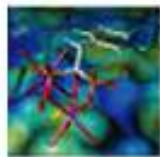
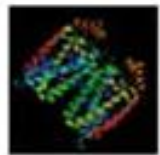


Bisphosphonates: Key Pharmacological Characteristics

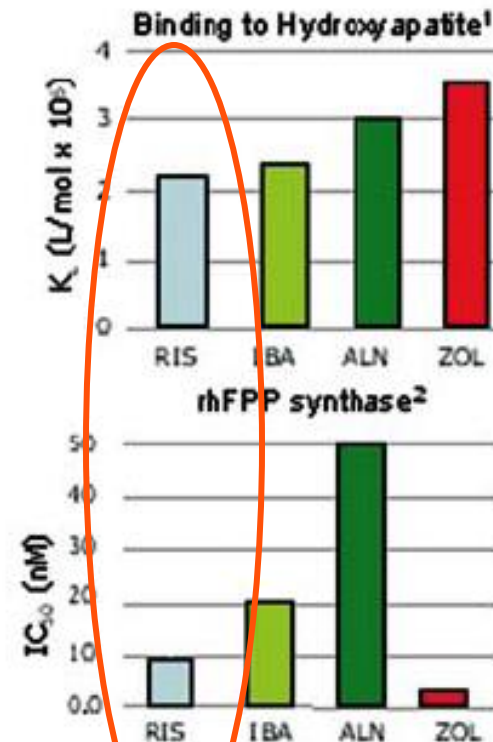


- Binding affinity for bone in vitro
 - Determines *in vivo* attachment to bone, potency and duration of effect



- FPP synthase inhibition in vitro
 - Determines antiresorptive potential

- Each BP has a distinct profile



1. Nancollas GH, et al. *Bone*. 2006;38: 617-627.

2. Updated from Dunford JE, et al. *J Pharmacol Exp Ther*. 2001;296:235-242.

FIGURE 6. Mineral binding and FPPs by alendronate, risedronate, ibandronate, and zoledronate, the four major BPs used in osteoporosis. Each BP has a distinct profile in terms of these properties.

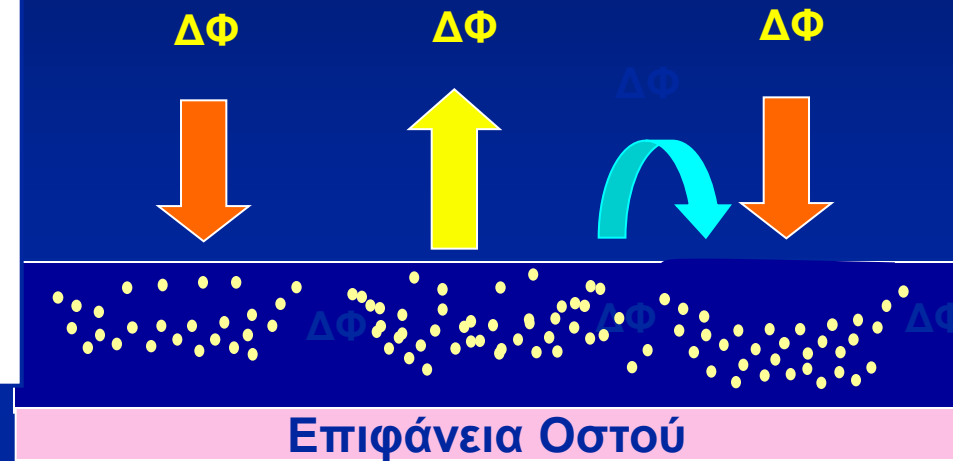
Προσρόφηση και αποδέσμευση των διφωσφονικών από τις επιφάνειες των οστών

•Χαμηλής συγγένειας $\Delta\Phi$

(π.χ.Ριζεδρονάτη)

- Ασθενέστερη προσρόφηση
- Υψηλότερη αποβολή
- Χαμηλού βαθμού επαναδέσμευση
- Μεγάλη διασπορά στο οστό
- Γρηγορότερη έναρξη δράσης

