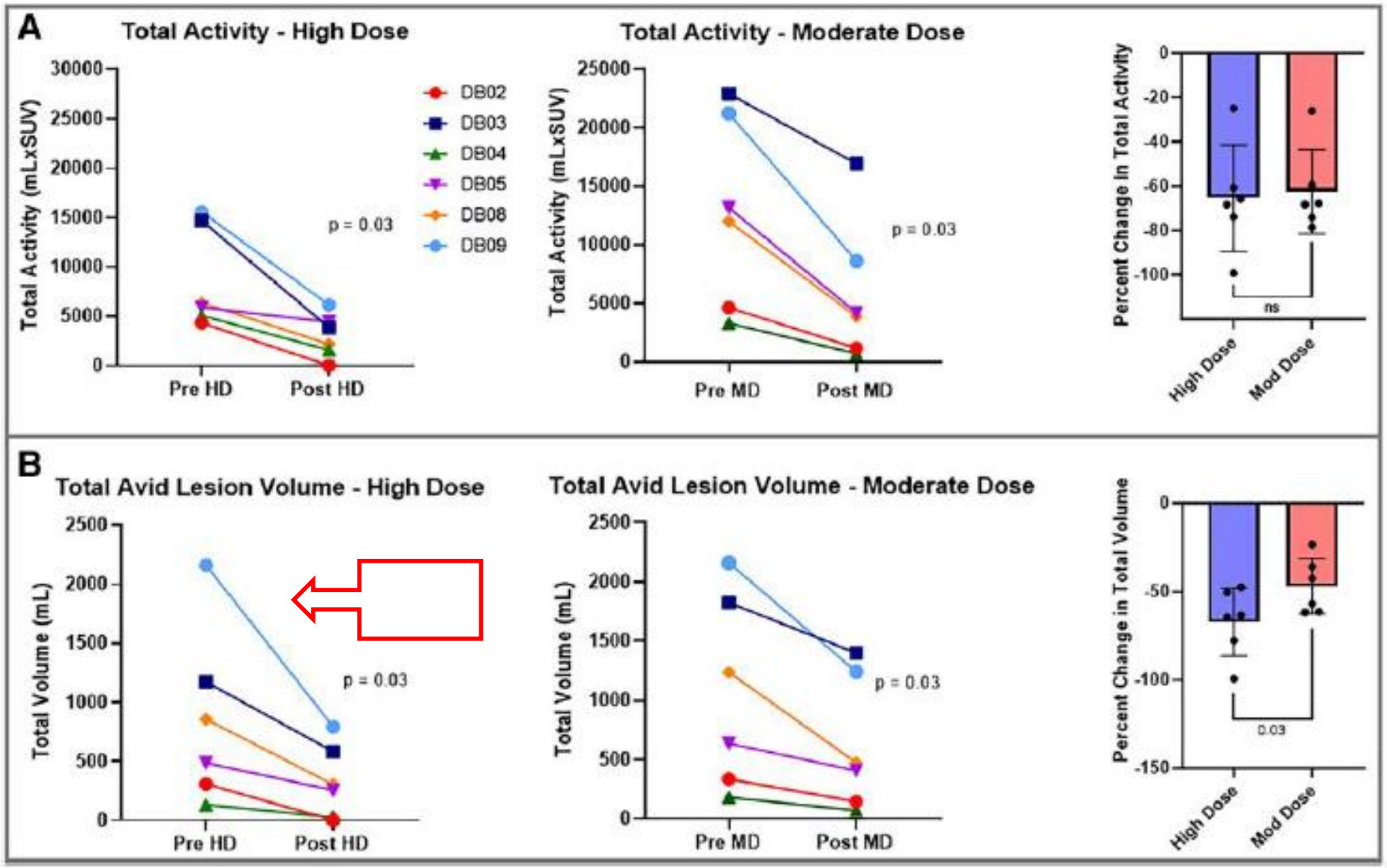
Σκοπός

- P: Ενήλικες (γυναίκες) ινώδη δυσπλασία και σχετικό οστικό άλγος > 3 μήνες (n=6)
- I: Denosumab (sub), 120 mg/ 3 μήνες
- C: Όχι, αλλά σύγκριση με προηγηθείσα θεραπεία denosumab (sub) στους ίδιους ασθενείς, 120 mg/ 1 μήνες (αρχική μελέτη: NCT03571191, φάσης 2, LF de Castro et al. N Engl J Med 2023)
- O: Αλλαγή σε: α) CTX, P1NP, β) ^{18}F-NaF PET/ CT, γ) βιοψίες βλαβών (6 μήνες)
- T: Θεραπεία
- T: Case series, open label, χωρίς placebo, 6,5-12 μηνών

