Η αντικαταγματική δράση της Ιβανδρονάτης

Study type	Details	Main finding
Prospective clinical trial: **BONE**[1]	Randomised, double-blind, placebo-controlled, parallel group trial over 3 years	Ibandronate had 62% RRR in vertebral fractures vs. placebo*
Meta-analyses of clinical trials[2,3]	Randomised trial data analysed by annual cumulative exposure	Higher doses of ibandronate showed significant reductions in non-vertebral fractures in two meta-analyses of clinical trials
Observational study: **VIBE**[4]	Retrospective, observational analysis of two US databases including 64,182 women adherent to medication**	With monthly ibandronate 150mg, a statistically significantly lower rate of vertebral fractures and comparable rates of non-vertebral & hip fracture, vs. weekly bisphosphonates were observed Fracture rates after the 12-month observational period were <2%

***The BONE study was not powered for non-vertebral fractures, and did not demonstrate a reduction of non-vertebral fractures in the overall population. **Included some patients outside of European license**

1. Chesnut CH, *et al.* J Bone Miner Res 2004;19:1241–1249
2. Cranney A, *et al.* Osteoporos Int 2009;20:291–297
3. Harris ST, *et al.* Curr Med Res Opin 2008;24:237–245
4. Harris ST, *et al.* Bone 2009;44:758–765

Literature references for efficacy data on vertebral, hip and nonvertebral fractures

	Vertebral	Hip	Nonvertebral
Bonviva	a	b	b,c,d,e

a. BONE trial primary endpoint new vert fx 3 yr IBN 2.5mg daily. Chestnut C, *JBMR* 2004: 19:1241

b. VIBE observational study, nonvert & hip fx 1 yr same for IBN 150mg monthly as weekly BPs. Harris ST, *BONE* 2009; 44:758

c. BONE trial post-hoc high-risk subgroup (baseline hip T-score<-3.0) nonvert fx 3 yr IBN 2.5mg daily. Chestnut C, *JBMR* 2004; 19:1241

d. Meta-analysis trials nonvert fx, IBN high doses vs placebo. Harris ST, *CMRO* 2009; 20:291

e. Meta-analysis trials nonvert fx, IBN high doses vs 2.5mg daily. Cranney A, *Osteop Int* 2009; 20:291

JOURNAL OF BONE AND MINERAL RESEARCH
Volume 19, Number 8, 2004
Published online on March 29, 2004; doi: 10.1359/JBMR.040325

Effects of Oral Ibandronate Administered Daily or Intermittently on Fracture Risk in Postmenopausal Osteoporosis

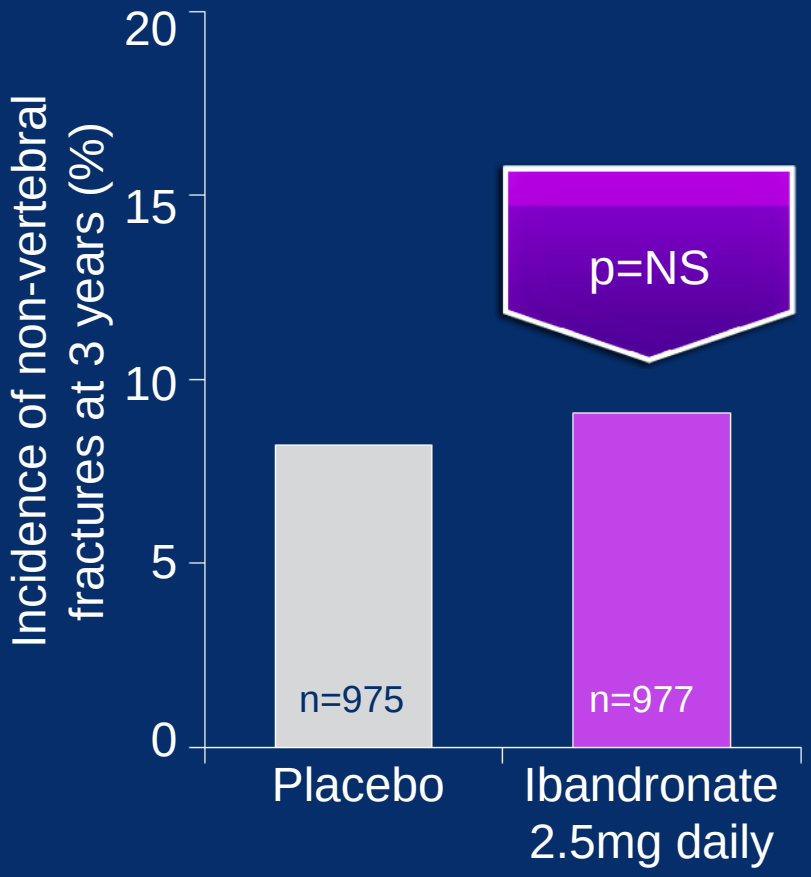
Charles H Chesnut III,[1] Arne Skag,[2] Claus Christiansen,[3] Robert Recker,[4] Jacob A Stakkestad,[5] Arne Hoiseth,[6] Dieter Felsenberg,[7] Hermann Huss,[8] Jennifer Gilbride,[9] Ralph C Schimmer,[10] and Pierre D Delmas[11] for the Oral Ibandronate Osteoporosis Vertebral Fracture Trial in North America and Europe (BONE)*