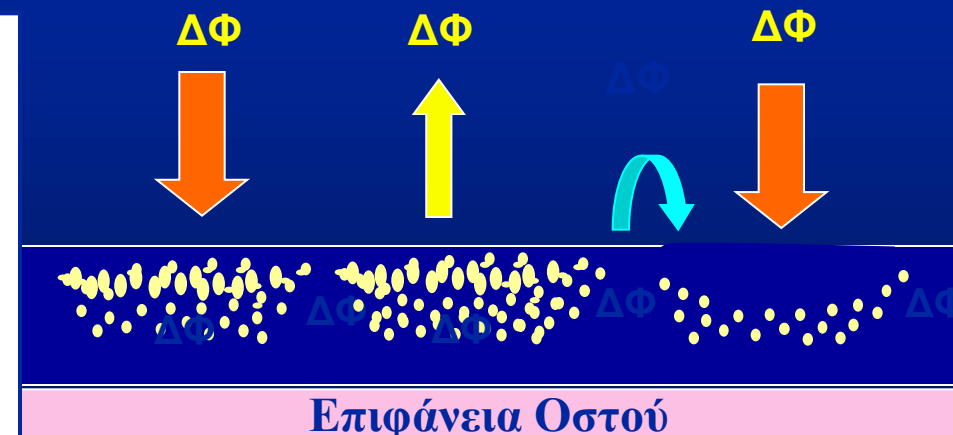
Η διαφορετική διασπορά των $\Delta\Phi$ στο οστό μπορεί να παίζει σημαντικό ρόλο στην αντικαταγματική τους δράση



•Υψηλής συγγένειας $\Delta\Phi$

(π.χ.Αλενδρονάτη)

- Ακόρεστη προσρόφηση
- Χαμηλότερη αποβολή
- Υψηλού βαθμού επαναδέσμευση
- Χαμηλή διασπορά στο οστό
- Βραδεία έναρξη δράσης



Clinical Investigations

Risedronate Rapidly Reduces the Risk for Nonvertebral Fractures in Women with Postmenopausal Osteoporosis

J. T. Harrington,¹ L.-G. Ste-Marie,² M. L. Brandi,³ R. Civitelli,⁴ P. Fardellone,⁵ A. Grauer,⁶ I. Barton,⁷ S. Boonen⁸

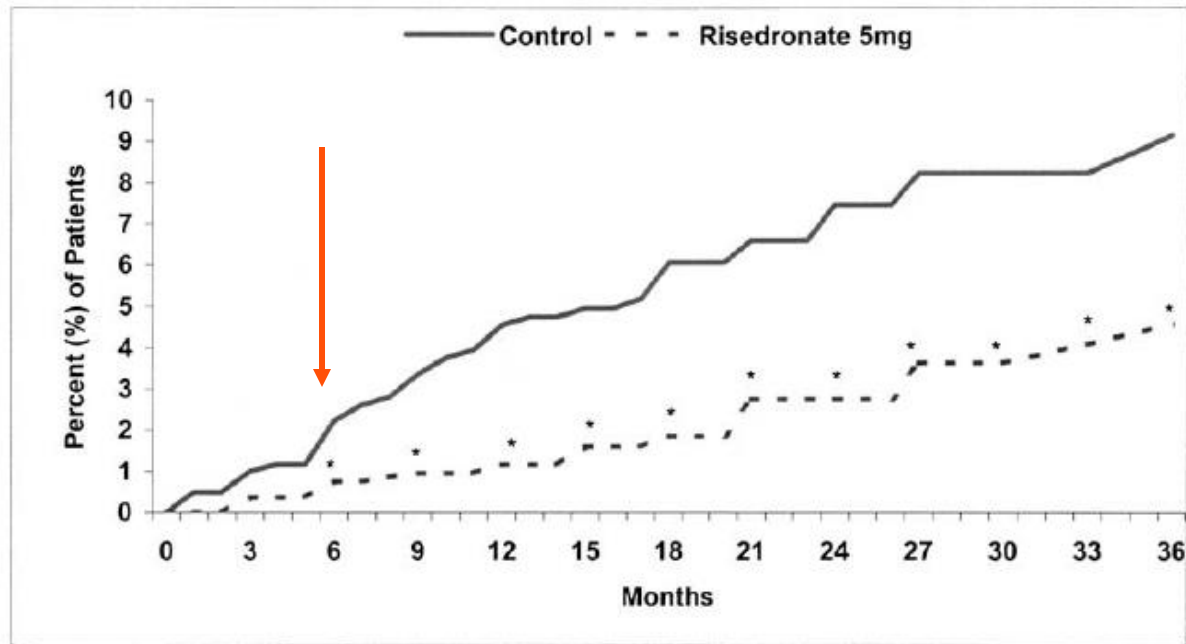


Fig. 2 Incidence of new osteoporosis-related nonvertebral fractures (Kaplan Meier method) in patients treated with placebo or risedronate 5 mg for up to 3 years (*significantly less than placebo group; $P \leq 0.01$). The 0–3 year fracture

incidence was 41/608 (9.1%) in the placebo group compared with 16/564 (4.6%) in the risedronate 5 mg group. The treatment effect of risedronate 5 mg was 59% (95% confidence interval, 27%, 77%; $P = 0.002$).

