



VII CONGRESSO NAZIONALE
SOCIETÀ ITALIANA DI OSTEONCOLOGIA
20-21 OTTOBRE 2022 ROMA

CON IL PATROCINIO DI



SAPIENZA
UNIVERSITÀ DI ROMA

Novità
sulla CTIBL indotta da terapia ormonale nei
pazienti con tumore mammario e prostatico e
relativo trattamento

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Università di Verona



Conflitti di interesse

- Ai sensi dell'art. 3.3 sul conflitto di interessi, pag 17 del Regolamento Applicativo Stato-Regioni del 5/11/2009, dichiaro che negli ultimi 2 anni ho avuto rapporti diretti di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:
 - Abiogen
 - Amgen
 - Chiesi
 - Sandoz
 - UCB pharma

Summary of existing evidence for adiposity in the life course and cancer risk

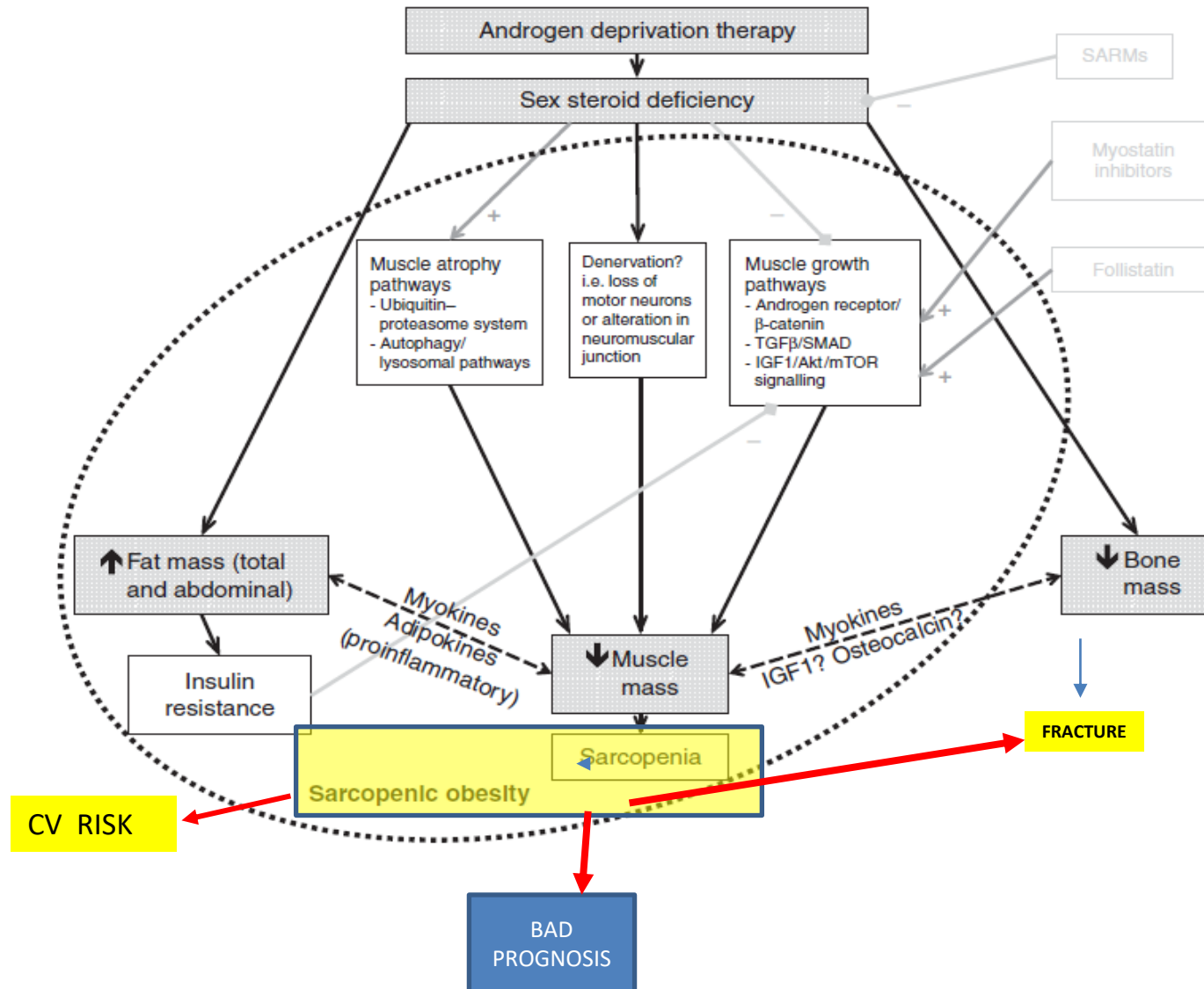
From: [The timing of adiposity and changes in the life course on the risk of cancer](#)

