# Νέα φάρμακα Οστεοπόρωσης

**Αθανάσιος Φούντας**
**Επιμελητής Α' Ενδοκρινολογίας**
**Μονάδα Ενδοκρινολογίας και Διαβητολογικό Κέντρο**
**Γενικό Νοσοκομείο Αθηνών 'Γ. Γεννηματάς'**

Μεταβολικά Νοσήματα των Οστών – Βιβλιογραφική Ενημέρωση
Αράχωβα, 29/03/2025

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osteoporosis

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## Medication-Related Osteonecrosis Successfully Treated With Hyperbaric Oxygen Therapy and Conservative Treatment: A Case Report.

Tanabe T, Kimura T, Sakata KI, Ohga N, Yanagawa-Matsuda A, Kobori Y.

Cureus. 2025 Feb 18;17(2):e79213. doi: 10.7759/cureus.79213. eCollection 2025 Feb.

PMID: 40115708 **Free PMC article.**

Medication-related osteonecrosis of the jaws (MRONJ) is a major side effect of the antiresorptive drugs used in treating patients with **osteoporosis** and cancer. MRONJ appears as prolonged inflammation affecting the maxilla or mandible, with necrotic bone exposure and intrao ...

2 Cite Share

## Selective modulation of the bone remodeling regulatory system through orthodontic tooth movement-a review.

Danz JC, Degen M.

Front Oral Health. 2025 Mar 6;6:1472711. doi: 10.3389/froh.2025.1472711. eCollection 2025.

PMID: 40115506 **Free PMC article.** Review.

Our aim was to elucidate the mechanisms and signaling pathways of the bone remodeling regulatory system (BRRS) as well as to investigate its clinical applications in **osteoporosis** treatment, orthopedic surgery, fracture management and orthodontic treatment. ...This approach ...

## Fermented soybean powder containing S-equol alleviates the **postmenopausal**

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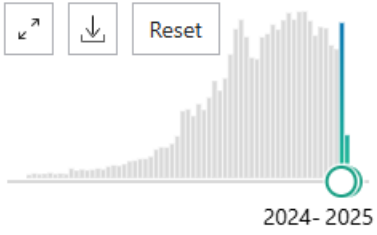
RESULTS BY YEAR

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PUBLICATION DATE

- 1 year
- 5 years
- 10 years
- From 2024/1/1 to 2025/2/28

TEXT AVAILABILITY

- Abstract
- Free full text
- Full text

1 Cite Share

Coffee and tea consumption on the risk of **osteoporosis**: a meta-analysis.

Li W, Xie Y, Jiang L.

Front Nutr. 2025 Mar 4;12:1559835. doi: 10.3389/fnut.2025.1559835. eCollection 2025.

PMID: 40104819 **Free PMC article.**

The pooled analysis showed that coffee consumption is significantly associated with a reduced risk of **osteoporosis** (odds ratio [OR] = 0.79, 95% confidence interval [CI]: 0.73-0.84, I (2) = 28.9%, p < 0.05). ...CONCLUSION: This meta-analysis suggests that long-term coffe

...

2 Cite Share

Study on the effect of Western medicine caltrate D combined with traditional Chinese medicine eight section brocade practice therapy on preventing **postmenopausal osteoporosis**.

Lan X, Sun H, Shi K, Sun X, Wang T, Wang H.

Pak J Pharm Sci. 2025 Jan-Feb;38(1):1-6.

PMID: 40089924 Clinical Trial.

*Journal of Bone and Mineral Research*, 2024, **39**, 672–682
https://doi.org/10.1093/jbmr/zjae057
Advance access publication: April 5, 2024
**Clinical Trial**

# Oral daily PTH(1-34) tablets (EB613) in postmenopausal women with low BMD or osteoporosis: a randomized, placebo-controlled, 6-month, phase 2 study

**Liana Tripto-Shkolnik[1], Auryan Szalat[2], Gloria Tsvetov[3], Vanessa Rouach[4], Chana Sternberg[5], Anke Hoppe[6], Gregory Burshtein[6], Hillel Galitzer[6], Miranda Toledano[6], Gil Harari[7], Arthur C. Santora[6], Felicia Cosman[8,*]**

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[5]CSC Ltd., Shoham, 6080340, Israel
[6]Entera Bio Ltd., Jerusalem, 9112002, Israel
[7]Medistat Ltd., Tel Aviv-Yafo, 9641002, Israel
[8]Department of Medicine, Columbia University, New York, NY, 10032, United States

# Κλινικό Ερώτημα

- Η αποτελεσματικότητα και η ασφάλεια του per os teriparatide *vs* placebo σε μετ-εμμηνοπαυσιακές γυναίκες με οστεοπενία ή οστεοπόρωση

# Κριτήρια Ένταξης - Αποκλεισμού

- Γυναίκες ≥50 ετών σε εμμηνόπαυση για τουλάχιστον 3 χρόνια
  - T-score ≤-2.0 και ≥-3.5 ΟΜΣΣ/ισχίο

- Κριτήρια αποκλεισμού
  - Ιστορικό κατάγματος
  - Προηγηθείσα λήψη teriparatide - Διφωσφωνικων, οιστρογόνων, raloxifene τα τελευταία 2 έτη - Zolendronate τα τελευταία 10 έτη - Denosumab τα τελευταία 3 έτη
  - Υπό αγωγή με γλυκοκορτικοειδή (≥2.5 mg prednisone ή ισοδύναμο) ή λήψη τους το τελευταίο έτος σε ημερήσια δόση ≥5 mg για ≥1 εβδομάδα
  - Ιστορικό νόσου Paget ή άλλης οστικής νόσου, εξωτερικής ακτινοβολίας, ουρολιθίασης, πρωτοπαθούς υπερπαραθυρεοειδισμού
  - Διαταραχές θυρεοειδούς, ασβεστίου, μαγνησίου, φωσφόρου, Alp
  - 25(OH)D <20 ng/mL,  eGFR <45 mL/min

# Διάγραμμα Μελέτης

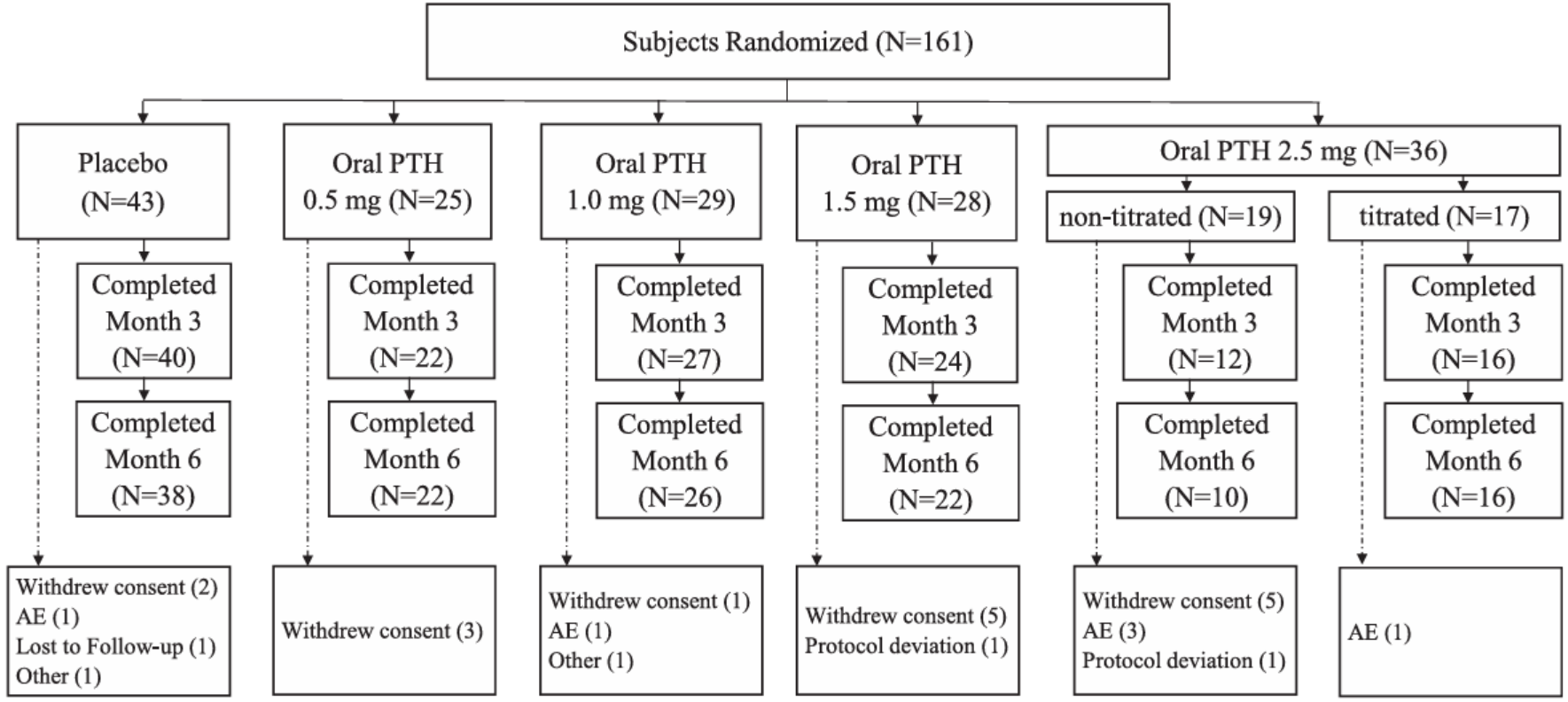



**Figure 1.** Subject Disposition.

# Πληθυσμός Μελέτης

**Table 1.** Baseline demographic and clinical characteristics.

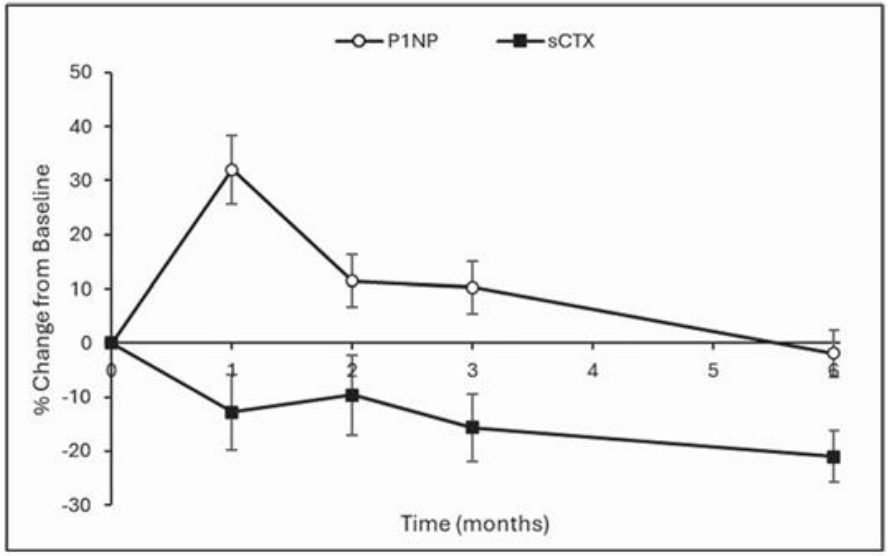
| *Variable* | Placebo | Oral PTH 0.5 mg | Oral PTH 1.0 mg | Oral PTH 1.5 mg | Oral PTH 2.5 mg non-titrated[a] | Oral PTH 2.5 mg titrated[a] | Total ($N = 161$) |
|---|---|---|---|---|---|---|---|
| | *Demographics, mean ± SD* | | | | | | |
| *N* | 43 | 25 | 29 | 28 | 19 | 17 | 161 |
| *Age, yr* | 59.9 ± 5.1 | 61.2 ± 6.0 | 62.4 ± 4.7 | 61.4 ± 6.5 | 62.4 ± 4.1 | 61.9 ± 5.3 | 61.3 ± 5.4 |
| *Height, cm* | 162.2 ± 4.5 | 159.7 ± 7.2 | 159.2 ± 5.6 | 160.6 ± 5.0 | 159.0 ± 6.6 | 158.7 ± 6.1 | 160.3 ± 5.8 |
| *Weight, kg* | 65.6 ± 13.0 | 68.7 ± 10.9 | 65.9 ± 13.7 | 65.2 ± 12.0 | 70.0 ± 10.6 | 65.1 ± 10.2 | 66.6 ± 12.0 |
| *BMI, kg/m²* | 25.0 ± 5.2 | 27 ± 4.0 | 25.9 ± 4.7 | 25.3 ± 4.9 | 27.7 ± 3.6 | 26.0 ± 4.6 | 26 ± 4.7 |
| | *Serum biochemical markers of bone formation and resorption, mean ± SD (PP1 Population)* | | | | | | |
| *N* | 40 | 21 | 25 | 23 | 10 | 13 | – |
| *PINP, ng/mL* | 64.7 ± 19.0 | 58.7 ± 20.8 | 60.5 ± 22.2 | 66.4 ± 23.0 | 68.6 ± 18.1 | 61.8 ± 18.9 | – |
| *Osteocalcin, ng/mL* | 24.4 ± 8.8 | 21.1 ± 4.3 | 24.7 ± 8.7 | 24.9 ± 6.7 | 32.6 ± 18.9 | 22.3 ± 13.3 | – |
| *Serum CTX, ng/mL* | 0.44 ± 0.20 | 0.36 ± 0.10 | 0.40 ± 0.20 | 0.46 ± 0.21 | 0.51 ± 0.26 | 0.43 ± 0.30 | – |
| | *BMD T Score, mean ± SD (PP2 Population)* | | | | | | |
| *N* | 43 | 25 | 29 | 28 | 19 | 17 | 161 |
| *LS* | −2.37 ± 0.65 | −2.45 ± 0.80 | −2.35 ± 0.71 | −2.32 ± 0.88 | −2.38 ± 0.69 | −2.02 ± 0.78 | −2.34 ± 0.74 |
| *FN* | −2.17 ± 0.54 | −2.16 ± 0.55 | −2.10 ± 0.62 | −2.02 ± 0.46 | −2.24 ± 0.49 | −2.30 ± 0.47 | −2.15 ± 0.53 |
| *TH* | −1.94 ± 0.61 | −1.94 ± 0.57 | −1.72 ± 0.61 | −1.77 ± 0.52 | −1.87 ± 0.67 | −1.85 ± 0.71 | −1.85 ± 0.61 |

# Αποτελέσματα (1)

| Biomarker | Oral PTH dose/placebo | Month 1[a] | | | | Month 2[b] | | | | Month 3 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | *N*[f] | Mean ± SE | *P*-value vs baseline[c] | *P*-value vs placebo[d] | *N*[f] | Mean ± SE | *P*-value vs baseline[c] | *P*-value vs placebo[d] | *N*[f] | Mean ± SE | *P*-value vs baseline[c] | *P*-value vs placebo[d] |
| PINP | Placebo | 40 | 0.2 ± 2.8 | .95 | | 37 | -3.3 ± 3.1 | .30 | | 40 | 1.8 ± 3.5 | .62 | |
| | 0.5 mg | 21 | 2.7 ± 4.2 | .52 | .44 | 21 | 6.7 ± 3.6 | .08 | .01 | 21 | 3.2 ± 4.9 | .53 | .33 |
| | 1.0 mg | 24 | 11.5 ± 3.1 | <.01 | .008 | 25 | 5.2 ± 3.3 | .13 | .03 | 25 | 6.1 ± 3.1 | .07 | .17 |
| | 1.5 mg | 36 | 18.9 ± 3.7 | <.01 | <.0001 | 23 | 9.0 ± 4.1 | .04 | .007 | 23 | 2.3 ± 4.4 | .60 | .61 |
| | 2.5 mg non-titrated | 10 | 32.0 ± 6.3 | <.01 | <.0001 | 10 | 19.1 ± 7.1 | .03 | .0014 | 10 | 12.0 ± 6.3 | .09 | .0882[e] |
| | 2.5 mg titrated[a] | 13 | 18.5 ± 7.6 | .03 | .003 | 13 | 5.6 ± 7.6 | .41 | .0701 | 13 | 9.0 ± 7.3 | .25 | .1114[e] |
| Osteocalcin | Placebo | 40 | -2.9 ± 2.2 | .19 | | 37 | -1.8 ± 2.4 | .47 | | 40 | 1.4 ± 2.9 | .65 | |
| | 0.5 mg | 21 | 5.5 ± 4.0 | .18 | .05 | 21 | 5.2 ± 4.4 | .28 | .14 | 21 | 11.2 ± 4.8 | .03 | .054 |
| | 1.0 mg | 24 | 3.7 ± 3.5 | .30 | .12 | 25 | 0.7 ± 3.8 | .86 | .55 | 25 | 2.4 ± 4.3 | .44 | .53 |
| | 1.5 mg | 36 | 12.5 ± 2.3 | <.01 | <.0001 | 23 | 8.5 ± 3.3 | .02 | .02 | 23 | 12.4 ± 5.0 | .02 | .03 |
| | 2.5 mg non-titrated | 10 | 29.4 ± 8.2 | <.01 | <.0001 | 10 | 23.3 ± 8.3 | .02 | .0005 | 10 | 7.4 ± 5.2 | .19 | .3429 |
| | 2.5 mg titrated[a] | 13 | 14.0 ± 4.3 | <.01 | .0021 | 13 | 17.3 ± 3.2 | <.01 | .0002 | 13 | 20.5 ± 5.1 | <.01 | .0009 |
| Serum CTX | Placebo | 40 | 5.7 ± 5.4 | .30 | | 37 | 5.8 ± 5.2 | .27 | | 40 | 9.9 ± 7.5 | .19 | — |
| | 0.5 mg | 21 | 9.0 ± 8.4 | .29 | .66 | 21 | 5.8 ± 2.0 | .26 | .86 | 21 | 10.5 ± 7.7 | .19 | .87 |
| | 1.0 mg | 24 | 1.9 ± 5.6 | .74 | .70 | 25 | -3.8 ± 4.9 | .44 | .26 | 25 | -5.3 ± 5.6 | .35 | .73 |
| | 1.5 mg | 36 | -8.9 ± 3.9 | .03 | .64 | 23 | 0.5 ± 5.1 | .93 | .54 | 23 | 3.5 ± 7.0 | .62 | .84 |
| | 2.5 mg non-titrated | 10 | -12.8 ± 7.0 | .10 | .0006 | 10 | -3.3 ± 11.0 | .77 | .0032 | 10 | -13.1 ± 9.5 | .20 | .0004 |
| | 2.5 mg titrated[a] | 13 | -15.2 ± 6.9 | .05 | .6634 | 13 | -14.6 ± 10.1 | .17 | .9122 | 13 | -17.7 ± 8.4 | .06 | .5805 |

# Αποτελέσματα (2)

| Biomarker | Oral PTH dose/placebo | Month 6 | | | |
|---|---|---|---|---|---|
| | | *N*[f] | Mean ± SE | *P*-value vs baseline[c] | *P*-value vs placebo[d] |
| PINP | Placebo | 37 | 0.4 ± 3.4 | .90 | |
| | 0.5 mg | 21 | 7.8 ± 6.2 | .22 | .2426 |
| | 1.0 mg | 26 | -2.0 ± 4.2 | .64 | .6441 |
| | 1.5 mg | 21 | -4.9 ± 5.2 | .36 | .3405 |
| | 2.5 mg non-titrated | 7 | -6.1 ± 5.6 | .32 | .5337 |
| | 2.5 mg titrated[a] | 14 | 0.2 ± 6.0 | .98 | .9617 |
| Osteocalcin | Placebo | 37 | 1.0 ± 3.5 | .77 | |
| | 0.5 mg | 21 | 8.6 ± 5.5 | .14 | .15 |
| | 1.0 mg | 26 | -4.6 ± 4.5 | .32 | .23 |
| | 1.5 mg | 21 | 1.6 ± 5.3 | .76 | .92 |
| | 2.5 mg non-titrated | 7 | 6.9 ± 6.1 | .30 | .5923 |
| | 2.5 mg titrated[a] | 14 | 5.2 ± 5.0 | .32 | .3207 |
| Serum CTX | Placebo | 37 | 14.7 ± 7.9 | .07 | |
| | 0.5 mg | 21 | 13.7 ± 9.2 | .15 | .99 |
| | 1.0 mg | 26 | -9.3 ± 6.8 | .18 | .90 |
| | 1.5 mg | 21 | -6.7 ± 8.9 | .46 | .90 |
| | 2.5 mg non-titrated | 7 | -22.0 ± 7.9 | .03 | <.0001 |
| | 2.5 mg titrated[a] | 14 | -20.5 ± 6.2 | <.01 | .9388 |



# Αποτελέσματα (3)

**Table 3.** Percent change from baseline in BMD at different sites following 6-mo treatment with different doses of oral PTH.

| Parameter | Treatment arms | | | | | | |
|---|---|---|---|---|---|---|---|
| | Placebo ($N=38$) | 0.5 mg Oral PTH ($N=22$) | 1.0 mg Oral PTH ($N=26$) | 1.5 mg Oral PTH ($N=21$) | 2.5 mg Oral PTH (pooled) ($N=21$) | 2.5 mg Oral PTH (non-titrated) ($N=7$) | 2.5 mg Oral PTH (titrated) ($N=14$) |
| **LS** | | | | | | | |
| Mean (%) | −0.16 | −0.20 | 0.84 | 1.87 | 2.57 | 3.62 | 2.04 |
| SD (%) | 3.38 | 3.11 | 3.08 | 3.13 | 4.19 | 2.66 | 4.78 |
| SE (%) | 0.55 | 0.66 | 0.60 | 0.68 | 0.91 | 1.01 | 1.28 |
| *P*-value vs baseline[a] | .78 | .76 | .18 | .01 | .01 | .01 | .13 |
| *P*-value vs placebo[b] | | .91 | .43 | .01 | .002 | .007 | .02 |
| **FN** | | | | | | | |
| Mean (%) | −0.78 | −0.01 | −0.38 | 0.77 | 1.98 | 1.64 | 2.14 |
| SD (%) | 3.84 | 2.07 | 2.67 | 3.25 | 2.48 | 1.28 | 2.93 |
| SE (%) | 0.62 | 0.44 | 0.52 | 0.71 | 0.54 | 0.48 | 0.78 |
| *P*-value vs baseline[a] | .22 | .98 | .48 | .29 | <.01 | .01 | .02 |
| *P*-value vs placebo[b] | | .35 | .61 | .06 | .001 | .06 | .003 |
| **TH** | | | | | | | |
| Mean (%) | −0.50 | 0.73 | 0.27 | 1.10 | 1.34 | 0.88 | 1.57 |
| SD (%) | 2.78 | 2.31 | 2.30 | 2.78 | 2.75 | 2.48 | 2.94 |
| SE (%) | 0.45 | 0.49 | 0.45 | 0.61 | 0.60 | 0.94 | 0.79 |
| *P*-value vs baseline[a] | .28 | .15 | .56 | .09 | .04 | .38 | .07 |
| *P*-value vs placebo[b] | | .08 | .25 | .03 | .01 | .20 | .01 |

