

TERAPIE MEDICHE DELL'OSSO:UPDATE

Osteoporosi e CTIBL: Quali novità

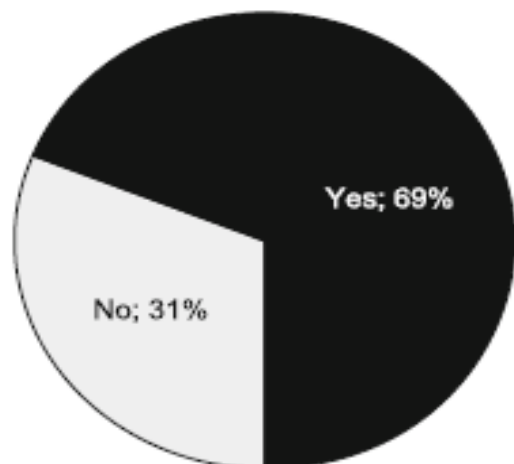
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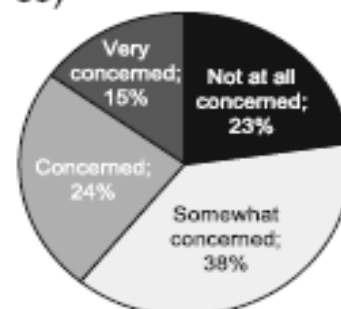
Awareness, concern, and communication between physicians and patients on bone health in cancer

A

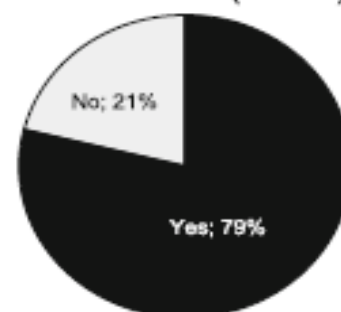
Q. Are you aware that AI therapy can lead to bone loss? (n = 111)



Q. If aware, how concerned are you about bone loss due to AI therapy? (n = 85)

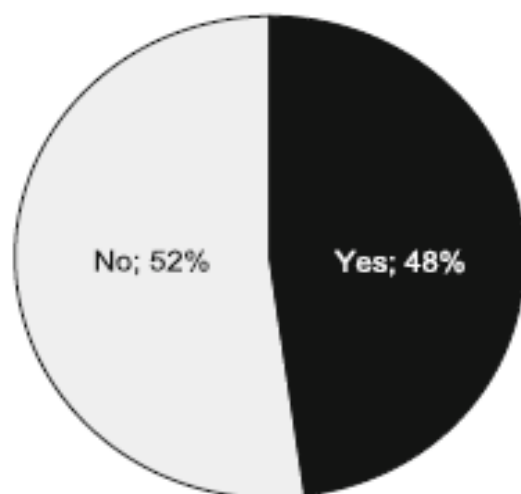


Q. If aware, have you and your physician (or another member of your healthcare team) discussed how this therapy could lead to bone loss? (n = 85)

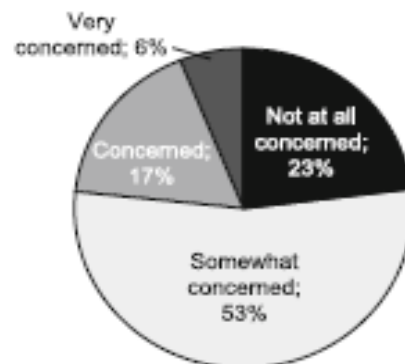


Awareness, concern, and communication between physicians and patients on bone health in cancer

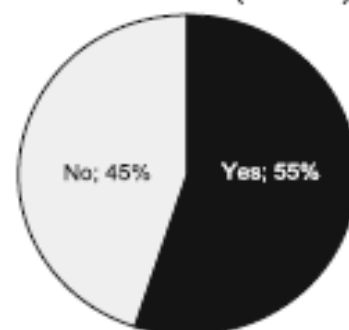
Q. Are you aware that ADT can lead to bone loss? (n = 96)



Q. If aware, how concerned are you about bone loss due to ADT? (n = 46)



Q. If aware, have you and your physician (or another member of your healthcare team) discussed how this therapy could lead to bone loss? (n = 46)



Bone health in a prospective cohort of postmenopausal women receiving aromatase inhibitors for early breast cancer (Mean age 62.5)

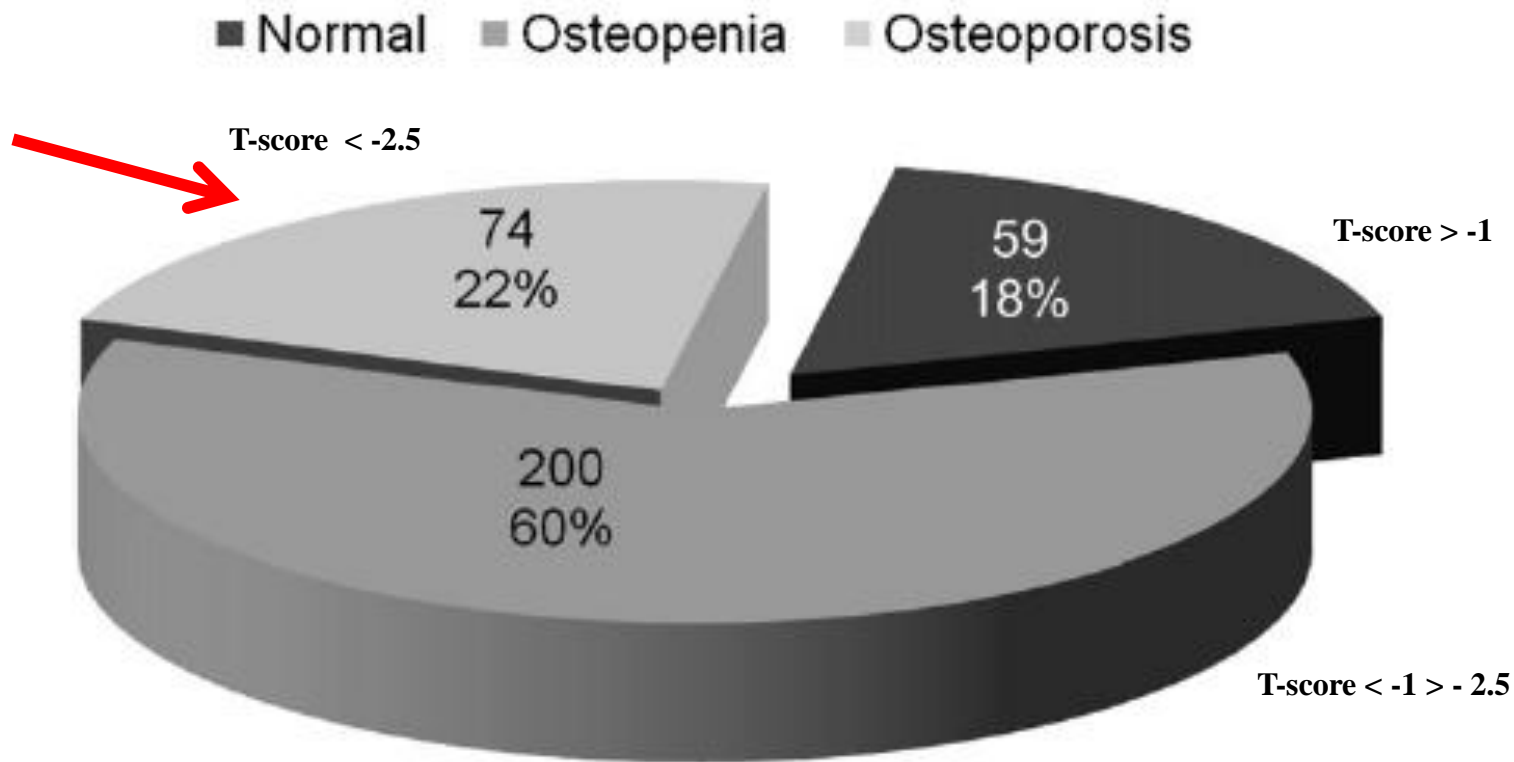
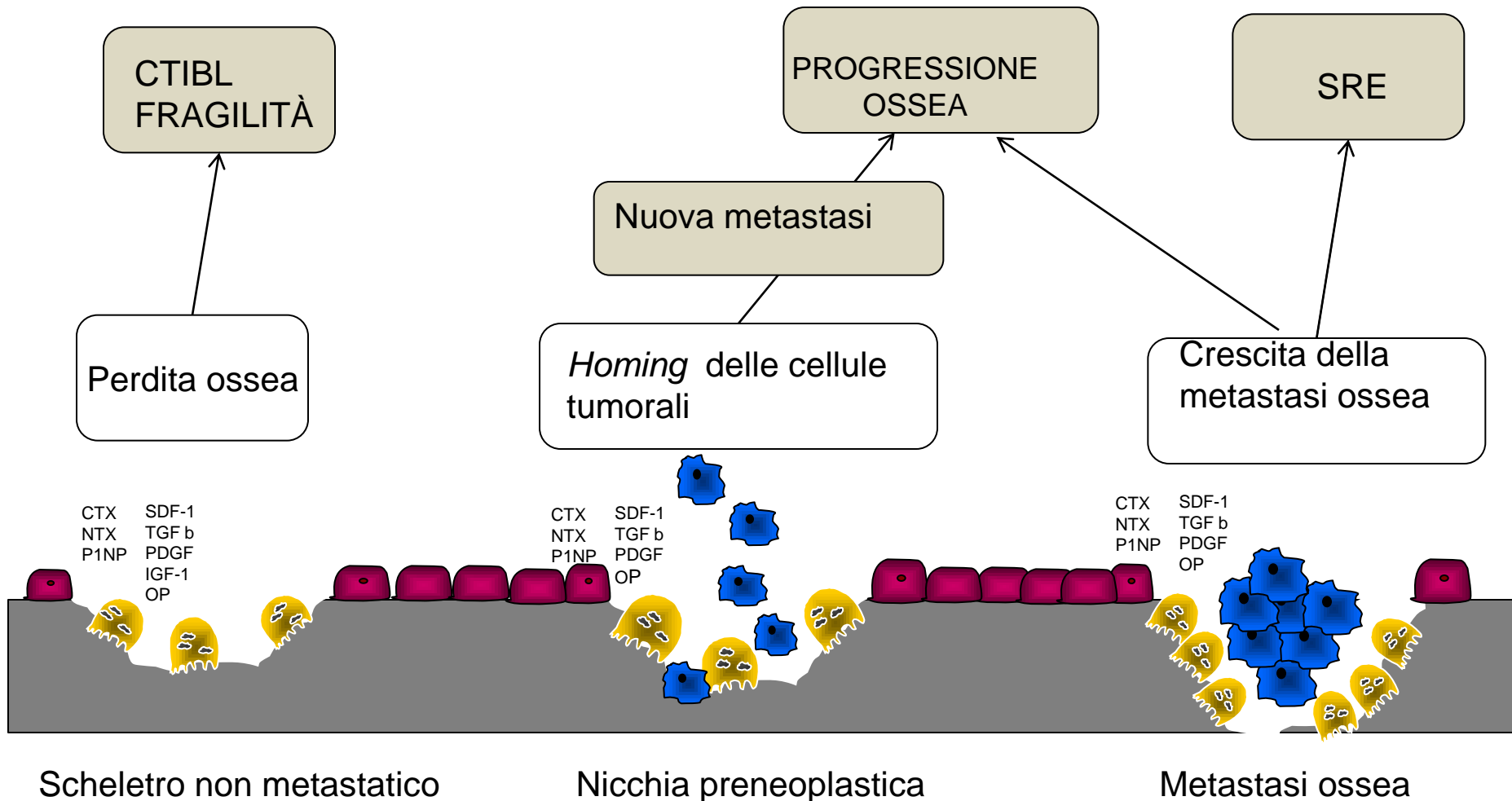


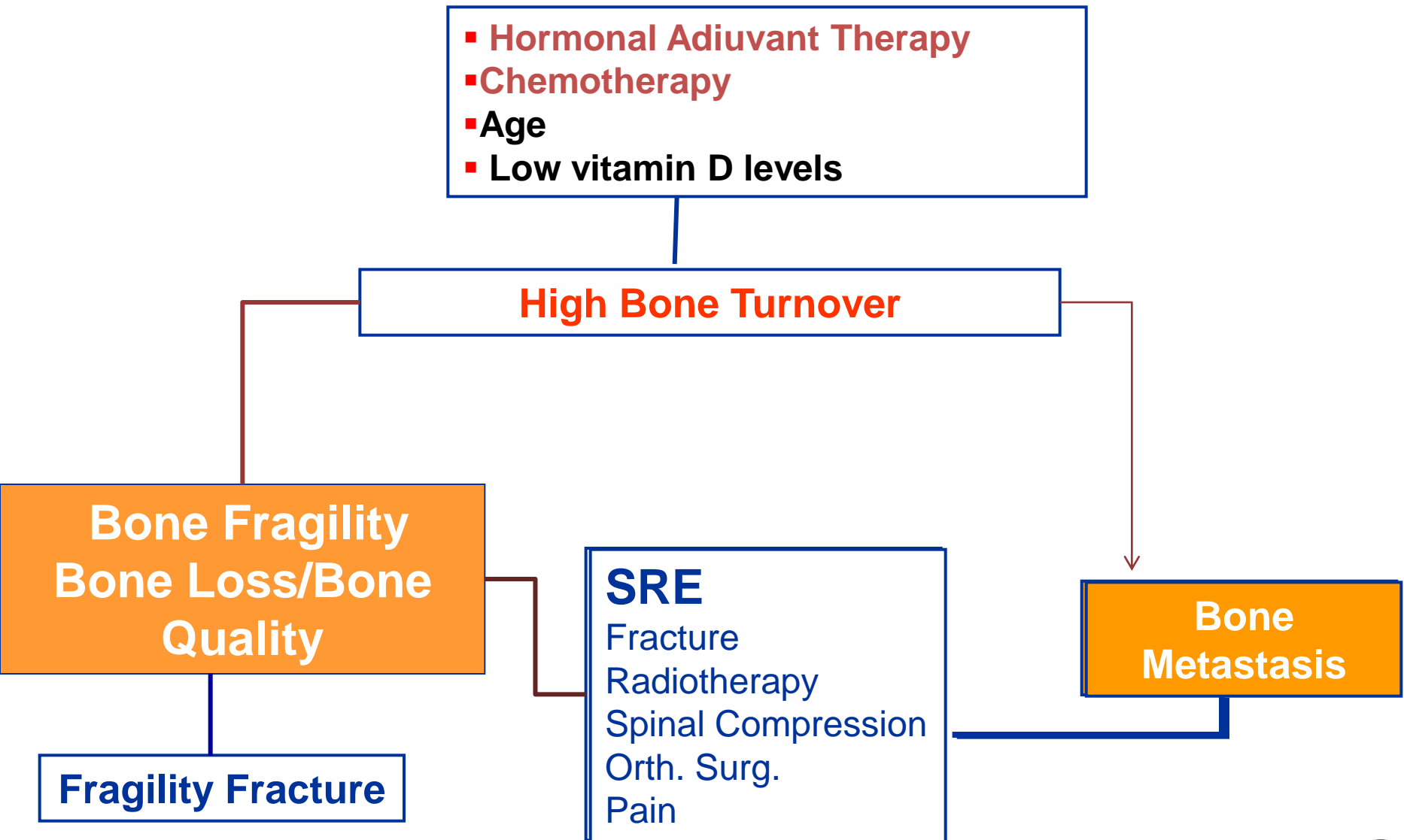
Fig 3. Baseline BMD according to WHO'94 criteria.