Cancer	Early life body weight (childhood, adolescence, early adulthood)	Adulthood body weight
Premenopausal breast cancer ¹	–	–
Postmenopausal breast cancer ²	–	+
Endometrial cancer ²	+	+ +
Aggressive prostate cancer ³	–	+
Colorectal cancer ⁴	+	+
Liver cancer	+	+
Pancreatic cancer	+ +	+
Kidney cancer	+	+

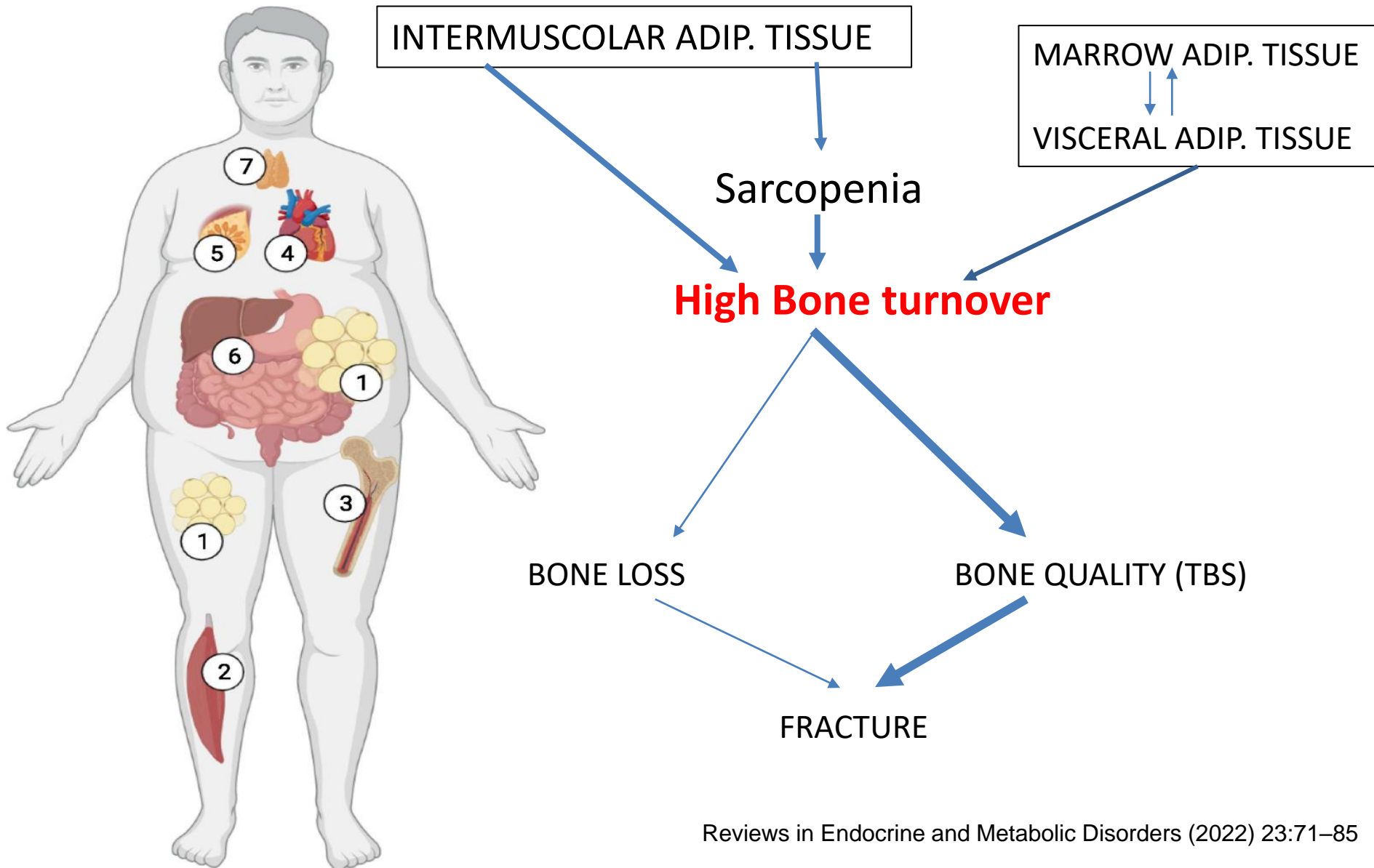
Visceral obesity and incident cancer and cardiovascular disease: An integrative review of the epidemiological evidence