# Ασφάλεια

- Χωρίς διαφορά στις ΑΕ στις δόσεις 0.5-1.5 mg *vs* placebo
- Στα 2.5 mg συχνότερες ΑΕ (non-titrated: 89.5%, titrated: 82.4%) *vs* placebo (67.4%) – παρόμοιες με αυτές της υποδόριας χορήγησης (αίσθημα παλμών – ναυτία – ζάλη – κεφαλαλγία).
- 19/161 αποσύρθηκαν - 10/19 drug-related – 4/10 στα 2.5 mg αλλά κανείς στο σχήμα τιτλοποίησης
- Χωρίς διαφορές στην εμφάνιση επεισοδίων υπερασβεστιαιμίας

# Περιορισμοί Μελέτης

- Μικρό δείγμα
- Μικρή διάρκεια μελέτης
- Αλλαγή πρωτοκόλλου κατά τη διάρκεια της μελέτης

*Journal of Bone and Mineral Research*, 2024, **39**, 202–210
https://doi.org/10.1093/jbmr/zjae016
Advance access publication: January 29, 2024
**Clinical Trial**

# Equivalence trial of proposed denosumab biosimilar GP2411 and reference denosumab in postmenopausal osteoporosis: the ROSALIA study

**Sławomir Jeka[1], Eva Dokoupilová[2,3], Alan Kivitz[4], Paweł Żuchowski[1], Barbara Vogg[5,*], Natalia Krivtsova[5], Susmit Sekhar[5], Samik Banerjee[5], Arnd Schwebig[5], Johann Poetzl[5], Jean-Jacques Body[6], Richard Eastell[7]**

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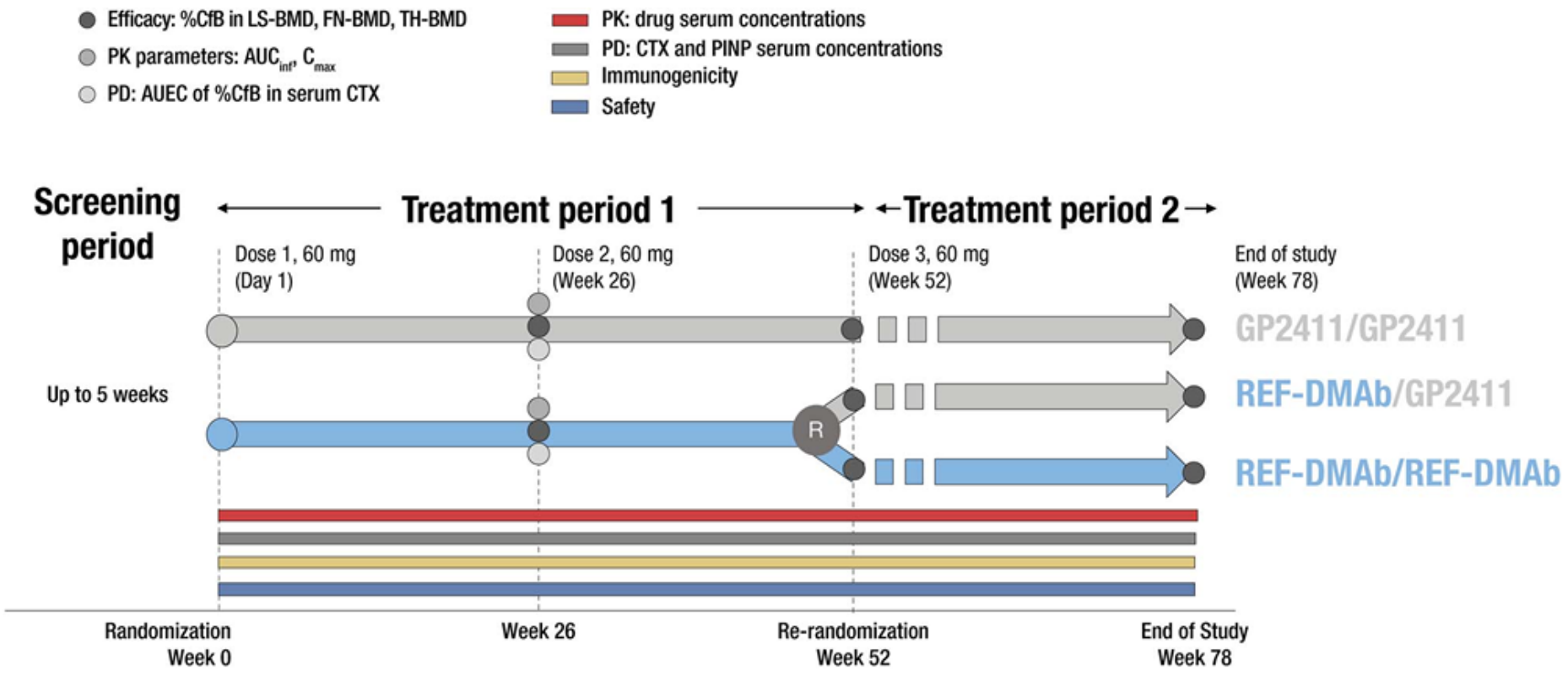
[6]Department of Medicine, University Hospital Brugmann, Université Libre de Bruxelles (ULB), 1020 Brussels, BE, Belgium
[7]Division of Clinical Medicine, University of Sheffield, Sheffield S10 2TN, SYK, United Kingdom

# Κλινικό Ερώτημα

- Η αποτελεσματικότητα, ασφάλεια, φαρμακοκινητική, φαρμακοδυναμική και ανοσογονικότητα του βιο-ομοειδούς του Denosumab GP2411 (Sandoz) σε γυναίκες με μετ-εμμηνοπαυσιακή οστεοπόρωση

# Σχεδιασμός Μελέτης

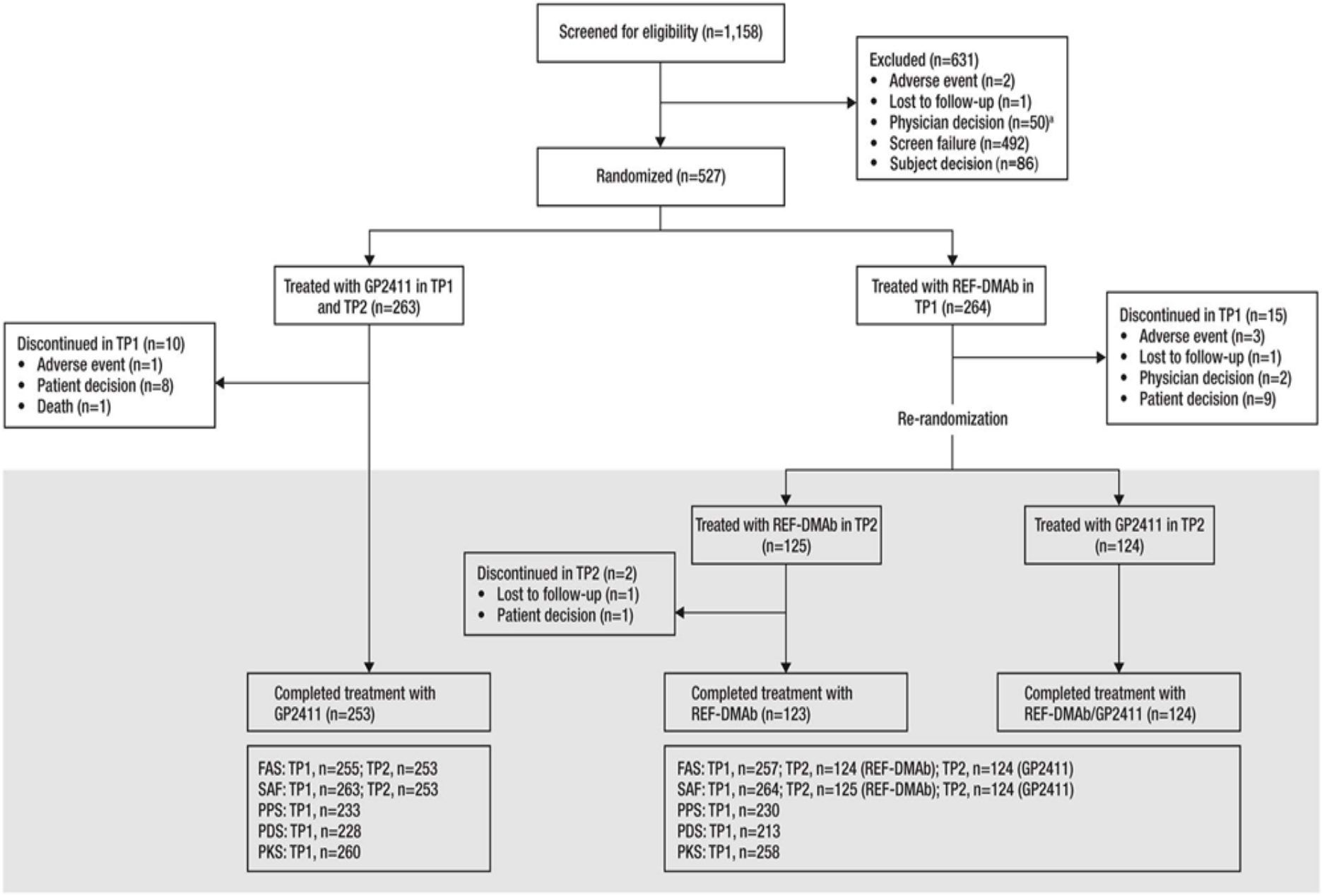
- Τυχαιοποιημένη, διπλή, τυφλή, πολυκεντρική μελέτη φάσης 3



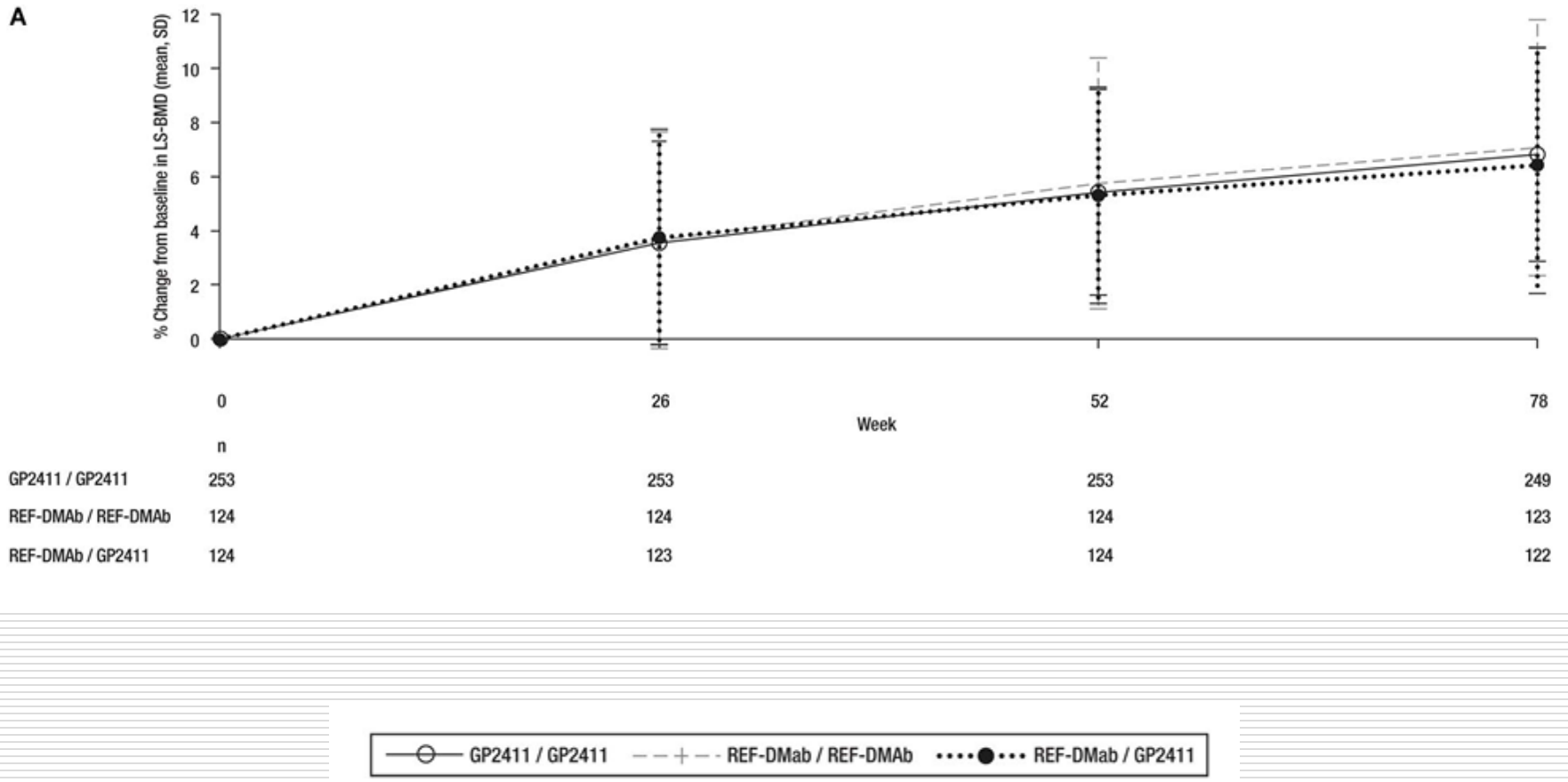
# Κριτήρια Ένταξης – Αποκλεισμού

- Μετ-εμμηνοπαυσιακές γυναίκες, 55-80 ετών, ΣΒ 50-90 kgr
  - T-score ≤-2.5 και ≥-4.0 ΟΜΣΣ

- Κριτήρια αποκλεισμού
  - Ιστορικό λήψης denosumab
  - Λήψη αντιοστεοπορωτικής αγωγής κατά το screening
  - Διφωσφωνικά για >3 έτη ή που διακόπηκαν λιγότερο από 1 χρόνο πριν το screening ή Ζολενδρονικό οξύ τα τελευταία 5 έτη
  - Ιστορικό τουλάχιστον 1 σοβαρού ή 2 ενδιάμεσης έντασης σπονδυλικών καταγμάτων ή κατάγματος ισχίου
  - 25(OH)D <20 ng/mL, υπό-/υπερασβεστιαιμία, νεφρική νόσος, υπο-/υπερπαραθυρεοειδισμός, υπο-/υπερθυρεοειδισμός
  - Λήψη κορτικοειδών εντός 3 μηνών από το screening


Screened for eligibility (n=1,158)
Excluded (n=631)
• Adverse event (n=2)
• Lost to follow-up (n=1)
• Physician decision (n=50)[a]
• Screen failure (n=492)
• Subject decision (n=86)
Randomized (n=527)
Treated with GP2411 in TP1 and TP2 (n=263)
Treated with REF-DMAb in TP1 (n=264)
Discontinued in TP1 (n=10)
• Adverse event (n=1)
• Patient decision (n=8)
• Death (n=1)
Discontinued in TP1 (n=15)
• Adverse event (n=3)
• Lost to follow-up (n=1)
• Physician decision (n=2)
• Patient decision (n=9)
Re-randomization
Treated with REF-DMAb in TP2 (n=125)
Treated with GP2411 in TP2 (n=124)
Discontinued in TP2 (n=2)
• Lost to follow-up (n=1)
• Patient decision (n=1)
Completed treatment with GP2411 (n=253)
Completed treatment with REF-DMAb (n=123)
Completed treatment with REF-DMAb/GP2411 (n=124)
FAS: TP1, n=255; TP2, n=253
SAF: TP1, n=263; TP2, n=253
PPS: TP1, n=233
PDS: TP1, n=228
PKS: TP1, n=260
FAS: TP1, n=257; TP2, n=124 (REF-DMAb); TP2, n=124 (GP2411)
SAF: TP1, n=264; TP2, n=125 (REF-DMAb); TP2, n=124 (GP2411)
PPS: TP1, n=230
PDS: TP1, n=213
PKS: TP1, n=258

# Αποτελεσματικότητα (1)



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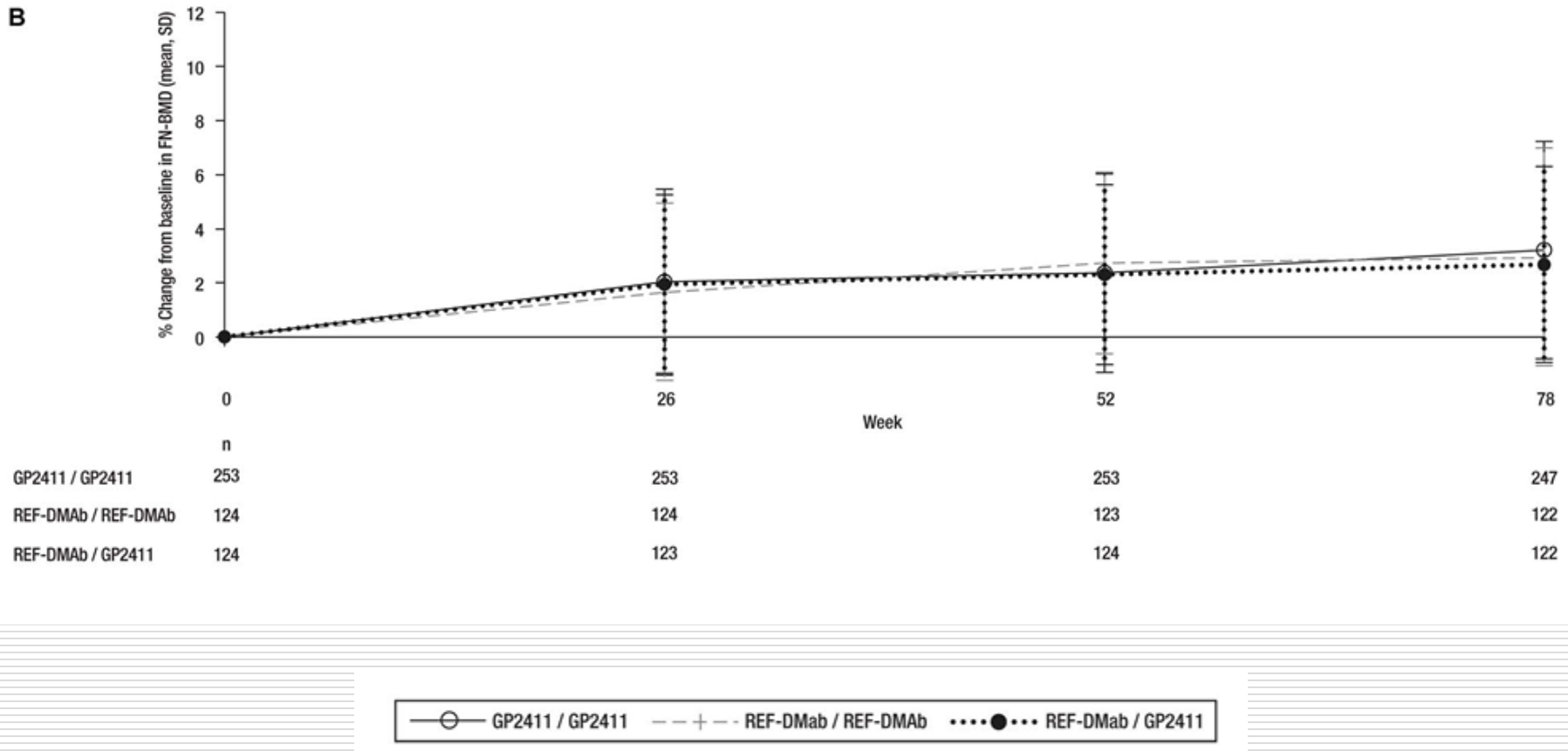