Elevato turnover osseo nei pazienti con carcinoma

ELEVATO TURNOVER OSSEO
(menopausa + terapia ormonale adiuvante + metastasi)

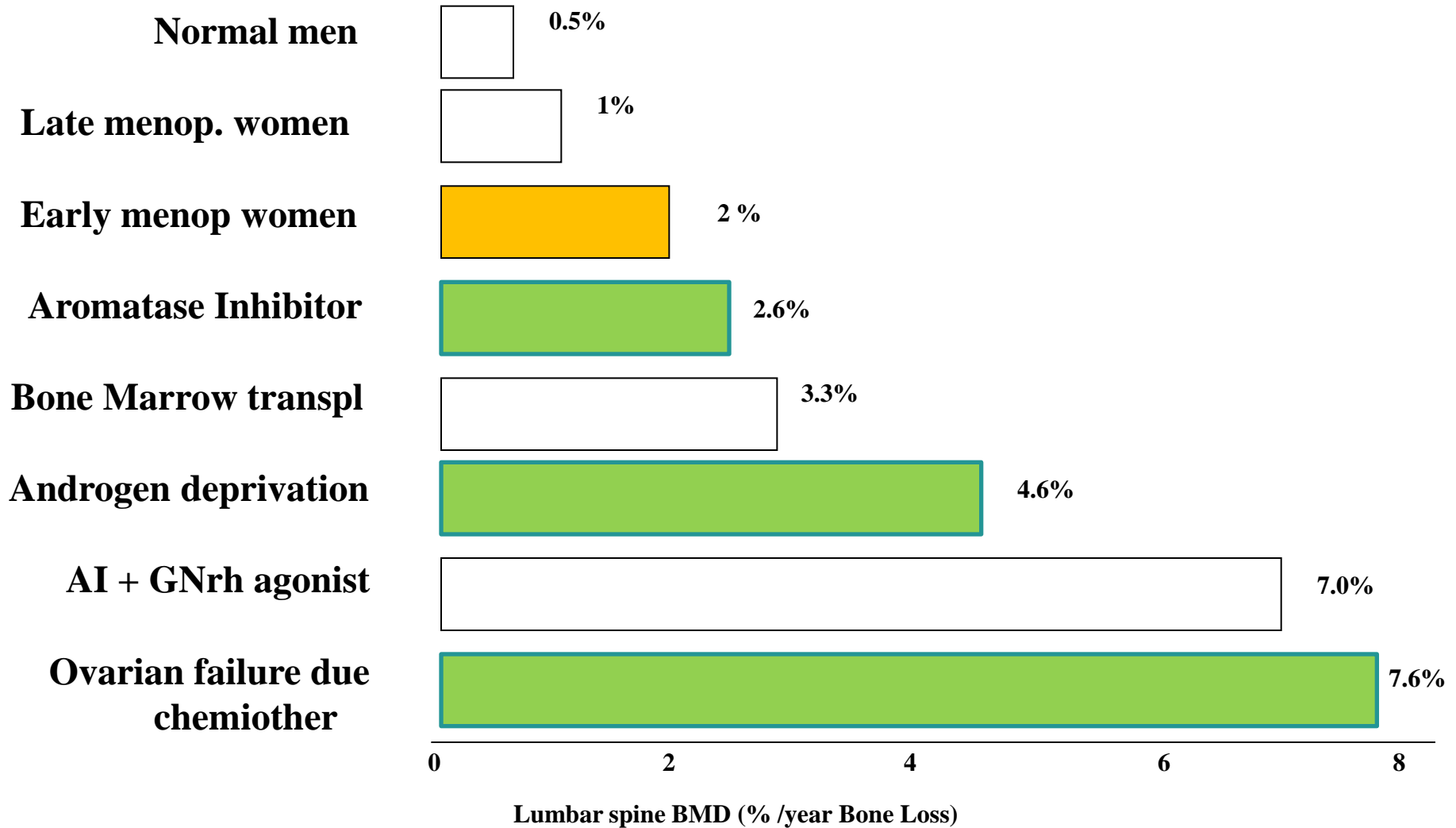


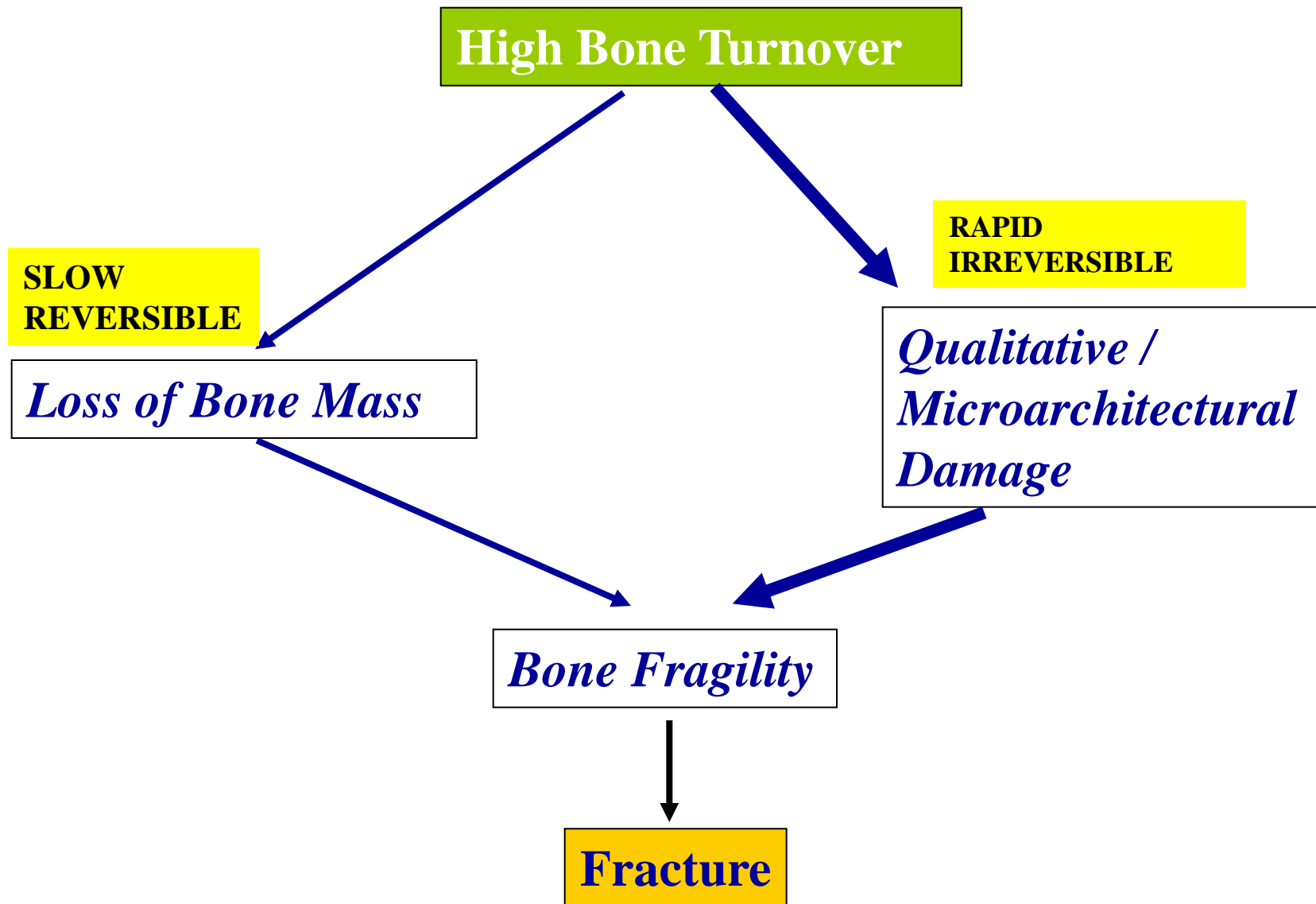
The “Bone Health” concept in Cancer Patients



CANCER TREATMENT INDUCED BONE LOSS

Rate of BMD Loss





High prevalence of vertebral fractures in women with breast cancer starting aromatase inhibitor therapy

Table 3. Number and severity of vertebral fractures with semiquantitative Genant analysis in 497 women with breast cancer

497 women 63 y.o

Vertebral level	Grade 1 (mild)	Grade 2 (moderate)	Grade 3 (severe)
T3	2	0	0
T4	2	0	0
T5	3	0	0
T6	14	1	0
T7	19	2	1
T8	10	4	1
T9	2	2	2
T10	5	1	2
T11	7	0	1
T12	8	7	4
L1	4	0	5
L2	4	3	1
L3	3	4	2
L4	2	1	1
L5	1	0	0
Total	86	25	20

19.1 % non vertebral Fx

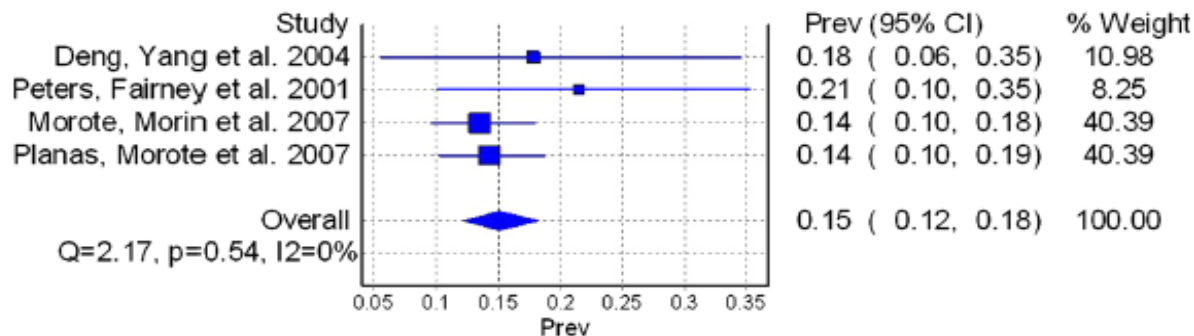
19.7% \geq 1 vertebral Fx

ETA'	< 60 aa	60-70 aa	>70 aa
% \geq 1 VFX	10.1	18.4	32.8

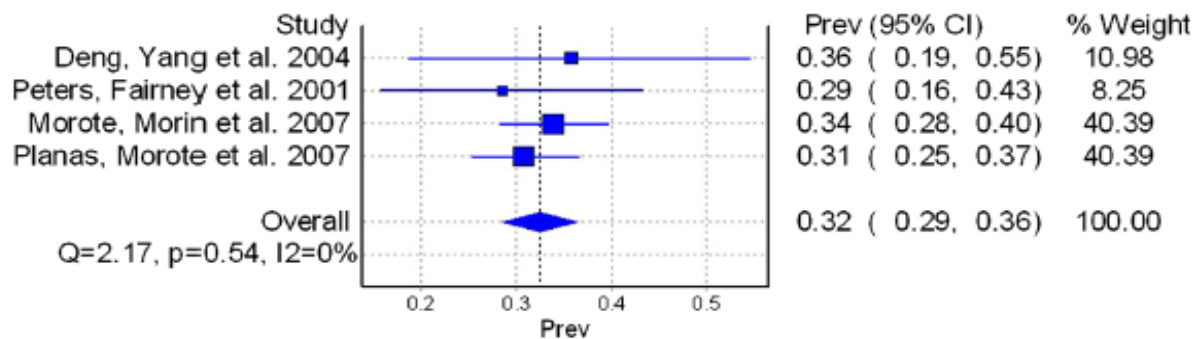
Bouvard B et al; Annals of Oncology, 2012

