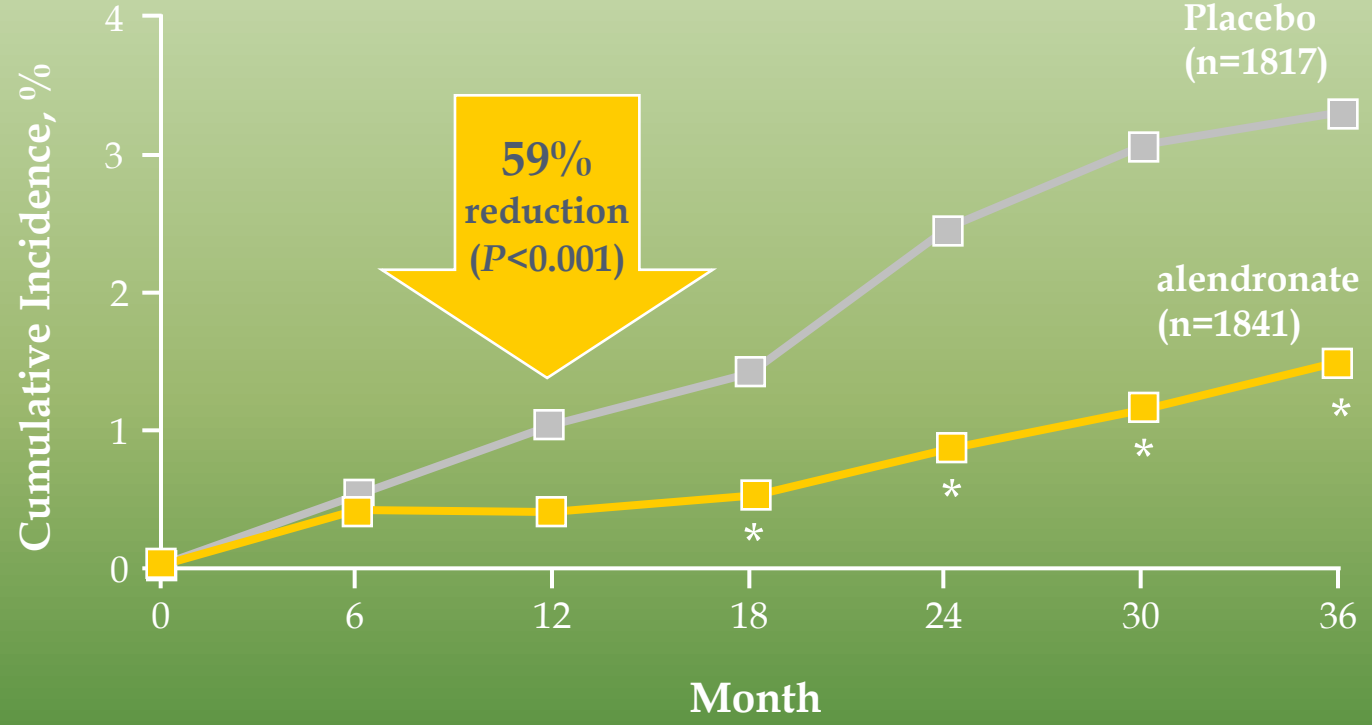
«Η ΑΛΕΝΔΡΟΝΑΤΗ»

ΕΥΑΓΓΕΛΙΑ Γ. ΚΑΣΚΑΝΗ
ΡΕΥΜΑΤΟΛΟΓΟΣ
Διδάκτωρ Πανεπιστημίου Αθηνών

Post hoc analyses of RCTs

Proven Vertebral Fracture Efficacy of alendronate™



- Alendronate reduced the incidence of multiple vertebral fractures by 90% at 3 years in women with prior fractures ($P<0.001$ vs placebo)

FIT = Fracture Intervention Trial

*Significant cumulative difference from placebo ($P<0.05$)

Adapted from Black DM, et al. *J Clin Endocrinol Metab.* 2000;85:4118–4124; Black DM, et al. *Lancet.* 1996;348:1535–1541; Black DM, et al. *Int J Clin Pract Suppl.* 1999;101:46–50.

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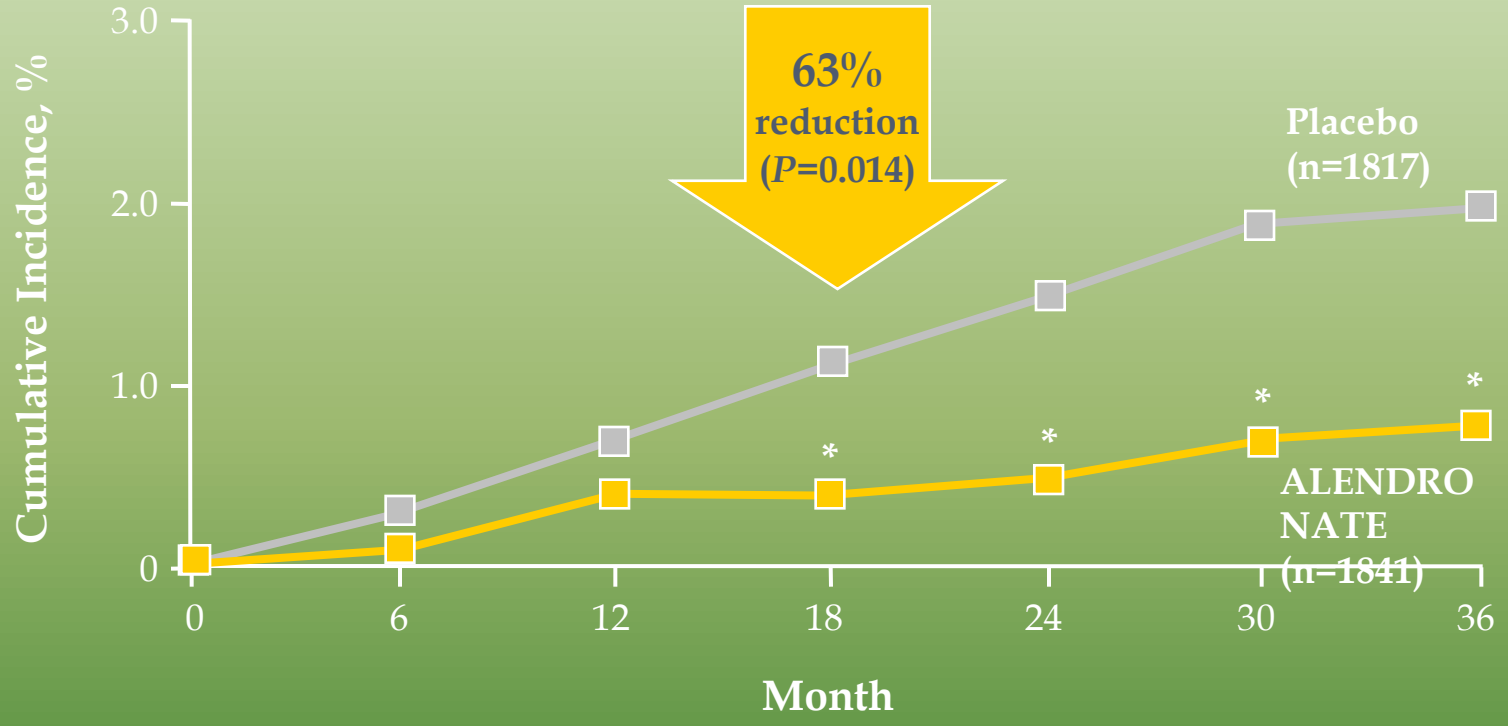
Post hoc analyses of RCTs