Σχεδιασμός μελέτης

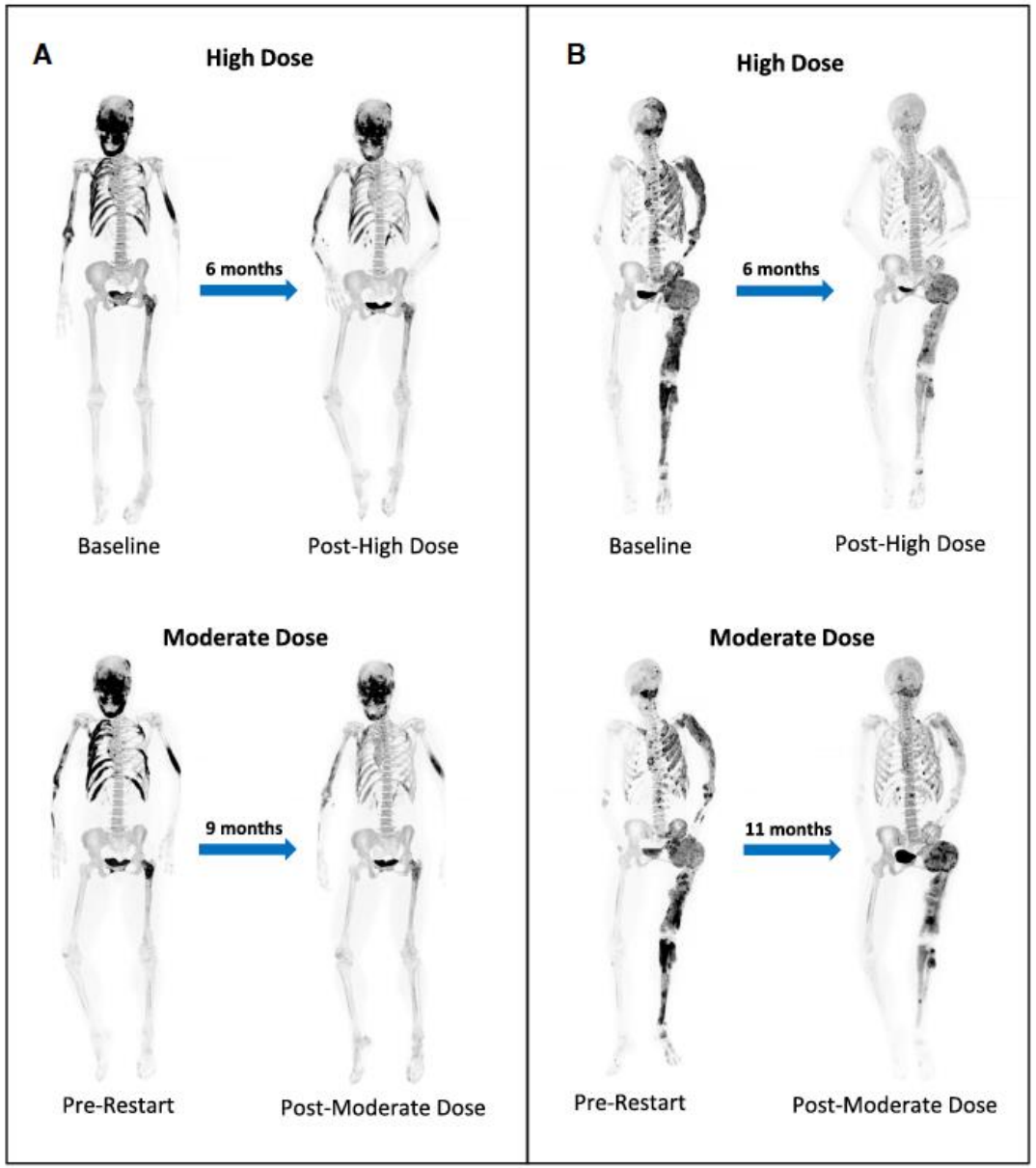


Κύρια έκβαση 1: ^{18}F-NaF PET/CT

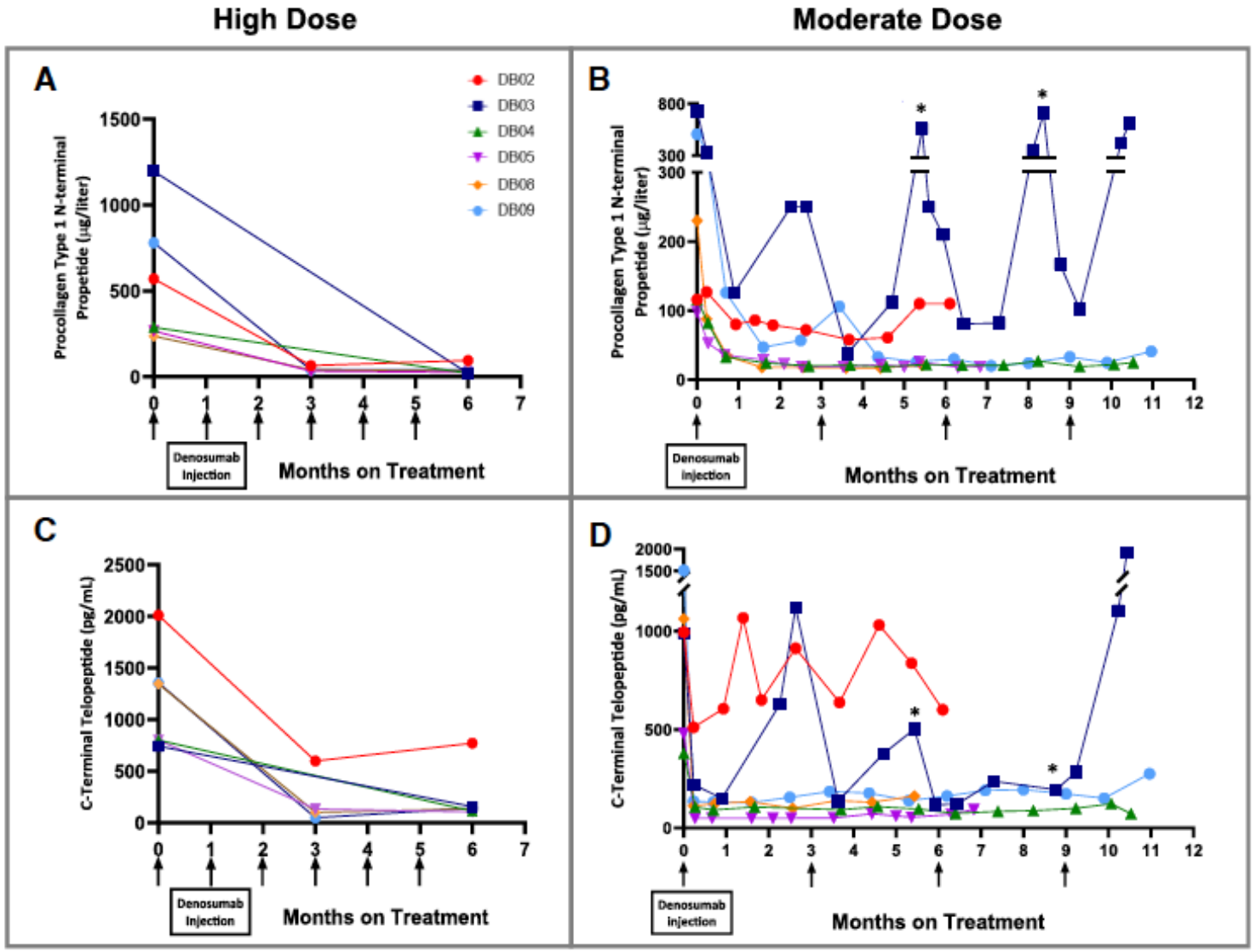


Median %

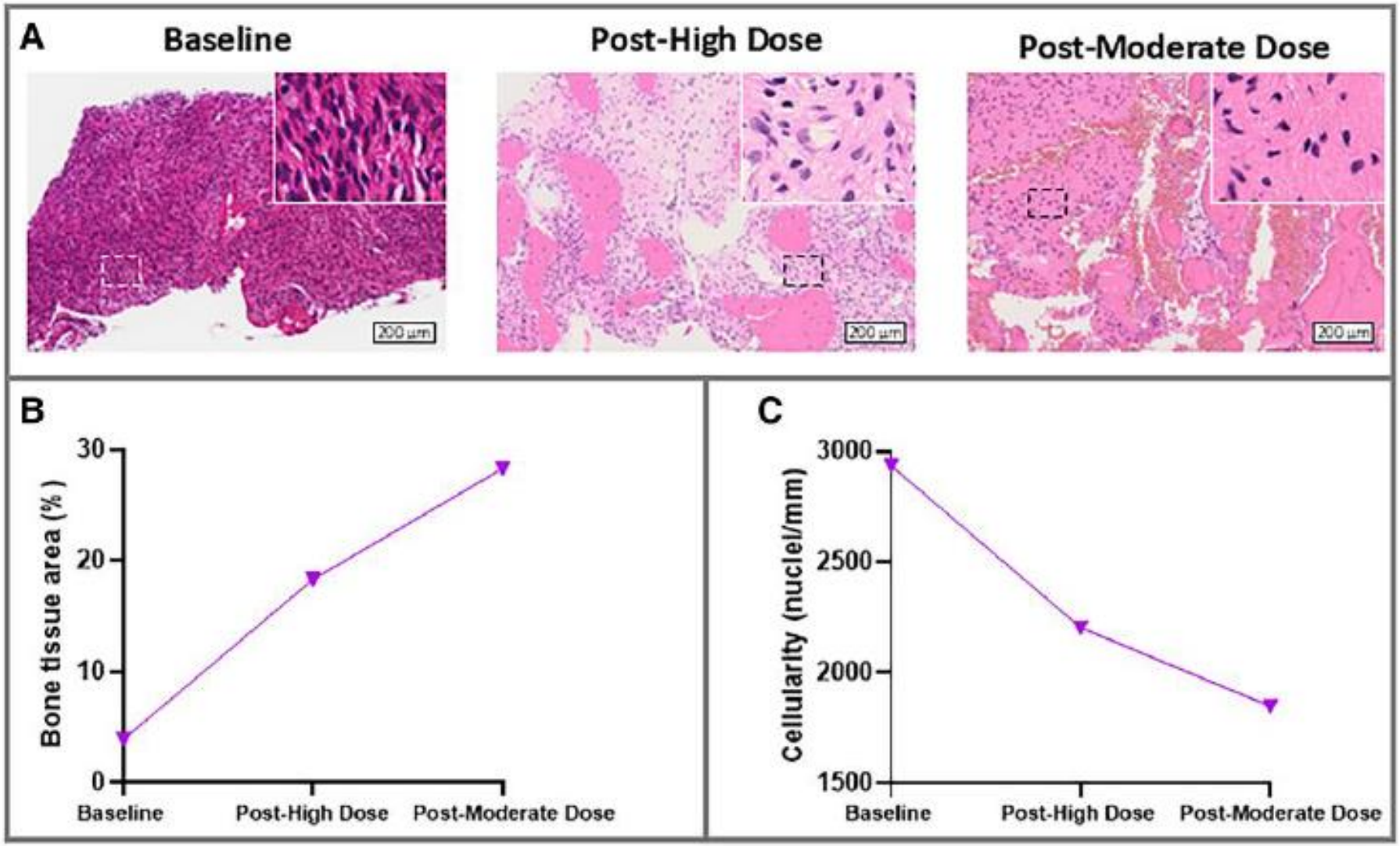
Κύρια έκβαση 1: ^{18}F-NaF PET/CT



Κύρια έκβαση 2: P1NP, CTX



Κύρια έκβαση 3: οστικές βιοψίες



The Journal of Clinical Endocrinology & Metabolism, 2025, **00**, 1–12
https://doi.org/10.1210/clinem/dgaf107
Advance access publication 3 March 2025
Clinical Research Article

The Efficacy and Safety of Denosumab for Treating Hypercalcemia in Primary Hyperparathyroidism: A Retrospective Study

An Song,[1,*] Yingyu Chen,[1,*] Rong Chen,[1] Shuzhong Liu,[2] Liyuan Kou,[1] Jiajia Wang,[1] Min Nie,[1] Yan Jiang,[1] Mei Li,[1] Weibo Xia,[1] Xiaoping Xing,[1] and Ou Wang[1]

[1]Key Laboratory of Endocrinology, Department of Endocrinology, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing 100730, China
[2]Department of Orthopaedic Surgery, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100730, China