Prevalence of osteoporosis in prostate cancer survivors: a meta-analysis

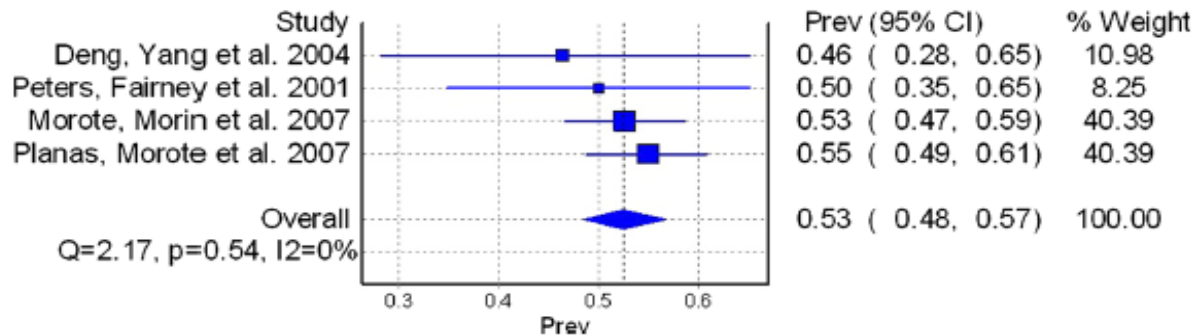
a Normal



b Osteopenia



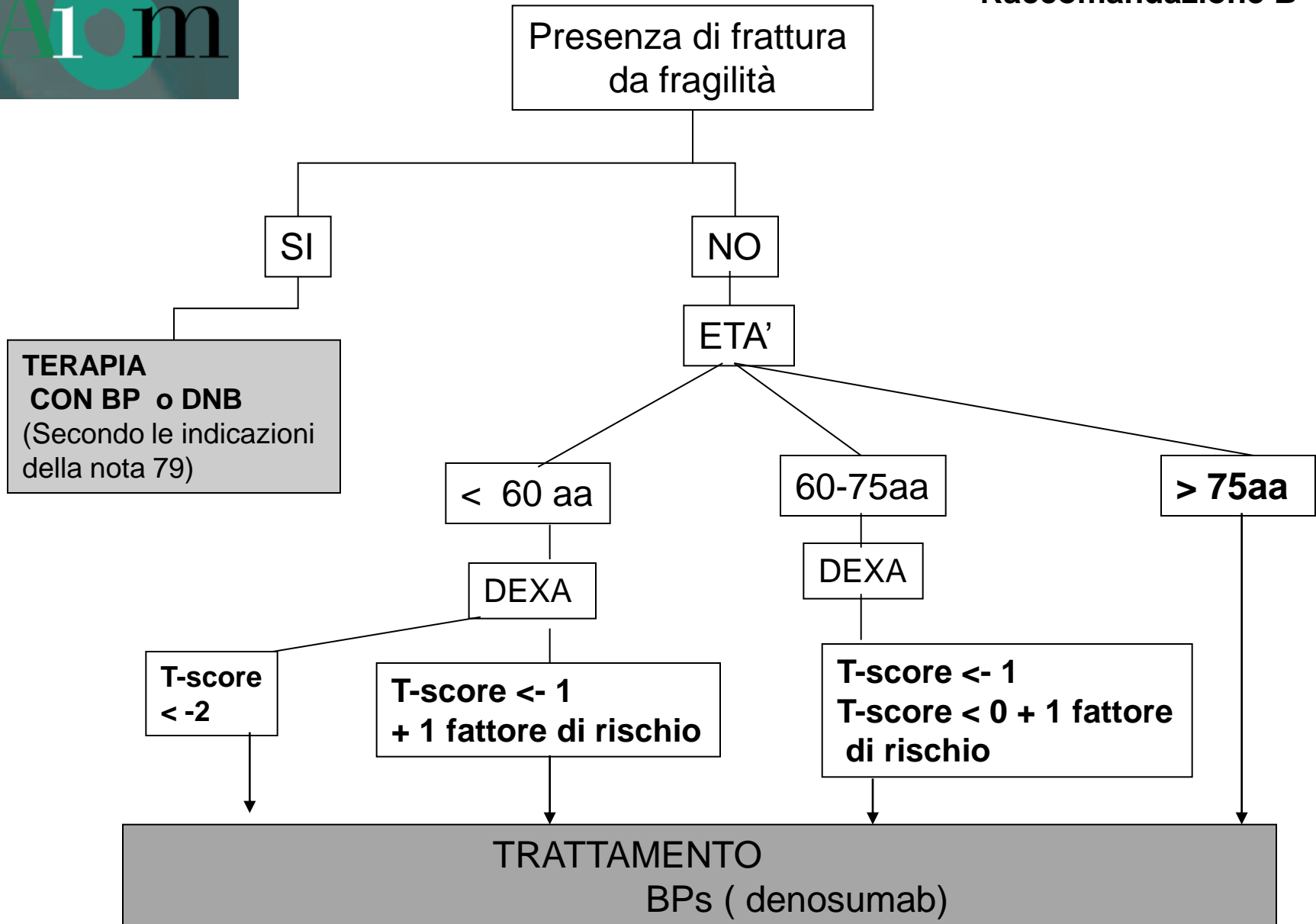
c Osteoporosis



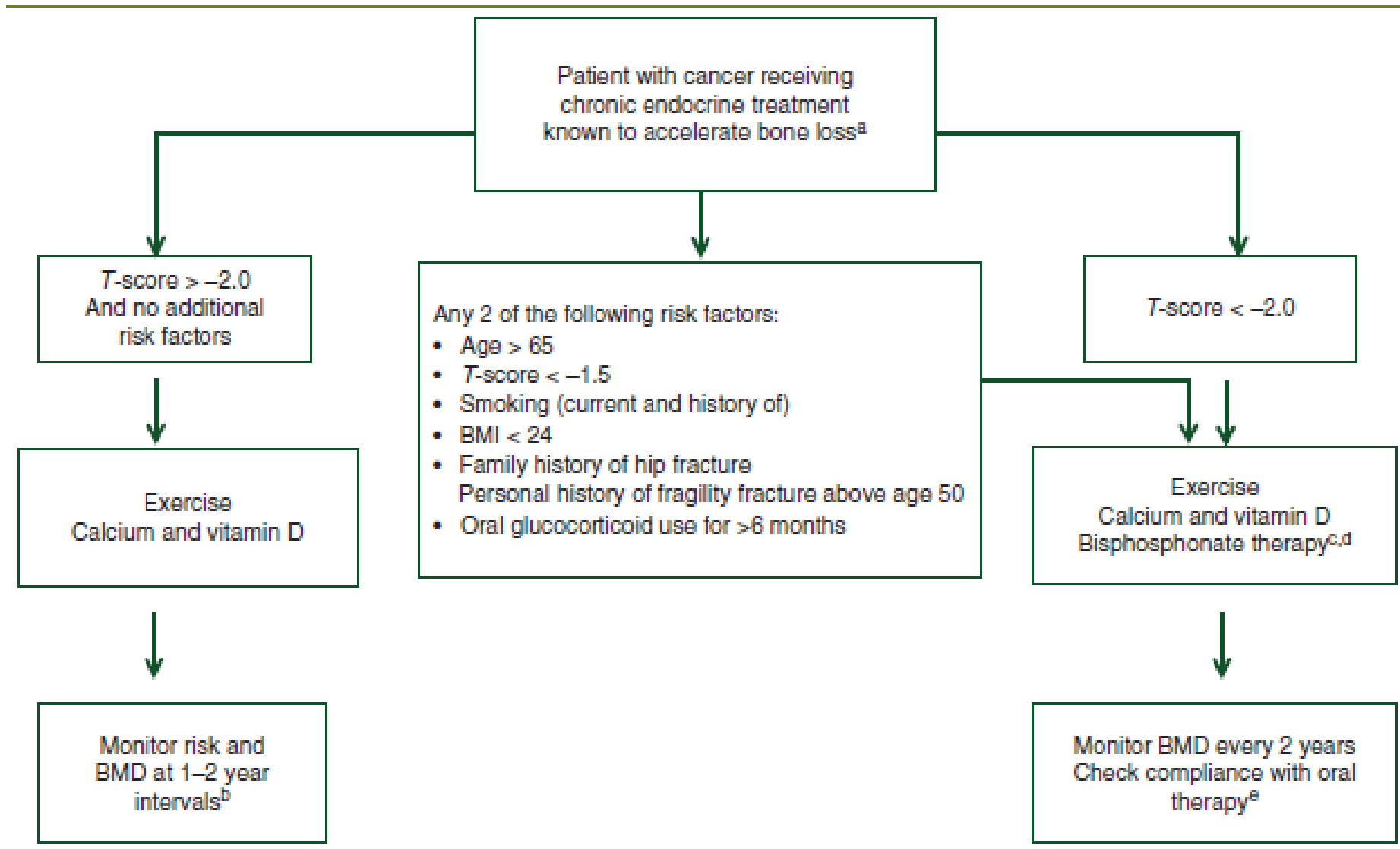
CATEGORIE AD ALTO RISCHIO DI CTIBL / FX

- **BC premenopausa dopo Kemio o K+ GnrH + TAM (anche dopo la sospensione della terapia adiuvante)**
- **BC pre- o postmenopausa alla sospensione TAM**
- **BC postmenopausa con switch TAM- AI**
- **BC postmenopausa in AI “giovani” (< 65 aa)**
- **PC men**

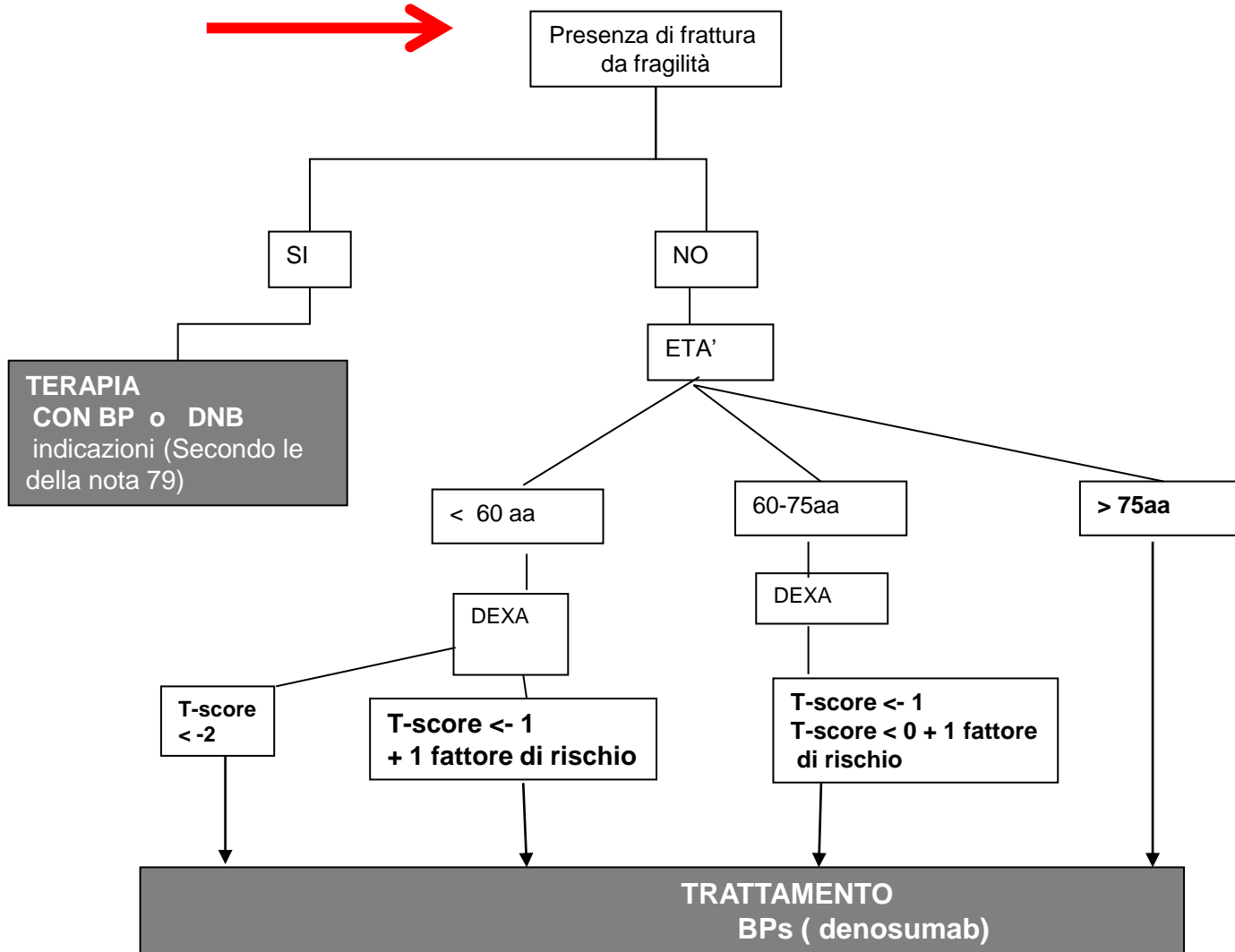




Bone health in cancer patients: ESMO Clinical Practice Guidelines[†]



ALGORITMO DECISIONALE NELLA CTIBL



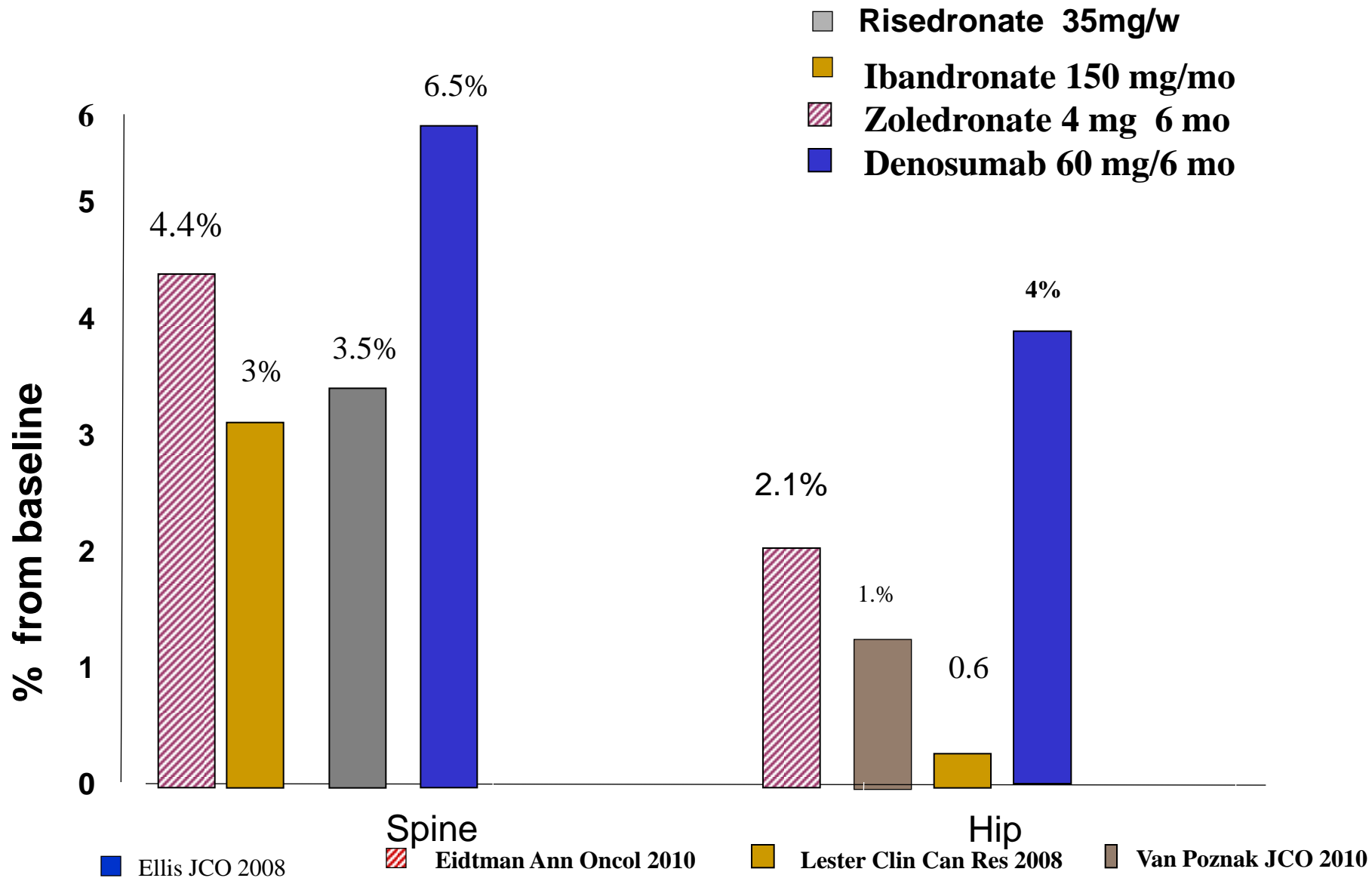
CTIBL IN PROSTATE CANCER- SPECIFIC GUIDELINES

GUIDELINES	Therapeutic Threshold	Treatment
EAU 2013	DEXA T-score <-2.5	DNB 60 mg/6 mo. ZOL 4 mg /6 mo.
NCCN 2013	FRAX HIP > 3% FRAX major FX >20%	AL 70 mg / week ZOL 5 mg /Year DNB 60mg/6 mo.