Proven Hip Fracture Efficacy of alendronate



- A significant reduction in relative risk was evident in women with and without fractures ($P<0.05$) at month 18 and month 36

FIT = Fracture Intervention Trial

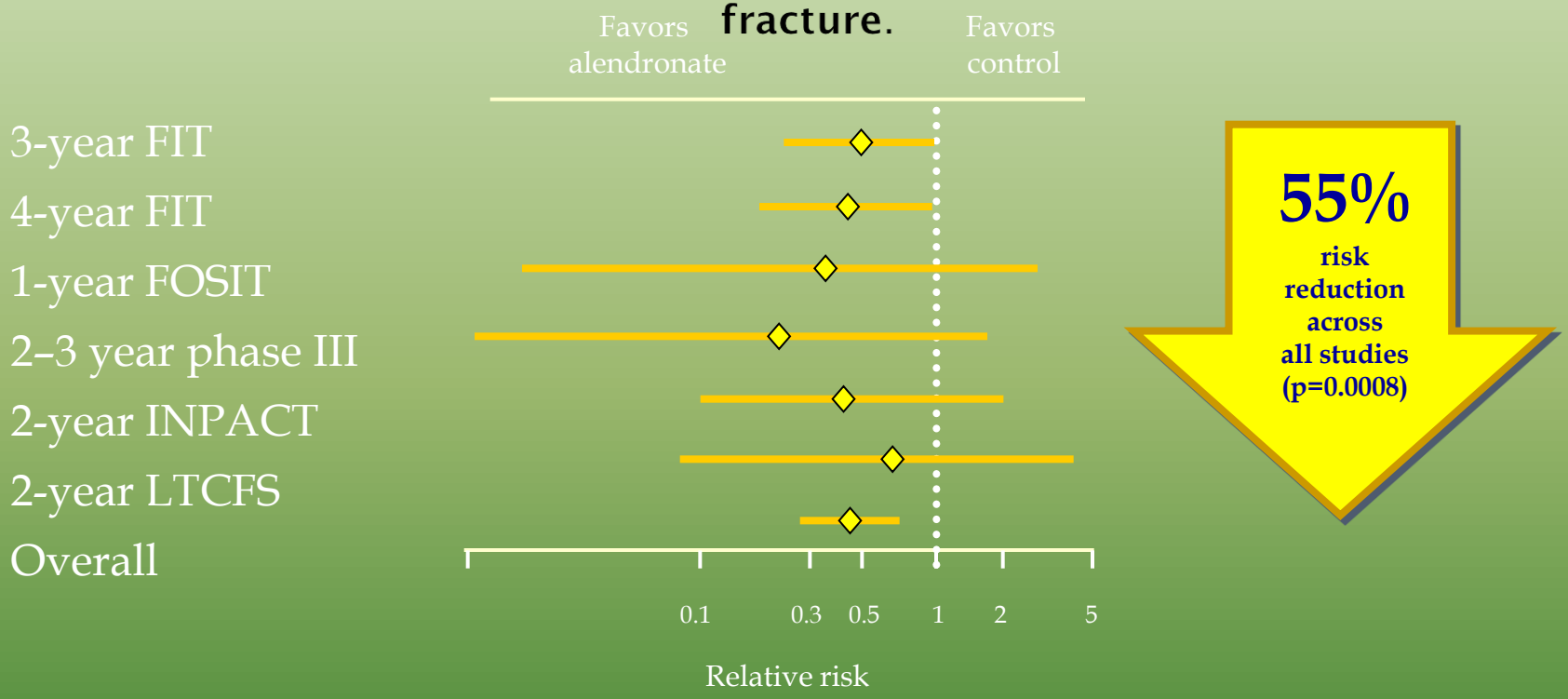
*Significant cumulative difference from placebo ($P<0.05$)

Adapted from Black DM, et al. *J Clin Endocrinol Metab.* 2000;85:4118–4124.

Meta-analysis of Alendronate Studies
Papapoulos SE 2005

Αποτελεσματικότητα της αλενδρονάτης στην μείωση της συχνότητας του κατάγματος του ισχίου

Data shown are for women with T-score of –2.5 or less or with a vertebral fracture.