Η αύξηση της οστικής πυκνότητας δεν αντικατοπτρίζει ανάλογη μείωση του σχετικού κινδύνου κατάγματος

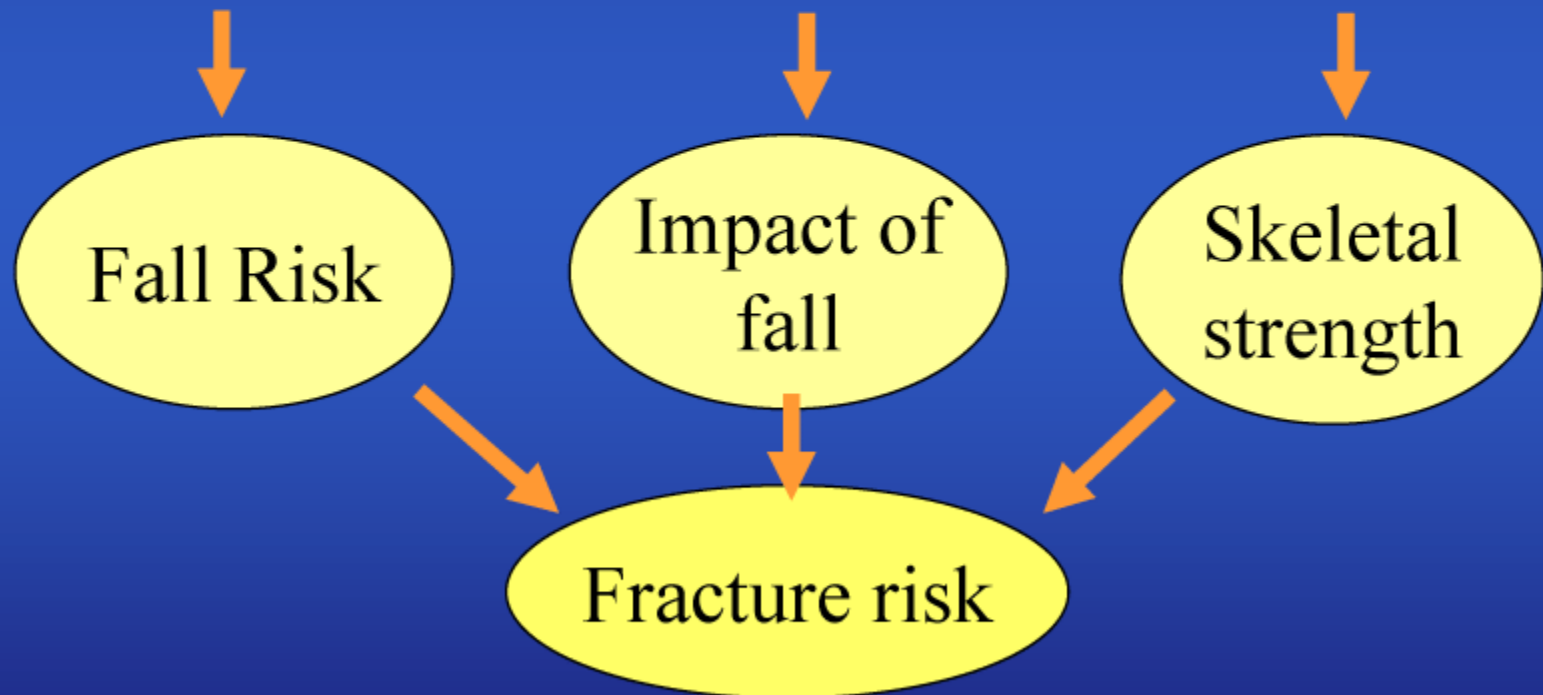
Μελέτες	Δ Οστ. Μάζας (%)	% μείωση του κινδύνου κατάγματος
PROOF (καλσιτονίνη) (Chesnut et al., Am.J.Med.2000)	0.5	36
MORE (ραλοξιφαίνη) (Ettinger et al., JAMA 1999)	2.6	30
FIT1 (αλενδρονάτη) (Black et al., Lancet 1996)	6.2	47
FIT2 (αλενδρονάτη) (Cummings et al., JAMA 1998)	6.8	44
VERT-NA (Actonel) (Harris et al., JAMA 1999)	5.2	41
VERT-MN (Actonel) (Reginster et al., Osteoporosis Int 2000)	6.3	49

Bone density is not the only factor of fracture risk ...