QUALI EVIDENZE PER PREVENZIONE/ TRATTAMENTO DELLA CTIBL?

- Le attuali linee guida indicano l'utilizzo dei bisfosfonati (BP) e DNB
- Tutti gli studi in BC con BPs e DNB hanno come end-point la prevenzione della perdita di BMD
- Vi è un unico studio (PC) con end-point la riduzione del rischio di frattura (DNB)
- Non è definita la posologia dei BPs da utilizzare (quella utilizzata per la PMO? Maggiore?)
- Non vi sono BPs registrati con indicazione CTIBL
- E' registrato (ma non rimborsabile) denosumab (PROLIA 60mg/6 mesi) in PC in ADT

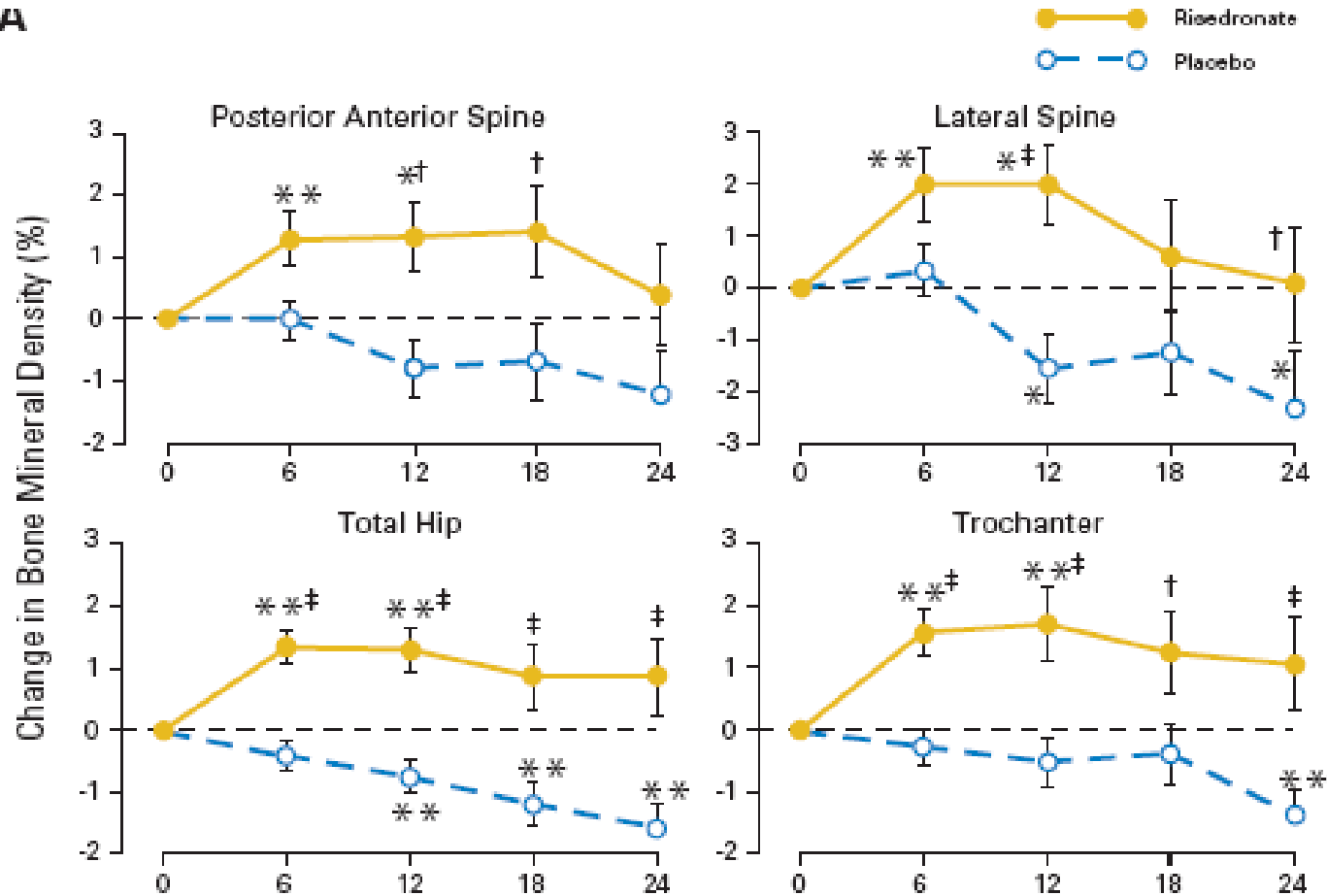
Effects of Antiresorptive therapy on BMD in BC Women treated with AI



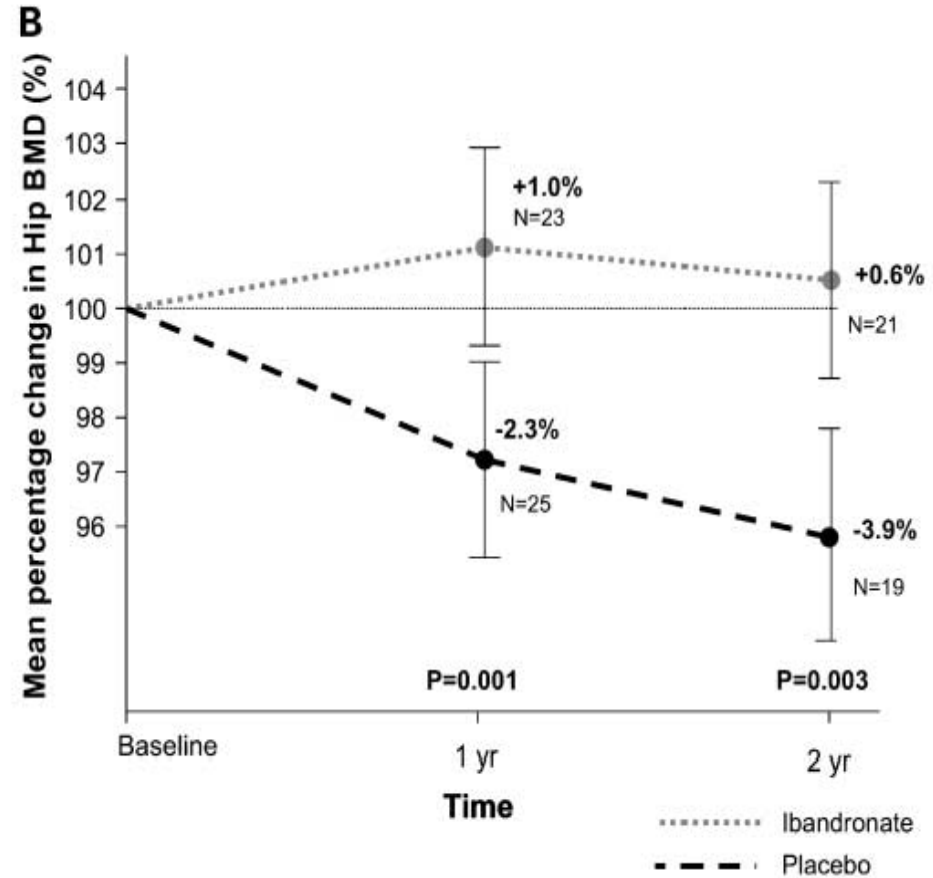
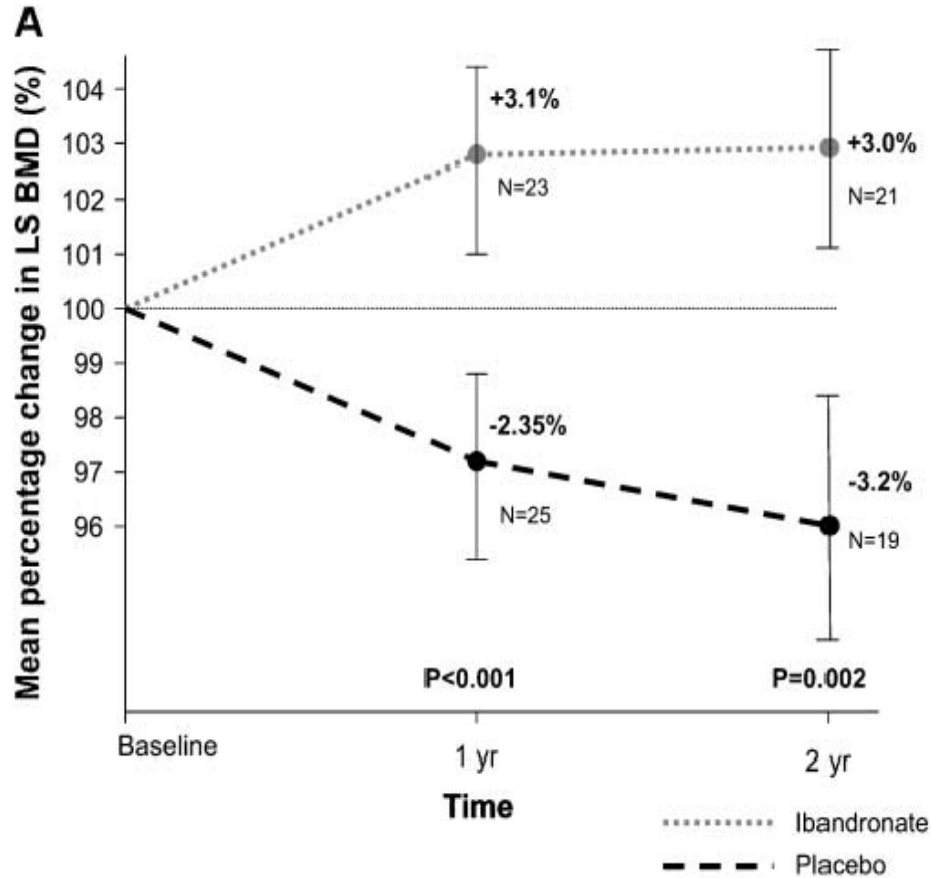
Risedronate Prevents Bone Loss in Breast Cancer Survivors: A 2-Year, Randomized, Double-Blind, Placebo-Controlled Clinical Trial

Susan L. Greenspan, Adam Brufsky, Barry C. Lembersky, Rajib Bhattacharya, Karen T. Vujevich, Subashan Perera, Susan M. Sereika, and Victor G. Vogel

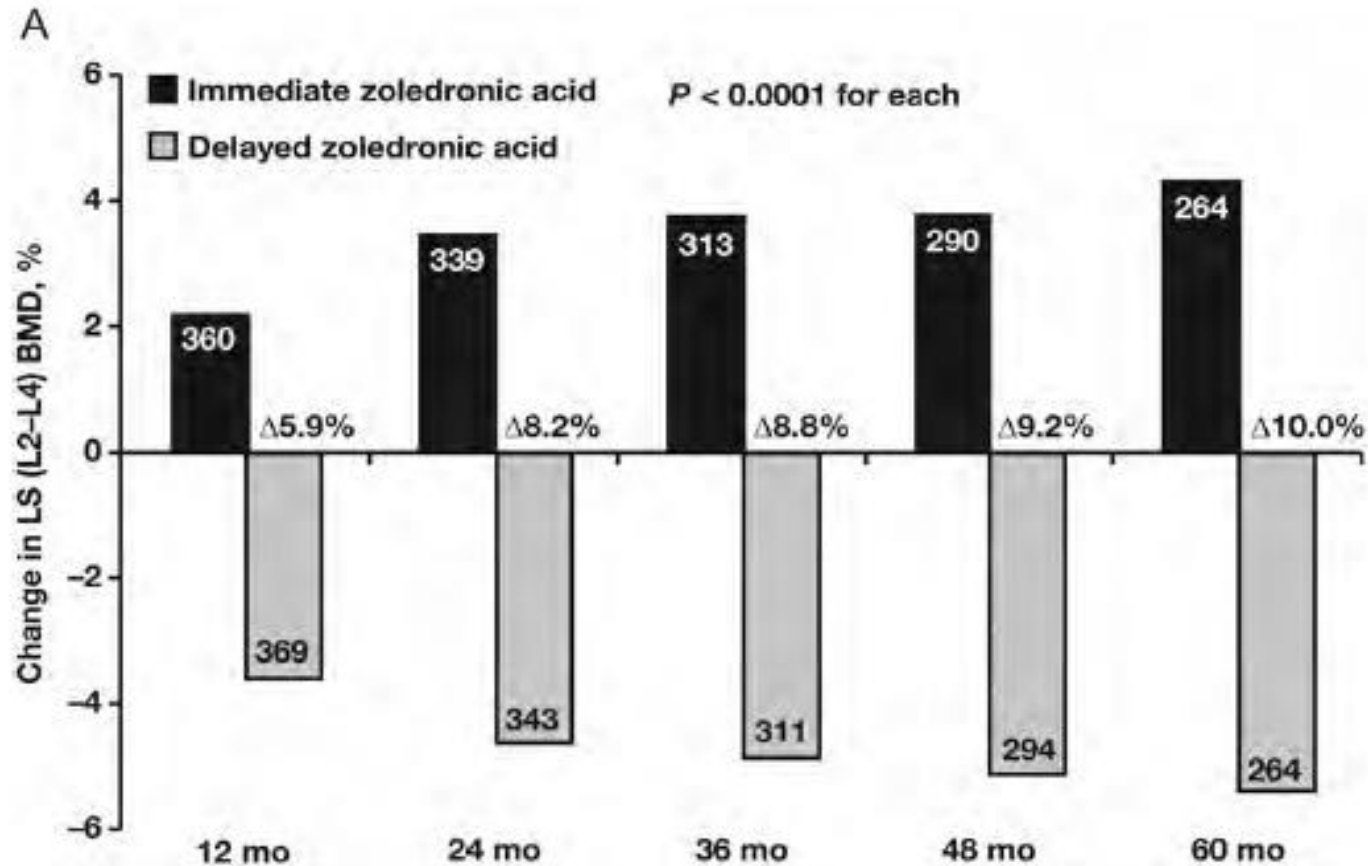
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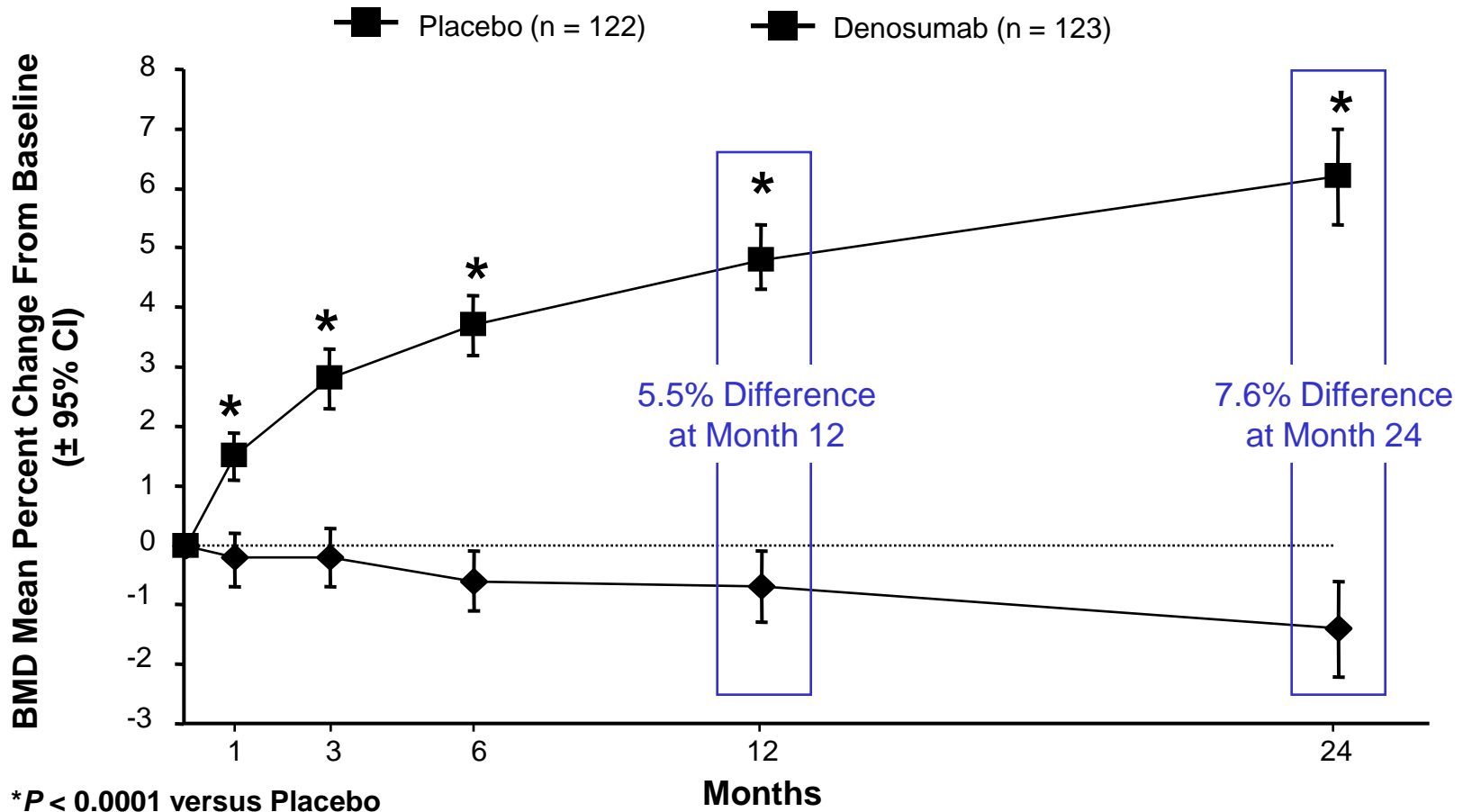
Prevention of Anastrozole-Induced Bone Loss with Monthly Oral Ibandronate during Adjuvant Aromatase Inhibitor Therapy for Breast Cancer