TABLE 1. SUMMARY OF BASELINE CHARACTERISTICS

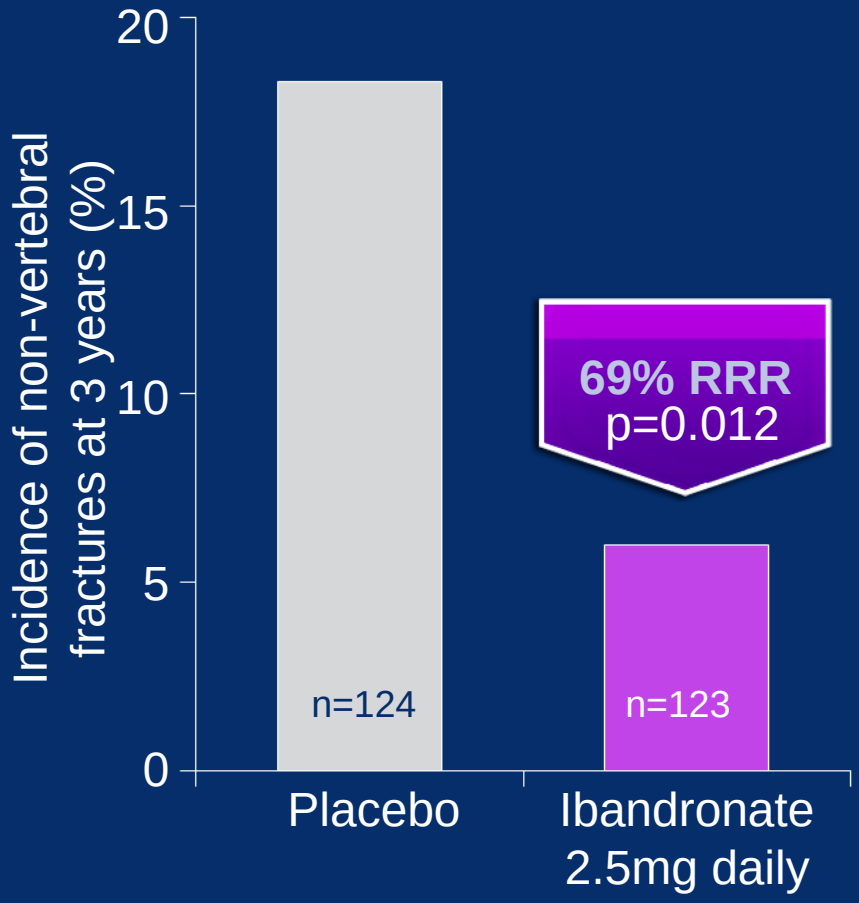
	Placebo (n = 975)	*Ibandronate (2.5 mg daily;* n = 977)	*Ibandronate (20 mg intermittent;* n = 977)
Age (years*)	69 (6)	69 (6)	69 (6)
Height (cm)	160 (6)	160 (6)	160 (6)
Weight (kg)	67 (11)	67 (11)	67 (11)
Time since menopause (years)	20.8 (7.8)	20.9 (8.0)	20.8 (8.0)
Patients with one fracture	906 (93%)	920 (94%)	917 (94%)
Patients with two fractures	421 (43%)	433 (44%)	413 (42%)
Lumbar spine BMD (T score)	−2.8 (0.9)	−2.8 (0.9)	−2.7 (0.9)
Femoral neck BMD (T score)	−2.0 (0.9)	−2.0 (0.9)	−2.0 (0.9)
Total hip BMD (T score)*	−1.7 (0.9)	−1.7 (0.8)	−1.7 (0.9)
Performed in selected centers only	(*n* = 224)	(*n* = 223)	(*n* = 229)
CTX/creatinine (g/mol)	0.25 (0.12)	0.26 (0.14)	0.26 (0.12)
NTX/creatinine (nmol/mmol)	61.23 (33.93)	64.63 (40.35)	63.59 (32.38)
Serum osteocalcin (ng/ml)	19.68 (7.71)	19.08 (9.25)	20.36 (9.38)
Serum BSAP (U/liter)	40.93 (18.24)	44.42 (20.70)	44.54 (19.03)

Η Ιβανδρονάτη μειώνει τα μη-σπονδυλικά κατάγματα σε ασθενείς υψηλού κινδύνου

Συνολικός πληθυσμός

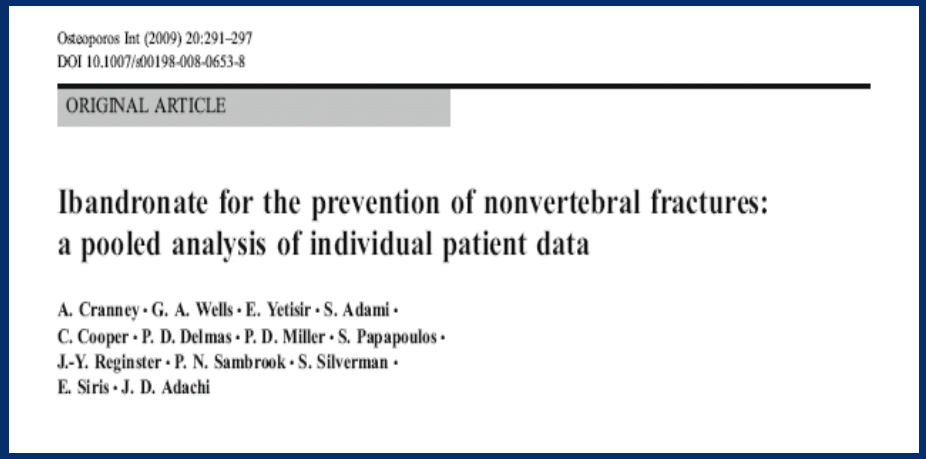


BMD στον αυχένα μηριαίου
T-score <–3.0 στην έναρξη*



*Post-hoc subgroup analysis
BMD = bone mineral density
Chesnut CH, *et al.* J Bone Miner Res 2004;19:1241–1249

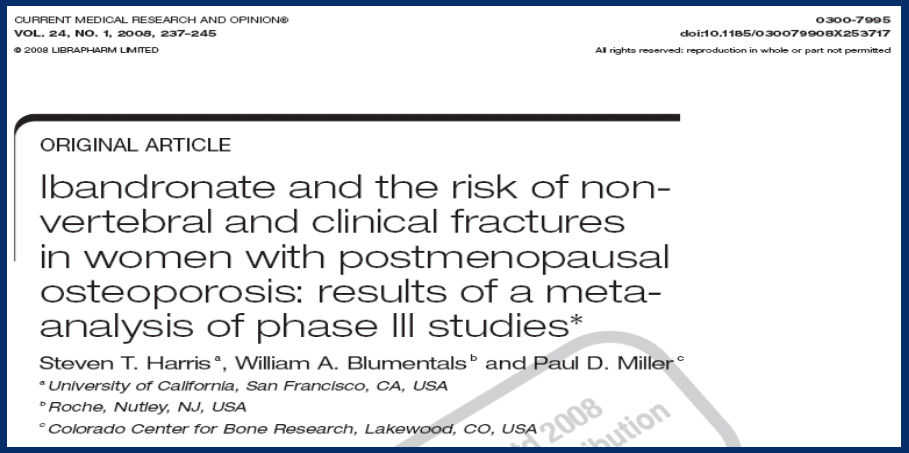
Δύο ξεχωριστές μετα-αναλύσεις επιβεβαιώνουν την προστασία από τα μη σπονδυλικά κατάγματα με την ιβανδρονάτη