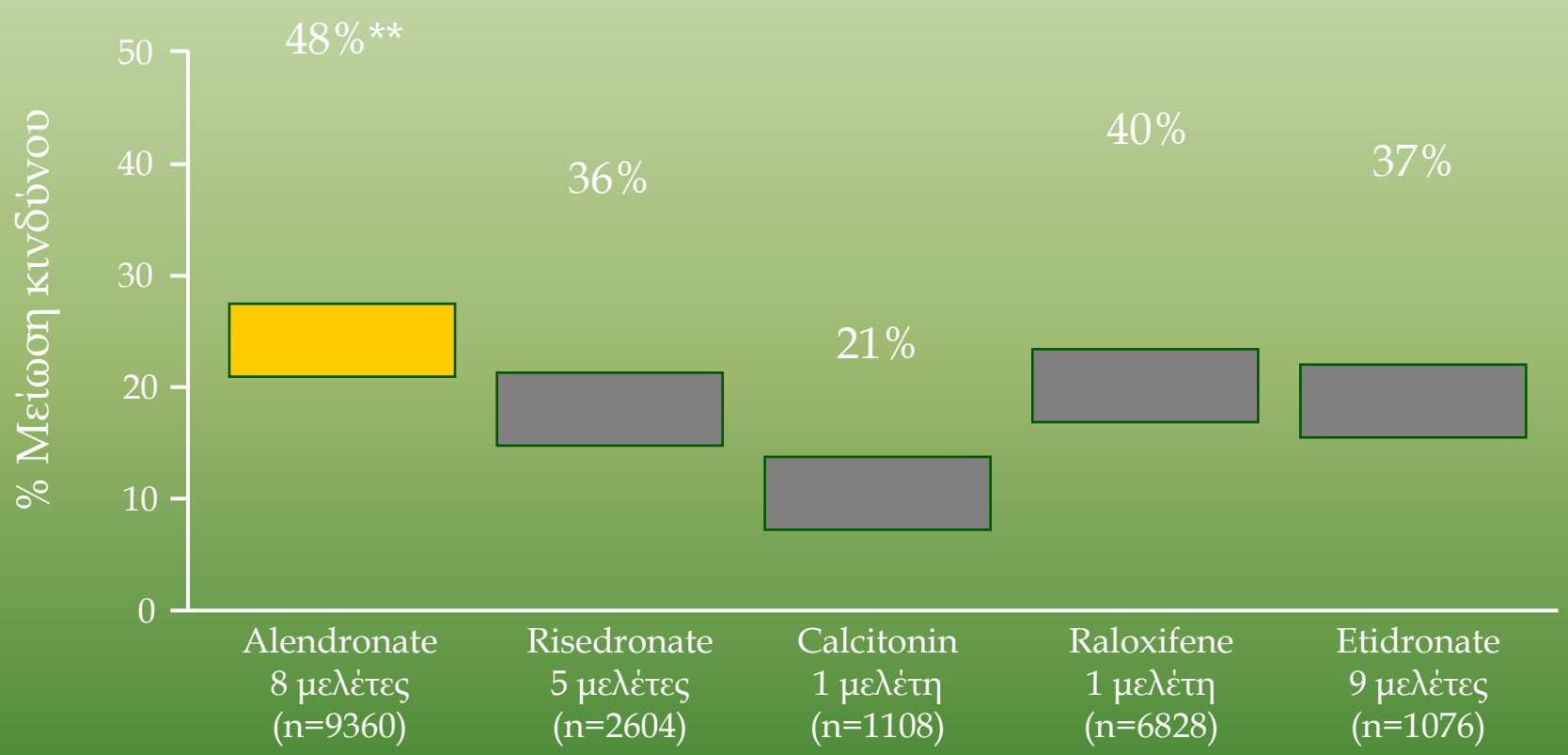


Meta-analysis of six randomized controlled trials of alendronate to examine consistency of effect and overall effect in reducing hip fractures in postmenopausal women

FIT=Fracture Intervention Trial; FOSIT=FOSAMAX™ International Trial; INPACT=Investigation of Postmenopausal Osteoporosis: Alendronate vs. Calcium Trial; LTCFS=Long-Term Care Facilities study

Papapoulos SE, Quandt SA, Liberman UA et al. Meta-analysisof the efficacy of alendronate for the prevention of hip fractures in postmenopausal women. Osteoporos Int 2005; 16:468–74.

Meta analyses of RCTs
Η Αλενδρονάτη προσέφερε μεγαλύτερη προστασία κατά των σπονδυλικών καταγμάτων*



*Data not representative of head-to-head trials; **p<0.01 vs. baseline

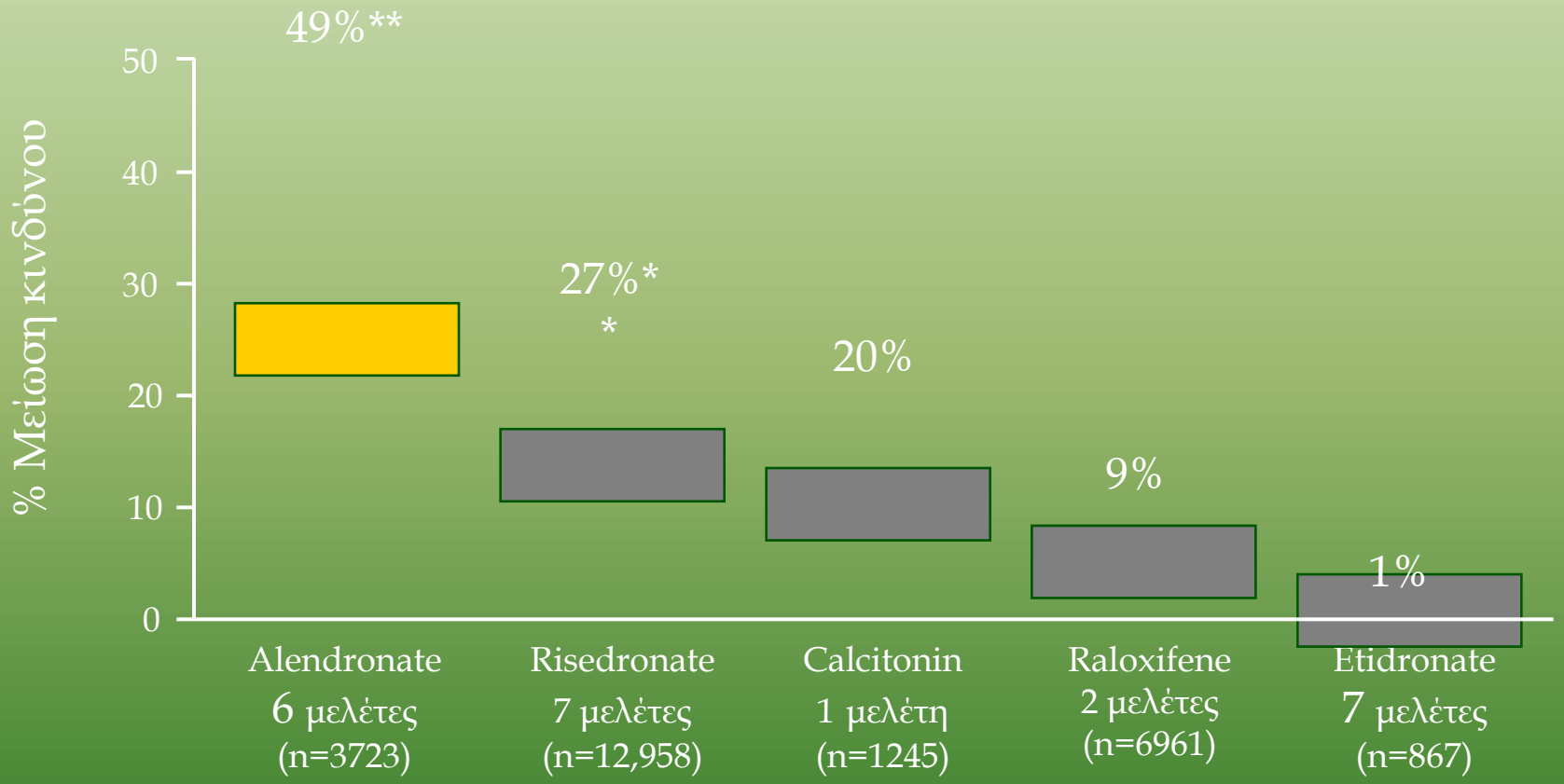
Meta-analysis to evaluate magnitude of treatment effects on fractures and BMD based on randomized controlled trials of different osteoporosis therapies

All data statistically significant vs. baseline

Adapted from Cranney A et al *Endocr Rev* 2002;23:570–578.