Zoledronic acid (zoledronate) for postmenopausal women with early breast cancer receiving adjuvant letrozole (ZO-FAST study): final 60-month results



Primary Endpoint: Percentage change from baseline in lumbar spine BMD vs Placebo



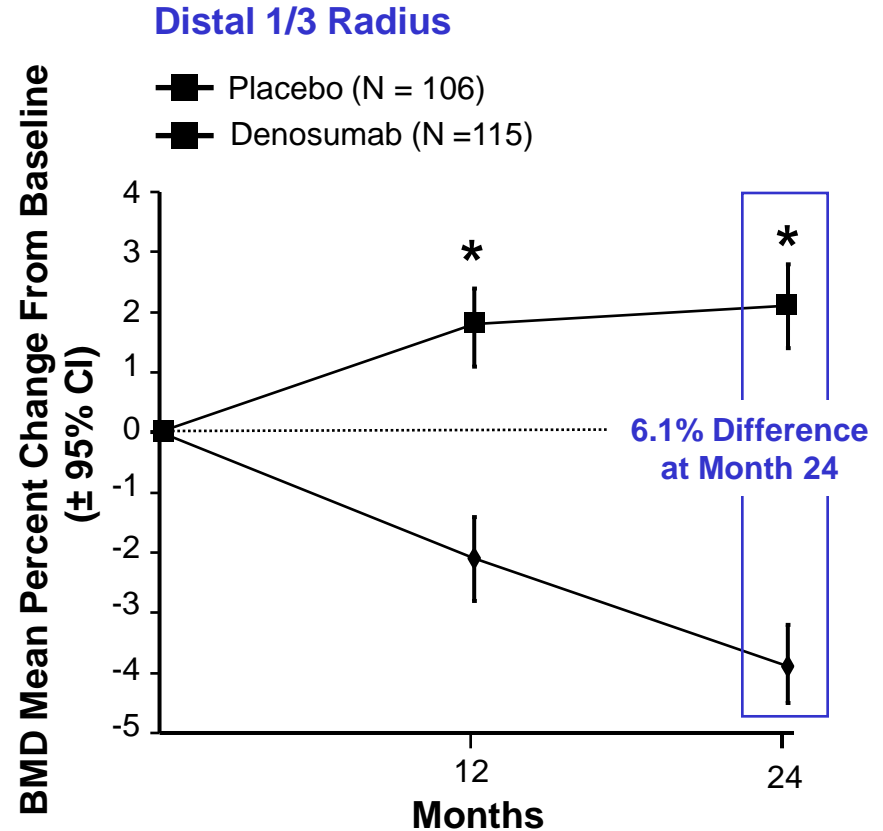
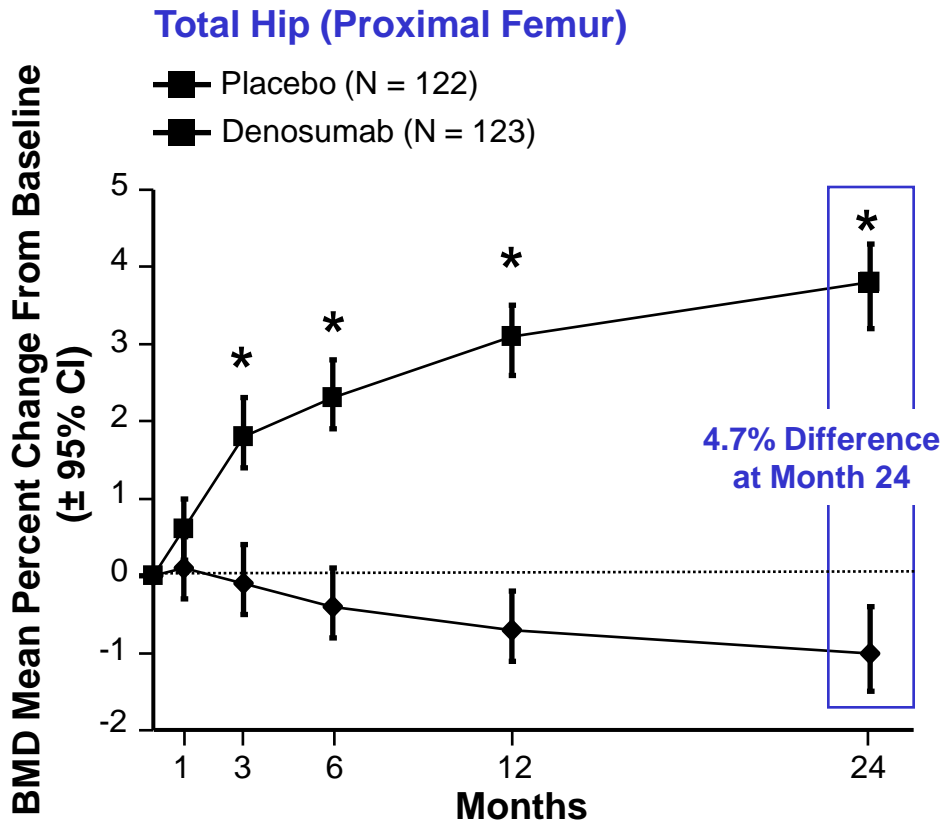
Ellis GK et al. *J Clin Oncol.* 2008;26:4875-4882.

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Denosumab 60 mg/ 6 mo.