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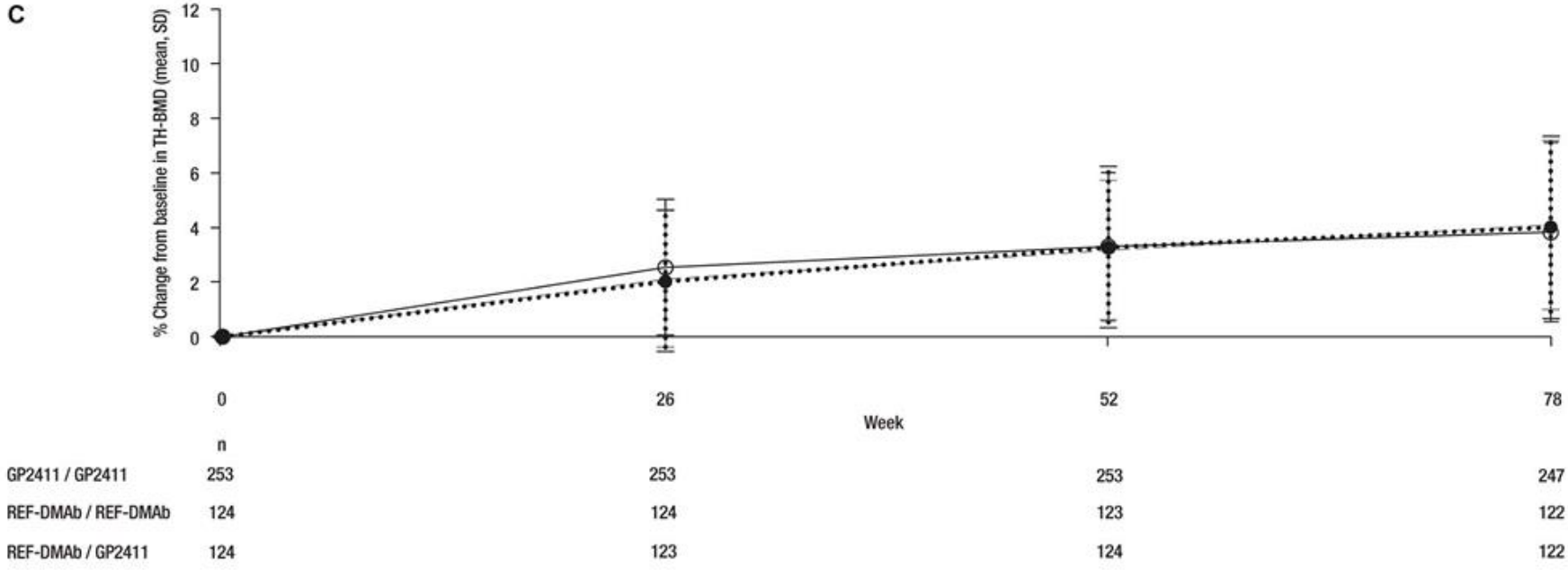

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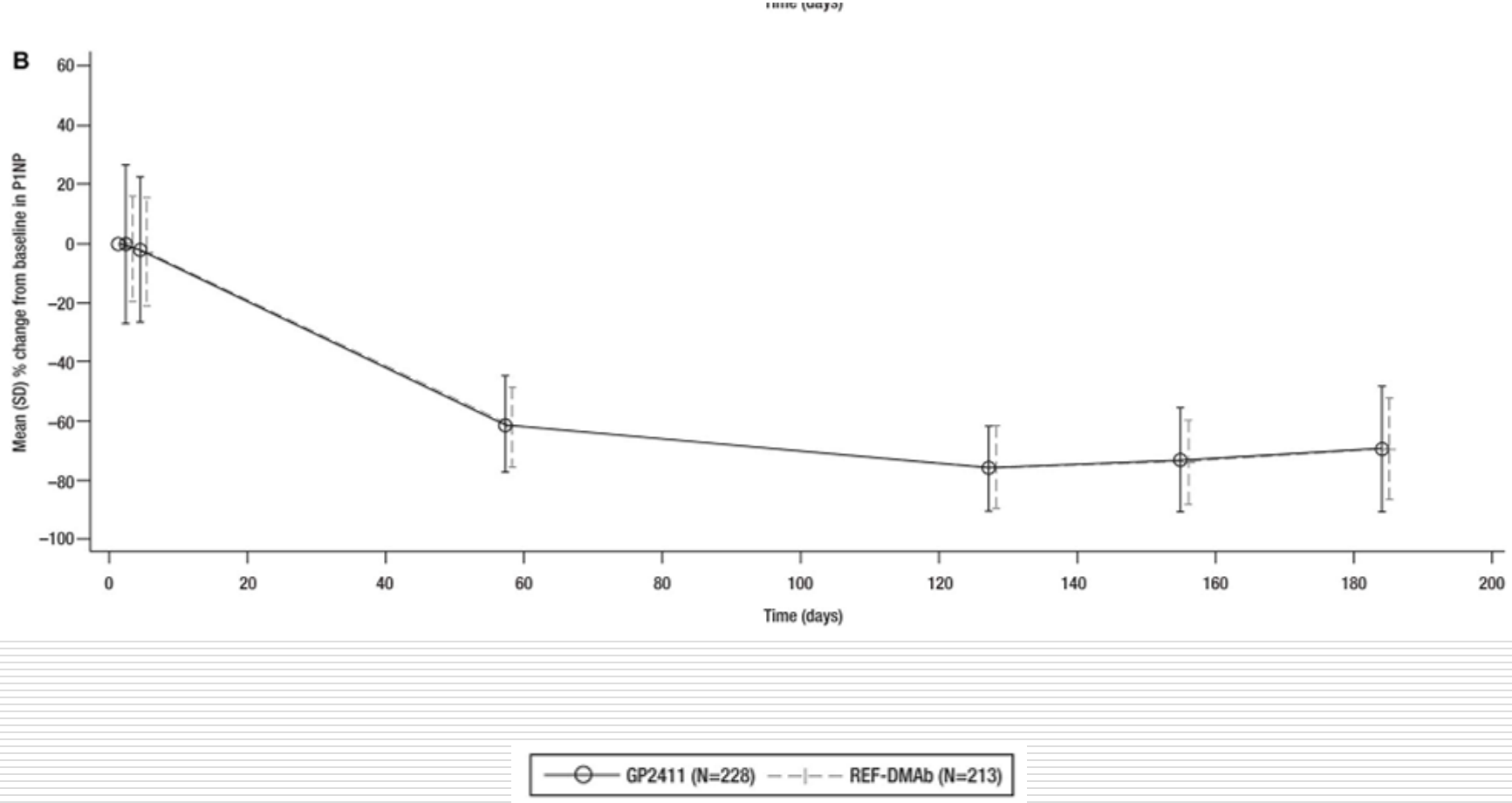
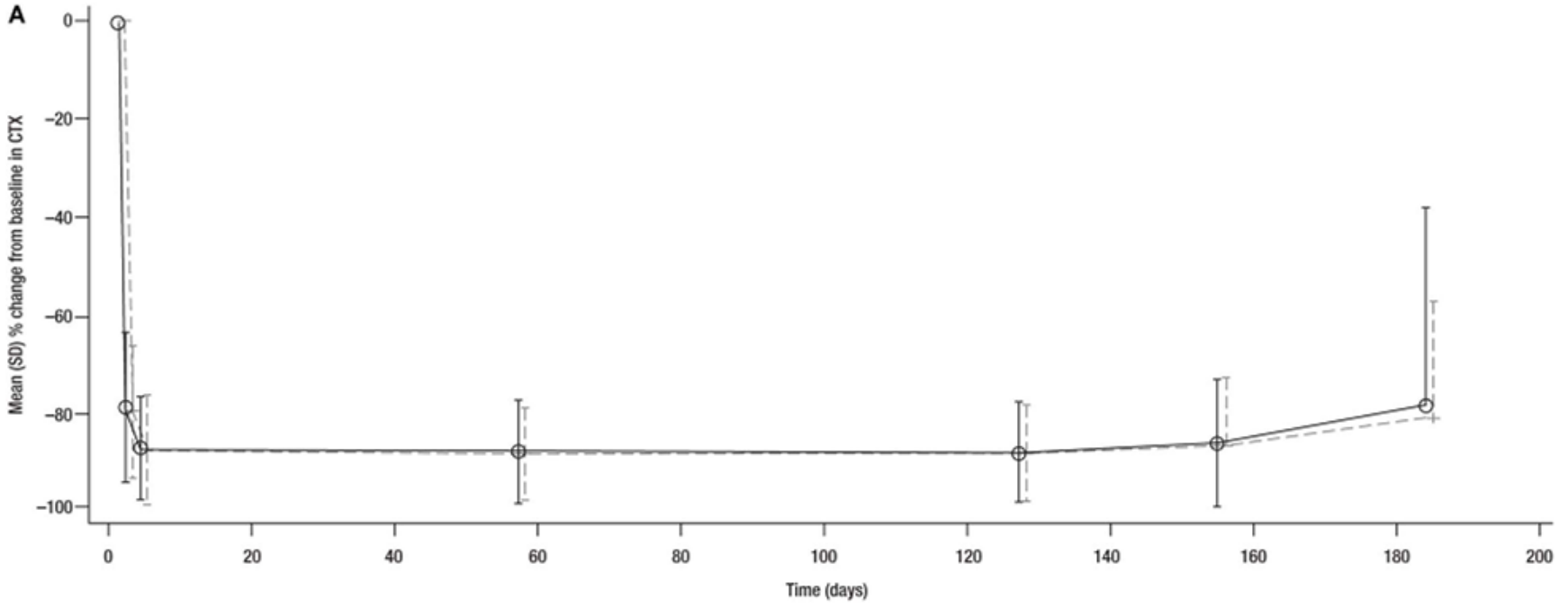


# Αποτελεσματικότητα (5)

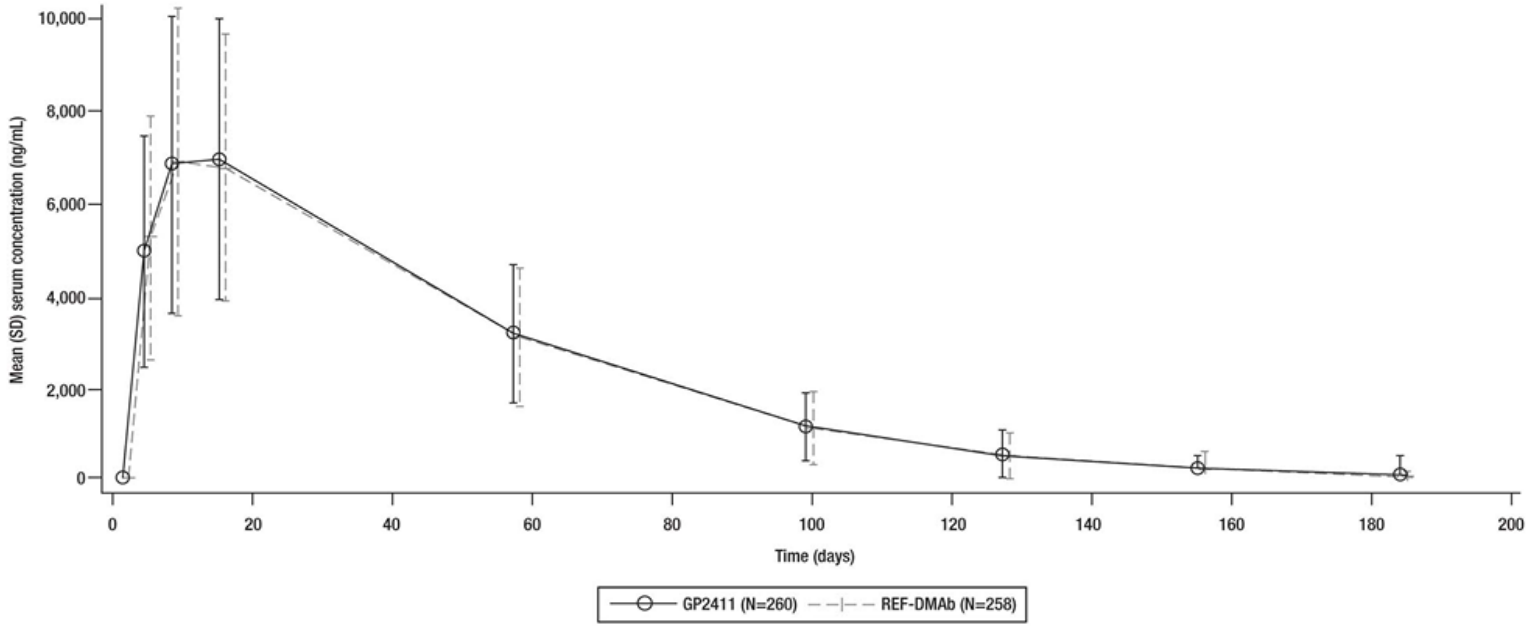


# Φαρμακοκινητική – Φαρμακοδυναμική

**Table 2.** PK and PD evaluation after the first treatment dose.

| | Adjusted geometric mean | | Geometric mean ratio GP2411/REF-DMAb | |
|---|---|---|---|---|
| | GP2411 | REF-DMAb | PE | (90% CI) |
| $AUC_{inf}$ (day ∗ ng/mL) | 366 000 $n = 247$ | 369 000 $n = 246$ | 0.99 | (0.93, 1.05) |
| $C_{max}$ (ng/mL) | 6910 $n = 260$ | 7120 $n = 258$ | 0.97 | (0.92, 1.03) |
| | **GP2411** | **REF-DMAb** | **PE** | **(95% CI)** |
| AUEC %CfB in CTX (% ∗ day) | 15 800 $n = 228$ | 15 800 $n = 213$ | 1.00 | (0.98, 1.01) |

Abbreviations: $AUC_{inf}$, area under the serum concentration–time curve extrapolated to infinity; AUEC, area under the effect curve; $C_{max}$, maximum drug serum concentration; PD, pharmacodynamics; PE, point estimate; PK, pharmacokinetics; *n*, number of participants with evaluable parameters; REF-DMAb, reference denosumab.



# Ανοσογονικότητα

- Μονίμως αυξημένα (αν και σε χαμηλό τίτλο) δεσμευτικά αντισώματα
  - GP2411/GP2411: n =5 (2%)
  - REF-DMAb/REF-DMAb: n=5 (4%)
  - REF-DMAb/GP2411: n=3 (2.4%)
- Αδρανοποιητικά αντισώματα
  - 0.8% και στις 3 υπο-ομάδες
- Μη κλινικά σημαντική ανοσογονικότητα

# Ασφάλεια (1)

| | Treatment Period 1 | | | | Treatment Period 2 | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | GP2411 (n=263) | | REF-DMAb (n=264) | | GP2411/GP2411 (n=253) | | REF-DMAb/ REF-DMAb (n=125) | | REF-DMAb/ GP2411 (n=124) | |
| n, (%) | All grades | Grade 3–4 | All grades | Grade 3–4 | All grades | Grade 3–4 | All grades | Grade 3–4 | All grades | Grade 3–4 |
| At least one TEAE | 157 (59.7) | 13 (4.9) | 181 (68.6) | 10 (3.8) | 68 (26.9) | 5 (2.0) | 47 (37.6) | 2 (1.6) | 48 (38.7) | 2 (1.6) |
| Treatment-related | 36 (13.7) | 0 | 49 (18.6) | 0 | 7 (2.8) | 0 | 7 (5.6) | 0 | 5 (4.0) | 0 |
| At least one serious TEAE | 12 (4.6) | 9 (3.4) | 8 (3.0) | 5 (1.9) | 4 (1.6) | 3 (1.2) | 2 (1.6) | 1 (0.8) | 0 | 0 |
| Treatment-related | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Fatal serious TEAE | 1 (0.4)[a] | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Treatment-related | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| TEAE leading to study drug discontinuation | 1 (0.4) | 1 (0.4) | 4 (1.5) | 3 (1.1) | 0 | 0 | 0 | 0 | 0 | 0 |
| Treatment-related | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| TEAE leading to study discontinuation | 3 (1.1) | 1 (0.4) | 3 (1.1) | 2 (0.8) | 0 | 0 | 0 | 0 | 0 | 0 |
| Treatment-related | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

# Ασφάλεια (2)

- Σπονδυλικά Κατάγματα
  - GP2411/GP2411: n=25 (9.9%)
  - REF-DMAb/REF-DMAb: n=17 (13.6%)
  - REF-DMAb/GP2411: n=17 (13.7%)

- Μη σπονδυλικά – μη ισχίου κατάγματα
  - GP2411/GP2411: n=1 (0.4%)
  - REF-DMAb/REF-DMAb: n=0
  - REF-DMAb/GP2411: n=1 (0.8%)

# Περιορισμοί Μελέτης

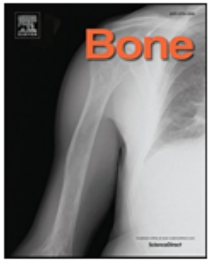
- Διάρκεια 18 μήνες
- Αλλαγή θεραπείας μόνο για 6 μήνες
- Κατάγματα ισχίου?
- Overshooting?

Bone 192 (2025) 117371

Contents lists available at ScienceDirect

Bone

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




Registered Report Stage II

# SB16 versus reference denosumab in postmenopausal women with osteoporosis: 18-month outcomes of a phase III randomized clinical trial

Yoon-Sok Chung [a,b], Bente Langdahl [c], Rafal Plebanski [d], Edward Czerwinski [e], Eva Dokoupilova [f,g], Jerzy Supronik [h], Jan Rosa [i], Andrzej Mydlak [j], Rafal Sapula [k], Anna Rowińska-Osuch [l], Ki-Hyun Baek [m], Audrone Urboniene [n], Robert Mordaka [o], Sohui Ahn [p], Young Hee Rho [p], Jisuk Ban [p], Richard Eastell [q,*]

# Κλινικό Ερώτημα

- Η αποτελεσματικότητα, ασφάλεια, φαρμακοκινητική, φαρμακοδυναμική και ανοσογονικότητα του βιο-ομοειδούς του Denosumab SB16 σε γυναίκες με μετ-εμμηνοπαυσιακή οστεοπόρωση

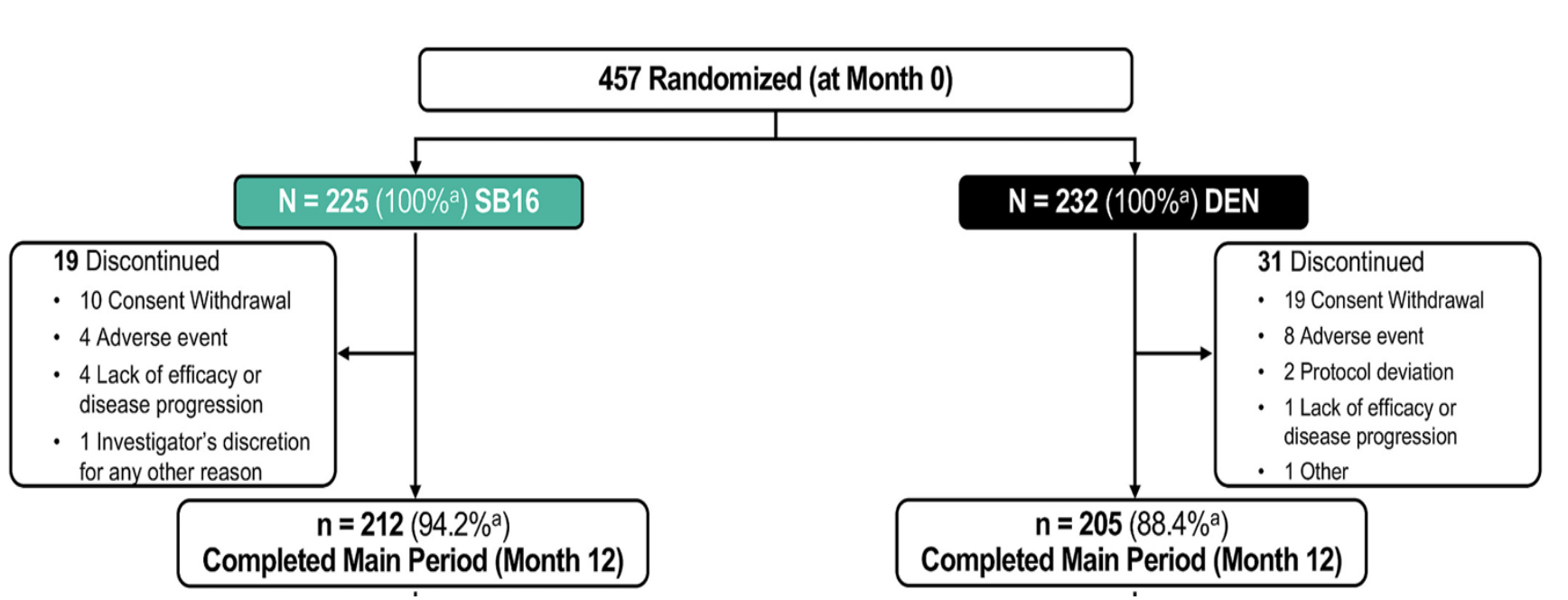
# Κριτήρια Ένταξης – Αποκλεισμού

- Μετ-εμμηνοπαυσιακές γυναίκες, 55-80 ετών
  - T-score ≤-2.5 και ≥-4.0 ΟΜΣΣ/ολικό ισχίο
  - Χωρίς προηγούμενη λήψη κάποιου βιολογικού παράγοντα