J Clin Endocrinol Metab 2025; Epub

Σκοπός

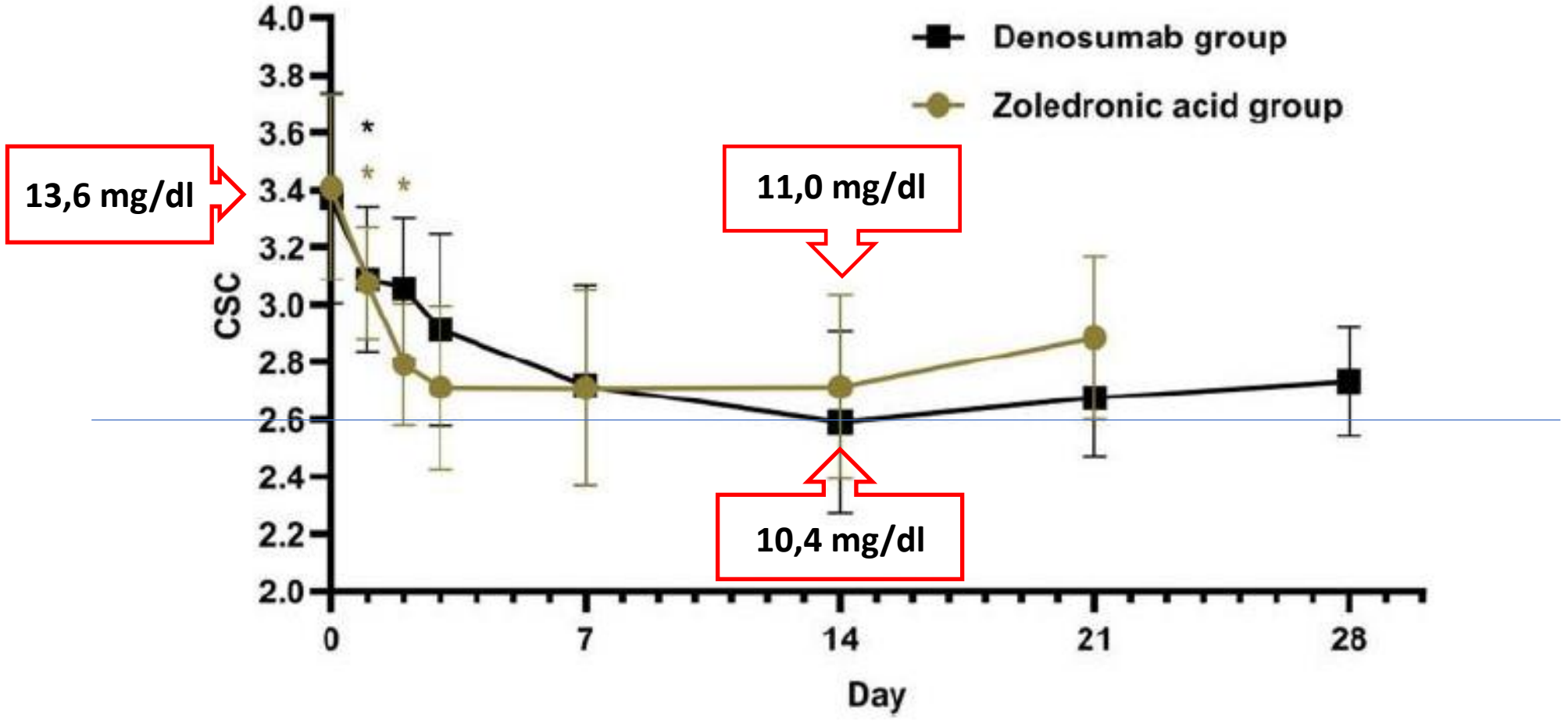
- P: Ενήλικες με PHPT και μέτρια/σοβαρή υπερασβεσιαιμία (διορθωμένο ασβέστιο > 12 mg/dl) (n=58)
- I: Denosumab (sub), 60 mg (120 mg 1 ασθενής) εφάπαξ
- C: Ζολεδρονικό οξύ (iv), 4 mg/ εφάπαξ
- O: Αλλαγή σε διορθωμένο ασβέστιο
- T: Θεραπεία
- T: RCT, open label, head-to-head, χωρίς placebo, ενός κέντρου, 12 μηνών

Δ.Δ. PHPT

	Dmab group *N* = 29	ZA group *N* = 29	*P*
Age at onset, years	54.14 ± 14.44	55.79 ± 14.57	.67
Pathology			
Pathological types	*n* = 26	*n* = 27	<.01
Hyperplasia, *n* (%)	1 (3.8%)	1 (3.7%)	
Adenoma, *n* (%)	11 (42.3%)	18 (66.7%)	
Atypical adenoma, *n* (%)	1 (3.8%)	6 (22.2%)	
Carcinoma, *n* (%)	13 (50.0%)	2 (7.4%)	
Concomitant treatment			
Calcitonin, *n* (%)	19 (65.6%)	23 (79.3%)	.38

Cinacalcet: v=2 vs. 0

Κύρια έκβαση



Κύρια έκβαση 1:
Πολλαπλή γραμμική παλινδρόμηση

Table 5. Multiple linear regression analysis of risk factors associated with ΔCa in the Dmab group

Independent variables	*B*	SE	β	95% CI	*P* value
Duration of disease	0.022	0.008	.301	0.005~0.038	.013
Serum CSCmax	0.360	0.143	.303	0.057~0.662	.023
Serum PTH at baseline	0.000	0.000	−.251	0.000~0.000	.057
Serum ALP	0.001	0.000	.608	0.001~0.002	<.001
Serum 25OHD	−0.024	0.006	−.369	−0.037~−0.010	.002

Ασφάλεια

	Dmab-P1 *N* = 13	Dmab-P2 *N* = 13	*P*
Serum PTH at baseline, pg/mL	1008.0 (708.5, 1539.5)	482.0 (343.5, 731.0)	.004
Serum PTH at D1~D3, pg/mL	838.5 (678.8, 1855.5)	473.0 (454.5, 704.0)	.05
Serum PTH at D7~D21, pg/mL	1168.0 (703.0, 2029.0)[b]	504.5 (385.0, 869.8)[b]	.01
Serum creatinine at baseline, μmol/L	98.5 ± 53.7	101.4 ± 58.0	.68
Serum creatinine at D1, μmol/L	103.1 ± 58.1	134.3 ± 89.0	.36
Serum creatinine at D3, μmol/L	83.5 ± 46.9	104.0 ± 59.8	.88
Serum creatinine at D7~D21, μmol/L	83.0 ± 35.3	99.5 ± 58.0	.49
ΔCreatinine, μmol/L	−4.0 (−23.5, −0.5)[b]	−6.0 (−13.0, −3.3)[b]	.33
Hypocalcemia after medication[c], *n* (%)	1 (7.7%)	0 (0%)	1.0

The Journal of Clinical Endocrinology & Metabolism, 2024, **109**, 879–901
https://doi.org/10.1210/clinem/dgad548
Advance access publication 14 September 2023
Meta-Analysis

Comparative Effectiveness of Therapeutic Interventions in Pregnancy and Lactation-Associated Osteoporosis: A Systematic Review and Meta-analysis