Effect on BMD at Cortical Bone Sites

Total Hip and Distal 1/3 Radius

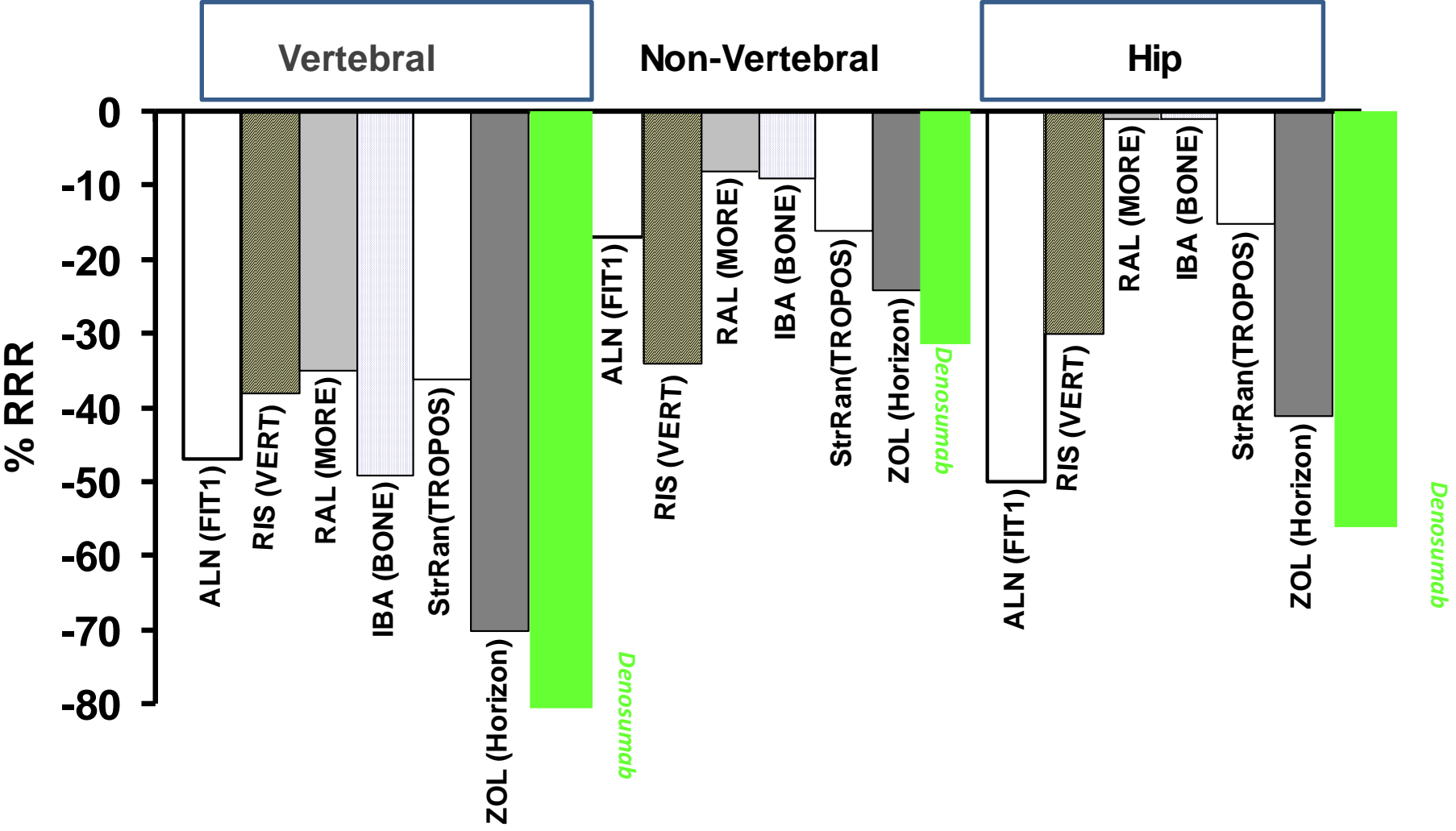


* $P < 0.0001$ versus Placebo

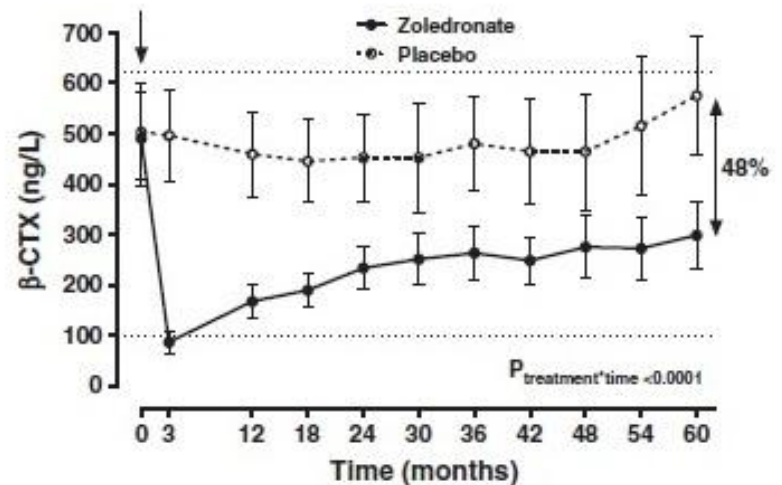
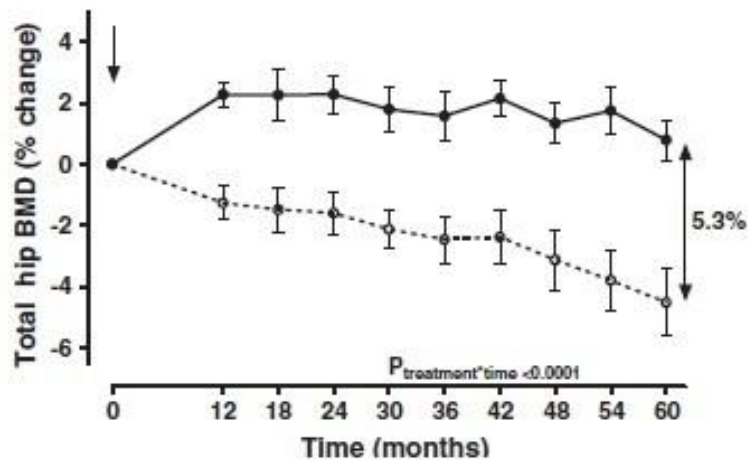
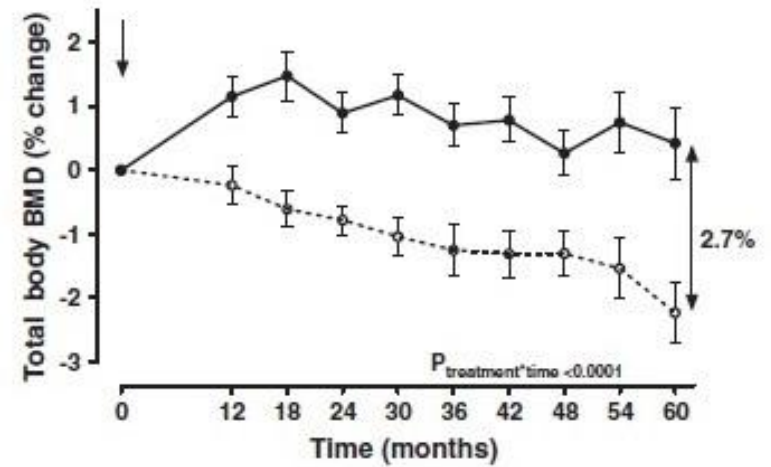
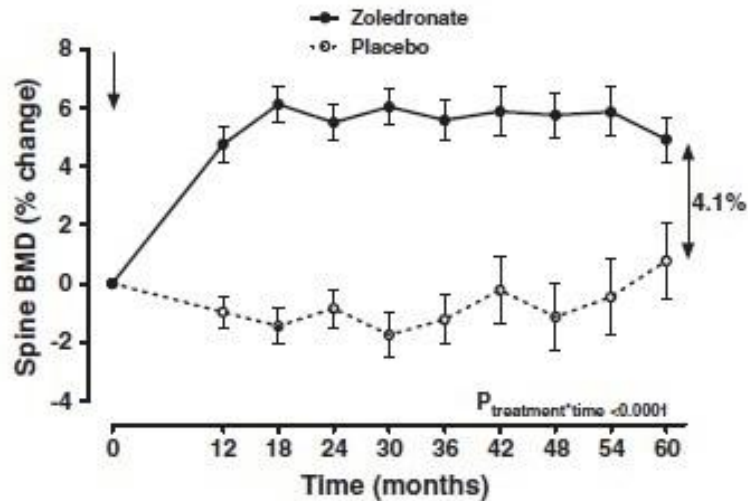
Effect of denosumab on bone mineral density in women receiving adjuvant aromatase inhibitors for non-metastatic breast cancer: subgroup analyses of a phase 3 study

Baseline covariate	Lumbar spine	Total hip	Femoral neck	1/3 radius
Duration of AI therapy				
≤6 months	5.4 (3.9, 6.8)*	3.7 (2.5, 5.0)*	3.6 (2.3, 4.8)*	3.8 (2.0, 5.5)*
>6 months	5.6 (4.7, 6.6)*	3.8 (3.0, 4.5)*	1.7 (0.6, 2.9)**	3.9 (2.7, 5.0)*
Type of AI therapy				
Non-steroidal	5.6 (4.7, 6.4)*	3.8 (3.1, 4.6)*	2.5 (1.5, 3.4)*	4.3 (3.3, 5.3)*
Steroidal	5.8 (3.7, 8.0)*	3.0 (1.4, 4.7)**	2.5 (0.3, 4.7)**	1.3 (-2.3, 4.8)
Prior tamoxifen				
Yes	5.3 (4.1, 6.5)*	4.3 (3.5, 5.1)*	2.6 (1.2, 4.0)**	3.8 (2.4, 5.1)*
No	5.8 (4.7, 6.8)*	3.3 (2.4, 4.3)*	2.4 (1.3, 3.6)*	3.9 (2.6, 5.3)*
Age				
<65 years	5.8 (4.8, 6.7)*	4.0 (3.2, 4.7)*	2.9 (1.8, 3.9)*	3.9 (2.8, 5.0)*
≥65 years	5.1 (3.7, 6.4)*	3.0 (1.6, 4.3)*	1.3 (-0.4, 2.9)	3.4 (1.4, 5.4)**
Time since menopause				
≤5 years	6.9 (5.3, 8.5)*	3.8 (2.8, 4.9)*	3.4 (1.7, 5.1)**	4.3 (2.5, 6.1)*
>5 years	5.1 (4.2, 6.0)*	3.8 (3.0, 4.6)*	2.2 (1.2, 3.3)*	3.9 (2.7, 5.1)*
Body mass index				
<25	5.5 (4.2, 6.8)*	3.5 (2.5, 4.5)*	2.6 (1.3, 3.9)**	3.4 (1.7, 5.0)**
≥25	5.6 (4.6, 6.6)*	3.9 (3.0, 4.8)*	2.4 (1.2, 3.6)*	4.2 (3.0, 5.4)*
T-score				
≤-1.0 ^a	5.4 (4.4, 6.4)*	3.8 (2.8, 4.7)*	2.1 (1.1, 3.2)**	4.0 (2.8, 5.1)*
>-1.0 ^a	5.8 (4.6, 7.0)*	3.8 (2.8, 4.7)*	3.7 (2.3, 5.0)*	3.2 (1.6, 4.8)**

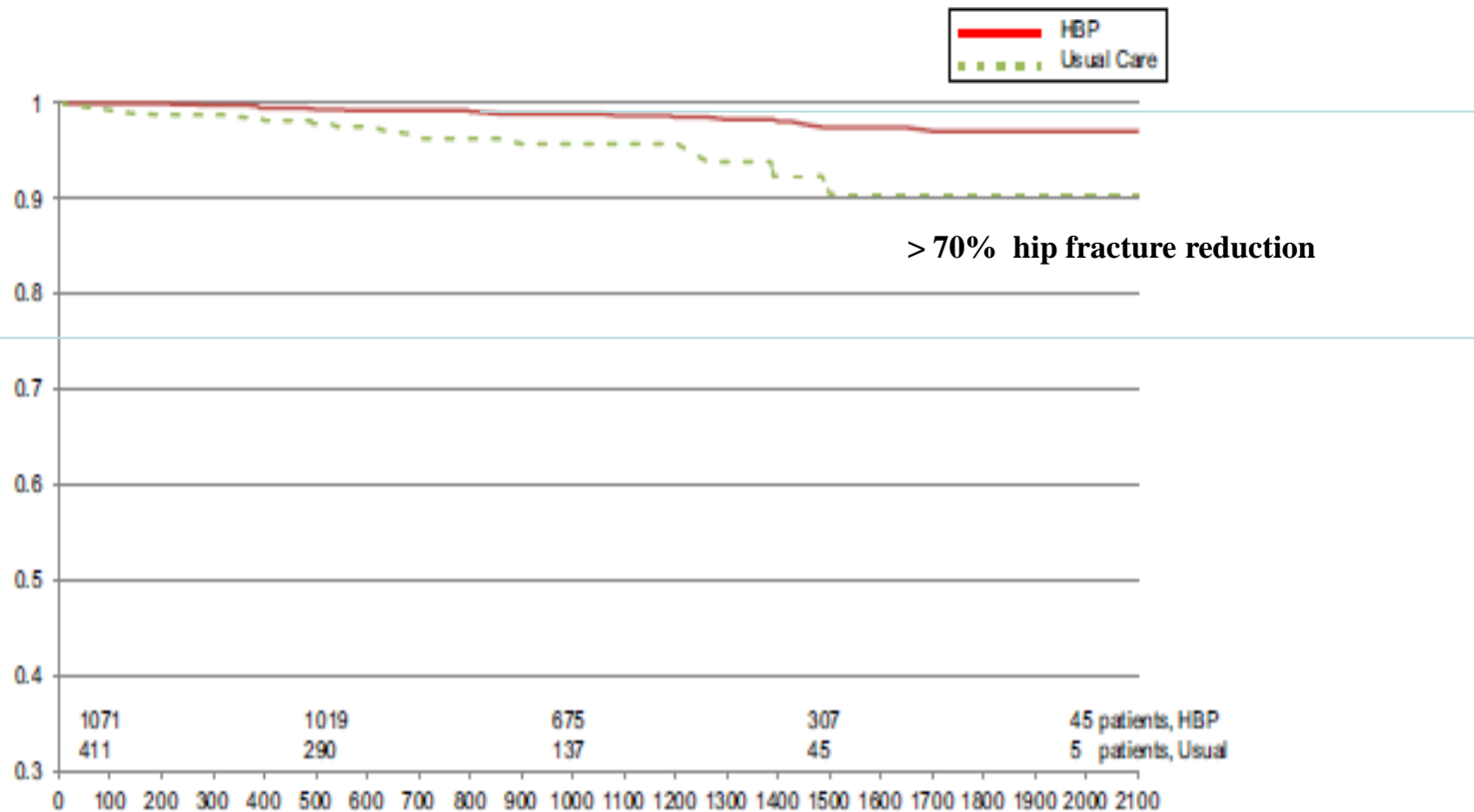
RRR of fractures in ad hoc pivotal trials



Persistenza d'effetto di singola infusione di acido zoledronico 5 mg/5anni

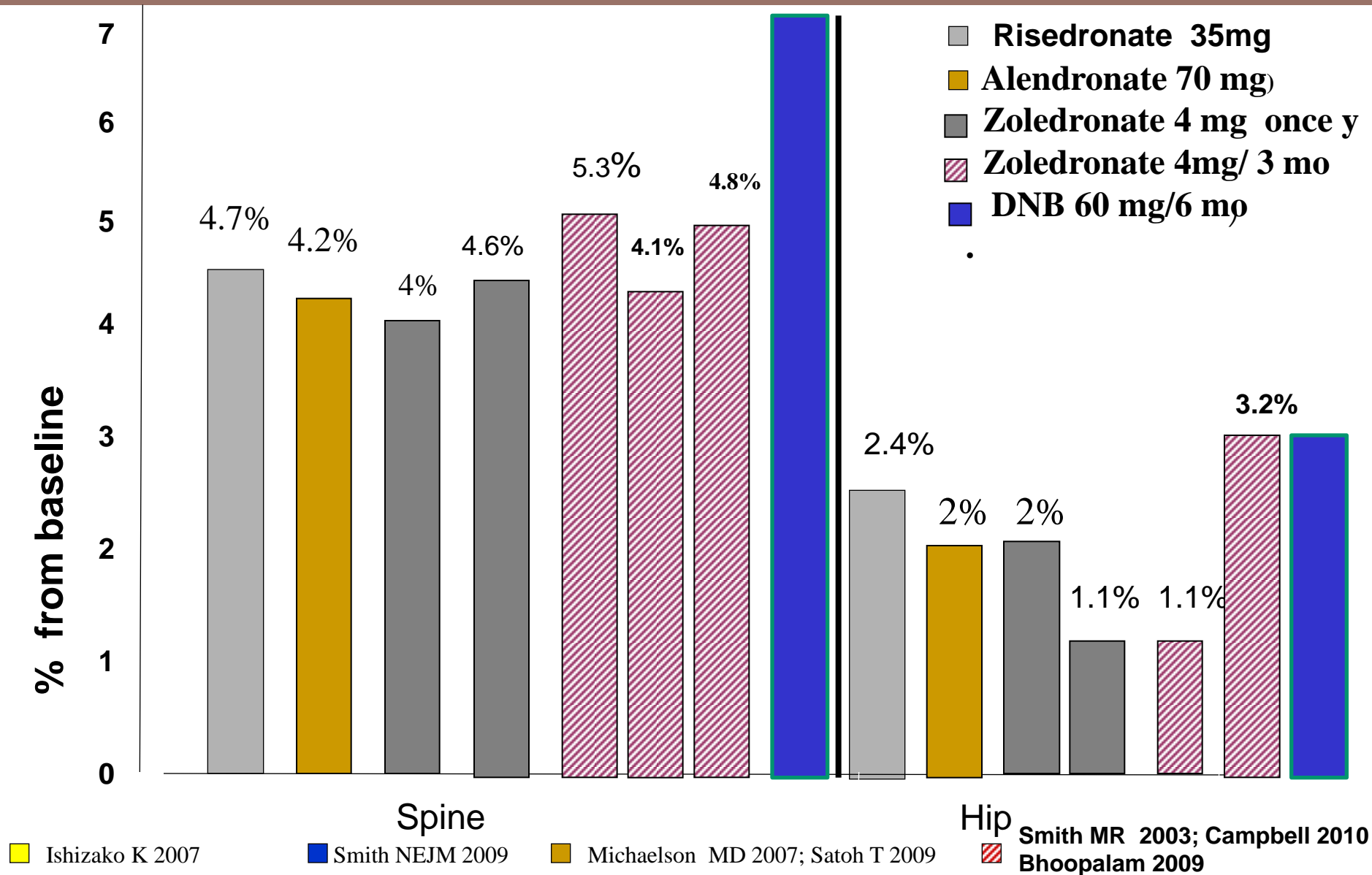


Osteoporosis Management Program Decreases Incidence of Hip Fracture in Patients With Prostate Cancer Receiving Androgen Deprivation Therapy