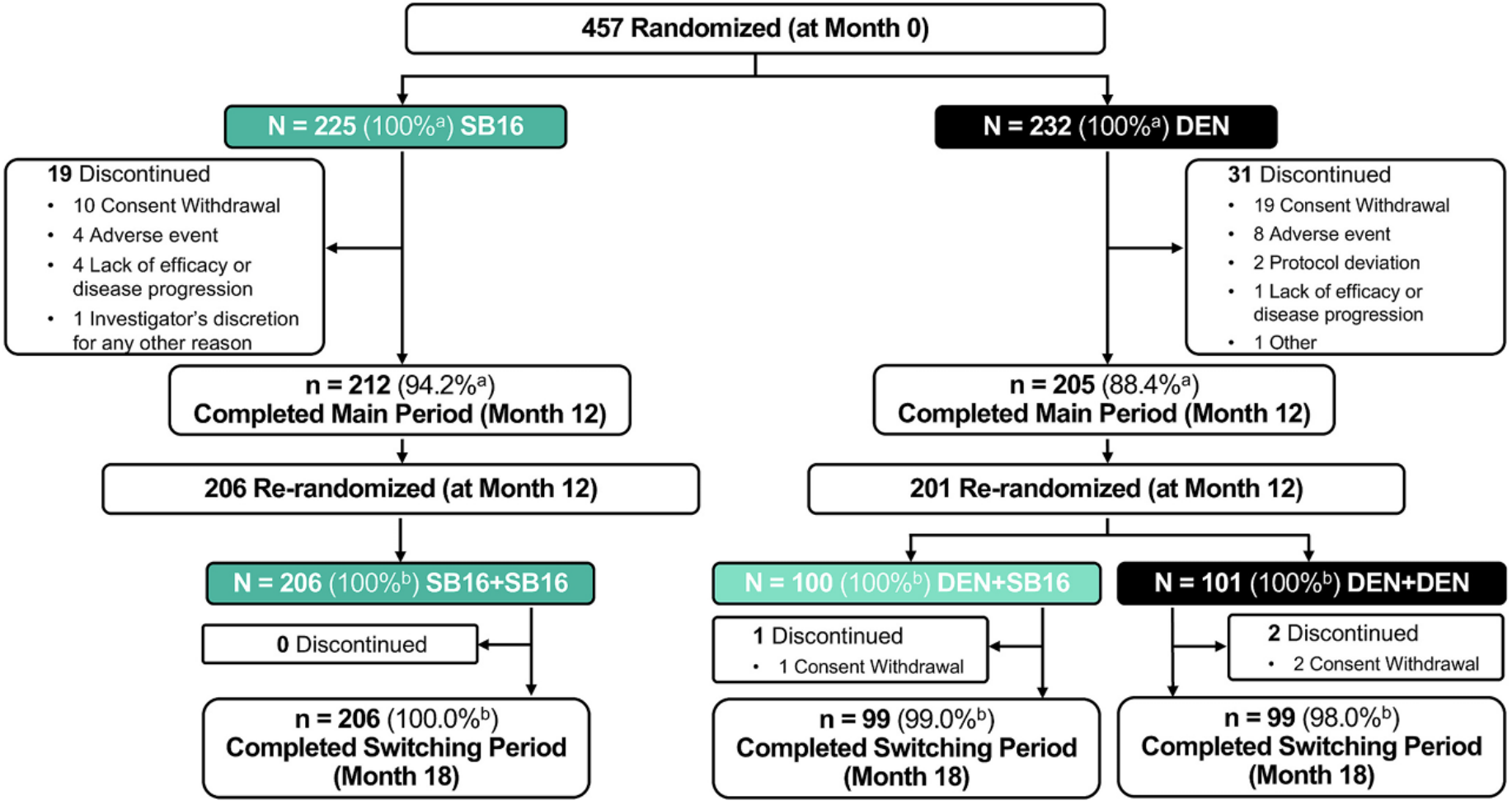
- Κριτήρια αποκλεισμού
  - Ιστορικό τουλάχιστον 1 σοβαρού ή 2 ενδιάμεσης έντασης σπονδυλικών καταγμάτων ή κατάγματος ισχίου
  - Ιστορικό αμφοτερόπλευρης αρθροπλαστικής ισχίου
  - Διφωσφωνικά για >3 έτη ή που διακόπηκαν λιγότερο από 1 χρόνο πριν το screening
  - 25(OH)D <20 ng/mL, υπο-/υπερασβεστιαιμία, eGFR <45 mL/min
  - Ενδοκρινικά αίτια οστεοπόρωσης

# Πληθυσμός – Σχεδιασμός Μελέτης (1)

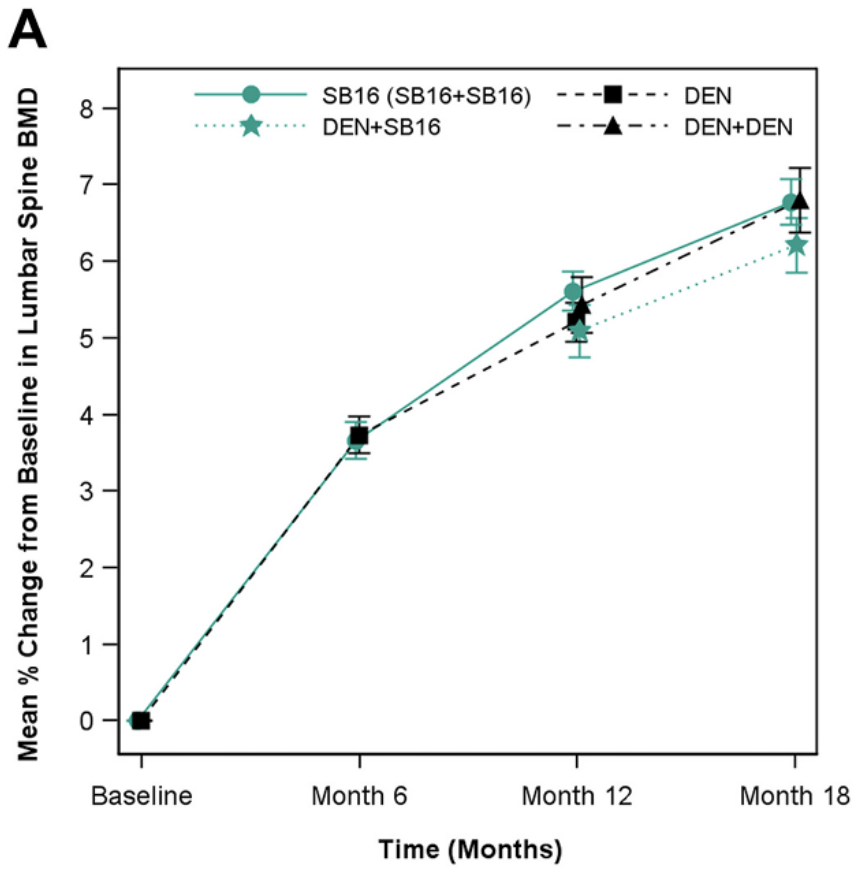
- Τυχαιοποιημένη, διπλή τυφλή, πολυκεντρική μελέτη Φάσης 3

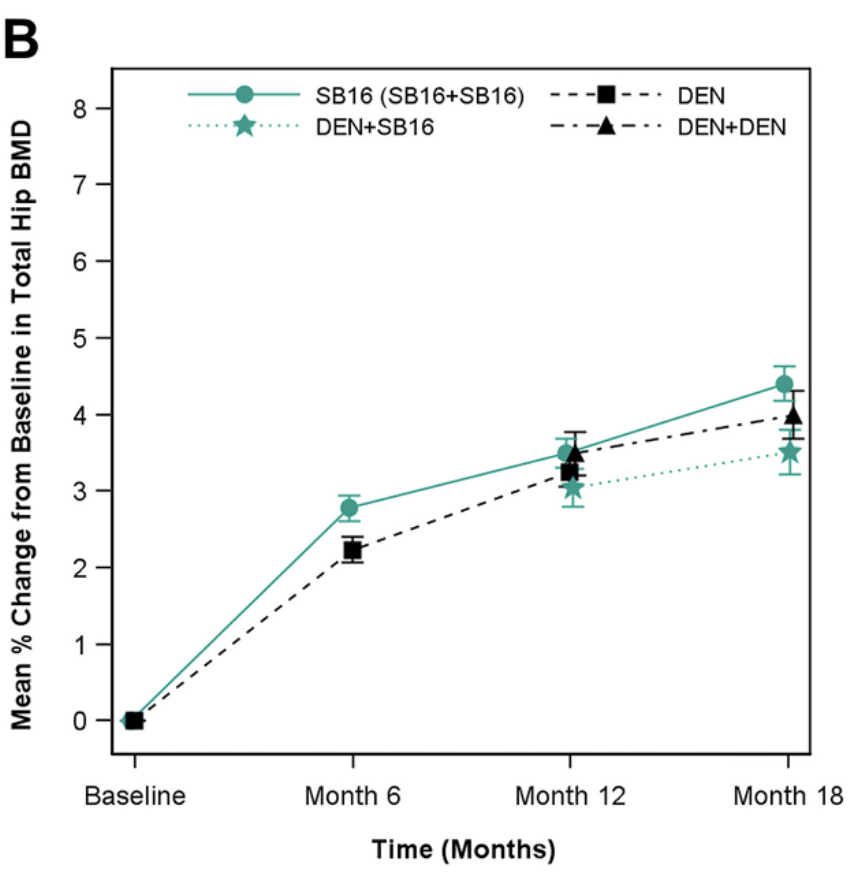


# Πληθυσμός – Σχεδιασμός Μελέτης (2)



# Αποτελεσματικότητα (1)



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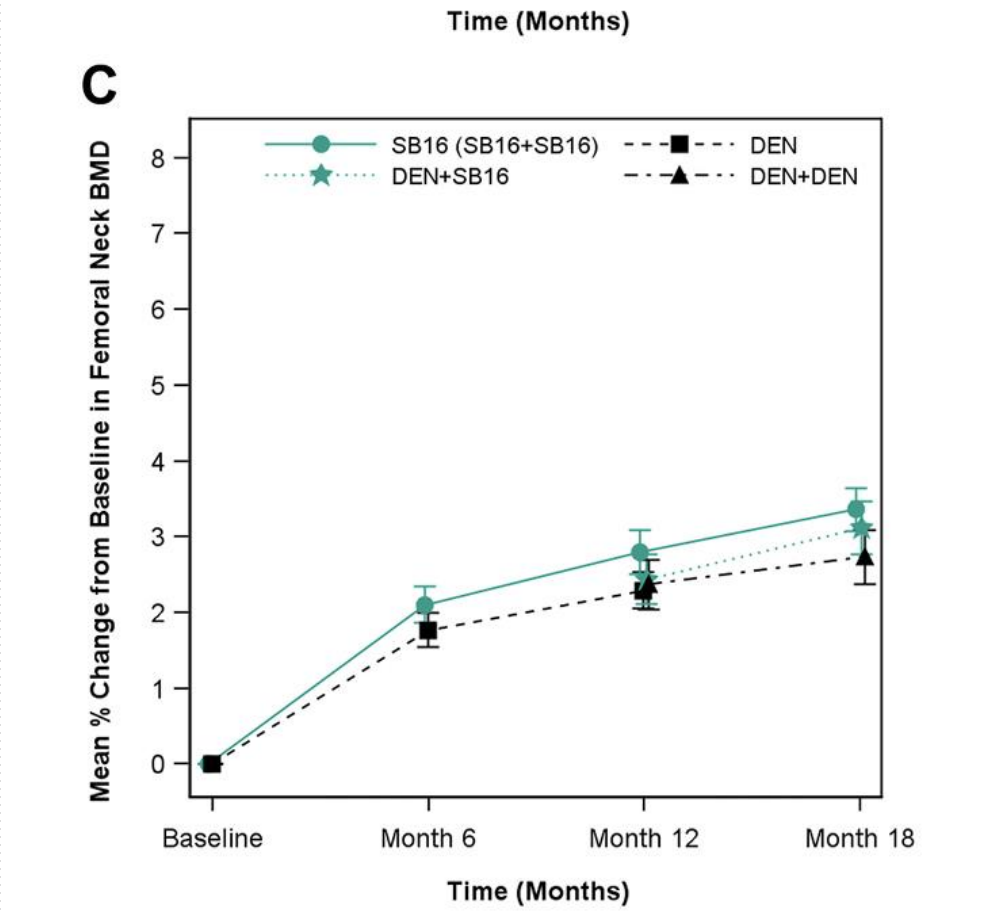
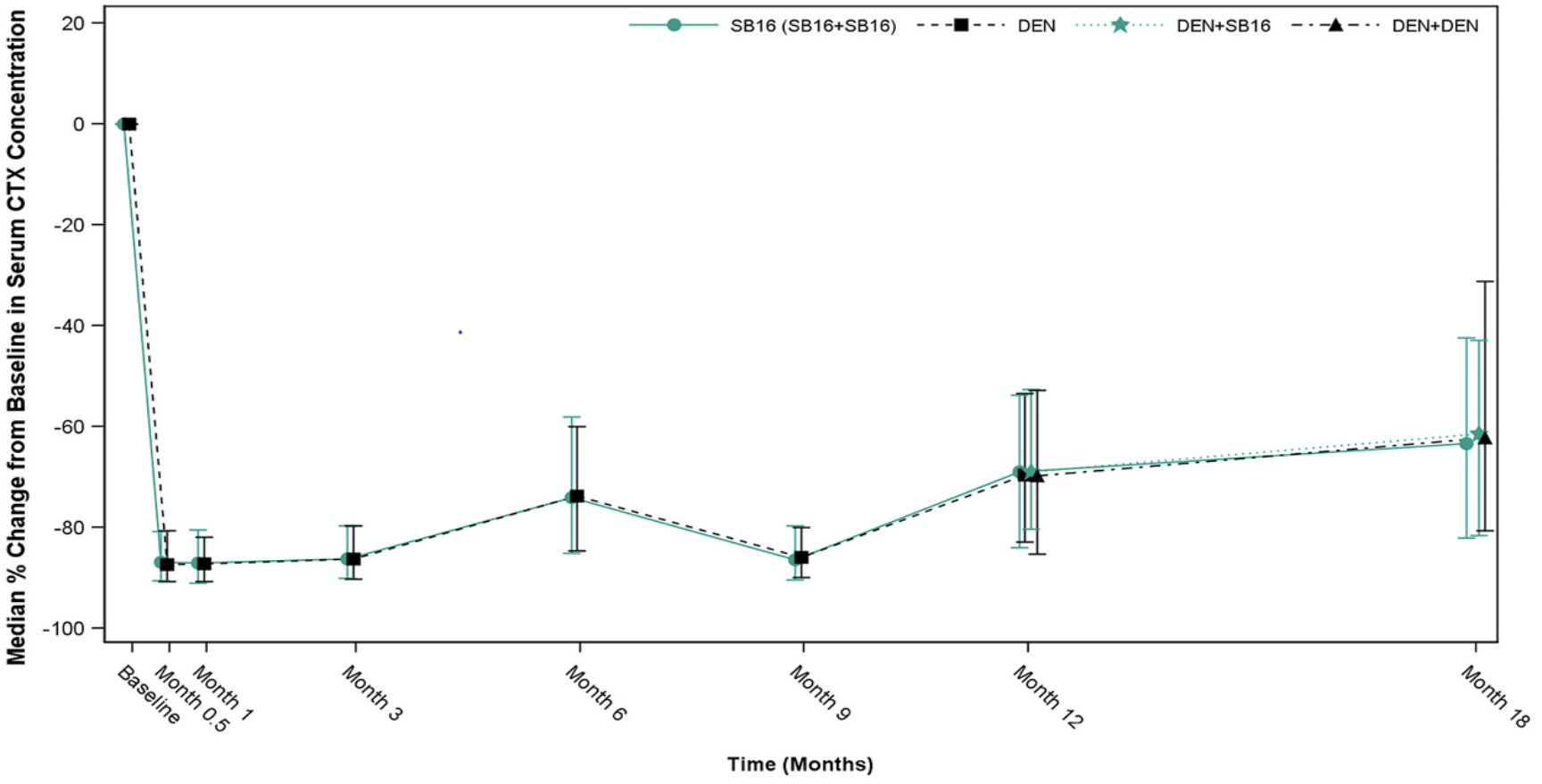
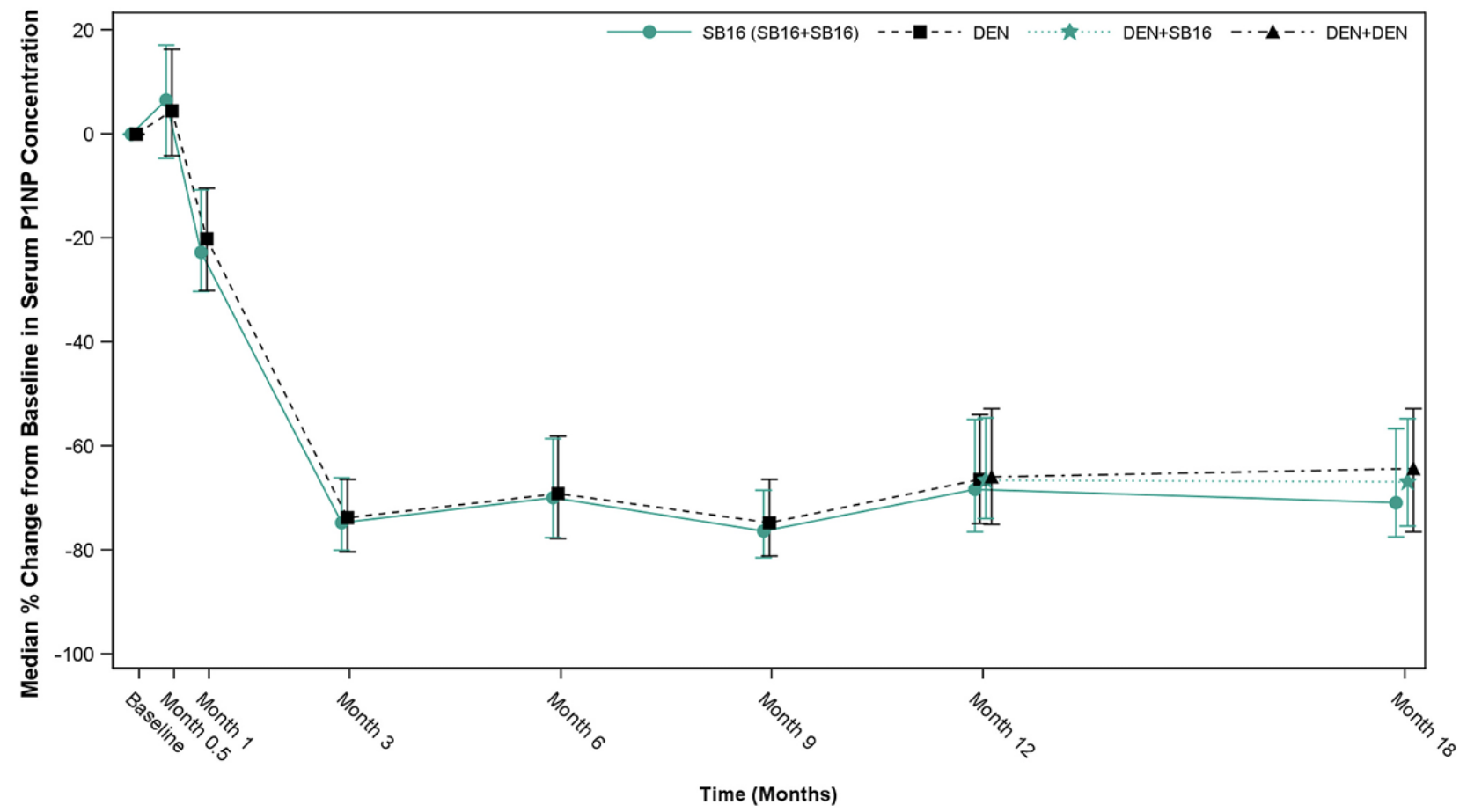


# Φαρμακοδυναμική (1)



# Φαρμακοδυναμική (2)



# Ανοσογονικότητα

- Θετικά δεσμευτικά αντισώματα
  - SF-16/SF-16: n=0
  - REF-DMAb/REF-DMAb: n=0
  - REF-DMAb/SF-16: n=1 (1%)

- Αδρανοποιητικά αντισώματα
  - 0% και στις 3 υπο-ομάδες

# Ασφάλεια

**Table 2**
Safety profiles during the switching period (SAF2)[a].

| Number of subjects experiencing | SB16 + SB16 | DEN+SB16 | DEN+DEN |
|---|---|---|---|
| | N = 206 | N = 100 | N = 101 |
| | n (%) | n (%) | n (%) |
| At least one TEAE | 73 (35.4) | 29 (29.0) | 35 (34.7) |
| TEAEs related to IP | 3 (1.5) | 0 (0.0) | 0 (0.0) |
| TEAEs of special interest | 2 (1.0) | 0 (0.0) | 0 (0.0) |
| Hypocalcemia | 2 (1.0) | 0 (0.0) | 0 (0.0) |
| At least one serious TEAE | 4 (1.9) | 2 (2.0) | 1 (1.0) |
| Injection site reactions | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| TEAEs leading to death | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Frequently reported (> 2 %) TEAEs | 39 (18.9) | 12 (12.0) | 15 (14.9) |
| Arthralgia | 7 (3.4) | 1 (1.0) | 2 (2.0) |
| Bronchitis | 5 (2.4) | 1 (1.0) | 2 (2.0) |
| COVID-19 | 5 (2.4) | 1 (1.0) | 2 (2.0) |
| Headache | 5 (2.4) | 2 (2.0) | 2 (2.0) |
| Hypercholesterolemia | 7 (3.4) | 1 (1.0) | 1 (1.0) |
| Nasopharyngitis | 1 (0.5) | 1 (1.0) | 4 (4.0) |
| Upper respiratory tract infection | 5 (2.4) | 0 (0.0) | 0 (0.0) |
| Vitamin D deficiency | 5 (2.4) | 5 (5.0) | 2 (2.0) |

Abbreviations: DEN, denosumab; IP, investigational product; N, number of patients in the SAF2; n, number of patients with event; PTH, parathyroid hormone; SAF2, safety analysis set 2; TEAE, treatment emergent adverse event.

# Περιορισμοί Μελέτης

- Διάρκεια 18 μήνες
- Αλλαγή θεραπείας μόνο για 6 μήνες
- Χωρίς έλεγχο καταγμάτων
- Overshooting?