Panagiotis Anagnostis,[1] Kalliopi Lampropoulou-Adamidou,[2] Julia K. Bosdou,[3] Georgios Trovas,[2] Petros Galanis,[4] Efstathios Chronopoulos,[2] Dimitrios G. Goulis,[1] and Symeon Tournis[2]

[1]Unit of Reproductive Endocrinology, 1st Department of Obstetrics and Gynecology, Medical School, Aristotle University of Thessaloniki, Thessaloniki 56403, Greece
[2]Laboratory for the Research of Musculoskeletal System "Th. Garofalidis", School of Medicine, National and Kapodistrian University of Athens, KAT General Hospital, Athens 14561, Greece
[3]Unit for Human Reproduction, 1st Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Thessaloniki 11527, Greece
[4]Clinical Epidemiology Laboratory, Faculty of Nursing, National and Kapodistrian University of Athens, Athens 11527, Greece

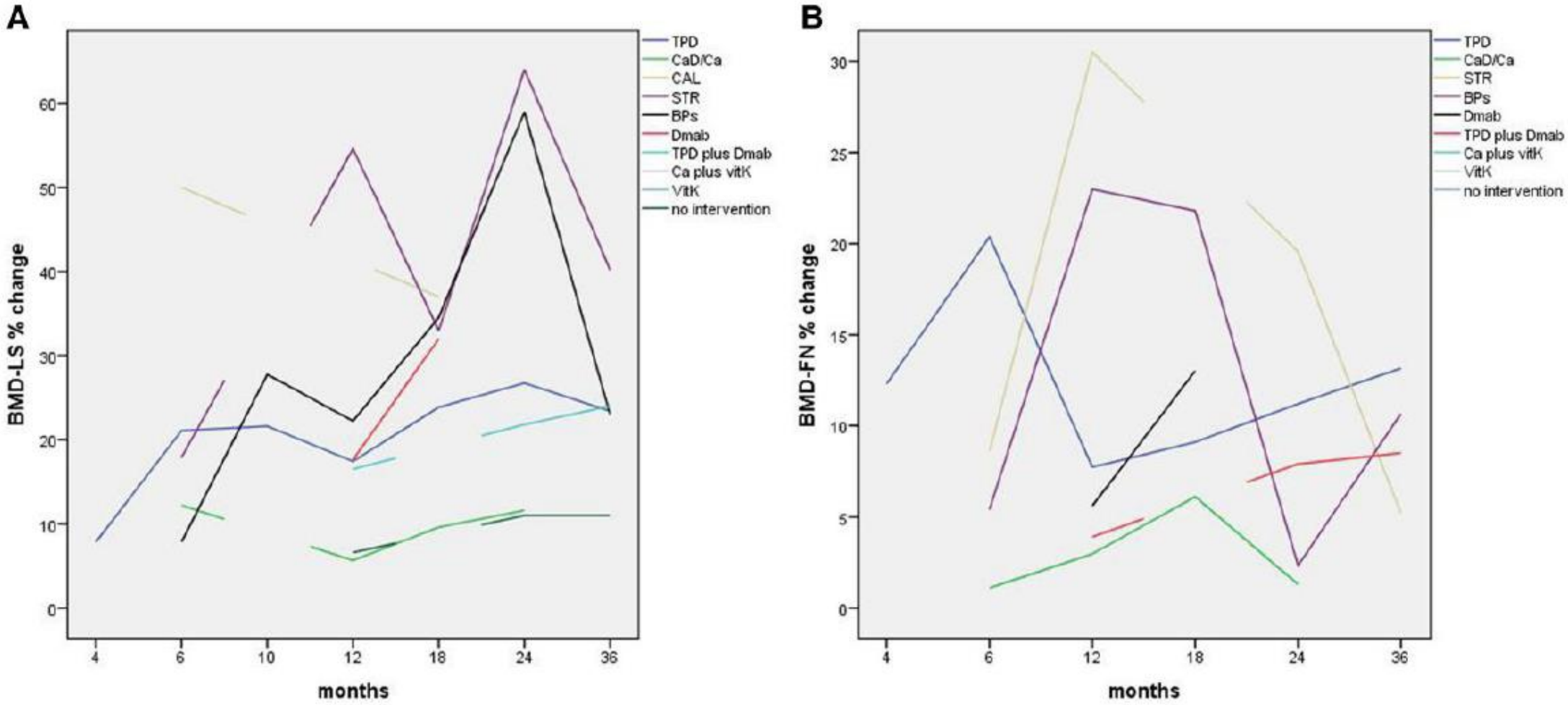
Correspondence: Panagiotis Anagnostis, MD, MSc, PhD, FRSPH, Medical School, Aristotle University of Thessaloniki, Mitropoleos 73, Thessaloniki 54622, Greece. Email: pan.anagnostis@gmail.com.

J Clin Endocrinol Metab 2024; 109: 879-901

Σκοπός

- P: Ενήλικες γυναίκες (19 – 42 ετών) με οστεοπόρωση κατά την εγκυμοσύνη/γαλουχία (**ν=451**)
- I: Ασβέστιο ±βιταμίνη D (ή αλφακαλσιδόλη) ή διφωσφονικά ή denosumab ή τεριπαρατίδη ή ρανελικό στρόντιο ή romosozumab ή αλληλοδιάδοχη θεραπεία
- C: Όχι (συνήθως) ή ασβέστιο ±βιταμίνη D
- O: α) αλλαγή BMD, β) επίδραση σε κατάγματα
- T: Θεραπεία
- T: Συστηματική ανασκόπηση μελετών παρατήρησης (οι περισσότερες case reports και case series), **65 μελέτες** (και μετανάλυση 2 μελετών), follow-up 6 μήνες – 22 έτη