Meta analyses of RCTs

Η Αλενδρονάτη προσέφερε μεγαλύτερη προστασία κατά των μή σπονδυλικών καταγμάτων*

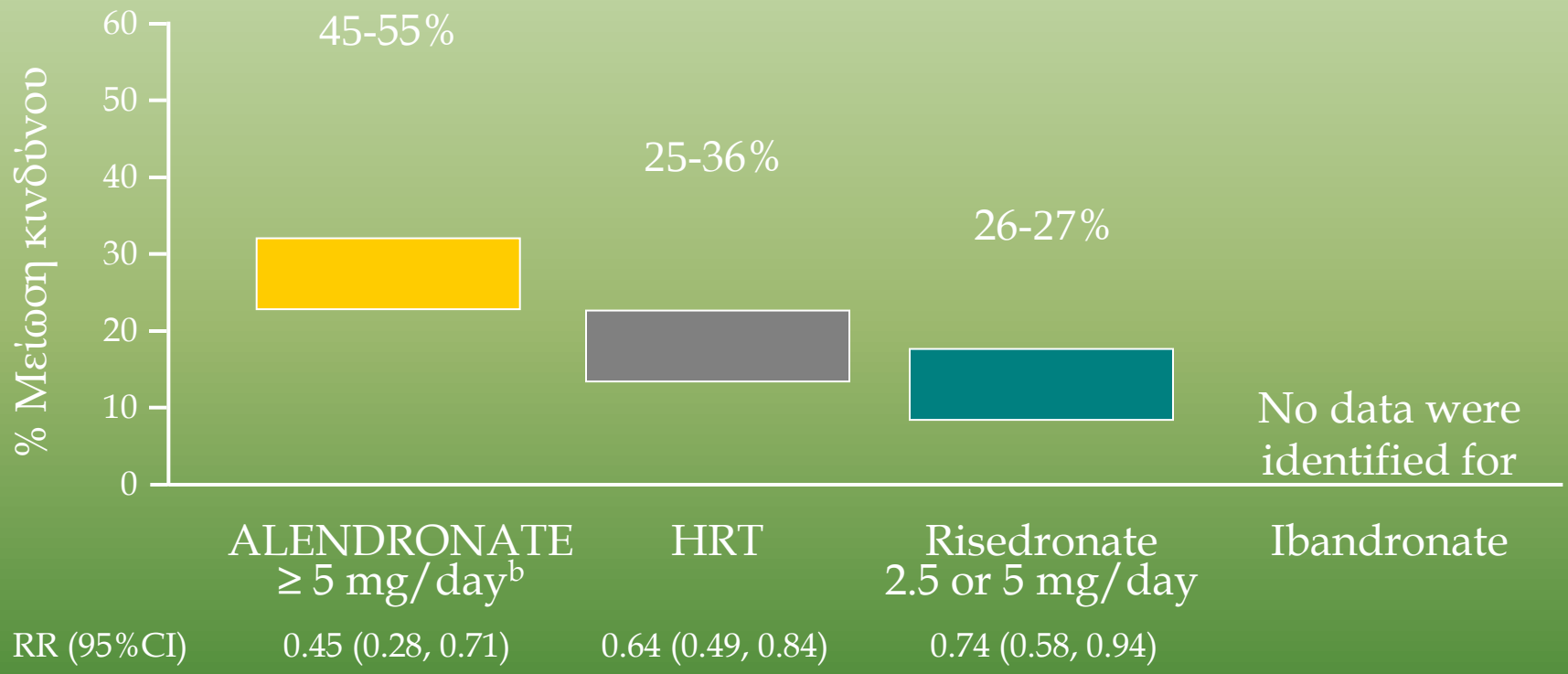


*Data not representative of head-to-head trials; **p<0.01 vs. baseline

Meta-analysis to evaluate magnitude of treatment effects on fractures and BMD based on randomized controlled trials of different osteoporosis therapies

Adapted from Cranney A et al *Endocr Rev* 2002;23:570–578.

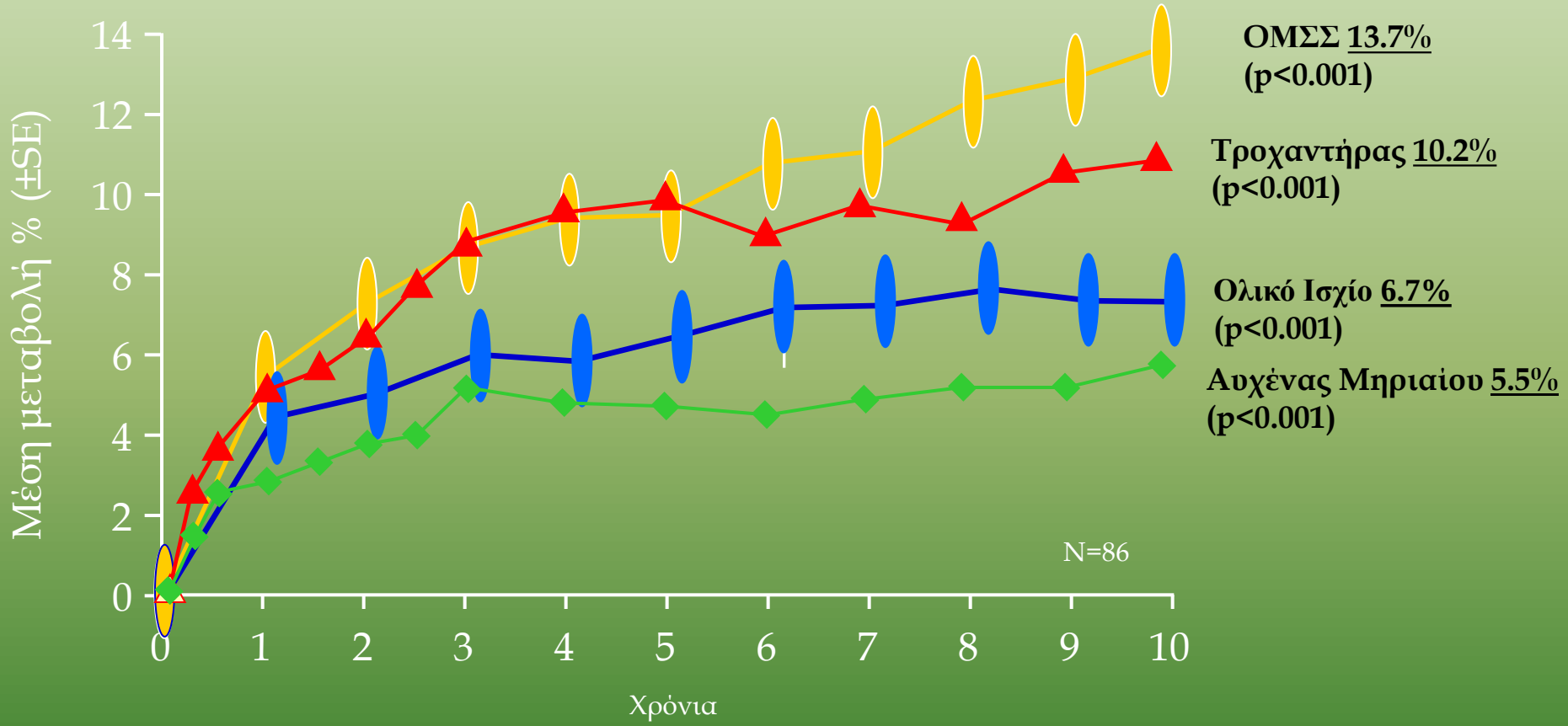
Meta analyses of RCTs
Η Αλενδρονάτη προσέφερε μεγαλύτερη προστασία κατά των καταγμάτων του ισχίου