Archives of Osteoporosis (2024) 19:119
https://doi.org/10.1007/s11657-024-01480-6

ORIGINAL ARTICLE

# Efficacy and safety of weekly liquid alendronate in Korean postmenopausal women with osteoporosis: a 12-month, multi-center, randomized trial

Seungjin Baek[1] · Seong Hee Ahn[2] · Namki Hong[1] · Da Hea Seo[2] · Seongbin Hong[2] · Yumie Rhee[1]

Received: 9 September 2024 / Accepted: 12 November 2024 / Published online: 26 November 2024
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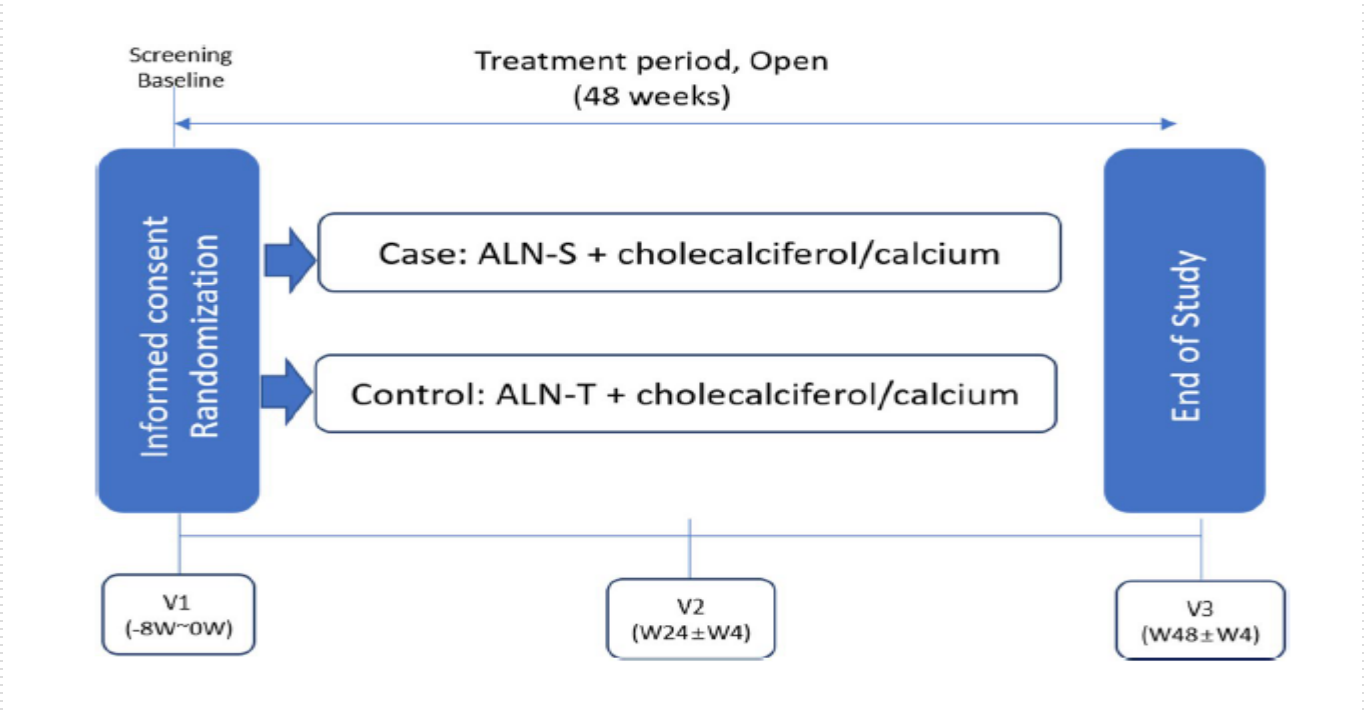
# Κλινικό Ερώτημα

- Η αποτελεσματικότητα και η ασφάλεια της υγρής αλενδρονάτης (70 mg σε 20 mL διάλυμα solution μαζί με 110 mL νερό) σε μετ-εμμηνοπαυσιακές γυναίκες με οστεοπόρωση

# Διάγραμμα Μελέτης

- Προοπτική, τυχαιοποιημένη, ανοιχτή μελέτη 2 κέντρων στη Βόρεια Κορέα διάρκειας 12 μηνών



# Κριτήρια Ένταξης – Αποκλεισμού

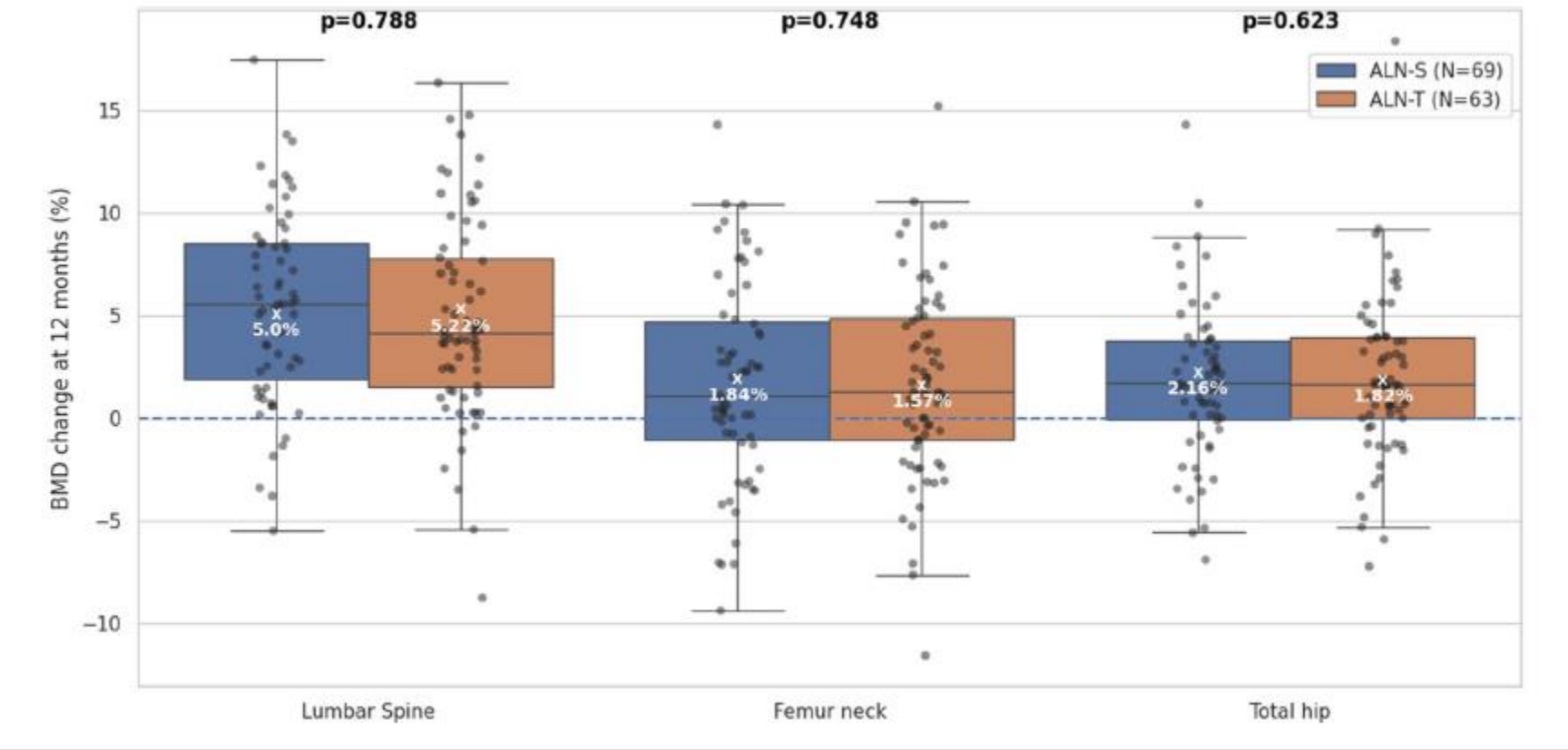
- Γυναίκες ≥50 ετών σε εμμηνόπαυση
  - T-score ≤-2.5 ΟΜΣΣ/ισχίο
  - T-score -1.0 έως -2.4 ΟΜΣΣ/ισχίο και ιστορικό κατάγματος
  - T-score -1.0 έως -2.4 ΟΜΣΣ/ισχίο και MOF >20% or HF >3%

- Όχι λήψη αντι-οστεοπορωτικής αγωγής τον προηγούμενο χρόνο
- Όχι ιστορικό ανεπιθύμητων ενεργειών σχετιζόμενων με τα διφωσφωνικά
- Όχι δευτεροπαθής οστεοπόρωση
- Όχι σοβαρή νεφρική, ηπατική ανεπάρκεια ή κακοήθεια

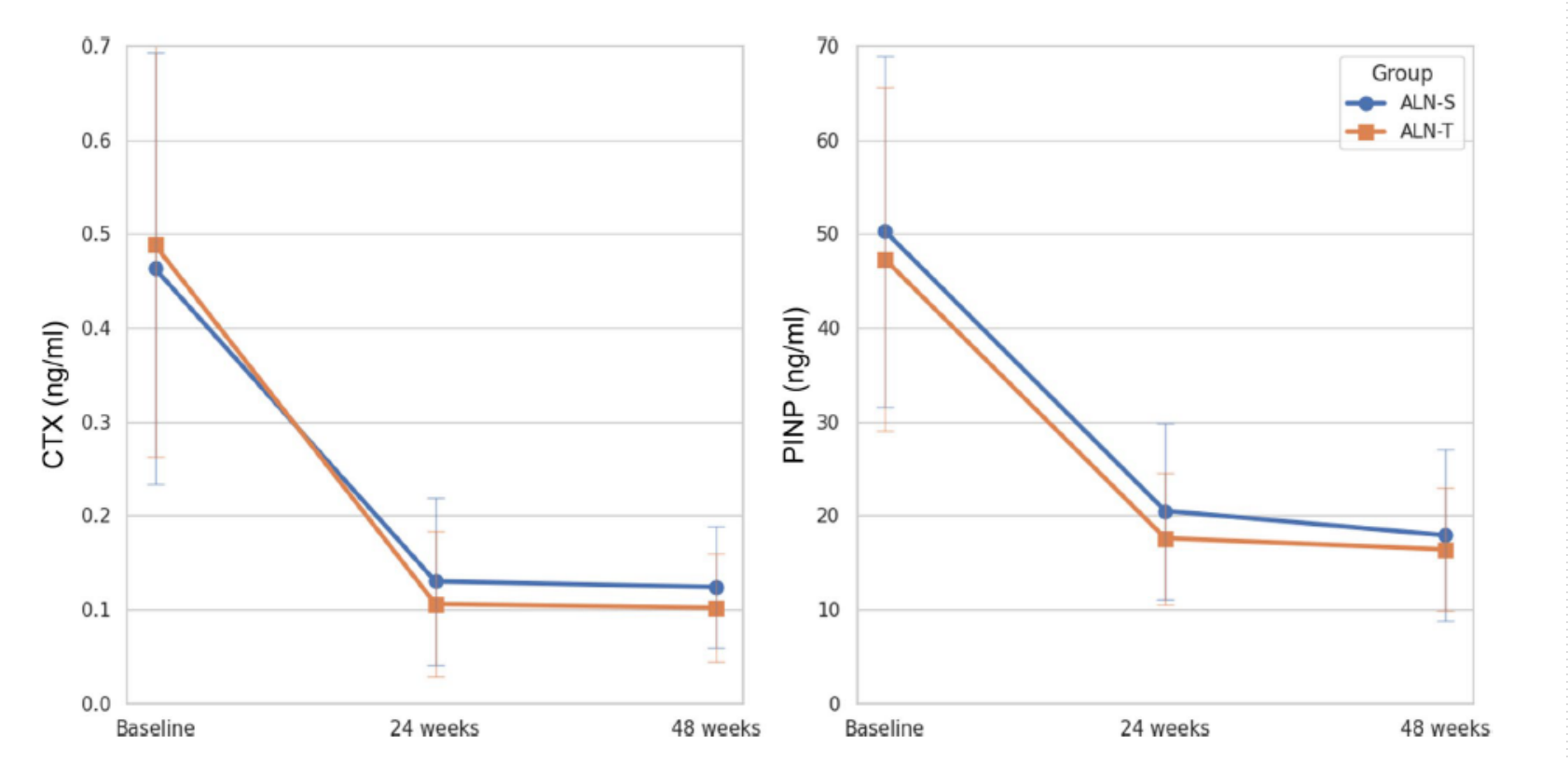
| | ALN-S ($N=69$) | | ALN-T ($N=63$) | | $p$ value |
|---|---|---|---|---|---|
| | Mean (or $N$) | SD (or %) | Mean (or N) | SD (or %) | |
| Age (years)* | 62.8 | 7.5 | 64.0 | 7.7 | 0.342 |
| Height (cm)* | 156.9 | 5.0 | 155.2 | 5.6 | 0.064 |
| Weight (kg)* | 55.4 | 7.7 | 55.5 | 7.2 | 0.923 |
| Systolic blood pressure (mmHg)* | 123.1 | 13.2 | 123.6 | 14.4 | 0.839 |
| Diastolic blood pressure (mmHg)* | 70.0 | 11.1 | 72.7 | 10.6 | 0.162 |
| Calcium (mg/dL)* | 9.3 | 0.3 | 9.3 | 0.3 | 0.633 |
| Phosphorus (g/dL)* | 3.8 | 0.5 | 3.7 | 0.4 | 0.763 |
| Albumin (g/dL)* | 4.5 | 0.3 | 4.5 | 0.2 | 0.749 |
| ALP (U/L)* | 74.8 | 21.3 | 68.4 | 17.3 | 0.060 |
| BUN (mg/dL)* | 15.1 | 4.0 | 15.8 | 4.2 | 0.305 |
| Creatinine (mg/dL)* | 0.7 | 0.1 | 0.7 | 0.1 | 0.875 |
| Total cholesterol (mg/dL)* | 183.7 | 52.0 | 186.7 | 31.2 | 0.683 |
| Parathyroid hormone (pg/mL)* | 40.8 | 22.5 | 38.7 | 13.6 | 0.518 |
| 25-hydroxy vitamin D (ng/mL)* | 29.5 | 9.1 | 31.2 | 9.3 | 0.292 |
| Baseline CTX (ng/mL)* | 0.467 | 0.231 | 0.492 | 0.229 | 0.528 |
| Baseline PINP (ng/mL)* | 51.0 | 18.5 | 47.7 | 18.7 | 0.309 |
| Baseline LSBMD ($g/cm^2$)* | 0.744 | 0.089 | 0.728 | 0.079 | 0.277 |
| Baseline LS T-score* | −2.4 | 0.7 | −2.5 | 0.7 | 0.526 |
| Baseline FN BMD ($g/cm^2$)* | 0.600 | 0.100 | 0.577 | 0.079 | 0.153 |
| Baseline FN T-score* | −2.1 | 0.7 | −2.2 | 0.6 | 0.295 |
| Baseline TH BMD ($g/cm^2$)* | 0.705 | 0.079 | 0.702 | 0.074 | 0.829 |
| Baseline TH T-score* | −1.4 | 0.6 | −1.4 | 0.6 | 0.693 |
| FRAX: major osteoporotic fracture (%)* | 10.3 | 5.2 | 11.4 | 5.4 | 0.224 |
| FRAX: hip fracture (%)* | 3.7 | 2.7 | 4.2 | 2.8 | 0.246 |
| Previous fracture history† | 21 | 30.4 | 20 | 31.7 | 0.871 |
| Parents' hip fracture history† | 6 | 8.7 | 9 | 14.3 | 0.312 |
| Current smoking†† | 1 | 1.4 | 2 | 3.2 | 0.606 |
| Alcohol > 3 units/day | 0 | 0.0 | 0 | 0.0 | NA |
| History of glucocorticoid†† | 0 | 0.0 | 1 | 1.6 | 0.477 |
| History of rheumatoid arthritis | 0 | 0.0 | 0 | 0.0 | NA |
| Secondary osteoporosis†† | 6 | 8.7 | 2 | 3.2 | 0.278 |

*ALN-S*, alendronate oral solution; *ALN-T*, alendronate oral tablet; *CTX*, C-telopeptide; *PINP*, procollagen type 1 N-terminal propeptide; *LS*, lumbar spine; *BMD*, bone mineral density; *FN*, femoral neck; *TH*, total hip; *FRAX*, fracture risk assessment tool

# Αποτελέσματα (1)



# Αποτελέσματα (2)



# Αποτελέσματα (3)

| | ALN-S ($N=83$) | | ALN-T ($N=84$) | | $p$ value |
|---|---|---|---|---|---|
| | $N$ | % | $N$ | % | |
| TEAE* | 23 | 27.7 | 22 | 26.2 | 0.825 |
| ADR* | 11 | 13.3 | 6 | 7.1 | 0.192 |
| SAE** | 0 | 0.0 | 2 | 2.4 | 0.497 |
| SADR | 0 | 0.0 | 0 | 0.0 | NA |
| GI disorders* | 8 | 9.6 | 7 | 8.3 | 0.768 |
| Cardiac disorders** | 2 | 2.4 | 3 | 3.6 | 1.000 |
| Musculoskeletal and connective tissue disorders** | 7 | 8.4 | 2 | 2.4 | 0.099 |
| Hepatobiliary disorder** | 3 | 3.6 | 1 | 1.2 | 0.367 |
| Infections and infestation** | 4 | 4.8 | 6 | 7.1 | 0.746 |
| Neoplasms benign, malignant, and unspecified** | 0 | 0.0 | 1 | 1.2 | 1.000 |
| General disorders and administration site conditions** | 2 | 2.4 | 2 | 2.4 | 1.000 |
| Nervous system disorders** | 2 | 2.1 | 2 | 2.1 | 1.000 |
| Skin and subcutaneous tissue disorders** | 1 | 1.2 | 3 | 3.6 | 0.620 |
| Respiratory, thoracic, and mediastinal disorders** | 0 | 0.0 | 1 | 1.2 | 1.000 |
| Renal and urinary disorders** | 0 | 0.0 | 2 | 2.4 | 0.497 |
| Endocrine disorders** | 2 | 2.4 | 0 | 0.0 | 0.246 |
| Psychiatric disorders** | 0 | 0.0 | 1 | 1.2 | 1.000 |
| Reproductive system and breast disorders** | 0 | 0.0 | 1 | 1.2 | 1.000 |

*ALN-S*, alendronate oral solution; *ALN-T*, alendronate oral tablet; *TEAE*, treatment-emergent adverse event; *ADR*, adverse drug reaction; *SAE*, serious adverse event; *SADR*, serious adverse drug reaction; *chi-square test, **Fisher's exact test

# Περιορισμοί Μελέτης

- Ανοιχτή μελέτη
- Διάρκεια 12 μηνών
- Μικρός αριθμός συμμετεχόντων

*Journal of Bone and Mineral Research*, 2024, **39**, 661–671
https://doi.org/10.1093/jbmr/zjae054
Advance access publication: April 13, 2024
**Clinical Trial**

# Effects of vitamin D3, omega-3s, and a simple strength training exercise program on bone health: the DO-HEALTH randomized controlled trial

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# Υπόθεση

- Η επίδραση (μονήρης και συνδυαστική) της βιταμίνης D, Ω3 και της άσκησης κατ' οίκον στη BMD (υπο-ανάλυση της μελέτης DO-HEALTH)

# DO-HEALTH

- Τυχαιοποιημένη, διπλή τυφλή, πολυκεντρική μελέτη (7 κέντρα – 5 Ευρωπαϊκές χώρες)

- 6 παραμέτρους φυσικής υγείας (ΣΑΠ – ΔΑΠ, Short Physical Performance Battery score, Montreal Cognitive Assessment Score, επίπτωση μη σπονδυλικών καταγμάτων, λοιμώξεις)

# Κριτήρια Ένταξης – Αποκλεισμού

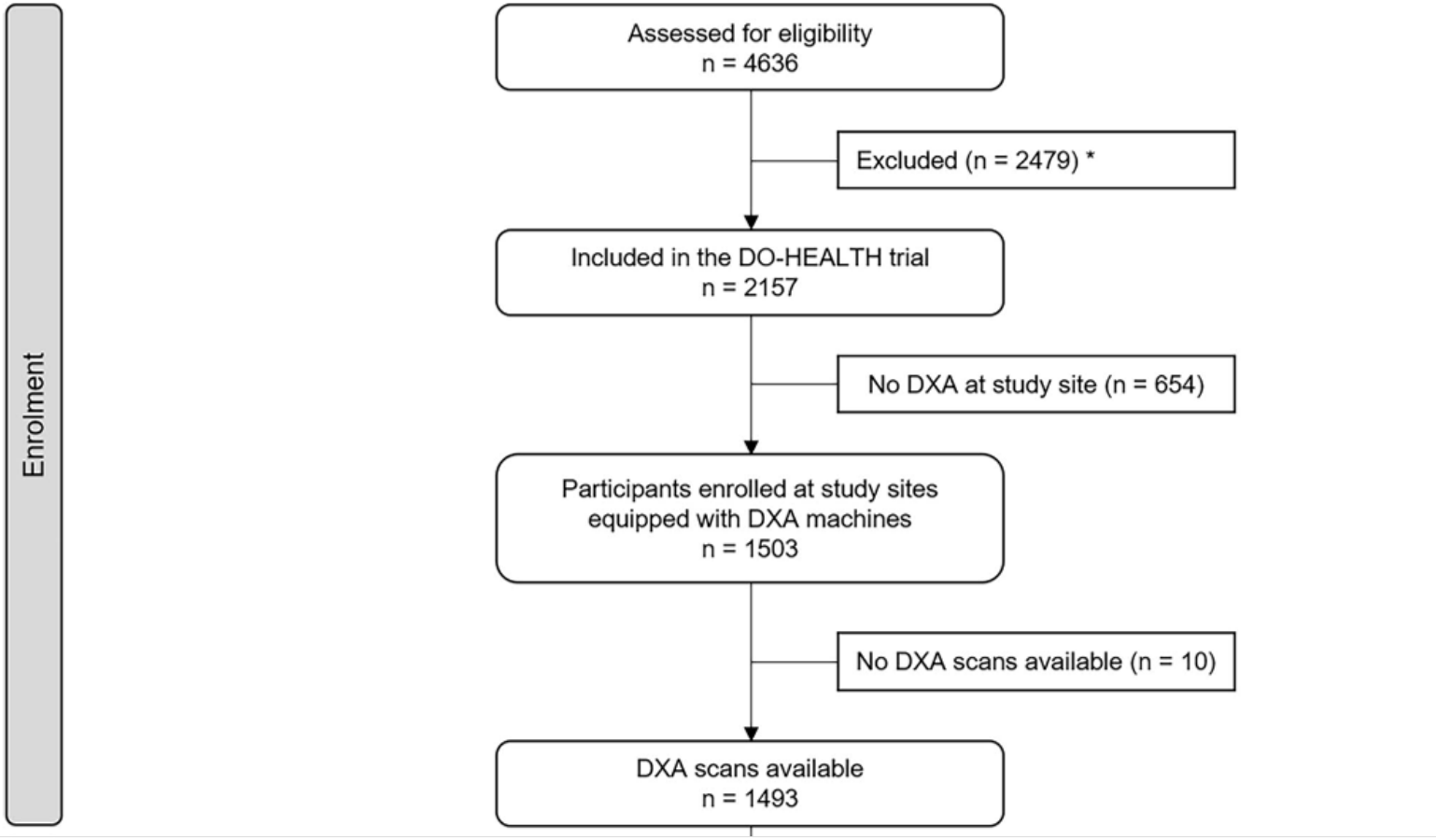
- Άντρες και γυναίκες ≥70 ετών
  - Επαρκής κινητικότητα
  - ≥24 στο Mini Mental State Examination
  - Περιορισμός ασβεστίου έως 500 mg/d, vitamin D έως 800 IU/d και καθόλου Ω3 για τουλάχιστον 3 έτη