Κύρια έκβαση 1

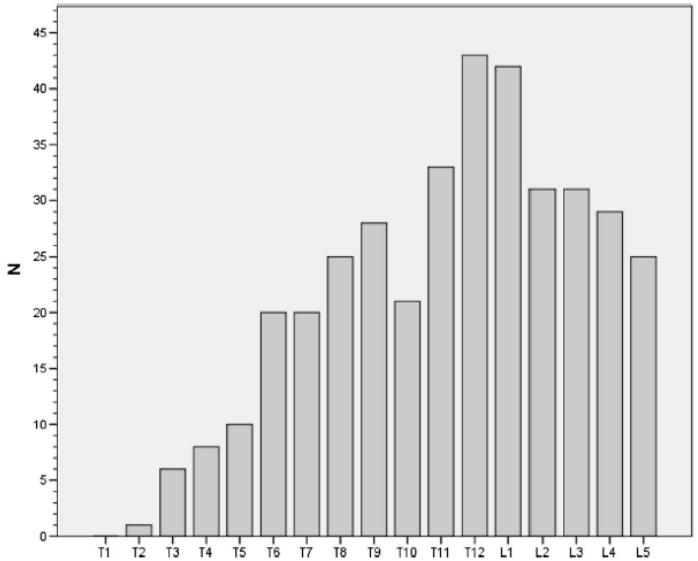


Κύρια έκβαση 2

- Συνολικά, νέο κάταγμα σε 64 ασθενείς (14%)
  - 10 σε επόμενη κύηση

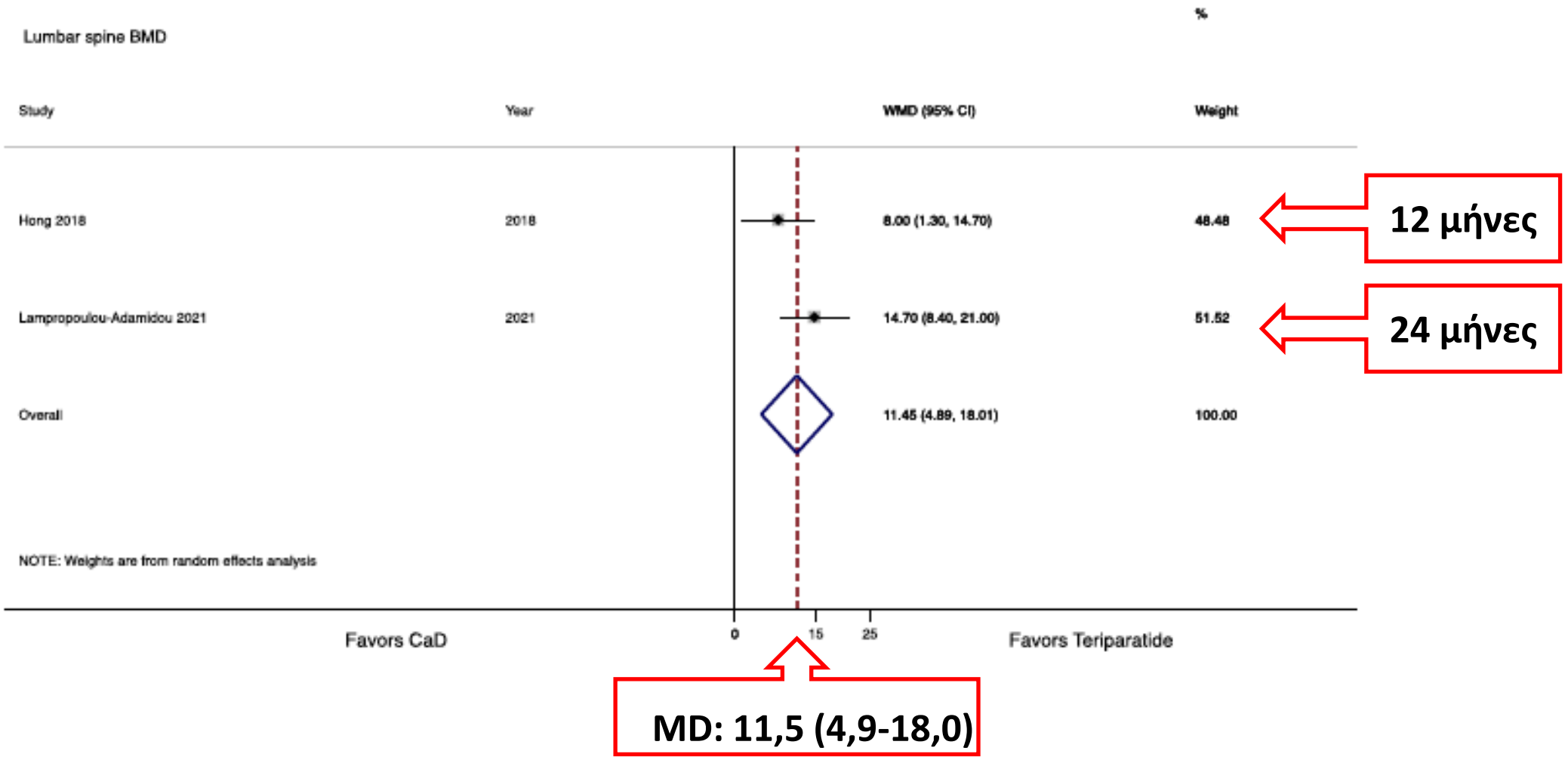
- Στη μεγαλύτερη μελέτη (ν=107), νέο κάταγμα σε 26 ασθενείς (24%)
  - 30 ασθενείς είχαν επόμενη κύηση
    - 6 (20%) νέο κάταγμα