Osteoporos Int (2009) 20:291–297
DOI 10.1007/s00198-008-0653-8

ORIGINAL ARTICLE

Ibandronate for the prevention of nonvertebral fractures: a pooled analysis of individual patient data

A. Cranney · G. A. Wells · E. Yetisir · S. Adami · C. Cooper · P. D. Delmas · P. D. Miller · S. Papapoulos · J.-Y. Reginster · P. N. Sambrook · S. Silverman · E. Siris · J. D. Adachi


CURRENT MEDICAL RESEARCH AND OPINION®
VOL. 24, NO. 1, 2008, 237–245
0300-7995
doi:10.1185/03007990802537177
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ORIGINAL ARTICLE

Ibandronate and the risk of non-vertebral and clinical fractures in women with postmenopausal osteoporosis: results of a meta-analysis of phase III studies*

Steven T. Harris[a], William A. Blumentals[b] and Paul D. Miller[c]
[a] University of California, San Francisco, CA, USA
[b] Roche, Nutley, NJ, USA
[c] Colorado Center for Bone Research, Lakewood, CO, USA

- **Cranney *et al*. 2009**
  - **Ανασκόπηση δεδομένων από οκτώ τυχαιοποιημένες μελέτες**
  - **Ξεχωριστά δεδομένα ασθενών από τον πληθυσμό ITT**
  - **Σύγκριση υψηλότερων vs. χαμηλότερων δόσεων για τα καίρια μη σπονδυλικά κατάγματα**

- **Harris *et al*. 2008**
  - **Δεδομένα από τις μελέτες: BONE, IV Pivotal Fracture Trial, MOBILE και DIVA**
  - **Ξεχωριστά δεδομένα ασθενών από τον πληθυσμό ITT**
  - **Σύγκριση υψηλότερων δόσεων vs. placebo για τα μη σπονδυλικά κατάγματα**

Cranney A, *et al*. Osteoporos Int 2009;20:291–297

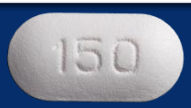
Harris ST, *et al*. Curr Med Res Opin 2008;24:237–245

Μετα-αναλύσεις: Σύγκριση υψηλότερων vs. χαμηλότερων ομάδων δόσεων

Higher doses

(ACE* ≥ 10.8mg)

Monthly oral† 150mg



Quarterly IV 3mg

Bimonthly IV 2mg NOT LICENSED

Cranney

Lower dose

(ACE* 5.5mg) Daily oral 2.5mg

Harris

Placebo

Placebo

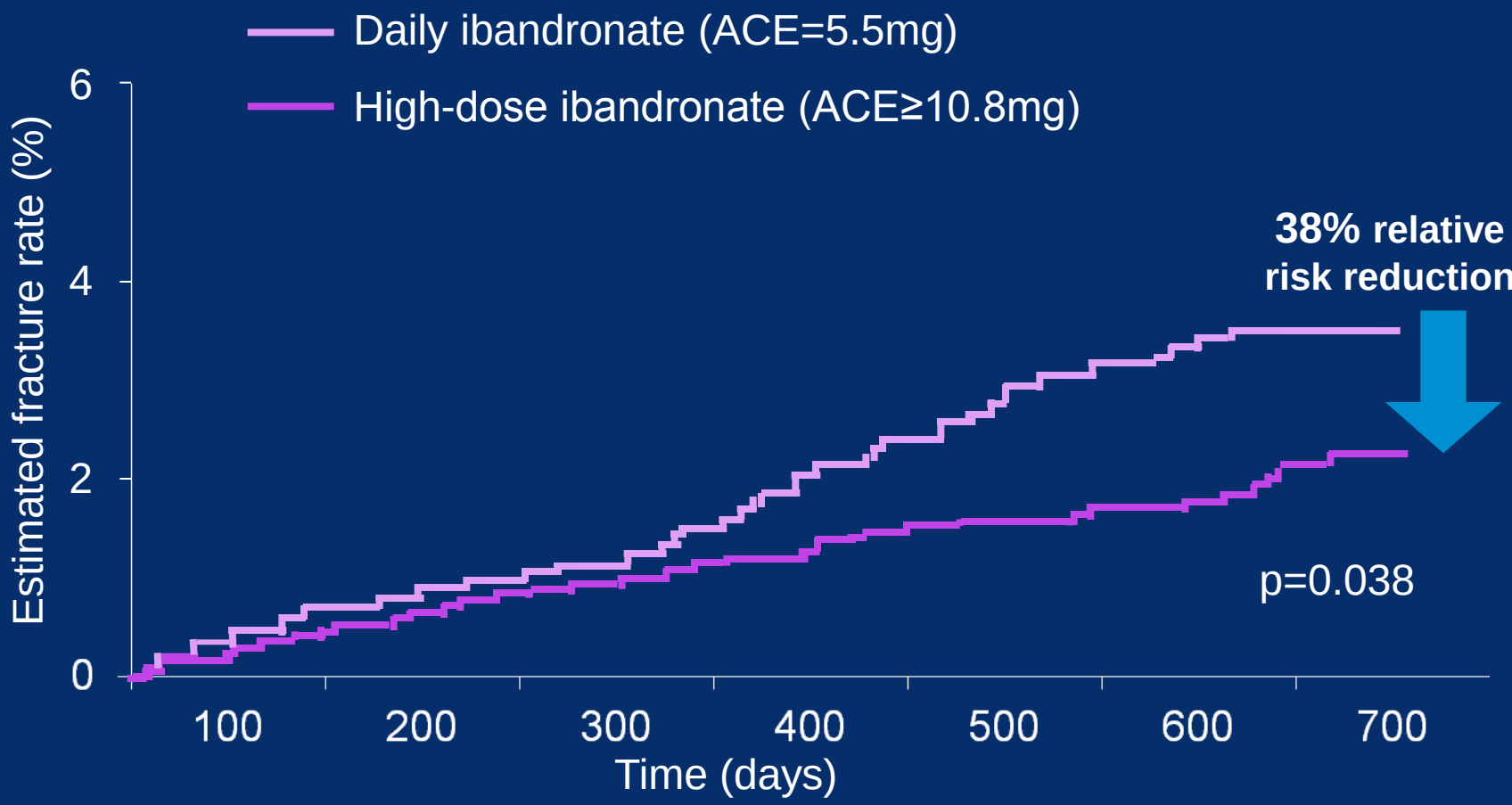
*ACE = annual cumulative exposure = dose x doses /year x absorption