Author/year	Design Population	Outcome	Visceral obesity measurement	Visceral obesity results	Summary
Breast cancer					
Agnoli (2010) ³²	Case-control study postmenopausal women, ORDET cohort. Follow-up 13.5 years Cases: 163 women Four matched controls per case	Breast cancer postmenopausal	WC > 86 cm	WC Adjusted RR = 1.23 (0.83–1.81)	WC Women—NS (post)
Agnoli (2015) ¹⁹	Case-cohort study 22 494 women 593 breast cancer cases EPIC—Italian centres European Prospective Investigation Into Cancer and Nutrition Followed up 15 years	Breast cancer (BC) Postmenopausal and premenopausal	WC > 80 cm	Whole cohort HR = 1.07(0.82–1.39) Premenopausal 0.77 (0.51–1.16) Postmenopausal 1.04 (0.69–1.57)	WC Women—NS (pre and post)
Bandera (2015) ³³	Case-control, AMBER Consortium, African American (AA) women Cases: 2104 ER+, 1070 ER– cases (including 491 TN cases) 12 060 controls	Breast cancer Premenopausal and postmenopausal Categorized according to hormone receptor status ER+, ER– and TN (ER–, PR– and HER2–)	WHR	Premenopausal ER+ tumours OR = 1.35 (1.01–1.80) Postmenopausal all tumour subtypes combined OR = 1.26 (1.02–1.56).	WHR Women risk (pre and post)
Park (2017) ³⁴	Cohort Sister Study, nationwide prospective cohort 50 884 participants aged 35 to 74 years old	Breast cancer Premenopausal and postmenopausal	WC (88 cm) WHR (0.85)	Premenopausal with normal BMI WC—NA WHR HR = 1.52 (0.89–2.61) Postmenopausal with normal BMI WC HR = 1.58 (1.02–2.46) WHR HR = 1.38 (1.02–1.85) Premenopausal with BMI ≥ 25 (overweight/obese)	Women Normal BMI WC and WHR—NS (pre) WC and WHR—risk (post) BMI ≥ 25 WC and WHR—NS (pre) WC and WHR—risk (post)
Chen (2016) ¹¹	Meta-analysis of prospective studies	Breast cancer Premenopausal and postmenopausal	WC per 10 cm WHR per 0.1 unit	Premenopausal BC—adjusted RRs WC RR = 1.05 (0.99–1.10) WHR RR = 1.07 (0.95–1.21) Postmenopausal BC WC RR = 1.06 (1.04–1.09)	Women WC—risk (post) WC—NS (pre) WHR—NS (pre and post)