Liberman UA, Hochberg MC, Geusens P et al. Hip and non-spine fracture risk reductions differ among antiresorptive agents: Evidence from randomised controlled trials. Int J Clin Pract 2006; 60: 1394–400.

Long-term extension analyses

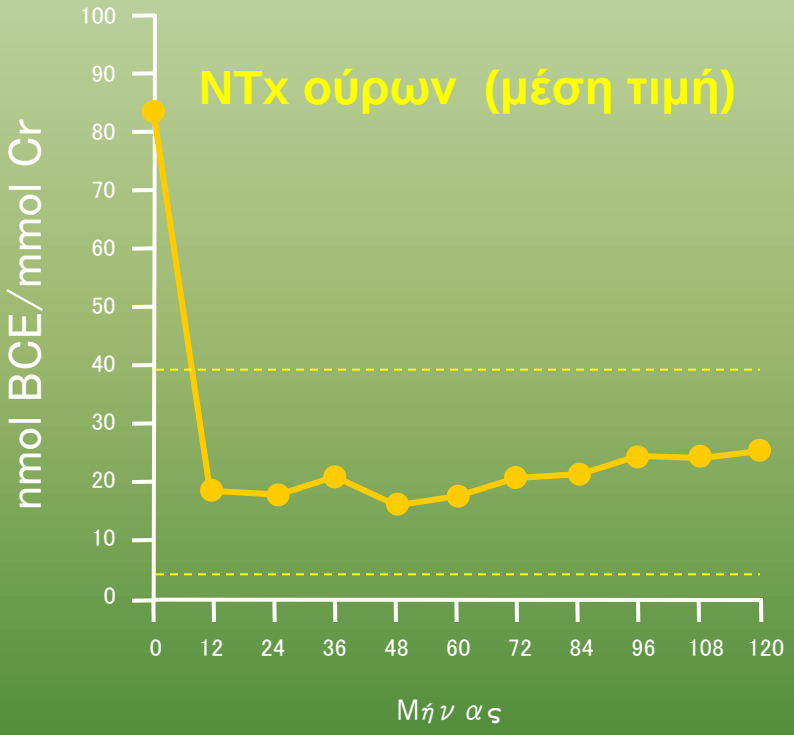
Ten years' experience with alendronate for osteoporosis in postmenopausal women

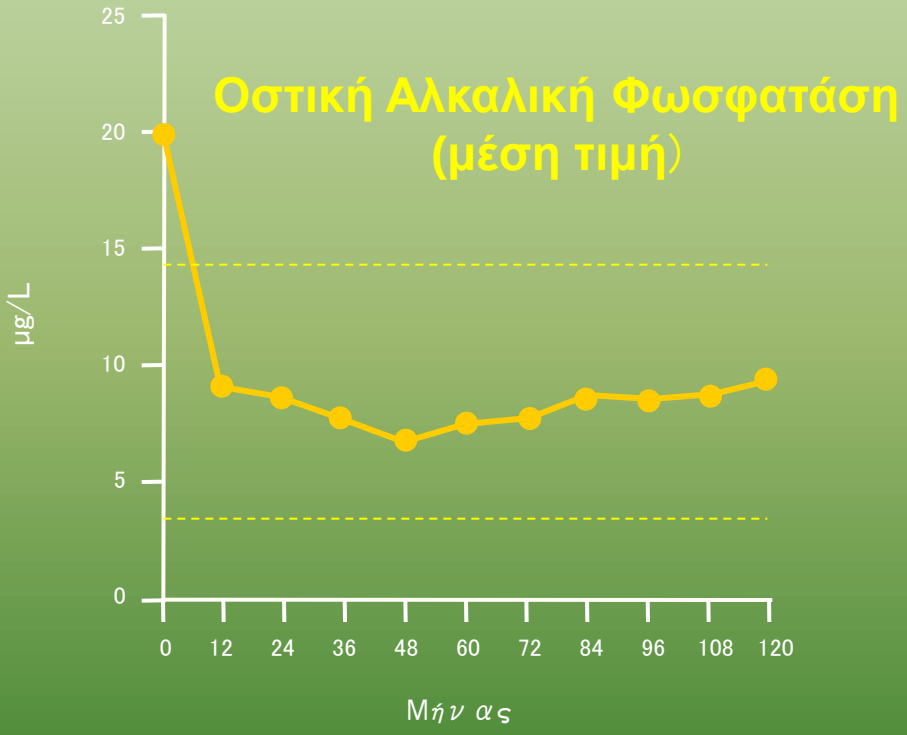


Η Αλενδρονάτη προσέφερε σταθερή βελτίωση της Οστικής Πυκνότητας για 10 χρόνια με καλή ανεκτικότητα The discontinuation of alendronate resulted in a gradual loss of effect, asmeasured by bone density and biochemical markers of bone remodeling

Adapted from Bone HG et al *N Engl J Med* 2004;350:1189–1199.