      Kyvernitakis I et al. Osteoporos Int 2018
    -

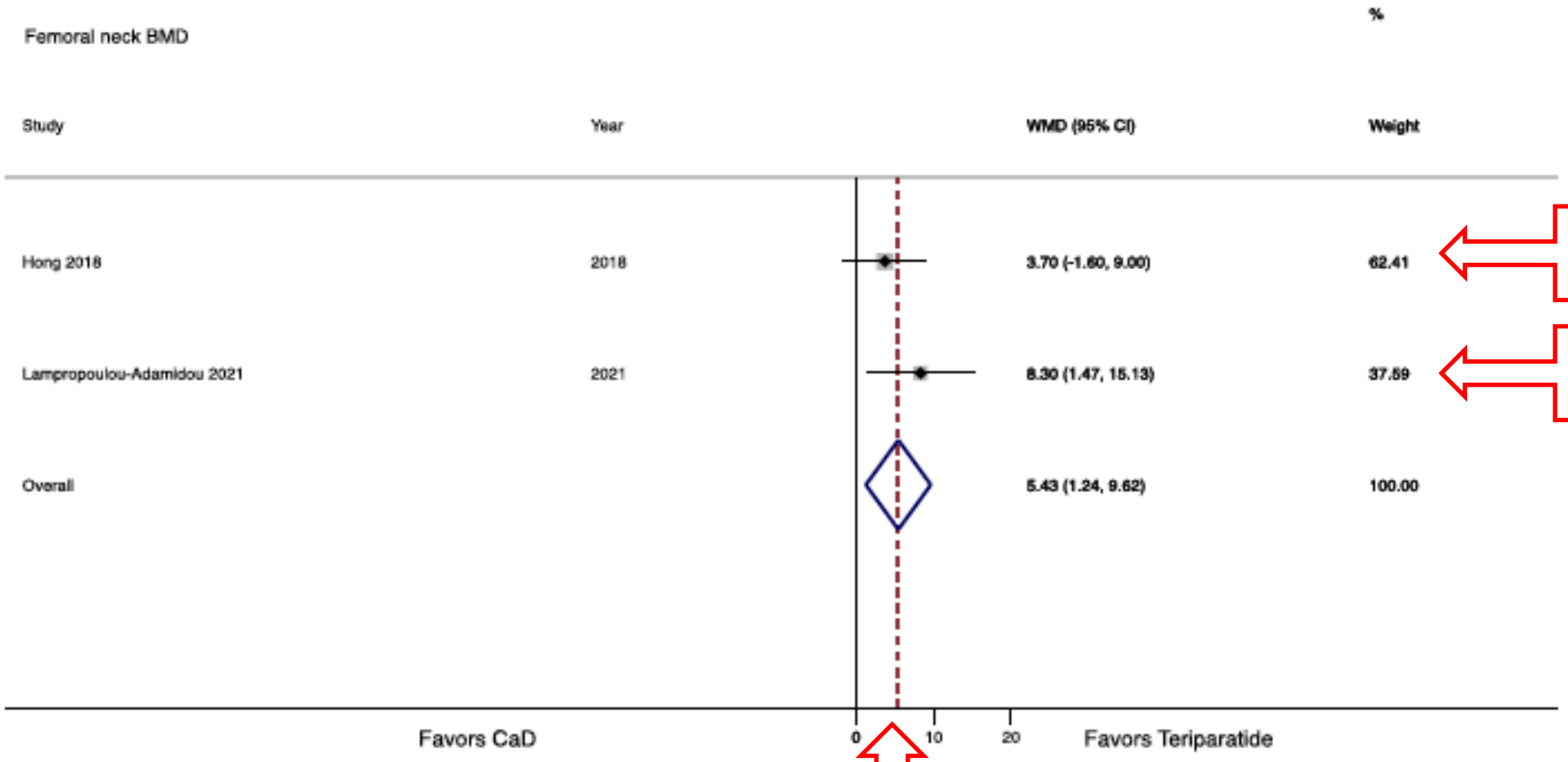


- Υποχώρηση άλγους στους περισσότερους ασθενείς

Μετα-ανάλυση: LS BMD (%)



Μετα-ανάλυση: FN BMD (%)



12 μήνες

24 μήνες

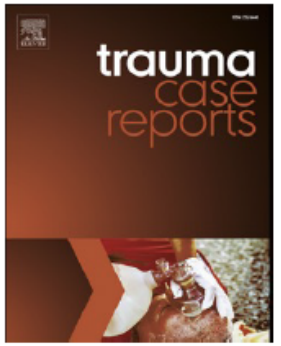
MD: 5,4 (1,2-9,5)

Trauma Case Reports 53 (2024) 101077

Contents lists available at ScienceDirect

Trauma Case Reports

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



Case Report

Monoclonal antibody anti-sclerostin for treatment of pelvic insufficiency fractures in adult hypophosphatasia: A case report

Pierre-Emmanuel Schwab [a,*], Alicia Dessain [c], Joshua Milby [b]

[a] *Missouri Orthopaedic Institute, Missouri University Health, Department of Orthopaedic Surgery, 1100 Virginia Avenue, Columbia, MO 65201, United States of America*

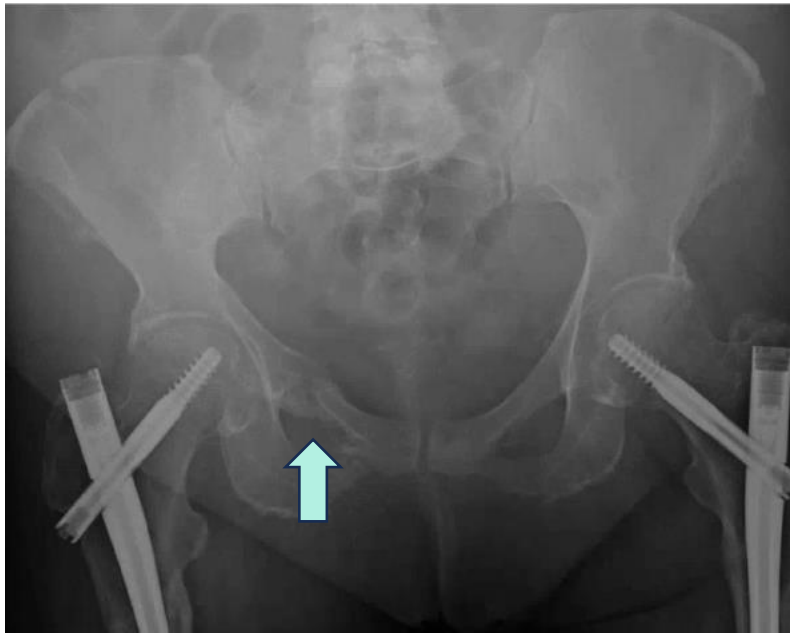
[b] *Cox Medical Center South, Missouri University Health, Department of Orthopaedic Trauma Surgery, 3801 S National Avenue, Springfield, MO 65807, United States of America*

[c] *Missouri University Health, Department of Pathology, 1 Hospital Drive, Columbia, MO 65201, United States of America*