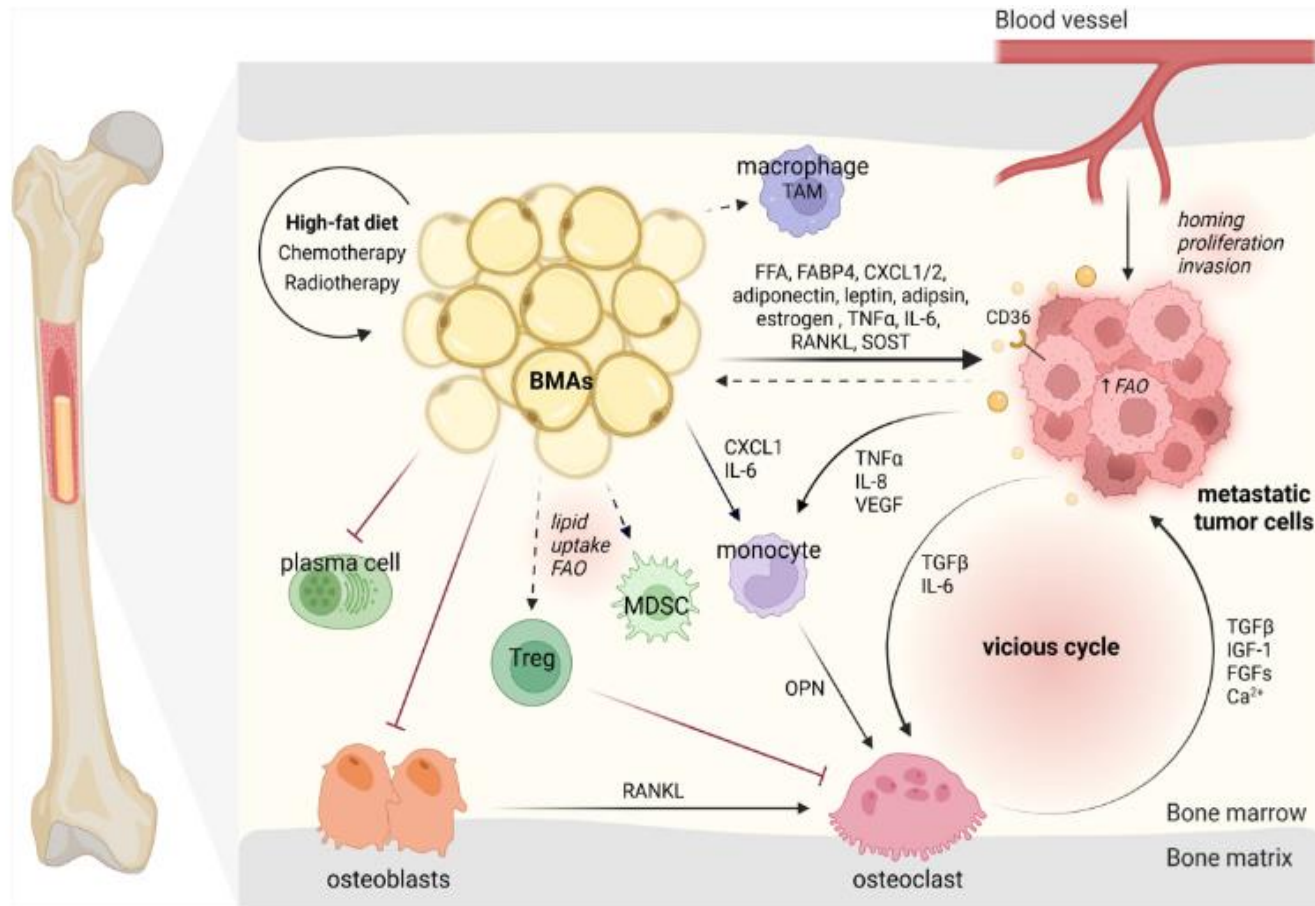
Osteosarcopenia: where bone, muscle, and fat collide