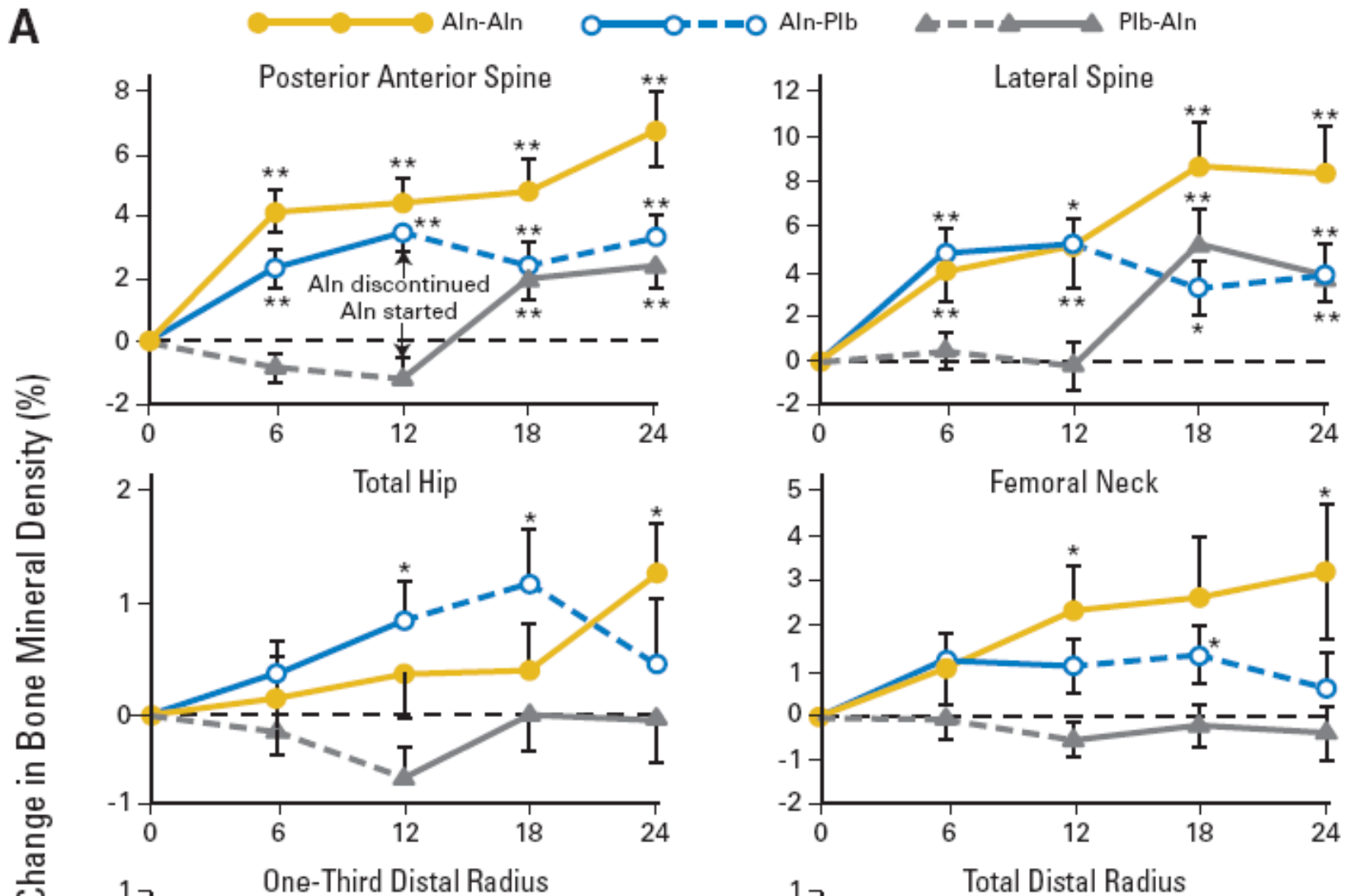
. Kaplan-Meier curve showing hip fracture-free survival. HBP, Healthy Bones Program. (Color version available online.)

Bone target agents: effects on BMD in Men with ADT Induced Bone Loss



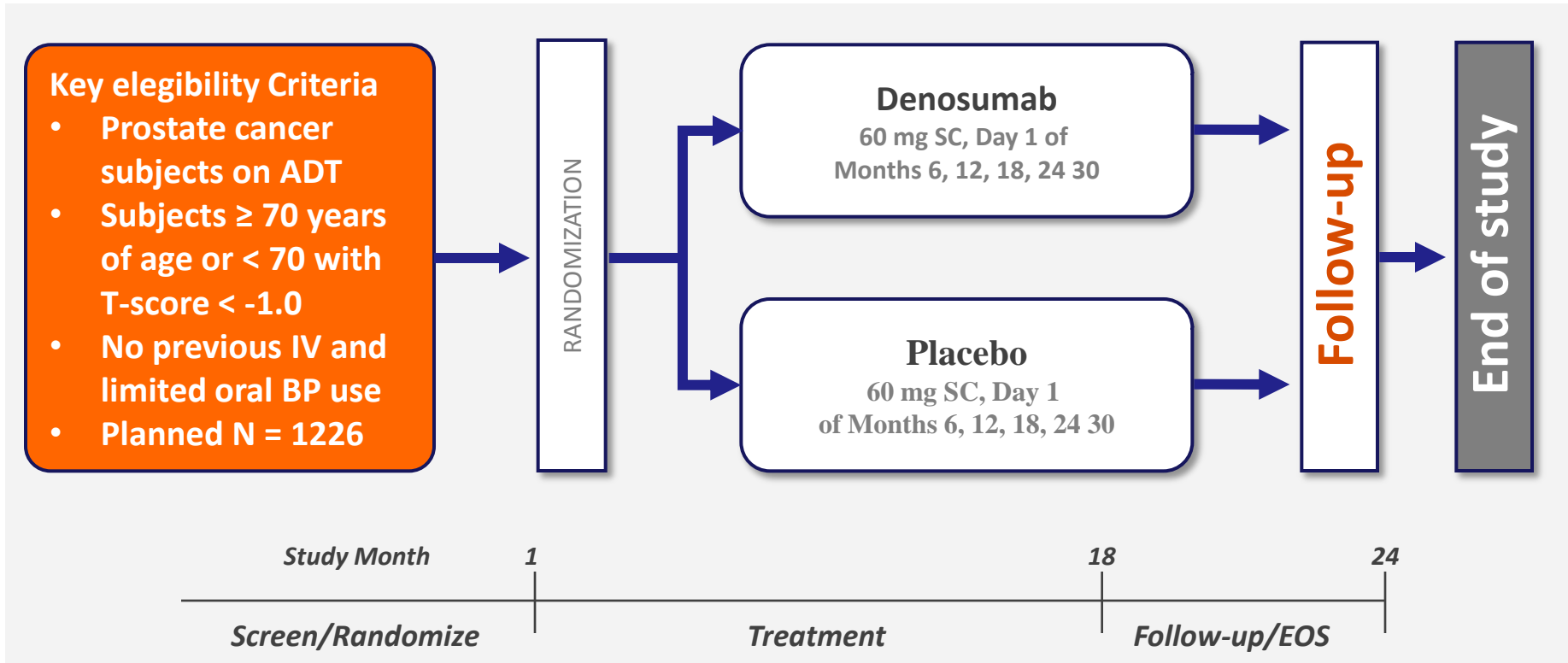
Skeletal Health After Continuation, Withdrawal, or Delay of Alendronate in Men With Prostate Cancer Undergoing Androgen-Deprivation Therapy

A



Prevention of Cancer Treatment Induced Bone Loss (CTIBL)

HALT-PC (20040138): Denosumab in ADT-Treated Prostate Cancer



Primary Endpoint: Percentage Change in Lumbar Spine BMD at Month 24

Secondary Objectives: Efficacy of denosumab compared with placebo on: Fractures and BMD at nonvertebral sites

Smith M et al. N Engl J Med, 361:745-55, 2009.

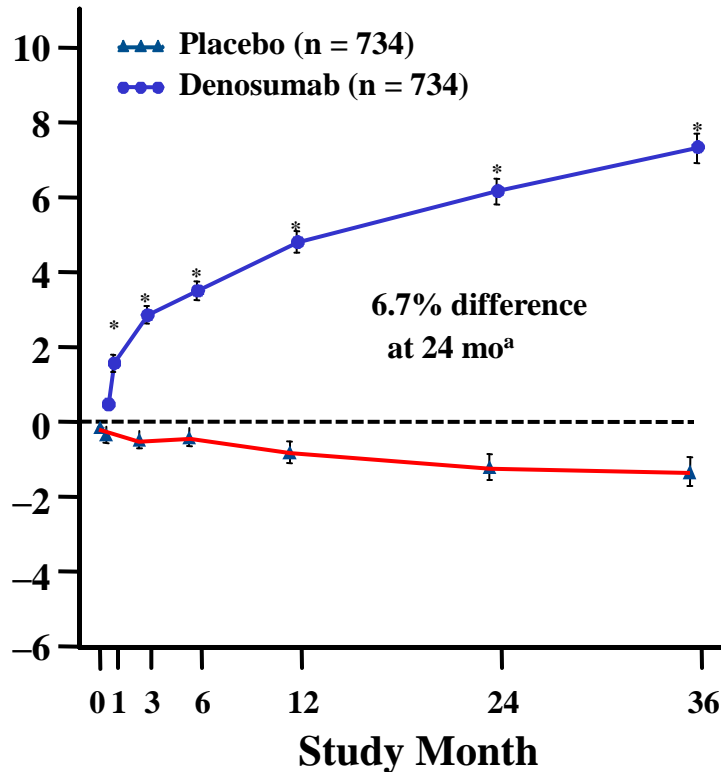
Enrico Cortesi

Baseline Characteristics (cont'd)

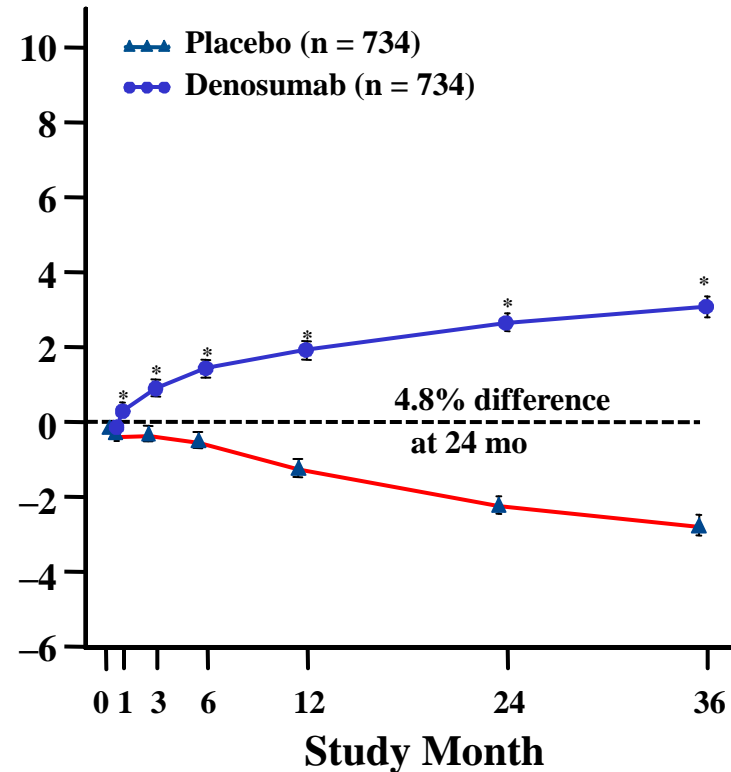
Characteristic	Placebo (n = 734)	SC Denosumab (n = 734)
Subjects with T-score < -2.5 at any site ^a , n (%)	111 (15.1)	105 (14.3)
Lumbar spine BMD T-score		
Median (range)	-0.6 (-4.8-7.6)	-0.5 (-6.8-7.3)
Mean ±SD	-0.4 ± 1.8	-0.3 ± 1.8
Total hip BMD T-score		
Median (range)	-1.0 (-3.6-3.1)	-0.9 (-3.6-3.3)
Mean ±SD	-0.9 ± 1.0	-0.9 ± 1.0
Femoral neck BMD T-score		
Median (range)	-1.5 (-3.5-1.9)	-1.5 (-3.8-3.0)
Mean ±SD	-1.4 ± 0.9	-1.4 ± 0.9