Long-term extension analyses
Ten years' experience with alendronate for osteoporosis in postmenopausal women





Η ΑΛΕΝΔΡΟΝΑΤΗ διατήρησε την Οστική Εναλλαγή σε φυσιολογικά προεμμηνοπαυσιακά επίπεδα κατά τη διάρκεια των 10 ετών

Bone HG et al *N Engl J Med* 2004;350(12):1189-1199;

Επίδραση στην ποιότητα του οστού

Από βιοψίες οστών η αλενδρονάτη

- **Βελτιώνει τη μικροαρχιτεκτονική στο σπογγώδες οστούν**
- **Αυξάνει ομοιογενώς την επιμετάλλωση στο σπογγώδες και φλοιώδες και μειώνει την πορωτικότητα**
- **Φυσιολογικό οστούν μετά και από δέκα έτη**

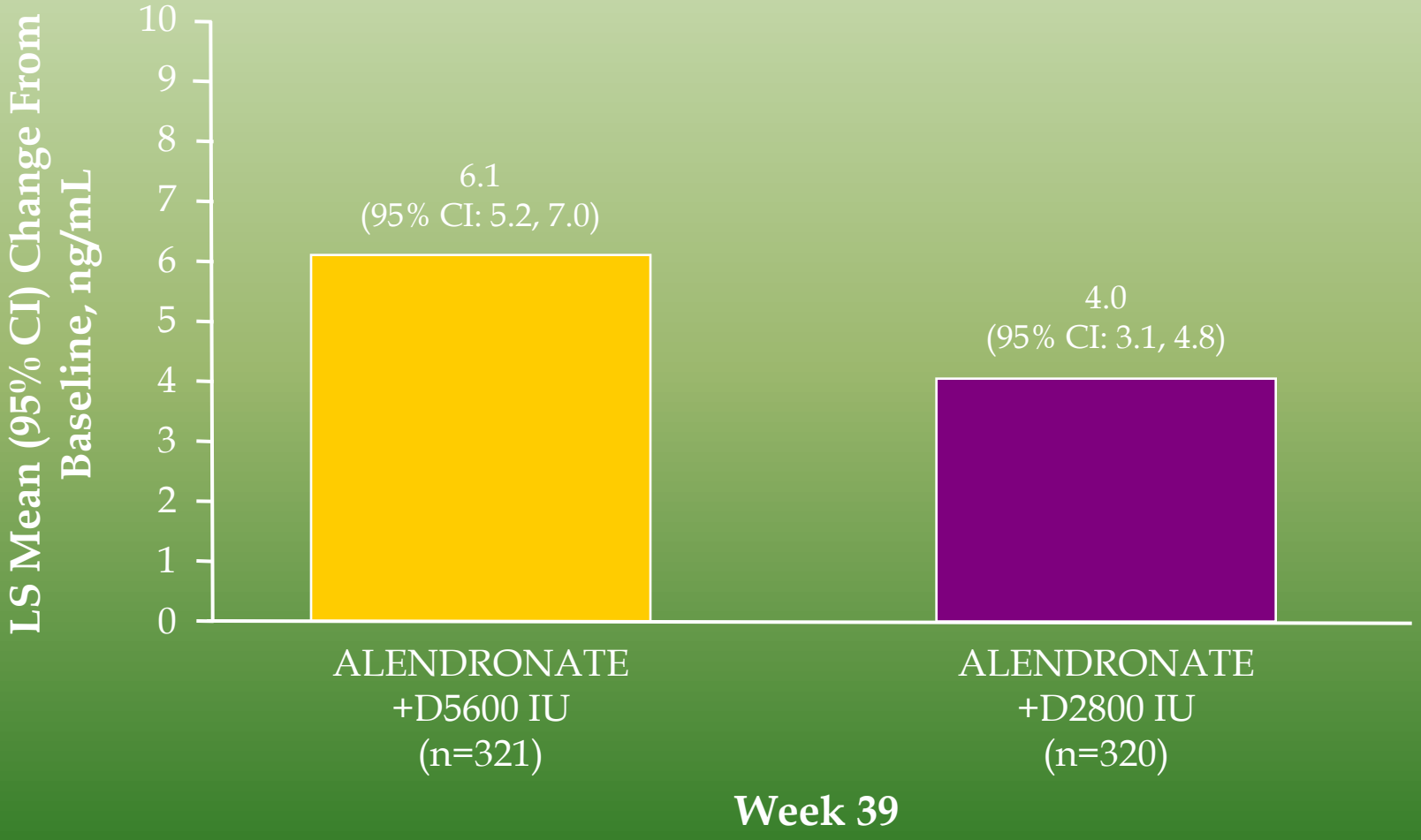
Από μελέτη ανάλυσης παραμέτρων αρχιτεκτονικής του ισχίου [Hip structure analysis (HAS)] η Αλενδρονάτη

- **Βελτιώνει τις γεωμετρικές παραμέτρους της δομής του ισχίου (cortical thickness, cross-sectional area, section modulus, and buckling ratio in the narrow neck, intertrochanteric region, and femoral shaft)**

- Boivin GY et al 2000. Bone.;27:687–94. Alendronate increases bone strength by increasing the mean degree of mineralization of bone tissue in osteoporotic women.
- Hochberg MC, J Clin Endocrinol Metab. 2002;87:1586–92.
- Recker R et al *Curr Med Res Opin* 2005;21:185–194
- JAMA, December 27, 2006—Vol 296, No. 24
- Greenspan et al 2005 J Bone Miner Res. 2005;20:1525–32. Effect of hormone replacement, alendronate, or combination therapy on hip structural geometry: a 3-year, double-blind, placebo-controlled clinical trial.