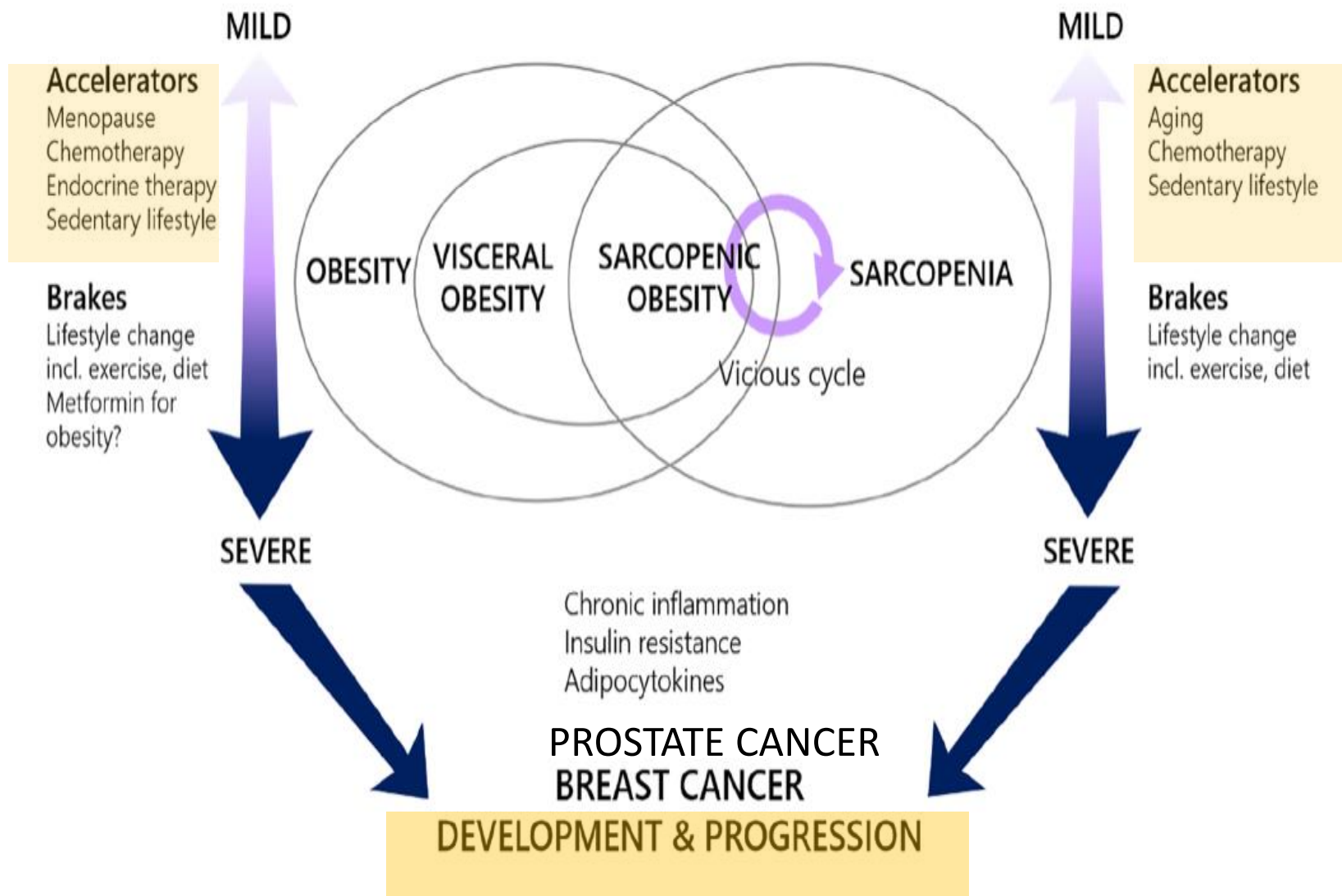


OBESITY= LOW GRADE INFLAMMATION

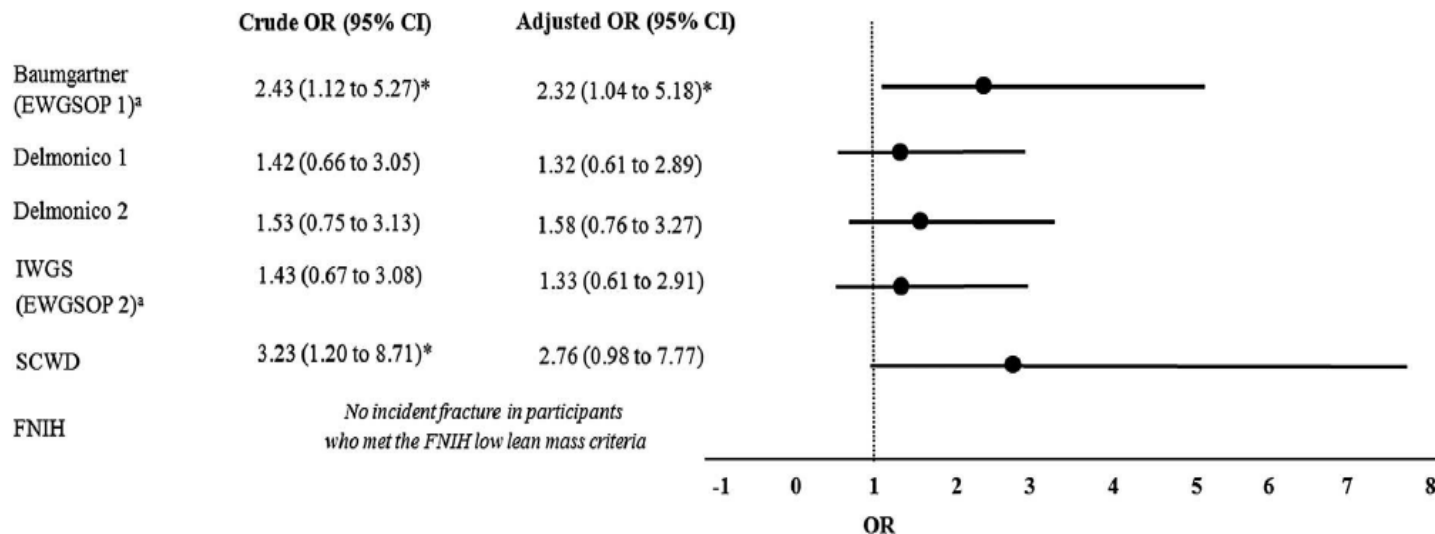


Distinct Metabolism of Bone Marrow Adipocytes and their Role in Bone Metastasis



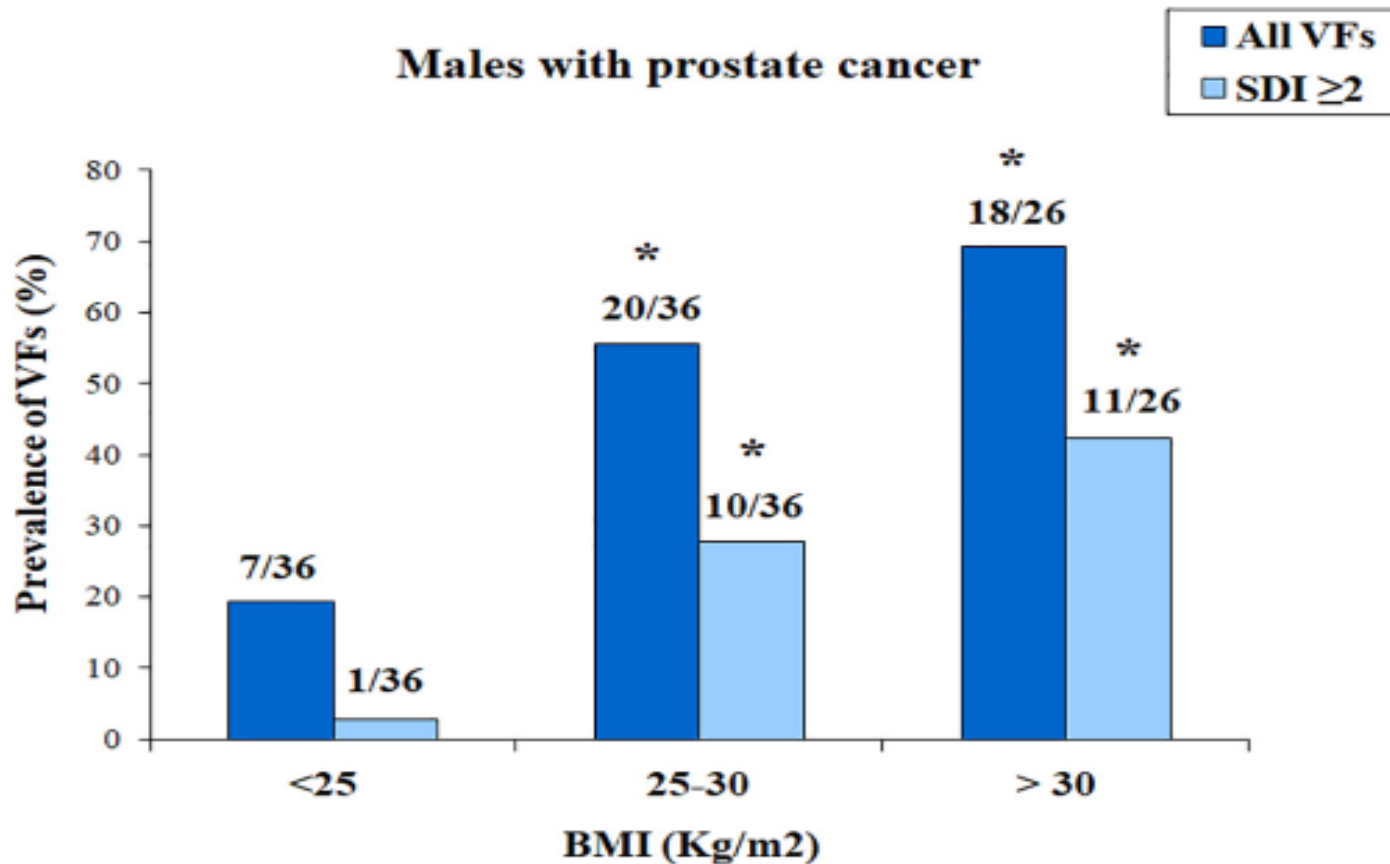