(e.g. 2.5 x 365 x 0.6% = 5.5mg ACE)

†Absorption for oral ibandronate = 0.6%

Cranney et al.

Το χρονικό διάστημα μέχρι την εμφάνιση μη σπονδυλικού κατάγματος παρατείνεται με την ιβανδρονάτη
ACE ≥10.8mg vs. low dose

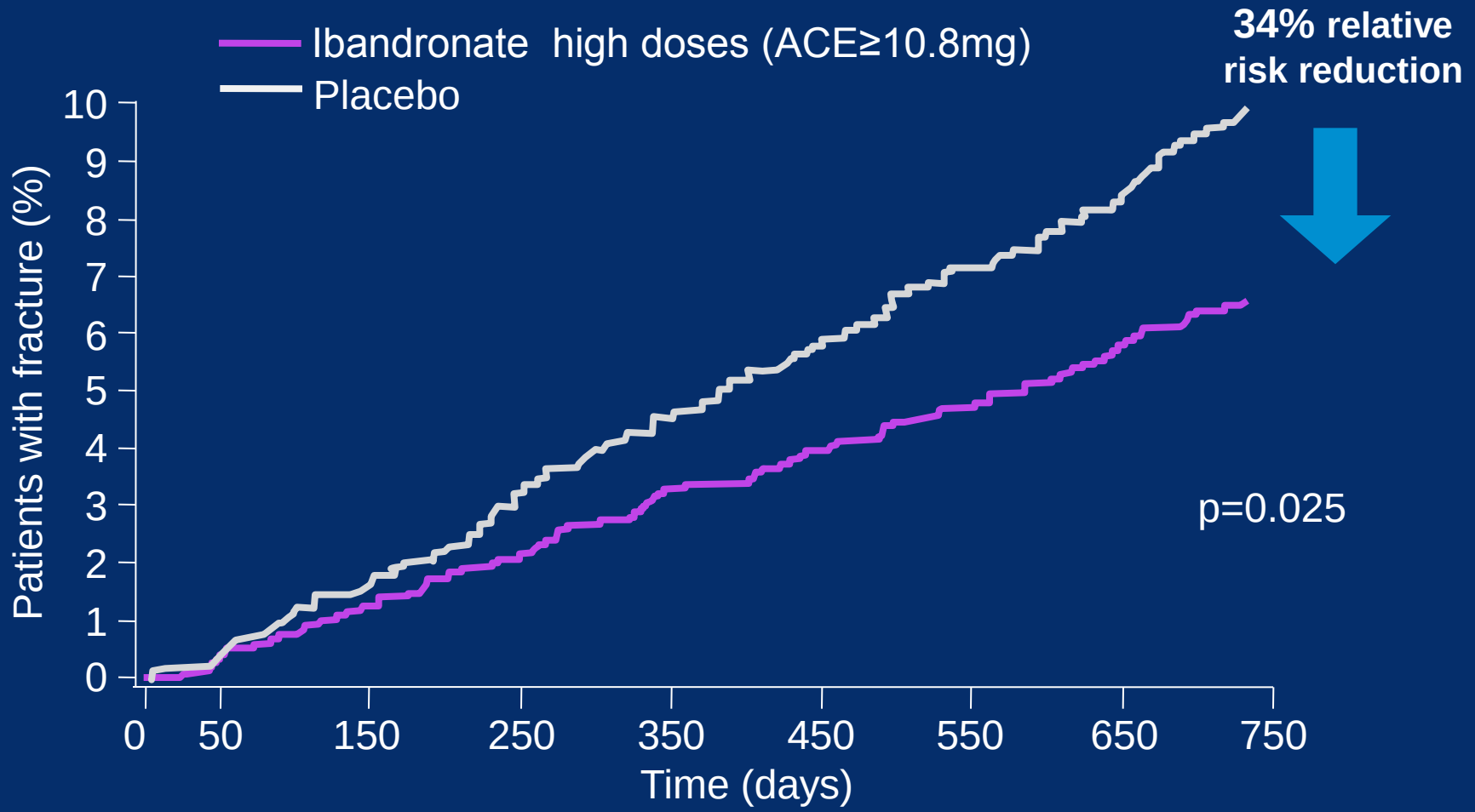


Adachi JD, *et al.* ASBMR Annual Meeting, 16–19 September 2007; Honolulu, HI. Poster M428.

Cranney A, *et. al.* Osteoporos Int 2009;20:291–297

Harris et al.