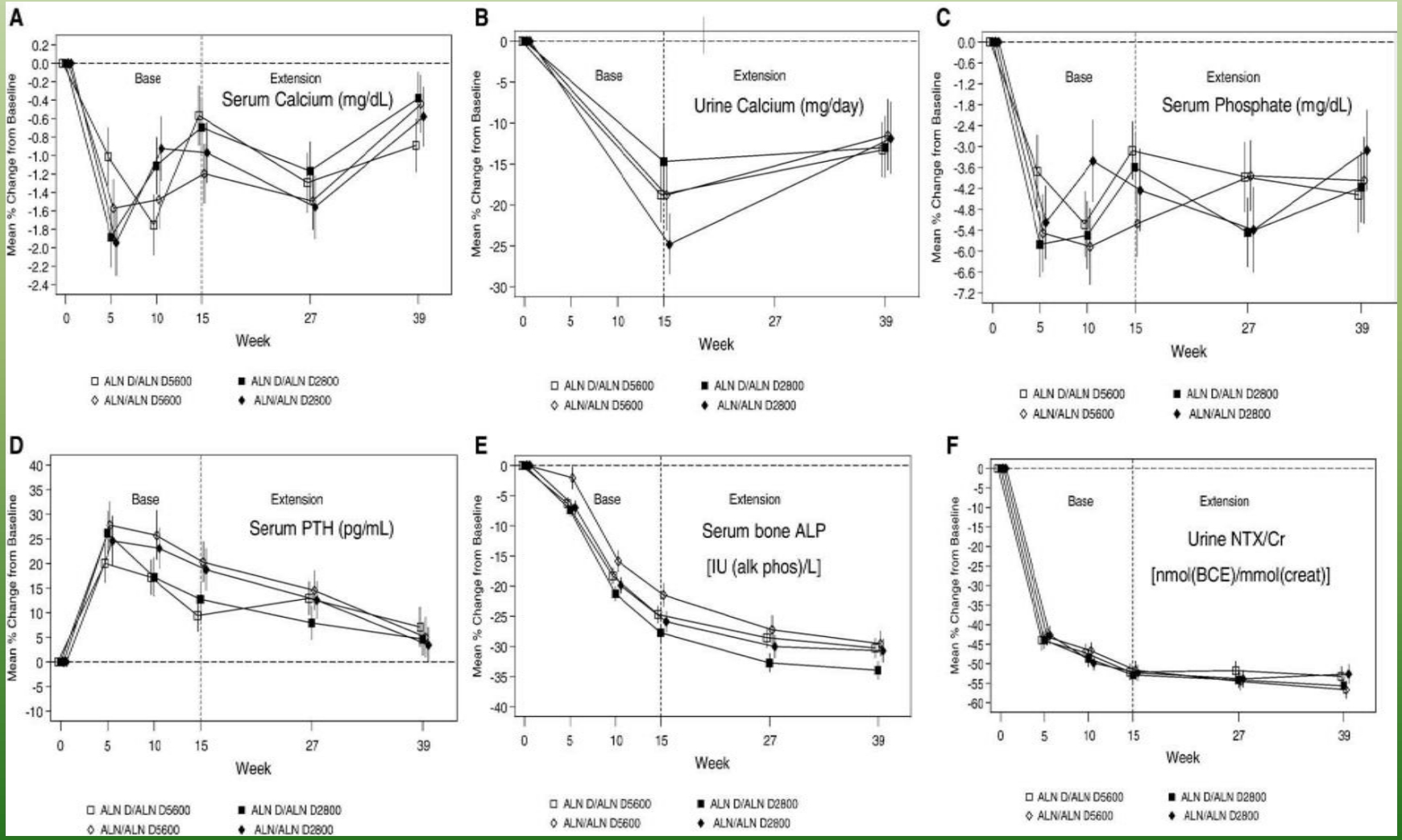
ALN+D5600

Βελτίωση των επιπέδων της βιταμίνης - D στις 39 εβδομάδες



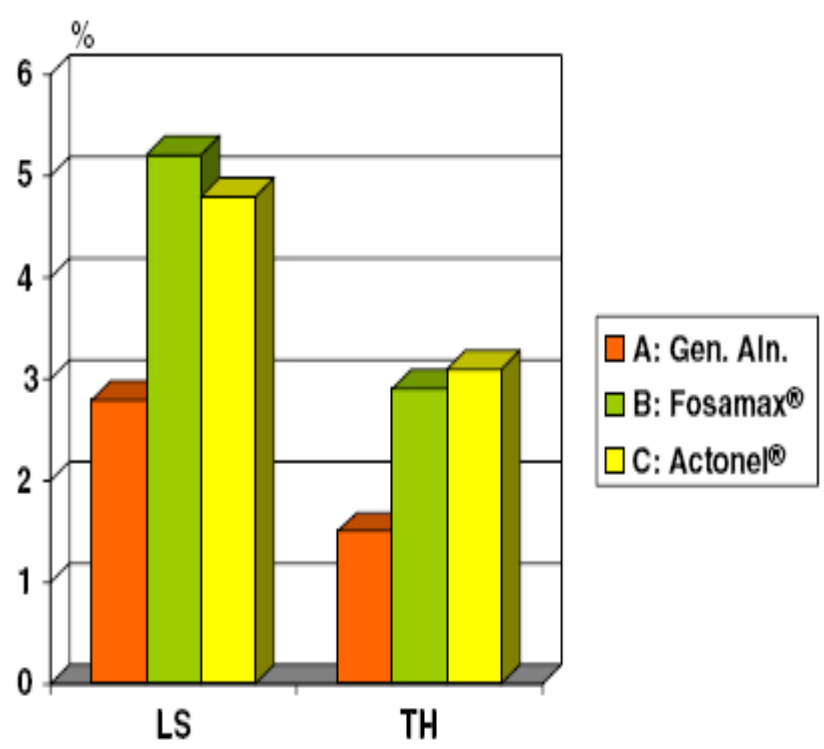
LS = least squares; CI = confidence interval

- **ALN+D5600**
  - **Βελτίωση όλων των βιοχημικών παραμέτρων**
  - **Το ποσοστό των ασθενών με υπερασβεστιουρία ήταν χαμηλό**



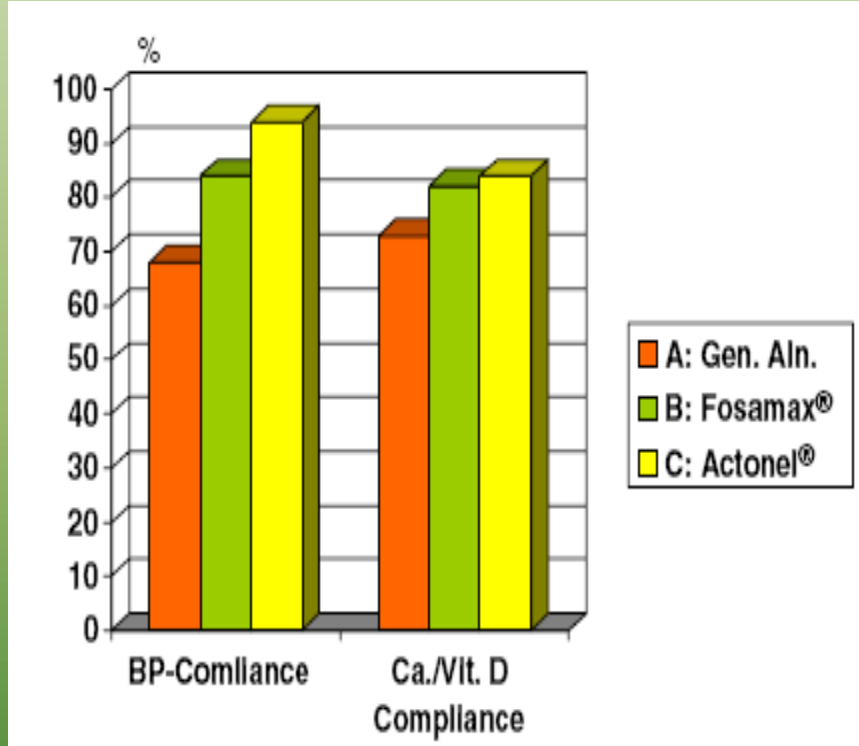
Bone 44 (2009) 639-647

Differences in persistence, safety and effcacy of generic and original branded once weekly bisphosphonates in patients with postmenopausal osteoporosis: 1-year results of a retrospective patient chart review analysis