- Κριτήρια αποκλεισμού (σχετικά με τα οστά)
  - Ιστορικό σημαντικής νόσου τα τελευταία 5 έτη (καρκίνος, έμφραγμα, ΑΕΕ)
  - Λήψη αναλόγων PTH, καλσιτριόλης ή αναλόγων της, καλσιτονίνης
  - Ιστορικό Νόσου Paget
  - Υπο/υπερπαραθυρεοειδισμός, επιληψία ή λήψη αντι-επιληπτικών

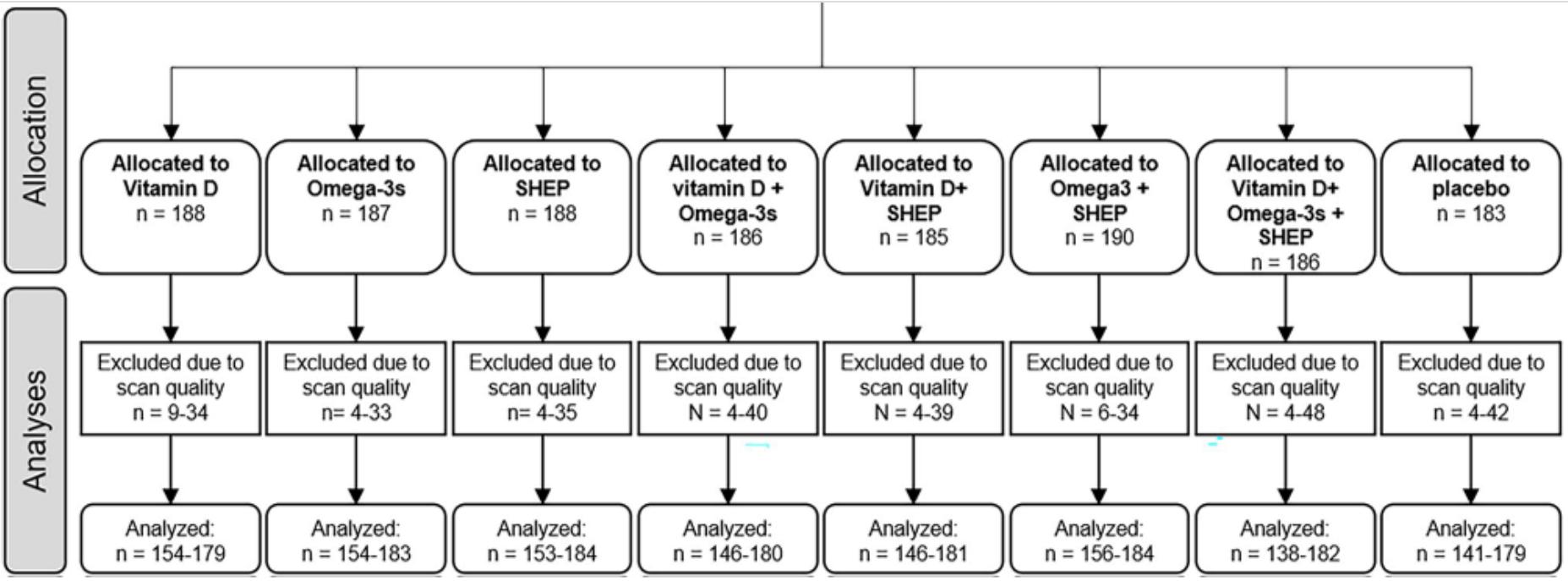
# Ιατρική Παρέμβαση

- Vitamin D:  2000 IU
- Ω3: 500 mg (EPA) και 1000 mg (DHA)
- Placebo
- SHEP: 5 ασκήσεις κινητικότητας του ισχίου, γόνατος, ΠΔΚ, θώρακα και κορμού – 3 σετ των 10 επαναλήψεων – 3 φορές τη βδομάδα

# Πληθυσμός Μελέτης (1)



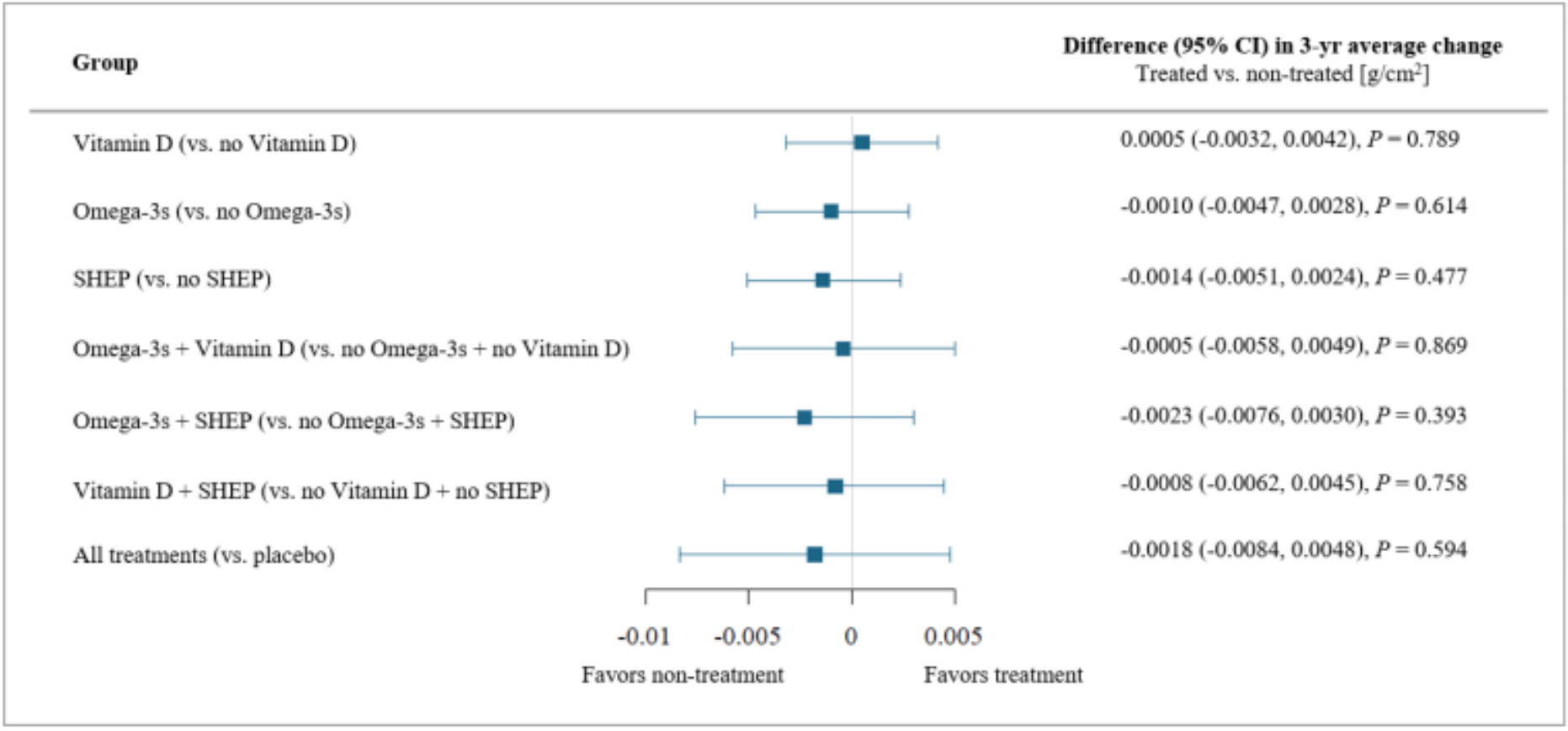
# Πληθυσμός Μελέτης (2)



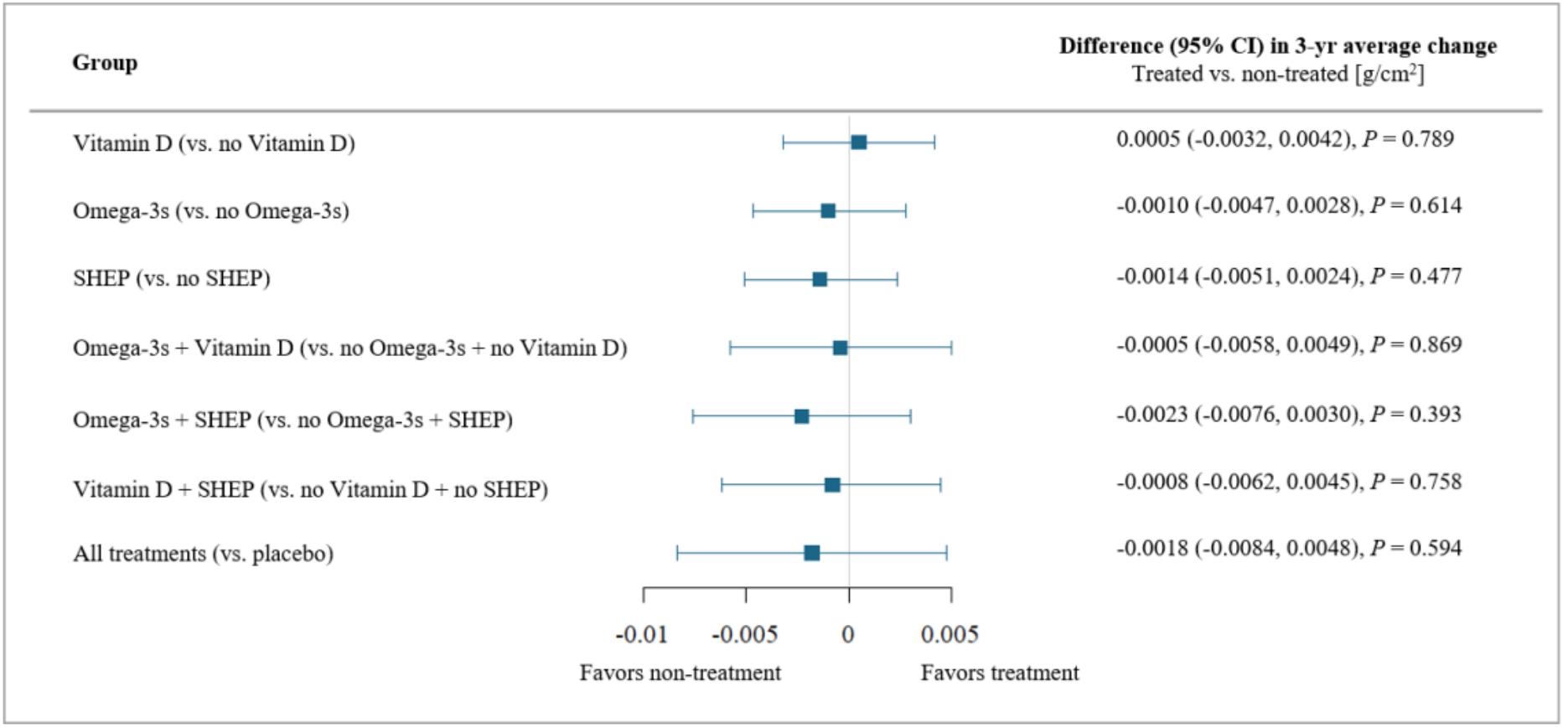
# Πληθυσμός Μελέτης (3)

- Baseline FN T-score -1.4
- Μέση 25[OH]D 21.9 ng/mL - 44% < 20 ng/mL
- 12% οστεοπόρωση, 55% οστεοπενία και 30% φυσιολογική BMD
- 162 (11%) με ιστορικό κατάγματος ευθραυστότητας την τελευταία 10ετία
- 7% λάμβαναν αντι-καταβολική αγωγή

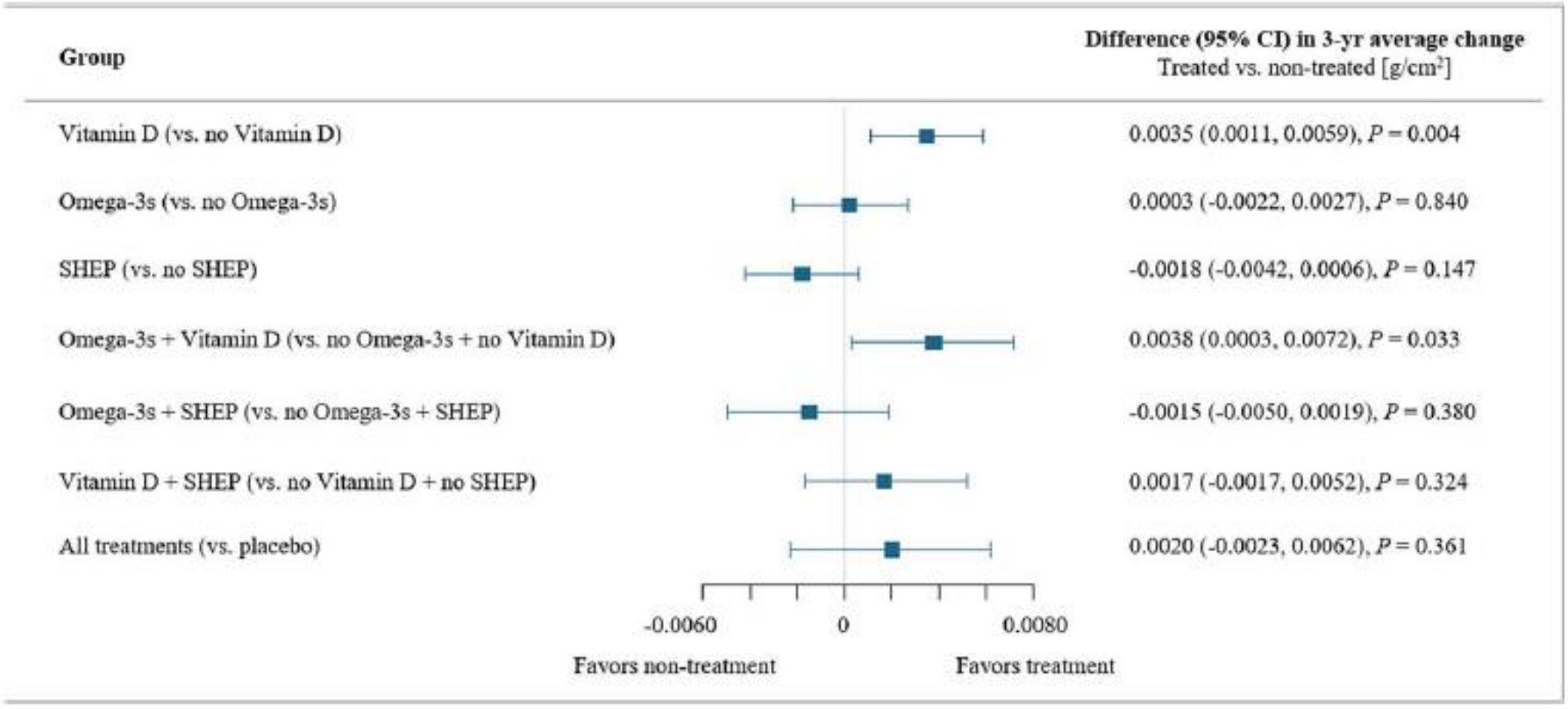
# Αποτελέσματα (1)



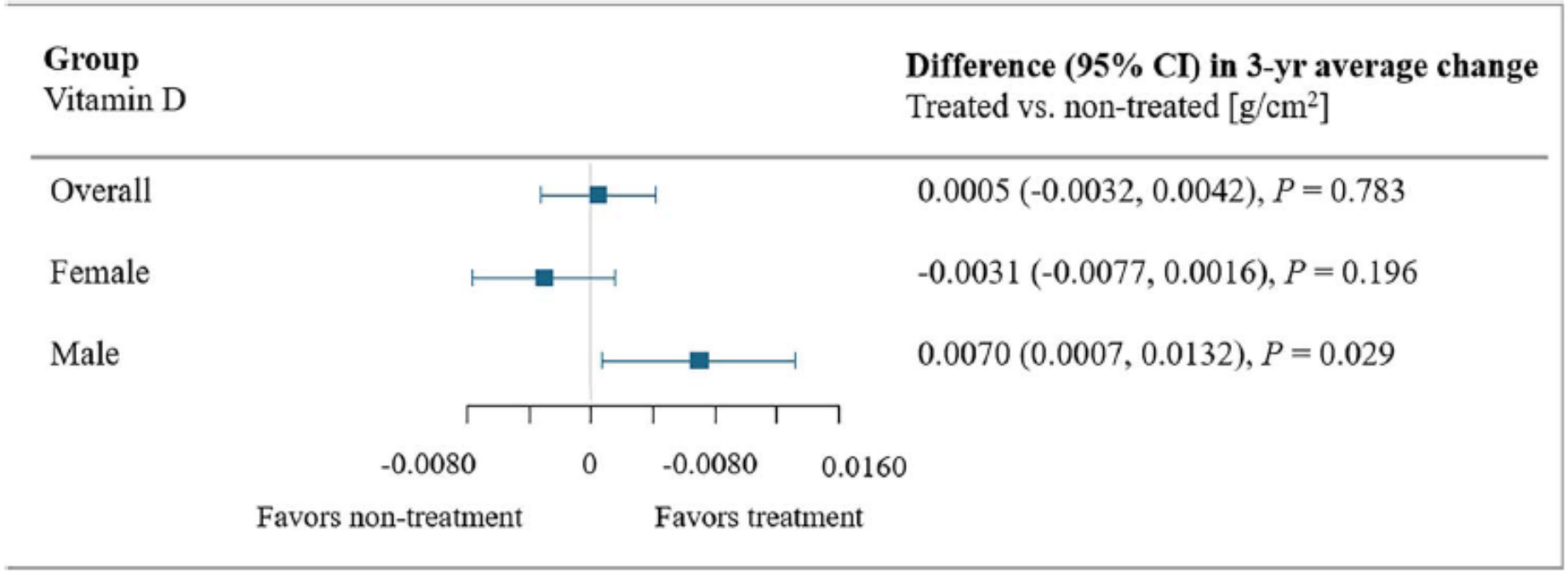
# Αποτελέσματα (2)



# Αποτελέσματα (3)



# Αποτελέσματα (4)



# Περιορισμοί Μελέτης

- Πληθυσμός μη ελεγχόμενος ως προς την επάρκεια βιταμίνης D, BMD, κίνδυνο καταγμάτων κατά το screening
- Ελάχιστη στατιστικά σημαντική αύξηση στο ολικό ισχίο 0.0035 g/cm$^2$ (≈0.4%) – LSC: 0.022 g/cm$^2$
- Μικτός πληθυσμός αναφορικά με την οστική μάζα → αδυναμία γενίκευσης των αποτελεσμάτων

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Journal of Orthopaedic Surgery and Research

SYSTEMATIC REVIEW Open Access

# Efficacy and safety of odanacatib in the treatment of postmenopausal women with osteoporosis: a meta-analysis

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# Ερώτημα

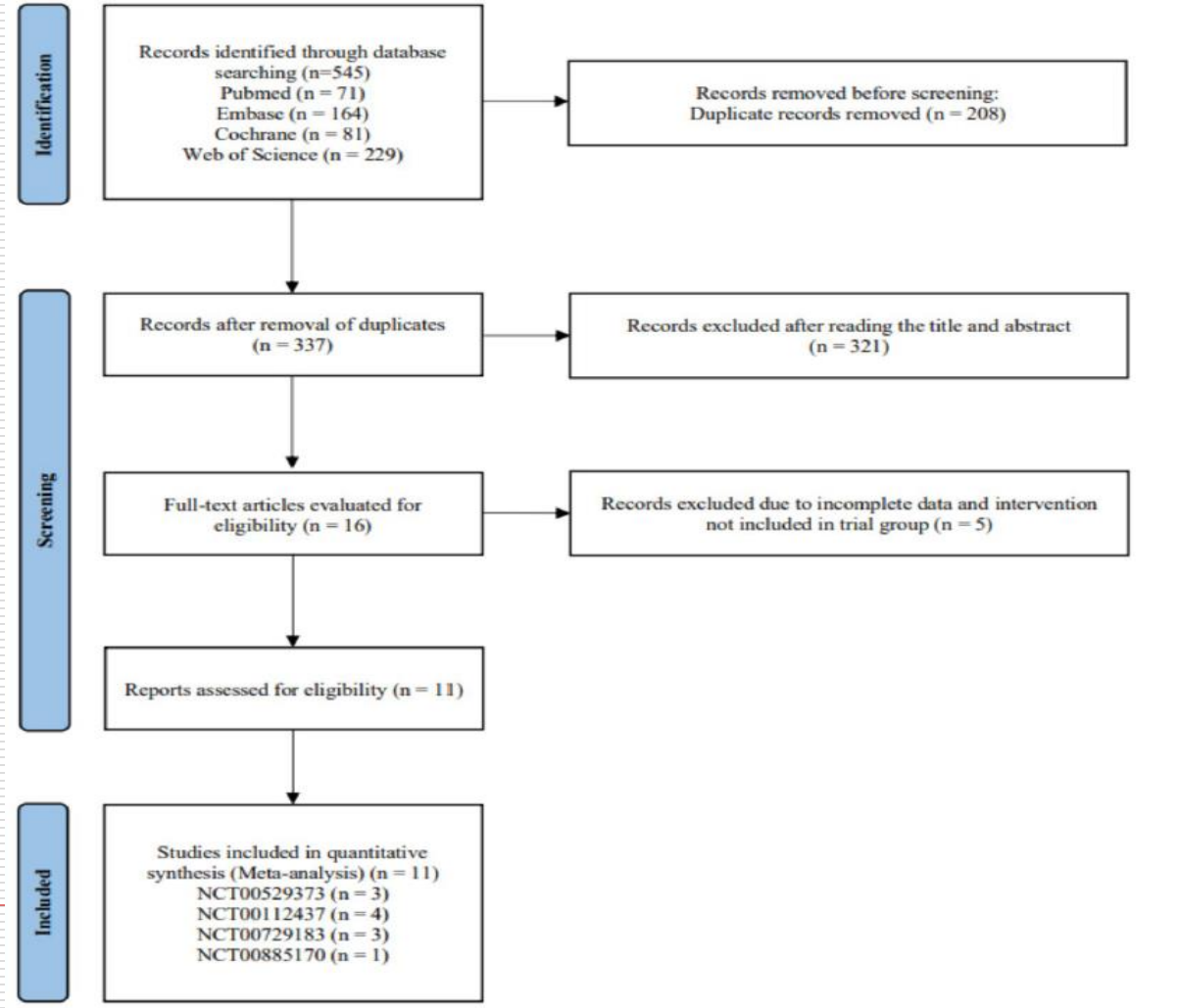
- Αποτελεσματικότητα (BMD, δείκτες οστικού μεταβολισμού) και ασφάλεια του Odanacatib σε γυναίκες με μετ-εμμηνοπαυσιακή οστεοπόρωση