Το χρονικό διάστημα μέχρι την εμφάνιση μη σπονδυλικού κατάγματος παρατείνεται με την ιβανδρονάτη
ACE ≥10.8mg vs. placebo



Harris ST, *et al.* Curr Med Res Opin 2008;24:237–245

Bone 44 (2009) 758–765

Contents lists available at ScienceDirect

Bone

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

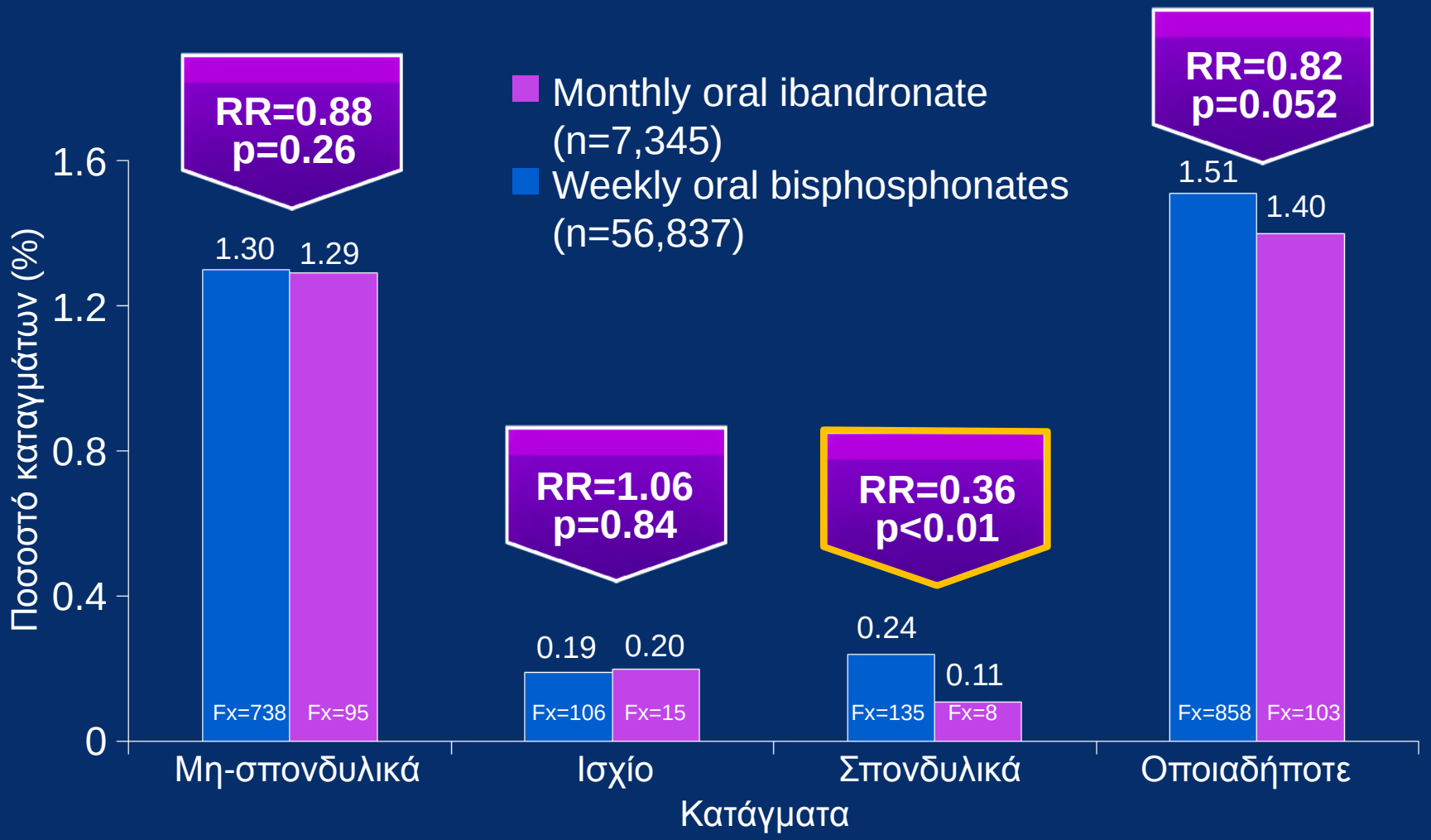
Risk of fracture in women treated with monthly oral ibandronate or weekly bisphosphonates: The eValuation of IBandronate Efficacy (VIBE) database fracture study

S.T. Harris [a,*], J.-Y. Reginster [b], C. Harley [c], W.A. Blumentals [d], S.A. Poston [e], C.E. Barr [f], S.L. Silverman [g]

- **Σκοπός:** σύγκριση ποσοστού καταγμάτων μετά από 1 έτος
  - ιβανδρονάτη vs. εβδομαδιαίων διφωσφονικών (ALN, RIS)
- **Πληθυσμός: 64.182** γυναίκες συμμορφούμενες στην αγωγή συμπεριλήφθησαν στην πρωταρχική ανάλυση
  - Δεδομένα ασθενών από τα συστήματα υγείας (i3 Research, i3 IMPACT)

Harris ST, *et al.* Bone 2009;44:758–765

Η μηνιαία ιβανδρονάτη έδειξε συγκρίσιμο ρυθμό μη-σπονδυλικών και ισχιακών καταγμάτων και χαμηλότερο ρυθμό σπονδυλικών καταγμάτων vs. των εβδομαδιαίων διφωσφονικών στους 12 μήνες