LS: A vs B and C p< 0.05 TH: A vs B and C p< 0.01

Fig. 2 Mean percent changes in lumbar spine (LS) and total hip (TH) after 12 months



BP: A vs B p< 0.03, A vs C p<0.01 Ca/D: A vs B and C p< 0.05

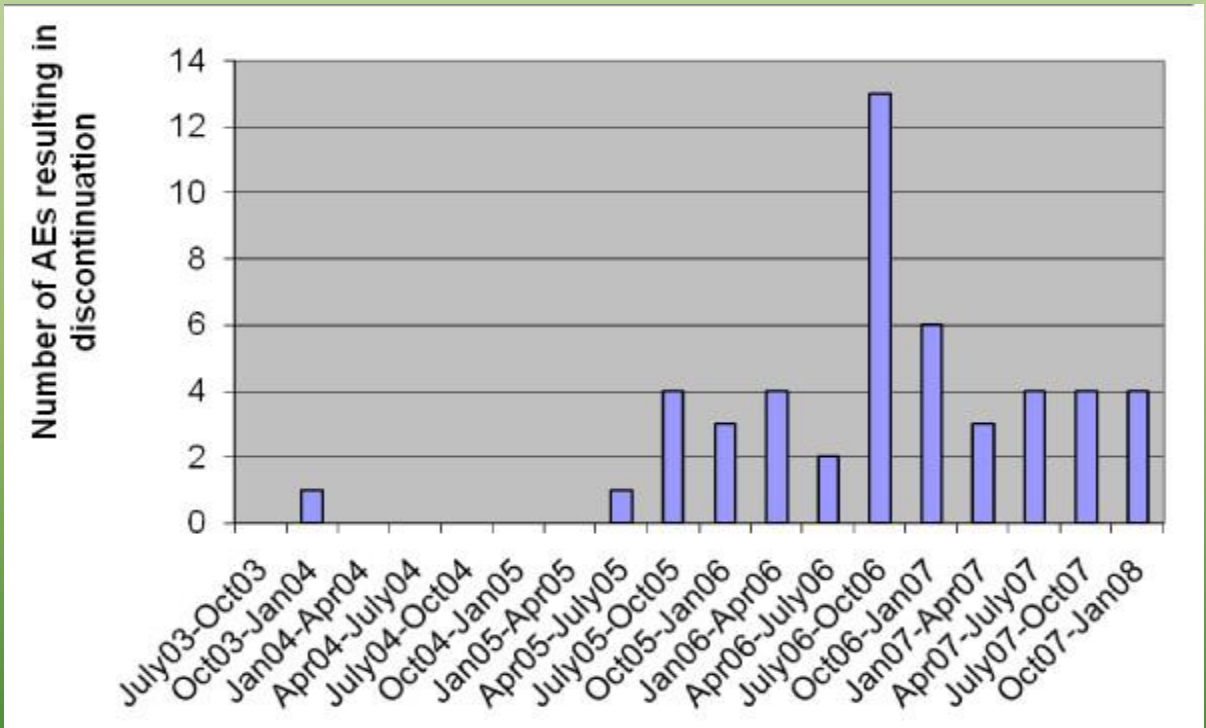
Fig. 1 Persistence with bisphosphonate therapy and calcium/vitamin D supplementation (% patients at month 12)

Rheumatol Int 2009 DOI 10.1007/s00296-009-0940-5 123

BMC Musculoskelet Disord 2010 Apr 14;11(1):68.

Adverse events, bone mineral density and discontinuation associated with generic alendronate among postmenopausal women previously tolerant of brand alendronate: a retrospective cohort study.

Grima DT, Papaioannou A, Airia P, Ioannidis G, Adachi JD



A rise in gastrointestinal (GI) adverse events (AEs) and a decline in bone mineral density (BMD) was observed in patients previously tolerant to brand alendronate shortly after generic versions were introduced in July 2005 to the Canadian market.

Long-term extension analyses
Ten years' experience with alendronate for osteoporosis in postmenopausal women
ΑΣΦΑΛΕΙΑ

Table 3. Adverse Events Reported during Years 8 through 10.*

Adverse Event	Discontinuation Group (N=83)	5-mg Alendronate Group (N=78)	10-mg Alendronate Group (N=86)
		number of women (percent)	
Any clinical event			
≥1	77 (92.8)	74 (94.9)	77 (89.5)
Serious	18 (21.7)	25 (32.1)	18 (20.9)
Cause of discontinuation	7 (8.4)	5 (6.4)	4 (4.7)
Any upper gastrointestinal event			
≥1	20 (24.1)	11 (14.1)	24 (27.9)
Serious	1 (1.2)	1 (1.3)	0
Cause of discontinuation	2 (2.4)	1 (1.3)	2 (2.3)
Esophageal event			
≥1	6 (7.2)	1 (1.3)	2 (2.3)
Dysphagia	2 (2.4)	0	0
Erosive esophagitis	2 (2.4)	1 (1.3)	0
Esophagalgia	0	0	1 (1.2)
Esophagitis	1 (1.2)	0	1 (1.2)
Odynophagia	1 (1.2)	0	0
Perforations, ulcers, or bleeding			
Duodenal ulcer	0	1 (1.3)	0

* The discontinuation group was treated with 20 mg of alendronate per day for two years and 5 mg daily for three years, followed by placebo for five years. The 10-mg group was treated with 10 mg daily for 10 years, and the 5-mg group was treated with 5 mg daily for 10 years.

Bone HG et al *N Engl J Med* 2004;350(12):1189-1199;

Αποτελεσματικότητα /ασφάλεια Αλενδρονάτης

- Αντικαταγματική δράση και αντικαταγματική δράση στο ισχίο επιβεβαιωμένη από κλινικές μελέτες, μεταναλύσεις και συγκριτικές μελέτες

- Ευνοική επίδραση στην ποιότητα του σπογγώδους οστού από βιοψίες (έως 10 έτη) αλλά και φλοιώδους από βιοψίες και μελέτη ανάλυσης παραμέτρων αρχιτεκτονικής του ισχίου [Hip structure analysis (HAS)]

- Μακροχρόνια (έως 10 έτη) αποτελεσματικότητα και ασφάλεια