# Στρατηγική Αναζήτησης

- PubMed, Embase, Cochrane Library, Web of Science έως 29/12/2023

- (P): Μετ-εμμηνοπαυσιακές γυναίκες με οστεοπόρωση ή χαμηλή οστική μάζα
- (I): Odanacatib
- (C): Placebo
- (O): BMD, δείκτες οστικού μεταβολισμού, ανεπιθύμητες ενέργειες
- (S): RCTs

# Διάγραμμα Ανασκόπησης



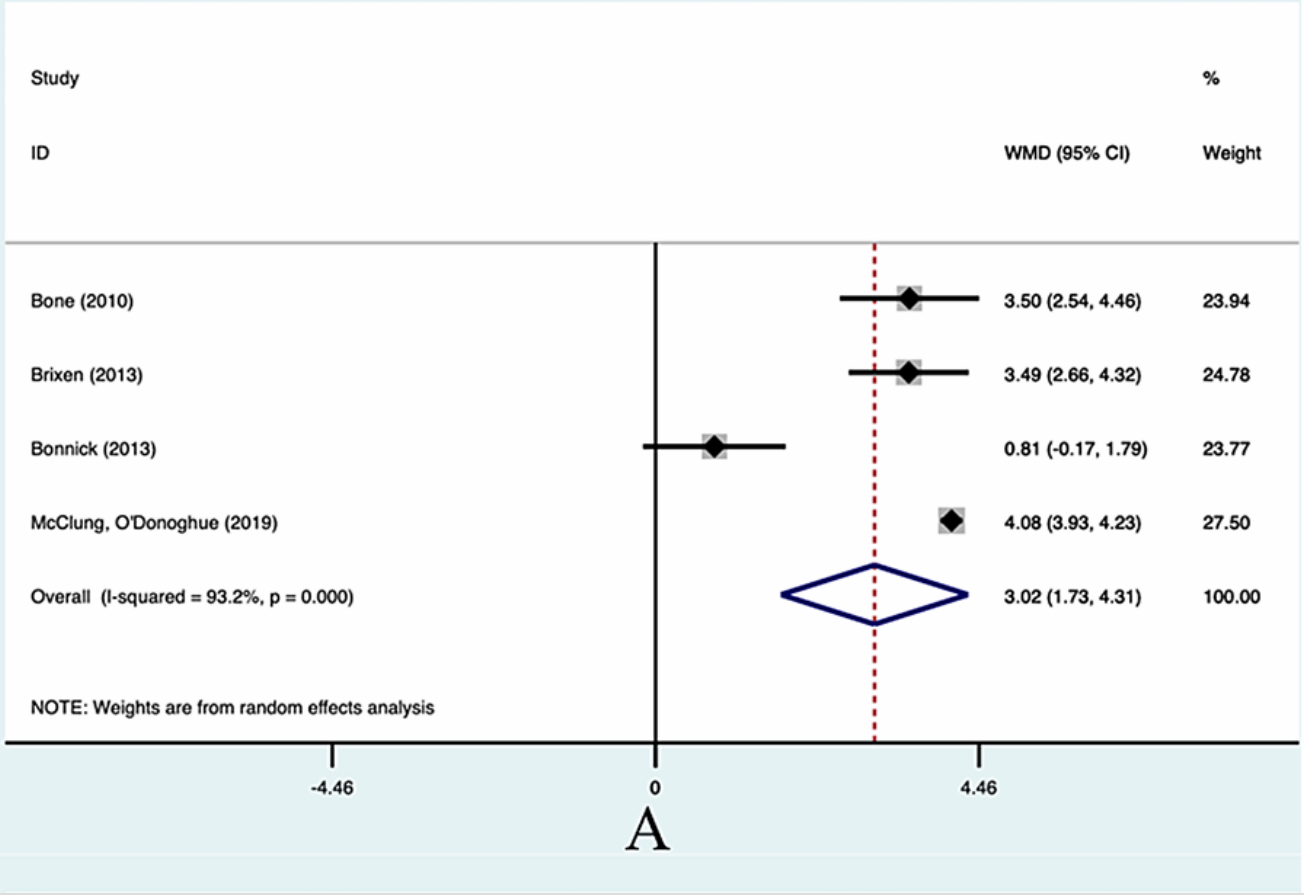
# Αναλυόμενες Μελέτες

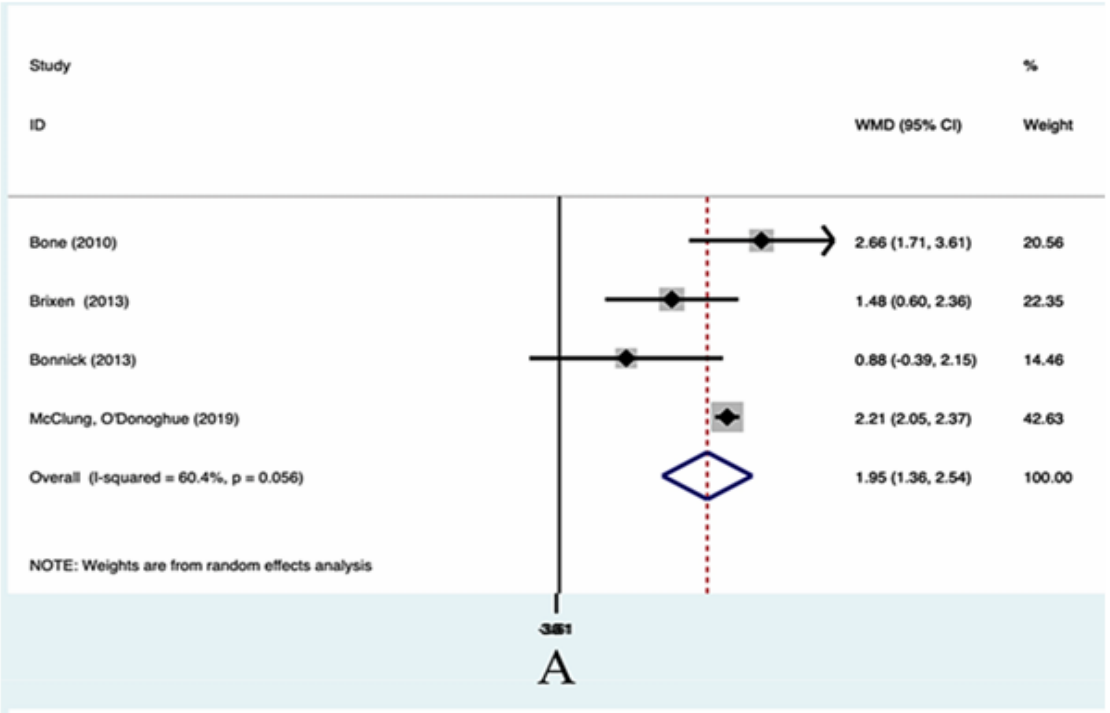
**Table 1** .

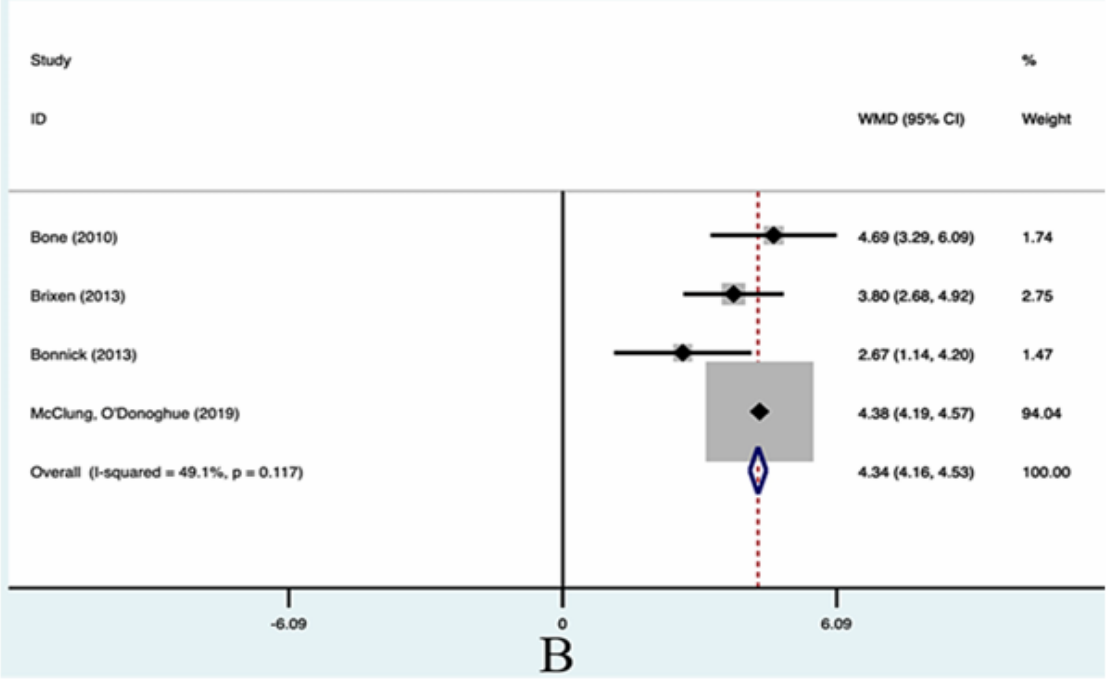
| Study | Year | Country | Sample size | | Age | | Intervention | | Outcome | Follow-up |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | EG | CG | EG | CG | EG | CG | | |
| M. R. McClung | 2019 | multicenter | 8043 | 8028 | 72.8 ± 5.4 | 72.9 ± 5.3 | 1.ODN 50 mg OW 2.vitamin D3 (5600 IU) and calcium | 1.Placebo OW 2.vitamin D3 (5600 IU) and calcium | Fractures, BMD, sCTx, uNTx/Cr, sBSAP, sP1NP, Adverse Events | 6, 12, 18, 24, 30, 36, 42, 48, 54, 60 months |
| H. G. Bone | 2010 | multicenter | 78 | 83 | 64.5 ± 8.1 | 65.9 ± 7.8 | 1.ODN 50 mg OW 2.vitamin D3 (2800 IU) and calcium | 1.Placebo OW 2.vitamin D3 (2800 IU) and calcium | BMD, sCTx, uNTx/Cr, sBSAP, sP1NP, Adverse Events | 12, 24months |
| K. Brixen | 2013 | multicenter | 109 | 105 | 63.9 ± 7.3 | 64.0 ± 6.2 | 1.ODN 50 mg OW 2. vitamin D3(5600 IU) 3.500 mg calcium | 1.Placebo 50 mg OW 2.vitamin D3(5600 IU) 3.500 mg calcium | BMD, CTX, P1NP, Adverse Events | 6, 12, 18, and 24 months |
| S. Bonnick | 2013 | multicenter | 122 | 121 | 71.5 ± 6.7 | 71.1 ± 6.8 | 1.ODN 50 mg OW 2.vitamin D3(5600 IU) 3.1200 mg calcium | 1.Placebo 50 mg OW 2.vitamin D3(5600 IU) 3.1200 mg calcium | BMD, uNTx/Cr, sCTx, sBSAP, sP1NP, Adverse Events | 1, 3, 6, 12, 18, and 24 months |

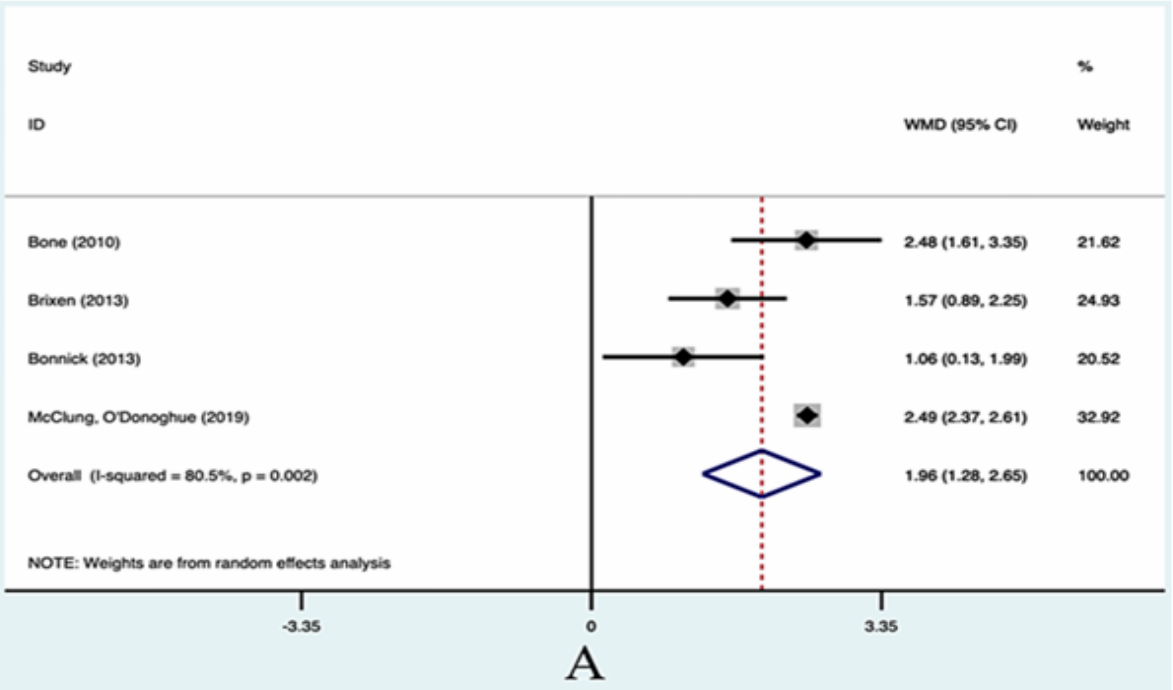
BMD, Bone Mineral Density; sCTx, serum C-telopeptides of type I collagen; uNTx/Cr, N-telopeptide/creatinine ratio; BSAP, bone-specific alkaline phosphatase; P1NP, N-terminal propeptide of Type I collagen

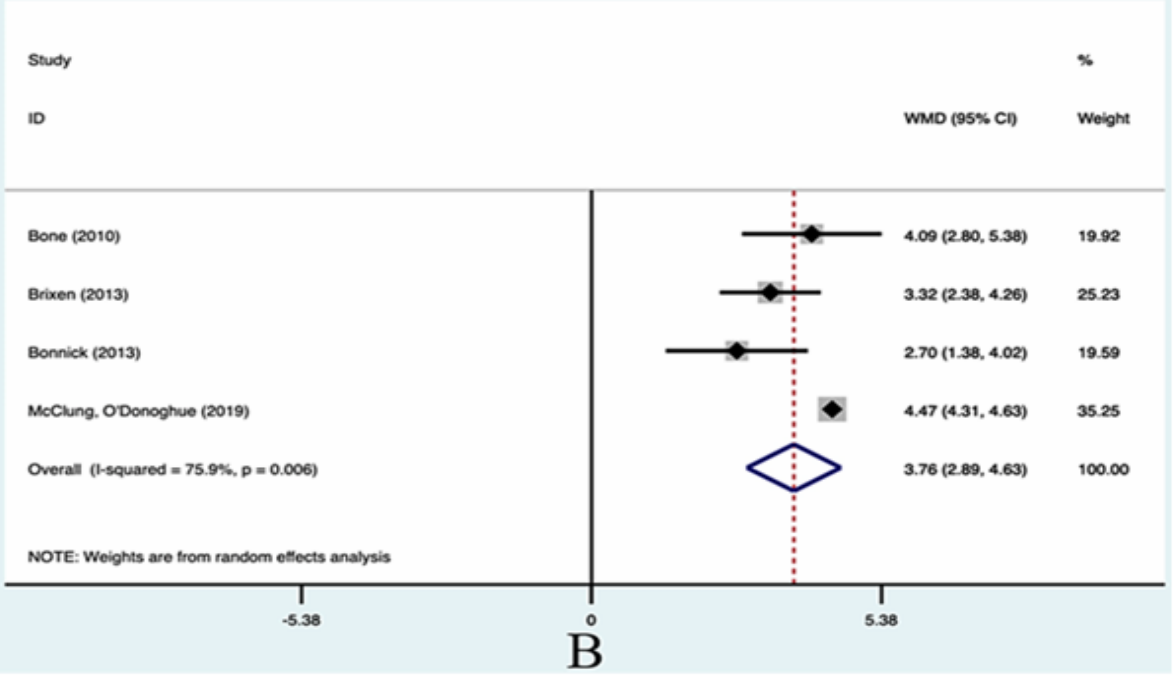
# Αποτελέσματα

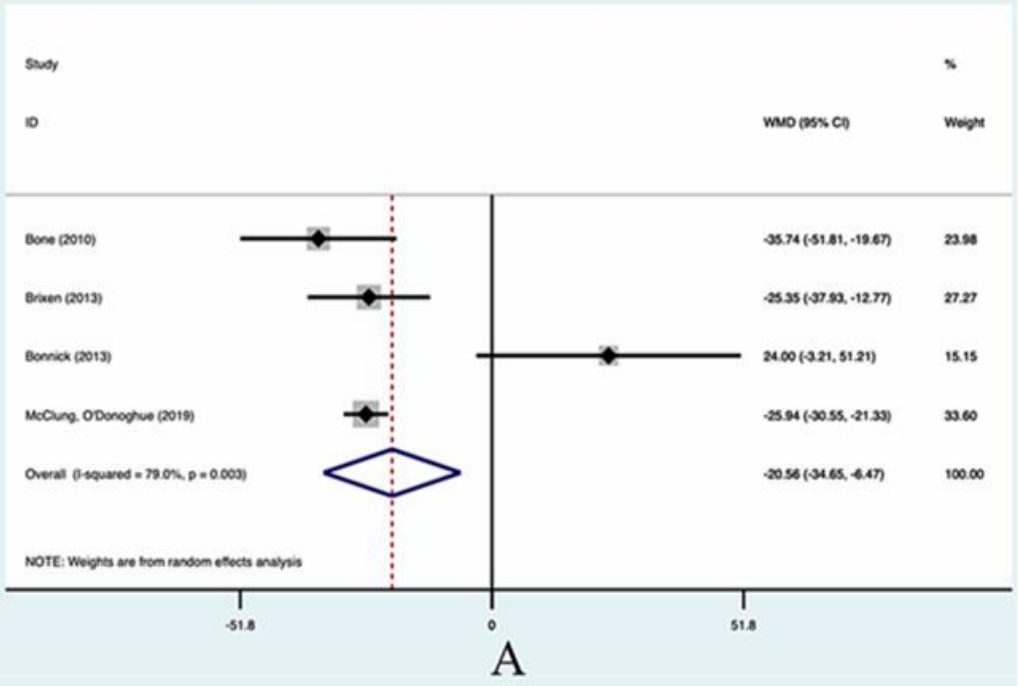


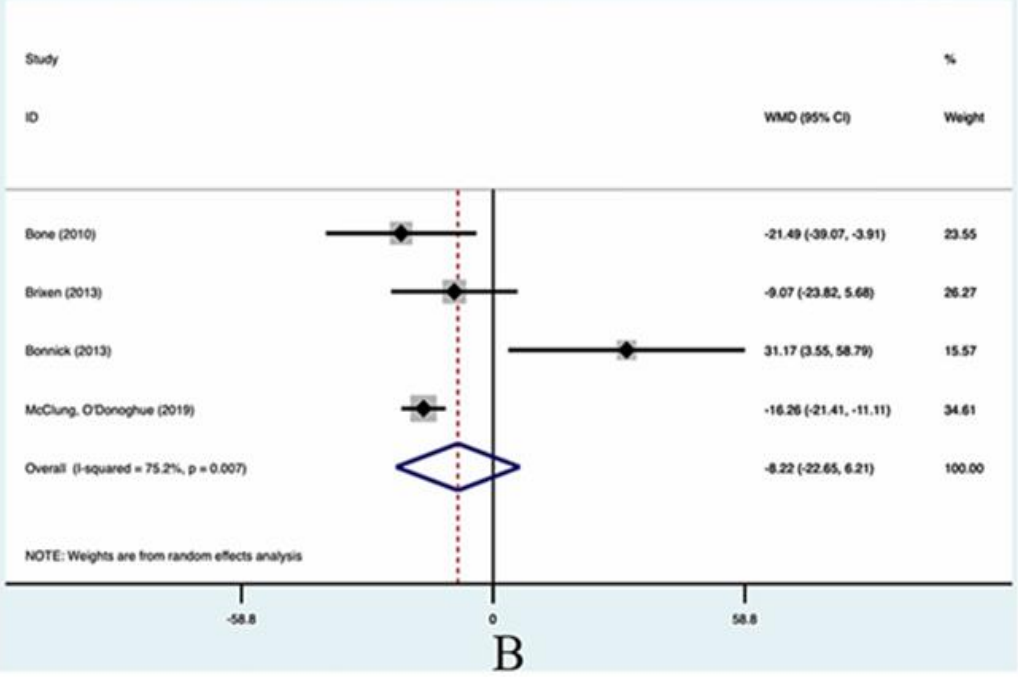

Study
ID
WMD (95% CI)
%
Weight
Bone (2010)
2.66 (1.71, 3.61)
20.56
Brixen (2013)
1.48 (0.60, 2.36)
22.35
Bonnick (2013)
0.88 (-0.39, 2.15)
14.46
McClung, O'Donoghue (2019)
2.21 (2.05, 2.37)
42.63
Overall (I-squared = 60.4%, p = 0.056)
1.95 (1.36, 2.54)
100.00
NOTE: Weights are from random effects analysis
3.61
A