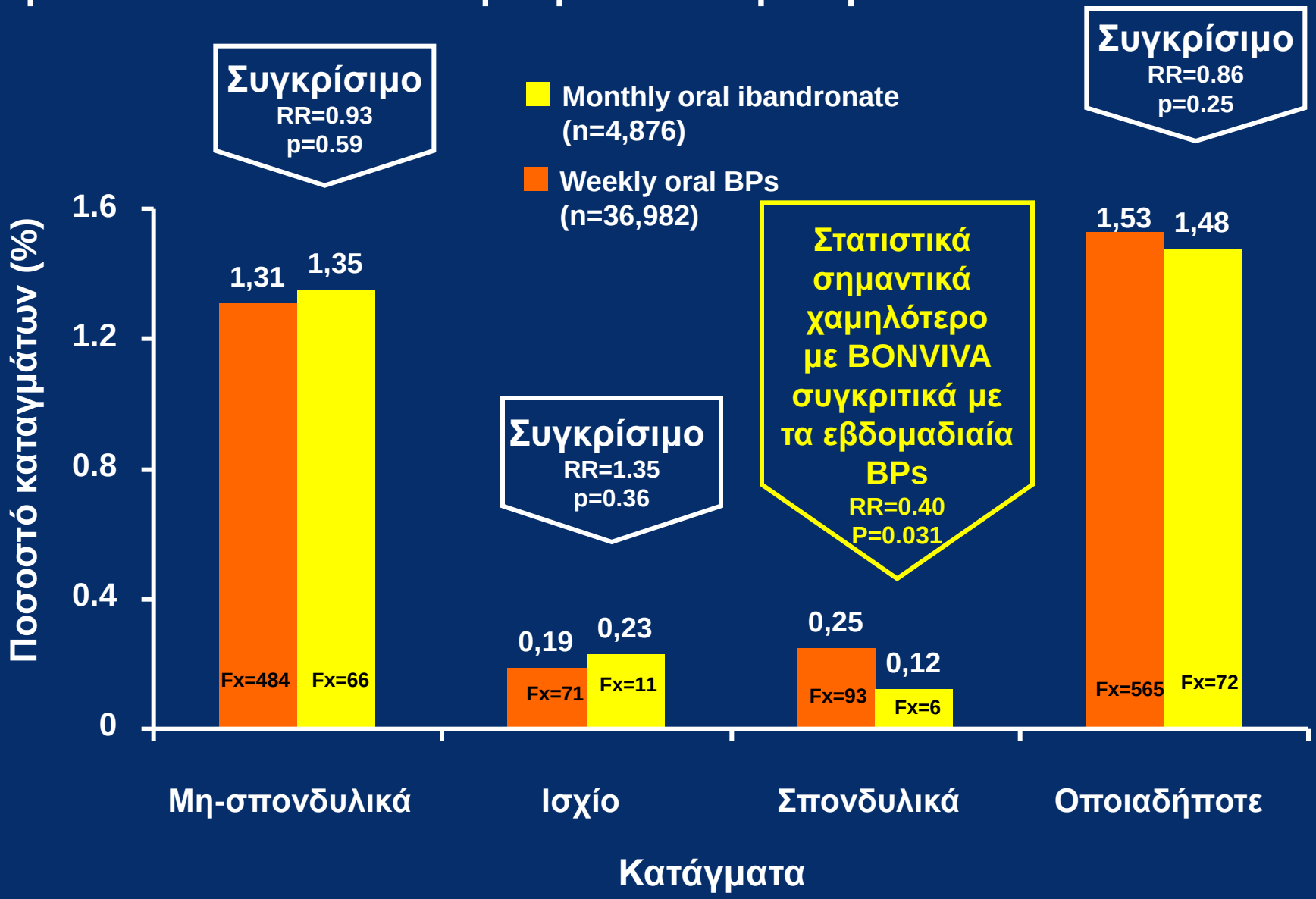


RR=adjusted RR (hazard ratio) using Cox regression controlling for potential confounding variables; population-based cohort study of persistent patient cohort with no refill gap >45 days (monthly) or 30 days (weekly); Fx = absolute number of fractures

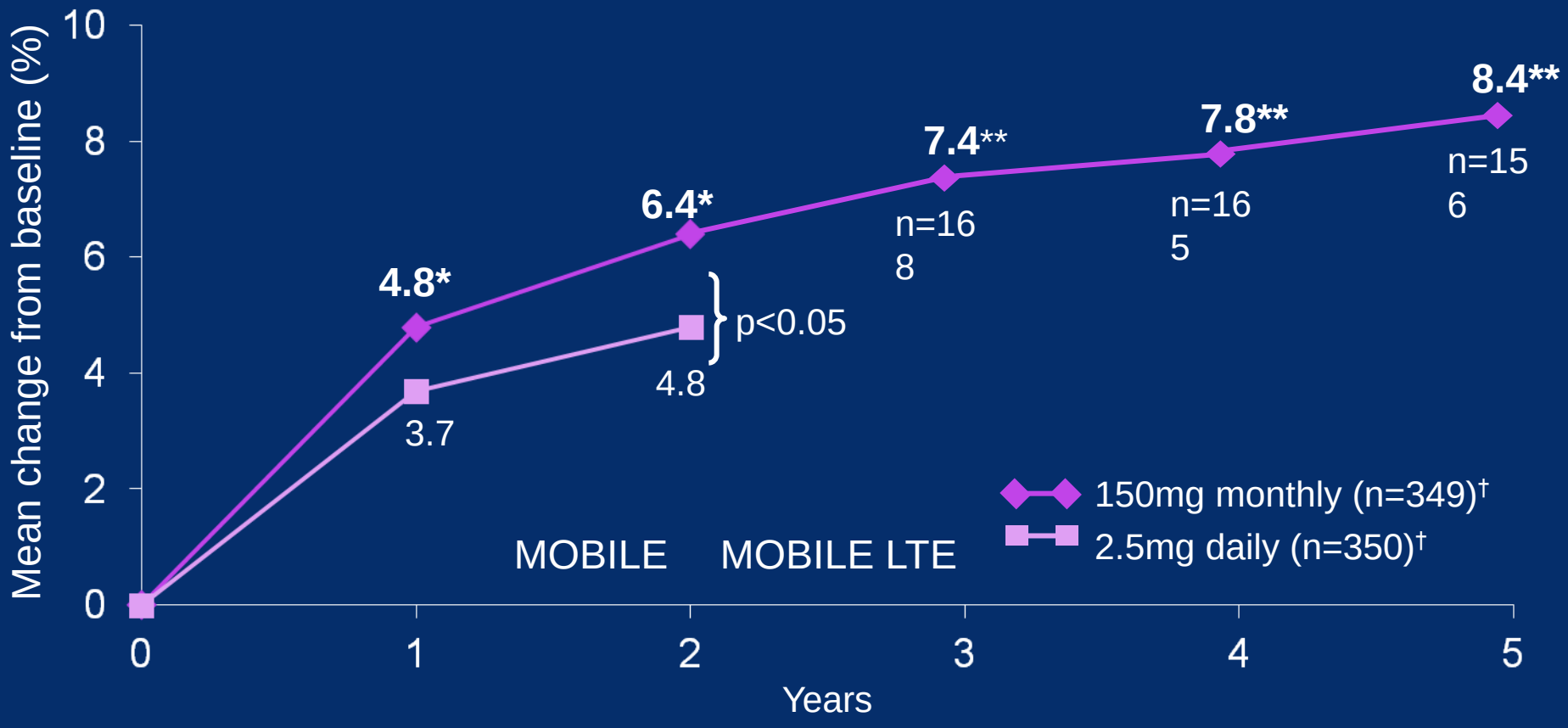
Harris ST, *et al.* Bone 2009;44:758–765