Low Lean Mass Predicts Incident Fractures Independently From FRAX: a Prospective Cohort Study of Recent Retirees



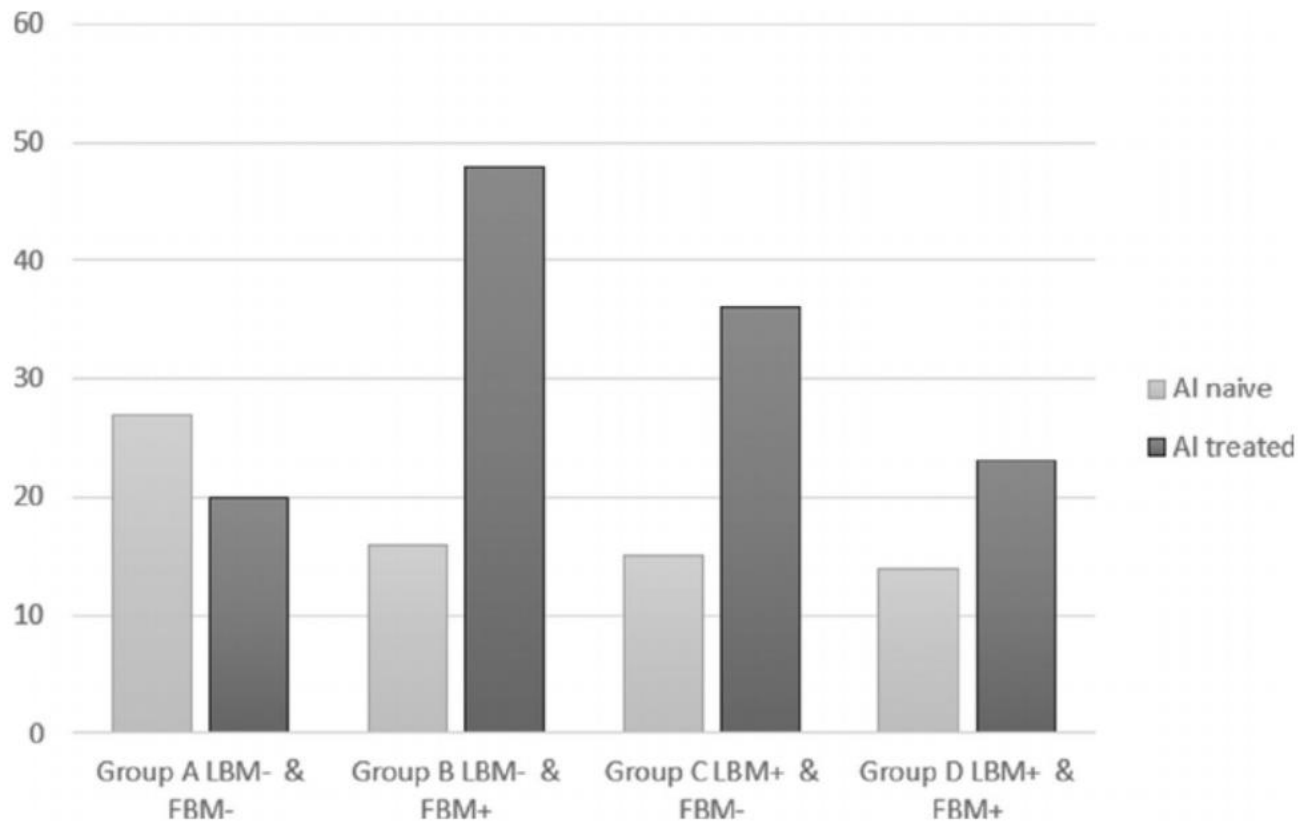
sarcopenia, and incidence of low trauma fracture over a 3-year follow-up ($n = 913$). Adjustment was made for gender, age, length of follow-up and FRAX probability with femoral neck BMD. OR = odds ratio; CI = confidence interval; EWGSOP = European Working Group on Sarcopenia in Older People;