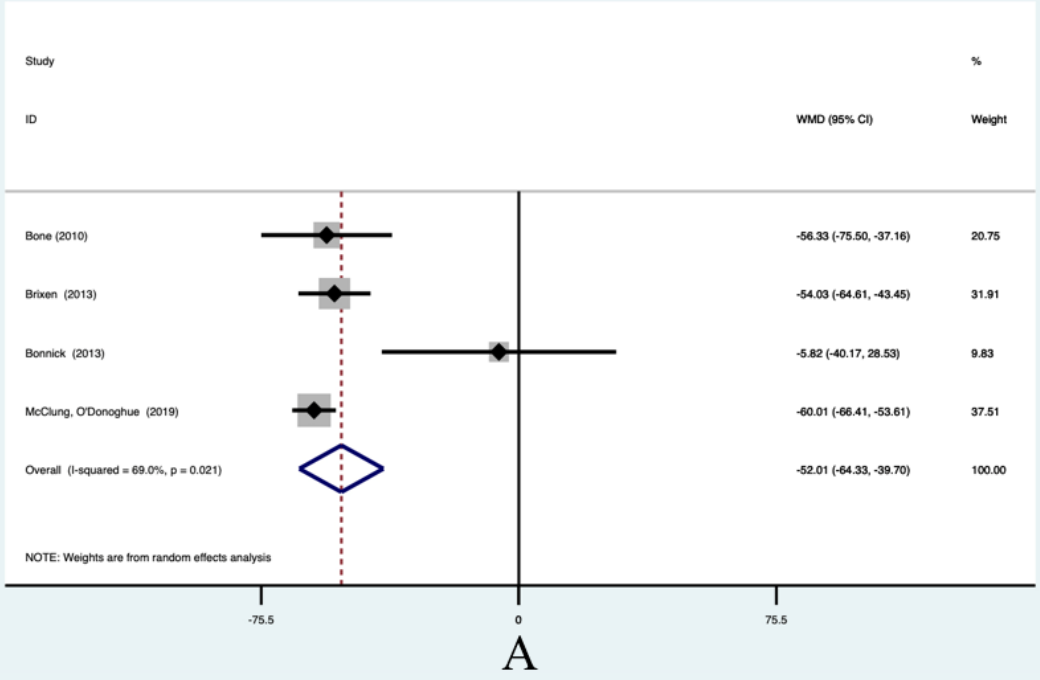

Study
ID
WMD (95% CI)
%
Weight
Bone (2010)
4.69 (3.29, 6.09)
1.74
Brixen (2013)
3.80 (2.68, 4.92)
2.75
Bonnick (2013)
2.67 (1.14, 4.20)
1.47
McClung, O'Donoghue (2019)
4.38 (4.19, 4.57)
94.04
Overall (I-squared = 49.1%, p = 0.117)
4.34 (4.16, 4.53)
100.00
-6.09
0
6.09
B


Study
ID
WMD (95% CI)
%
Weight
Bone (2010)
2.48 (1.61, 3.35)
21.62
Brixen (2013)
1.57 (0.89, 2.25)
24.93
Bonnick (2013)
1.06 (0.13, 1.99)
20.52
McClung, O'Donoghue (2019)
2.49 (2.37, 2.61)
32.92
Overall (I-squared = 80.5%, p = 0.002)
1.96 (1.28, 2.65)
100.00
NOTE: Weights are from random effects analysis
-3.35
0
3.35
A

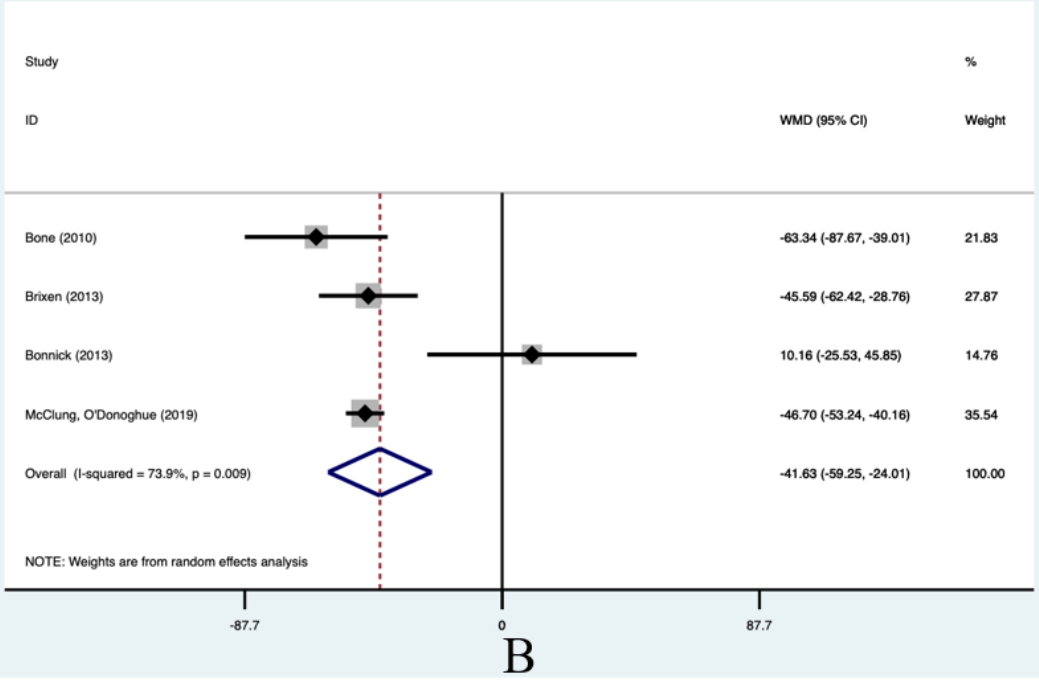

Study
ID
WMD (95% CI)
%
Weight
Bone (2010)
4.09 (2.80, 5.38)
19.92
Brixen (2013)
3.32 (2.38, 4.26)
25.23
Bonnick (2013)
2.70 (1.38, 4.02)
19.59
McClung, O'Donoghue (2019)
4.47 (4.31, 4.63)
35.25
Overall (I-squared = 75.9%, p = 0.006)
3.76 (2.89, 4.63)
100.00
NOTE: Weights are from random effects analysis
-5.38
0
5.38
B


Study
ID
WMD (95% CI)
%
Weight
Bone (2010)
-35.74 (-51.81, -19.67)
23.98
Brixen (2013)
-25.35 (-37.93, -12.77)
27.27
Bonnick (2013)
24.00 (-3.21, 51.21)
15.15
McClung, O'Donoghue (2019)
-25.94 (-30.55, -21.33)
33.60
Overall (I-squared = 79.0%, p = 0.003)
-20.56 (-34.65, -6.47)
100.00
NOTE: Weights are from random effects analysis
-51.8
0
51.8
A


Study
ID
WMD (95% CI)
%
Weight
Bone (2010)
-21.49 (-39.07, -3.91)
23.55
Brixen (2013)
-9.07 (-23.82, 5.68)
26.27
Bonnick (2013)
31.17 (3.55, 58.79)
15.57
McClung, O'Donoghue (2019)
-16.26 (-21.41, -11.11)
34.61
Overall (I-squared = 75.2%, p = 0.007)
-8.22 (-22.65, 6.21)
100.00
NOTE: Weights are from random effects analysis
-58.8
0
58.8
B

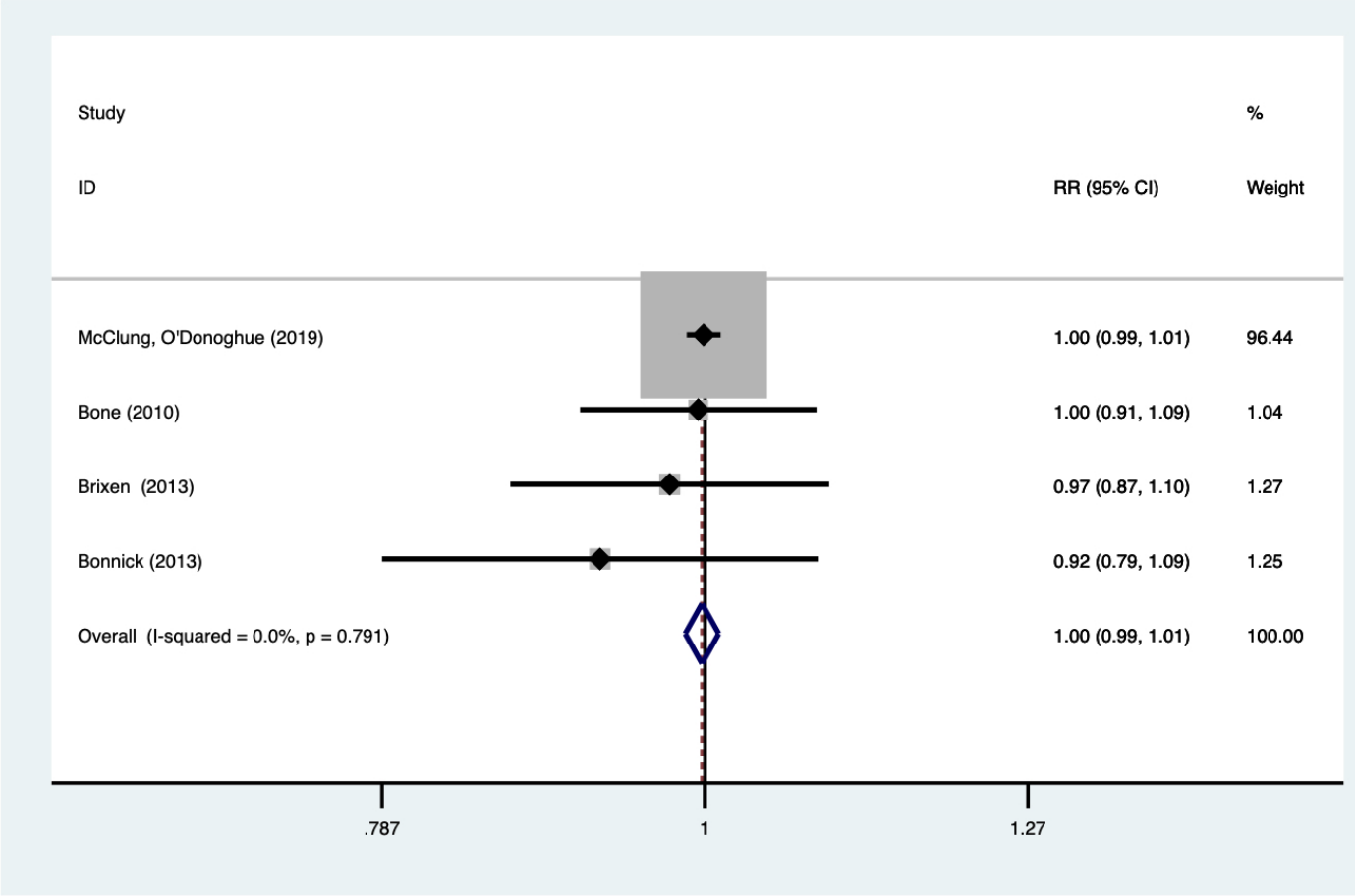

Study
ID
WMD (95% CI)
%
Weight
Bone (2010)
-56.33 (-75.50, -37.16)
20.75
Brixen (2013)
-54.03 (-64.61, -43.45)
31.91
Bonnick (2013)
-5.82 (-40.17, 28.53)
9.83
McClung, O'Donoghue (2019)
-60.01 (-66.41, -53.61)
37.51
Overall (I-squared = 69.0%, p = 0.021)
-52.01 (-64.33, -39.70)
100.00
NOTE: Weights are from random effects analysis
-75.5
0
75.5

A

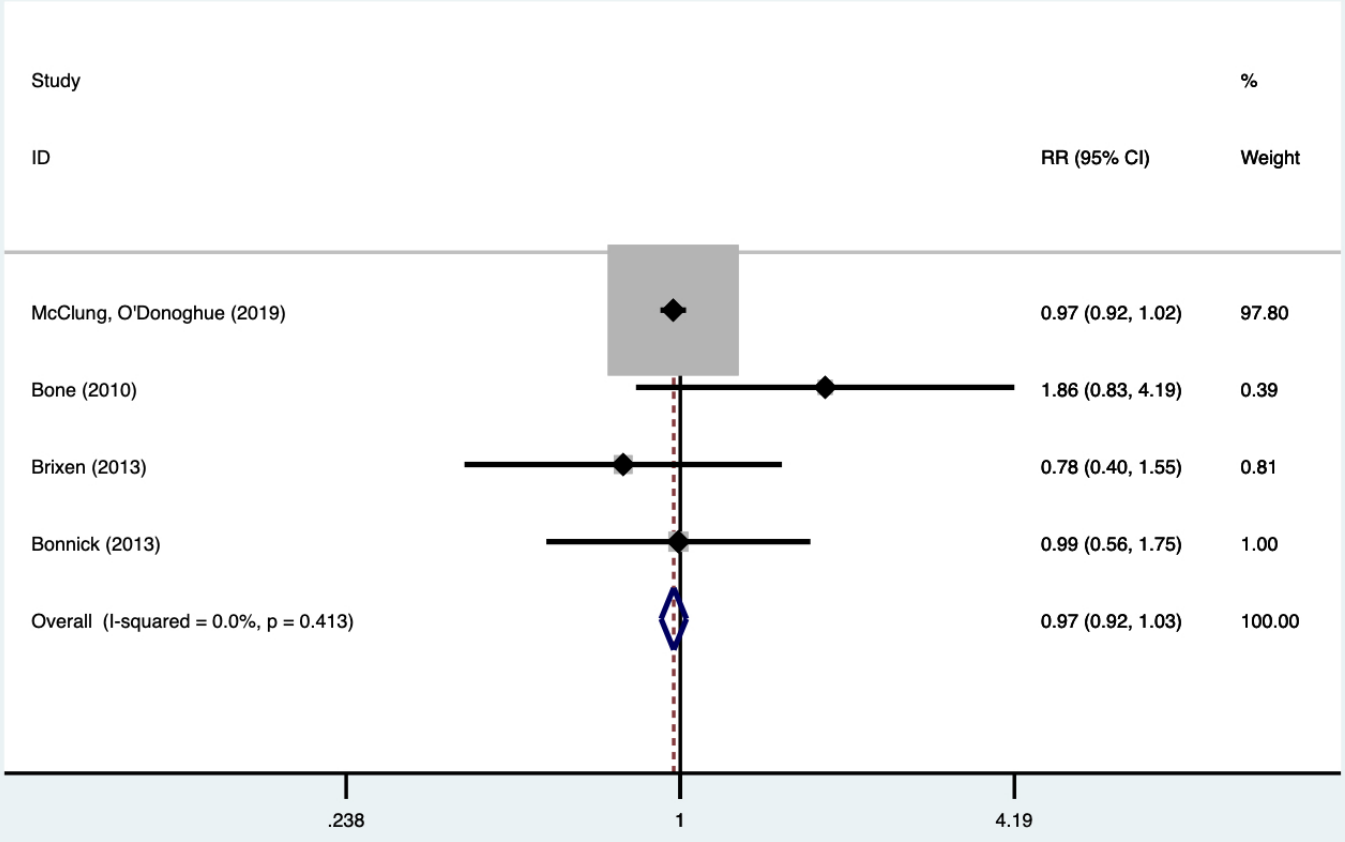

Study
ID
WMD (95% CI)
%
Weight
Bone (2010)
-63.34 (-87.67, -39.01)
21.83
Brixen (2013)
-45.59 (-62.42, -28.76)
27.87
Bonnick (2013)
10.16 (-25.53, 45.85)
14.76
McClung, O'Donoghue (2019)
-46.70 (-53.24, -40.16)
35.54
Overall (I-squared = 73.9%, p = 0.009)
-41.63 (-59.25, -24.01)
100.00
NOTE: Weights are from random effects analysis
-87.7
0
87.7

B

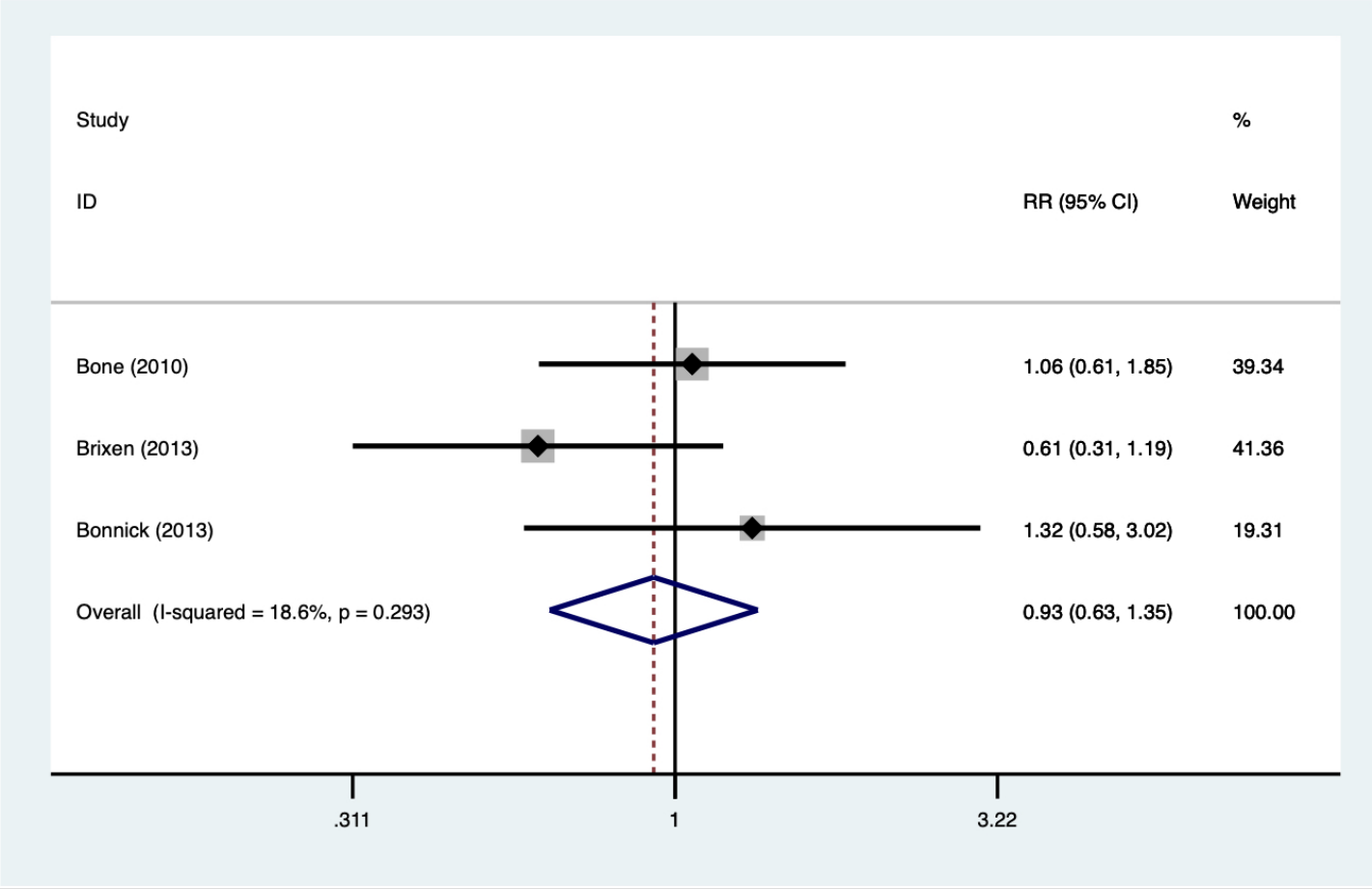
# Ασφάλεια (1)


Study
ID
RR (95% CI)
%
Weight
McClung, O'Donoghue (2019)
1.00 (0.99, 1.01)
96.44
Bone (2010)
1.00 (0.91, 1.09)
1.04
Brixen (2013)
0.97 (0.87, 1.10)
1.27
Bonnick (2013)
0.92 (0.79, 1.09)
1.25
Overall (I-squared = 0.0%, p = 0.791)
1.00 (0.99, 1.01)
100.00
.787
1
1.27

# Ασφάλεια (2)


Study
ID
RR (95% CI)
%
Weight
McClung, O'Donoghue (2019)
0.97 (0.92, 1.02)
97.80
Bone (2010)
1.86 (0.83, 4.19)
0.39
Brixen (2013)
0.78 (0.40, 1.55)
0.81
Bonnick (2013)
0.99 (0.56, 1.75)
1.00
Overall (I-squared = 0.0%, p = 0.413)
0.97 (0.92, 1.03)
100.00
.238
1
4.19

# Ασφάλεια (3)


Study
ID
RR (95% CI)
%
Weight
Bone (2010)
1.06 (0.61, 1.85)
39.34
Brixen (2013)
0.61 (0.31, 1.19)
41.36
Bonnick (2013)
1.32 (0.58, 3.02)
19.31
Overall (I-squared = 18.6%, p = 0.293)
0.93 (0.63, 1.35)
100.00
.311
1
3.22

Σας Ευχαριστώ