Αποτελέσματα Μελέτης VIBE σε ασθενείς με ΟΣΤΕΟΠΟΡΩΣΗ

Ενός Έτους Αναδρομική Μελέτη Παρατήρησης Καταγμάτων μηνιαίο BONVIVA έναντι εβδομαδιαία διφωσφονικά



Η μηνιαία ιβανδρονάτη έχει αποδείξει συνεχόμενες αυξήσεις της BMD στην ΟΜΣΣ κατά τη διάρκεια 5 ετών



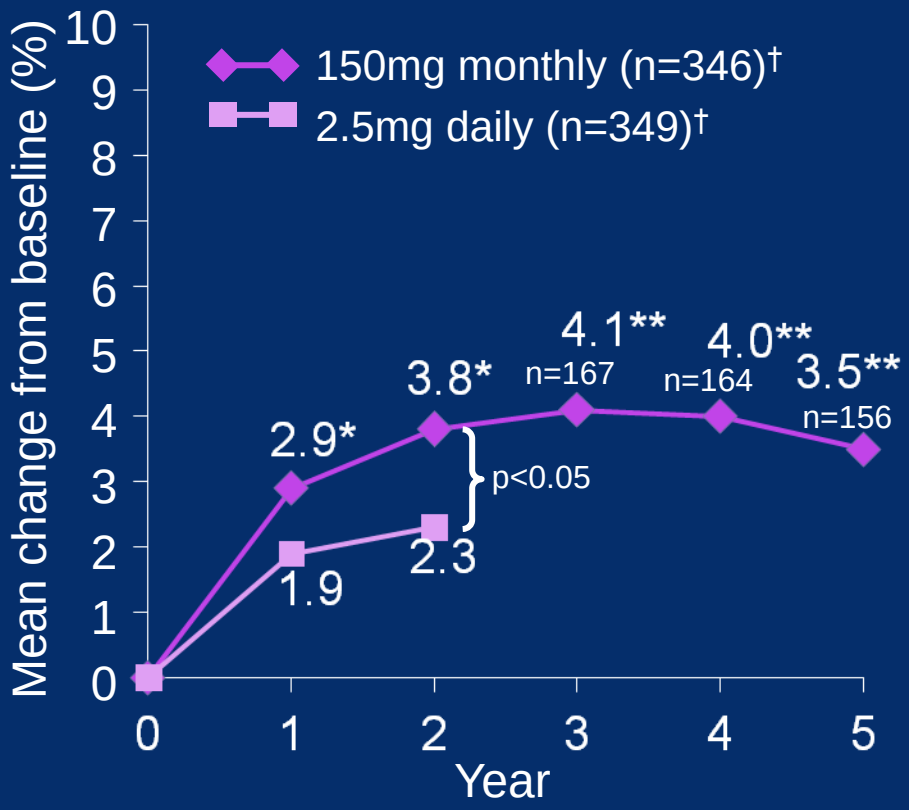
MOBILE ITT analysis; *p<0.05 vs. MOBILE baseline; **95% CI; †At 2 years; LTE = long-term extension

Miller PD, *et al.* J Bone Miner Res 2005;20:1315–1322; Reginster JY, *et al.* Ann Rheum Dis 2006;65:654–661

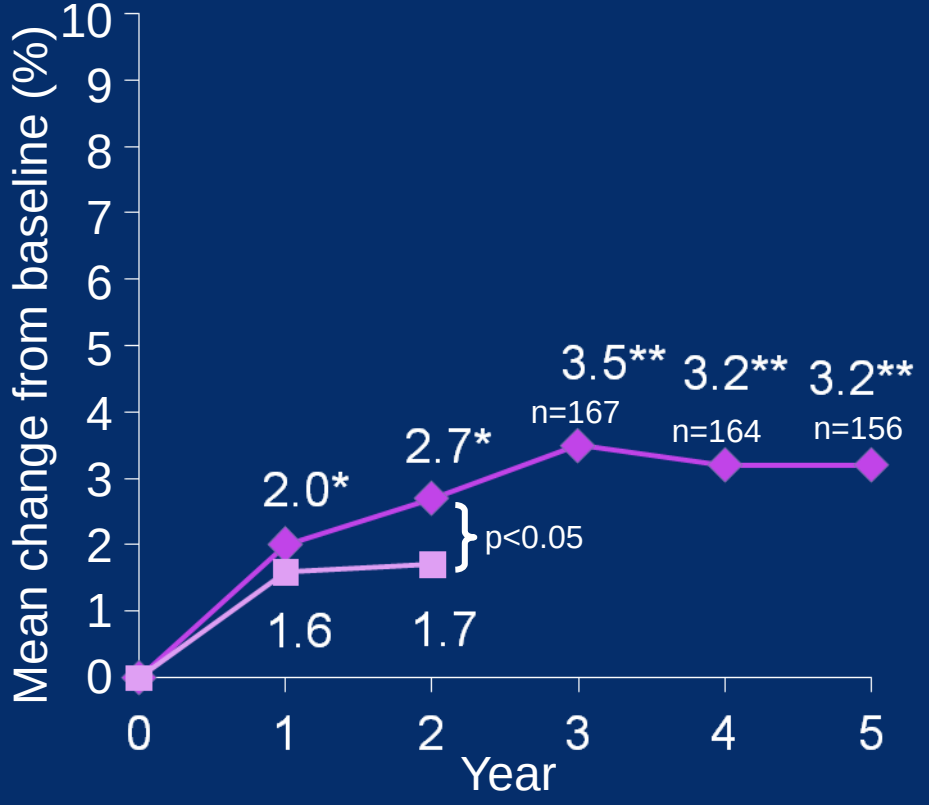
Felsenberg D, *et al.* Osteoporos Int 2009;20(Suppl.1):S15 (Abstract OC32)

Η μηνιαία ιβανδρονάτη διατήρησε τις αυξήσεις της BMD στο ισχίο κατά τη διάρκεια 5 ετών