Neuromuscular function
Environmental risks
Age

Type of fall
Energy reduction
External protection

Bone mass
Bone structure
Bone quality

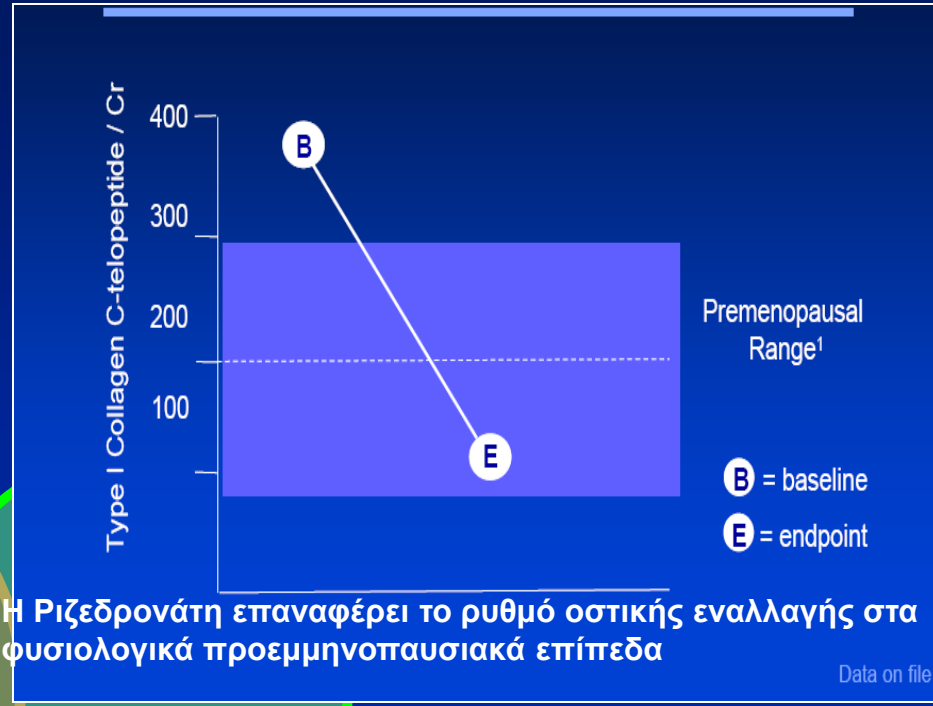


Η δύναμη του οστού εξαρτάται από την ποιότητα του Η κλινική αποδείξη της ρισεδρονάτης

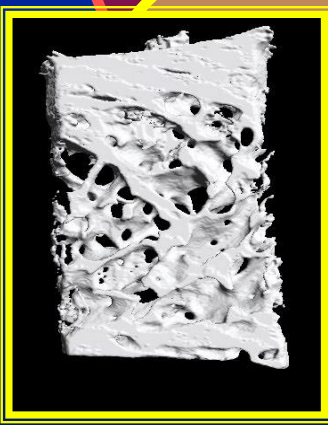
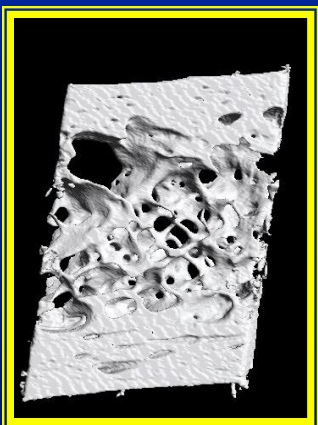
Table 1 Randomised controlled trials of bisphosphonates