Primary/Secondary End Point: BMD

Lumbar Spine



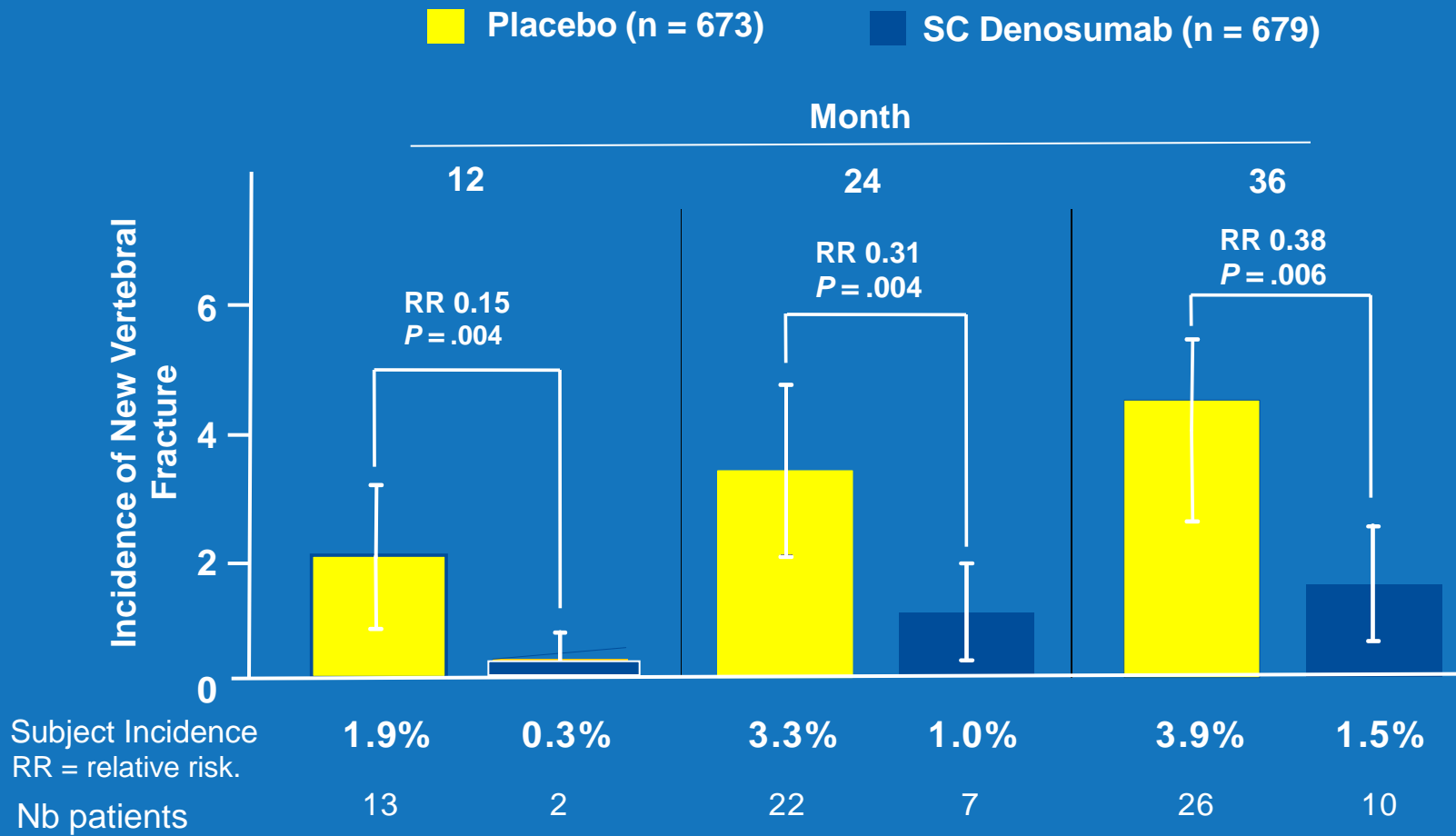
Total Hip



* $P \leq .001$ at all measured sites

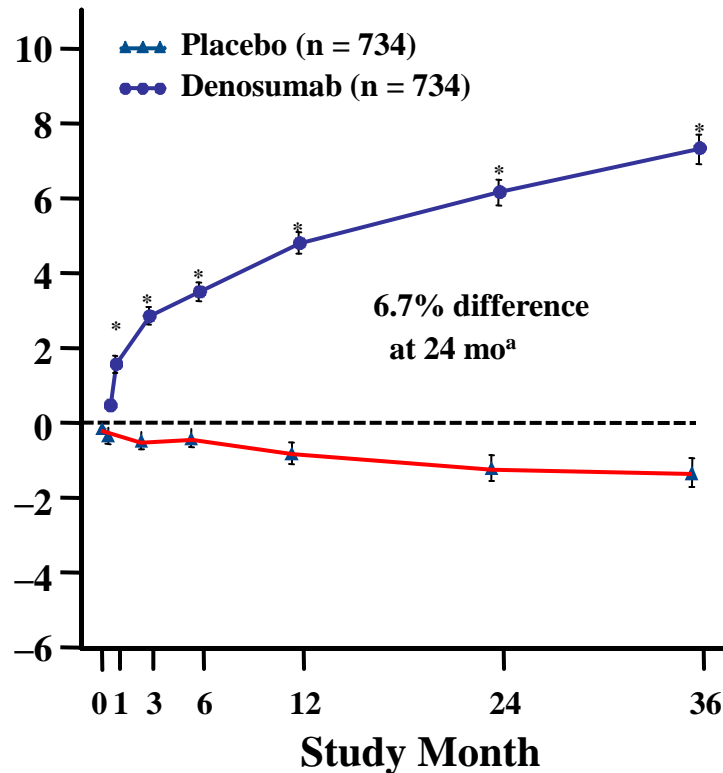
^aPrimary end point

Secondary End Point: New Vertebral Fractures

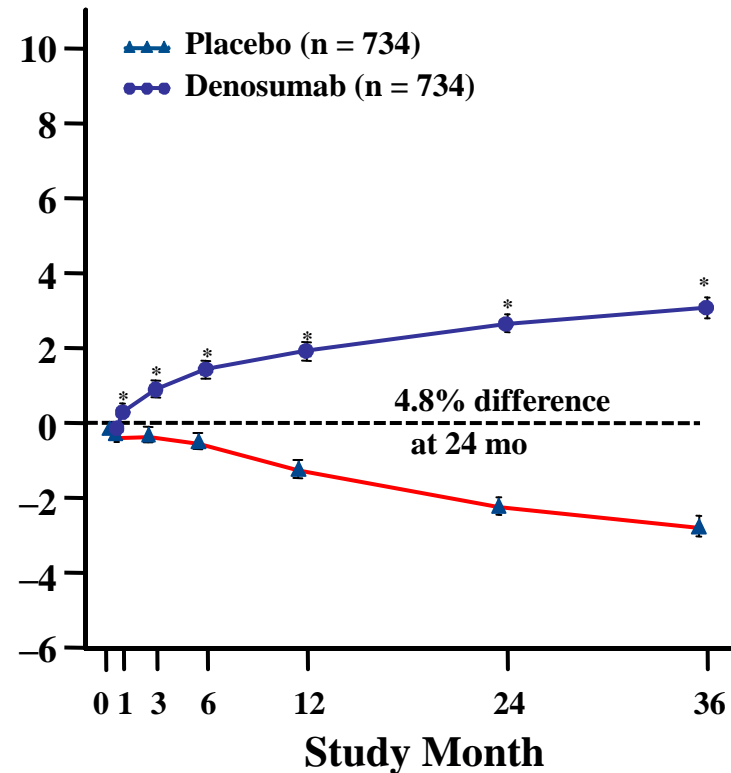


Primary/Secondary End Point: BMD

Lumbar Spine



Total Hip

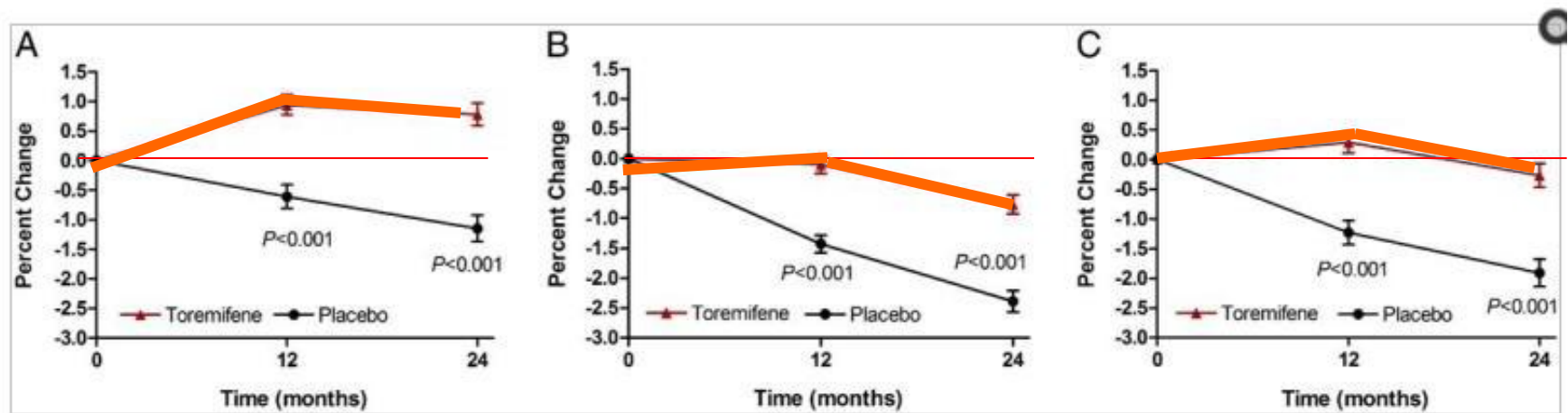


* $P \leq .001$ at all measured sites

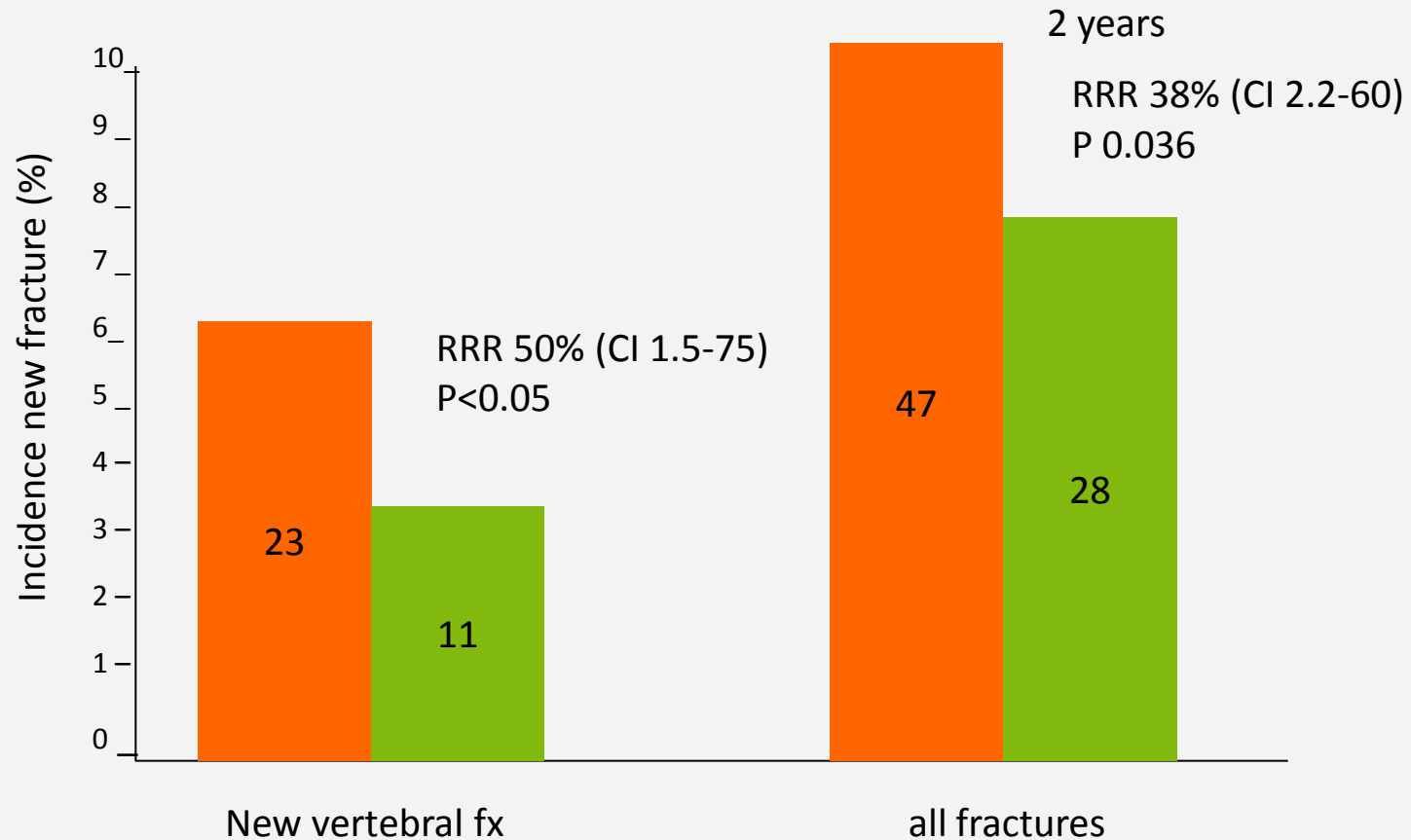
^aPrimary end point

TOREMIFENE REDUCES FRACTURE RISK IN MEN RECEIVING ANDROGEN DEPRIVATION THERAPY FOR PROSTATE CANCER

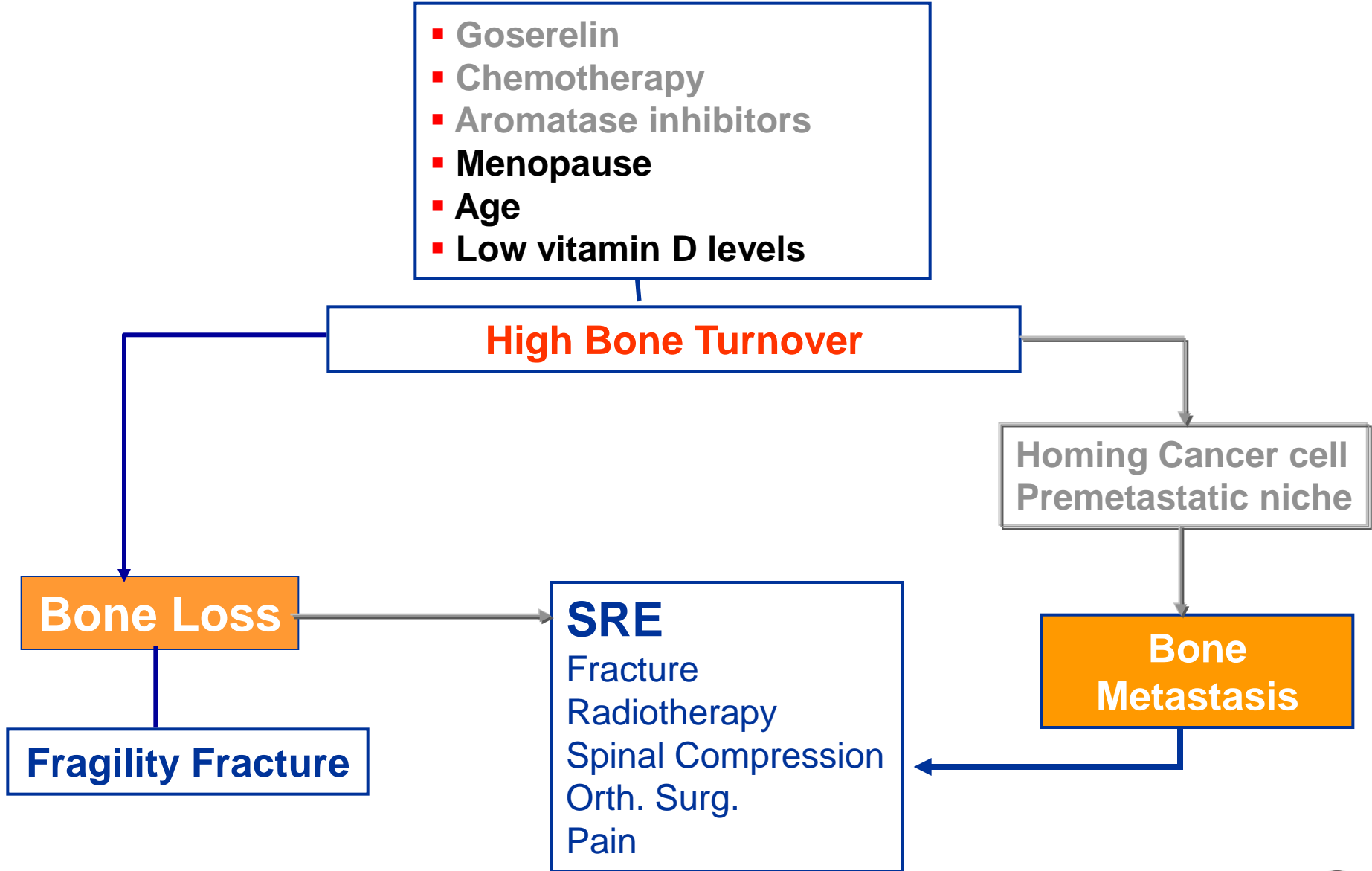
Changes in BMD of lumbar spine (A), total hip (B) and femoral neck (C)



TOREMIFENE REDUCES FRACTURE RISK IN MEN RECEIVING ANDROGEN DEPRIVATION THERAPY FOR PROSTATE CANCER



The “Bone Health” *concept* in Cancer Patients



CONCLUSIONI

- **LA normalizzazione del turnover (entro range 30-40 anni/premenopausale) permette la prevenzione della perdita di massa ossea , la prevenzione delle fratture (probabilmente l'effetto adiuvante (DSF e OS)**
- **Questo si puo' realizzare con amino BP e denosumab (indicazioni, rimborsabilità) alle dosi utilizzate per l'OP.Postmenop.**