Ολικό ισχίο



Αυχένας μηριαίου οστού



MOBILE ITT analysis; *p<0.05 vs. MOBILE baseline; **95% CI; †At 2 years; LTE = long-term extension

Miller PD, *et al.* J Bone Miner Res 2005;20:1315–1322; Reginster JY, *et al.* Ann Rheum Dis 2006;65:654–661

Felsenberg D, *et al.* Osteoporos Int 2009;20(Suppl.1):S15 (Abstract OC32)

EFFICACY OF MONTHLY ORAL and QUARTERLY IV IBANDRONATE IS MAINTAINED OVER 5 YEARS: THE MOBILE and DIVA LTE STUDY

MOBILE[1] 5 years	BMD increase (%)
LS (L2-L4)	8.4
Total Hip	3.5
FN	3.2
Trochanter	6.0

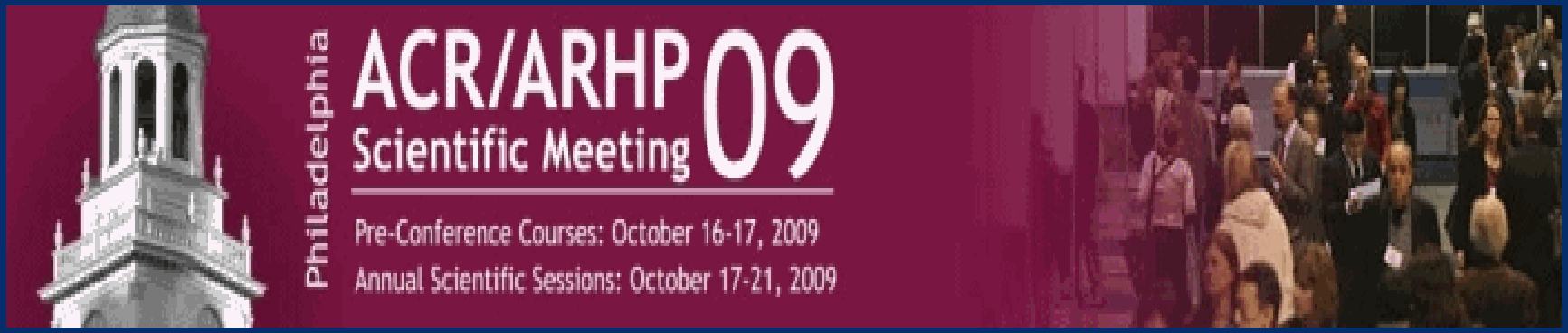
DIVA[2] 5 years	BMD increase (%)
LS (L2-L4)	8.1
Total Hip	2.8
FN	3.4
Trochanter	5.3

[1]D.Felsenberg et al. Osteoporo Int (2009) 20 (Suppl. 1): S5-S22
[2]G. Bianchi et al. Ann Rheum Dis 2009; 68 (Suppl. 3) : 494

Corticosteroid Induced Osteoporosis & IBN

Presentation: Once Monthly Oral Ibandronate Provides Significant Improvement in Lumbar Spine Bone Mineral Density in Postmenopausal Women Treated with Glucocorticoids for Inflammatory Rheumatic Diseases (ACR/ARHP Annual Scientific Meeting)

ONCE study (OsteoporosIs preventioN in glucoCorticoid-treated womeEn)



Leena Paimela, ORTON hospital, Invalid Foundation, Helsinki, Finland,
Markku Hakala, Rheumatism Foundation Hospital, Heinola, Finland,
Tuija Hienonen-Kempas, Roche Finland, Espoo, Finland and ONCE study group

Arthitis Rheum 2009;60 Suppl 10: 889 DOI:10.1002/art.25969

ONCE study design

- Randomized, Double-blind, Placebo-controlled, Parallel-group study in PMO women in Finland
- n = 140 (aged 50-85 years), ≥1 year since menopause
- Mean LS (L1-L4) BMD T-score ≥ -2.0
- Receiving treatment with 5-15mg/day of prednisolone
- Rheumatoid arthritis (48%), Polymyalgia rheumatica (36%), other Inflammatory rheumatic disease (16%)
- All pts received vit. D (800IU/day) and Ca (1000mg/day)
- **Primary Endpoint : Relative change (%) from baseline at 12 months in mean LS BMD**

Arthitis Rheum 2009;60 Suppl 10: 889 DOI:10.1002/art.25969

ONCE study results

Significant mean change from baseline in mean LS BMD

	Placebo	IBN 150mg	P value
6 months	0.3 %	2.6 %	
12 months	**-0.2%**	**3.3 %**	**<0.0001**

Arthitis Rheum 2009;60 Suppl 10: 889 DOI:10.1002/art.25969

Ανδρική Οστεοπόρωση & IBN

- 1 έτους, ελεγχόμενη με placebo, τυχαιοποιημένη (2:1), διπλά-τυφλή μελέτη
- n = 132 άνδρες (≥30 ετών) με πρωτοπαθή, ιδιοπαθή ή υπογοναδική οστεοπόρωση

- Baseline BMD T-score: FN ≤ -2.0 & LS ≤ -1.0 or
- Baseline BMD T-score: LS ≤ -2.0, FN ≤ -1.0 & ≥ -4.0 at any site
- Primary Endpoint: **mean % change from baseline in LS BMD at 1 year**
- Secondary Endpoints
  - mean % change from baseline at the FN, Total Hip and Trochanter
  - changes in sCTX
- All men received daily Ca (1000mg) and vit. D (400 IU)

Bone 46 (2010) 970-976

Efficacy and Safety of Once-monthly Oral Ibandronate in Men with Osteoporosis - STRONG study

ΑΠΟΤΕΛΕΣΜΑΤΑ

	Placebo (%)	IBN 150mg (%)	P value
LS	**0.9**	**3.5**	**<0.001**
FN	-0.2	1.2	0.012
TH	-0.3	1.8	<0.001
Trochanter	0.4	2.2	<0.005

- % decrease in median s-CTX levels: -51.7% (IBN) vs -20.8% (PLA)
- Well tolerated

Bone 46 (2010) 970-976