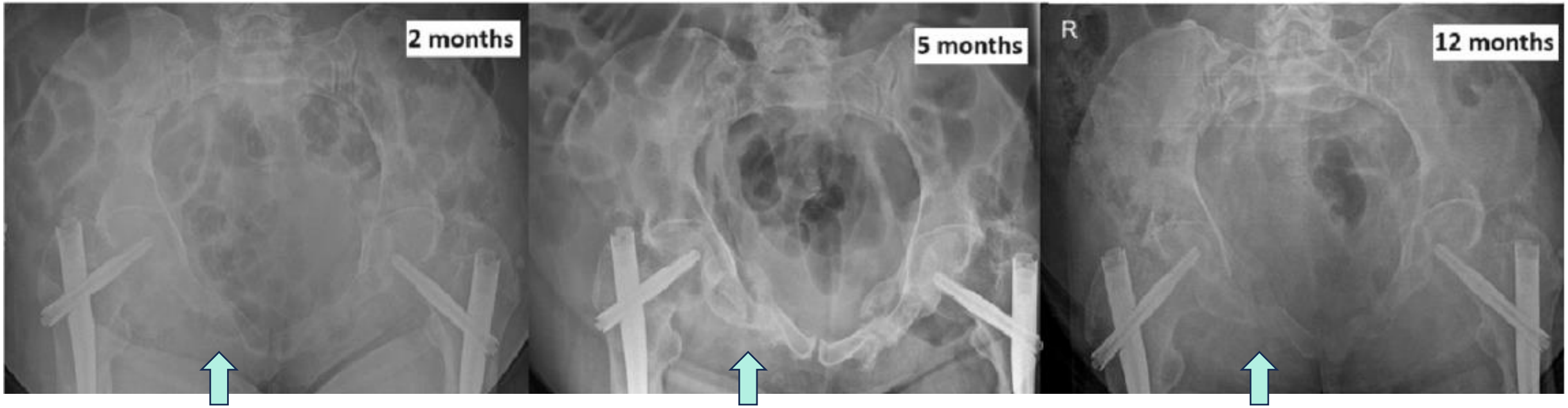
Trauma Case Rep 2024; 53: 101077

Σκοπός

- P: Ασθενής (67 ετών) με HPP και δυσεπούλωτο κάταγμα δεξιού λαγονίου (**ν=1**)
- I: Romosozumab (sub), 210 mg/μήνα
- C: Όχι
- O: α) επούλωση κατάγματος, β) ανακούφιση άλγους
- T: Θεραπεία
- T: Case report, 1 έτος



Κύρια έκβαση 1



Κύρια έκβαση 2

Table 1
Timeline.

Ortho visits	Initial visit	Second visit	Third visit	Fourth visit
Timeline	0 month	2 months	5 months	12 months
Romosozumab dose	None	Second	Fifth	Twelfth
VAS pain	10/10	6/10	0/10	0/10
Ambulatory status	Wheelchair use	Cane use	Cane use	No assistive device

VAS: Visual Analogic Scale.

Table 2
DEXA scan results.

DEXA scan timeline	T-Score lumbar spine	Lumbar spine BMD (g/cm^2)	BMD improvement from baseline	T-Score proximal radius	Proximal radius BMD (g/cm^2)	BMD improvement from baseline
Beginning	+1.0	1.100		−1.6	0.500	
6 months	+1.1	1.327	20.6 %	−1.3	0.764	52.8 %
12 months	+1.2	1.443	31.2 %	−1.1	0.852	70.4 %

DEXA: Dual-Energy X-ray Absorptiometry, BMD: Bone Mass Density.

20,6% & 31,2%

52,1% & 70,4%

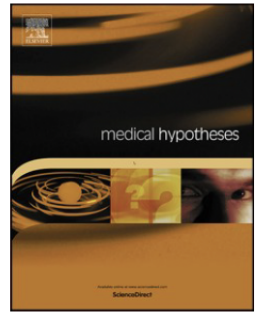
Denosumab: repurposing

Medical Hypotheses 146 (2021) 110379

Contents lists available at ScienceDirect

Medical Hypotheses

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



Check for updates

Treatment of nonalcoholic fatty liver disease with an anti-osteoporotic medication: A hypothesis on drug repurposing

Stergios A. Polyzos [*,1], Antonis Goulas

First Laboratory of Pharmacology, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece

Κλινική μελέτη

NCT05493761 Recruiting

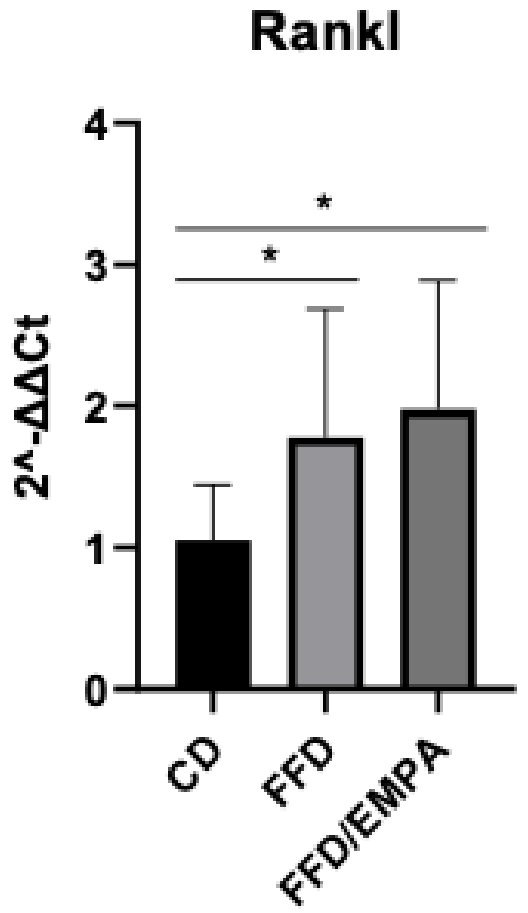
Effect of Anti-osteoporotic Medications on Nonalcoholic Fatty Liver Disease

Conditions

Nonalcoholic Fatty Liver | Osteoporosis, Postmenopausal

Locations

Thessaloniki, Greece

Thessaloníki, Greece (2)

FFD mice model