Study	Treatment regimen (n)	Duration (years)	Treatment completers, n (%)	Change in BMD, % (p-value)
Alendronate (ALN)				
Liberman et al. (13)	ALN 5-20 mg daily (597); placebo (397)	3	ALN 500 (84); placebo 365 (84)	ALN 10 mg vs. placebo: LS 8.8; FN 5.9; hip 2.5 (all < 0.001)
Black et al. (29)	ALN 5-10 mg daily (1022); placebo (1005)	3	ALN 981 (96); placebo 965 (96)	ALN vs. placebo: LS 6.2; FN 4.1; hip 4.7 (all < 0.001)
Cummings et al. (22)	ALN 5-10 mg daily (2214); placebo (2218)	4	ALN 2057 (93); placebo 2077 (94)	ALN vs. placebo: LS 6.6; FN 4.6; hip 5.0 (all < 0.001)
Pols et al. (12)	ALN 10 mg daily (950); placebo (958)	1	ALN 832 (88); placebo 865 (90)	ALN vs. placebo: LS 4.9; FN 2.5; hip 3.0 (all < 0.001)
Ibandronate (IBN)				
Chestnut III et al. (35)	IBN 2.5 mg daily (982); IBN 20 mg intermittent (982); placebo (982)	3	IBN daily 648 (66); IBN intermittent 662 (67); placebo 628 (64)	IBN daily/intermittent vs. placebo: LS 5.2/4.4; FN 3.4/3.0; hip 4.1/3.6 (all < 0.0001)
Risedronate (RIS)				
Harris et al. (30)	RIS 5 mg daily (813); placebo (815)	3	RIS 489 (60); placebo 450 (55)	RIS 5 mg vs. placebo: LS 4.3; FN 2.8; hip 4.0 (all < 0.05)
Reginster et al. (31)	RIS 5 mg daily (407); placebo (407)	3	RIS 251 (62); placebo 221 (54)	RIS 5 mg vs. placebo: LS 5.9; FN 2.1; hip 6.4 (all < 0.001)
McClung et al. (32)	RIS 2.5 mg daily (3093); RIS 5 mg daily (3104); placebo (3134)	3	RIS both doses 3093 (50); placebo 1584 (50)	RIS 2.5/5 mg vs. placebo: FN 2.1/3.4; hip 3.8/4.8 (NR)
Zoledronate (ZOL)				
Black et al. (33)	ZOL 5 mg yearly (3889); placebo (3876)	3	ZOL 5 mg 3248 (84); placebo 3269 (92)	ZOL vs. placebo: LS 6.7; FN 5.1; hip 6.0 (all < 0.001)
Lyles et al. (34)	ZOL 5 mg yearly (1065); placebo (1062)	3	ZOL 770 (72); placebo 746 (70)	FN at years 1, 2 and 3 with ZOL vs. placebo, respectively: 0.8 vs. -1.7, 2.2 vs. -2.1 and 3.6 vs. -0.7 Hip at years 1, 2 and 3 with ZOL vs. placebo, respectively: 2.6 vs. -1.0, 4.7 vs. -0.7 and 5.5 vs. -0.9 (all < 0.001)

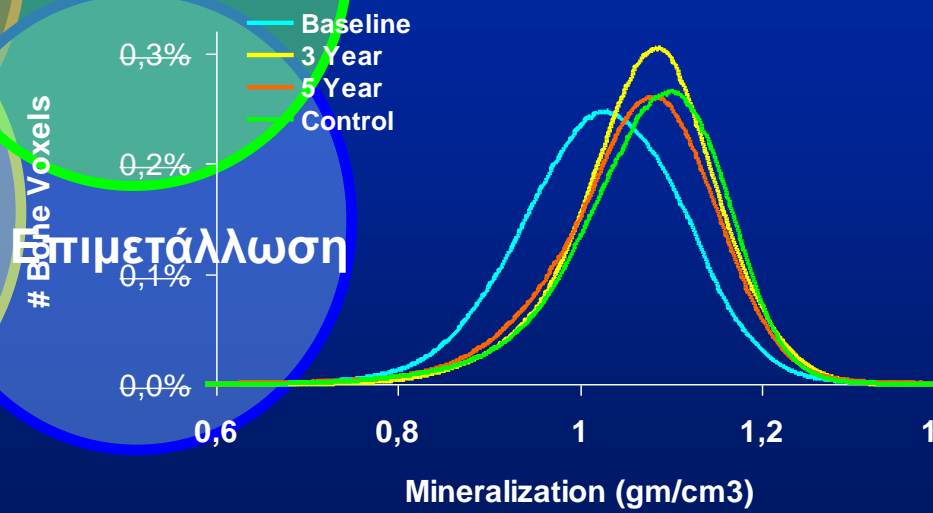
6,4 -2,3%



BMD, bone mineral density; FN, femoral neck; LS, lumbar spine; NR, not reported. *Int J Clin Pract*, December 2009, 63, 12, 1792-1804



Οστική



Βιοψίες λαγόνιου οστού πρόσφατα μετεμμηνοπαυσιακών γυναικών μετά ένα έτος αγωγής με ρισεδρονάτη

Η Επιμετάλλωση που προκαλεί η Ριζεδρονάτη είναι ανάλογη των προ-εμμηνόπαυσιακών επιπέδων