Prevalence of total vertebral fractures (VFs) and multiple/moderate/severe (SDI ≥ 2) in prostate cancer under androgen-deprivation therapies and stratified for body mass index (BMI).

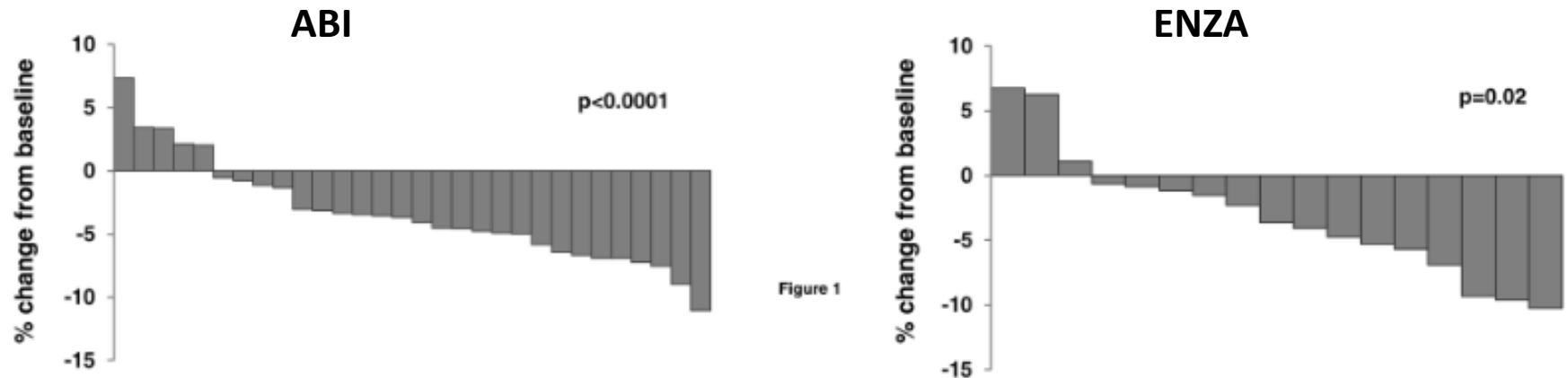


The Interaction of Lean Body Mass With Fat Body Mass Is Associated With Vertebral Fracture Prevalence in Women With Early Breast Cancer Undergoing Aromatase Inhibitor Therapy

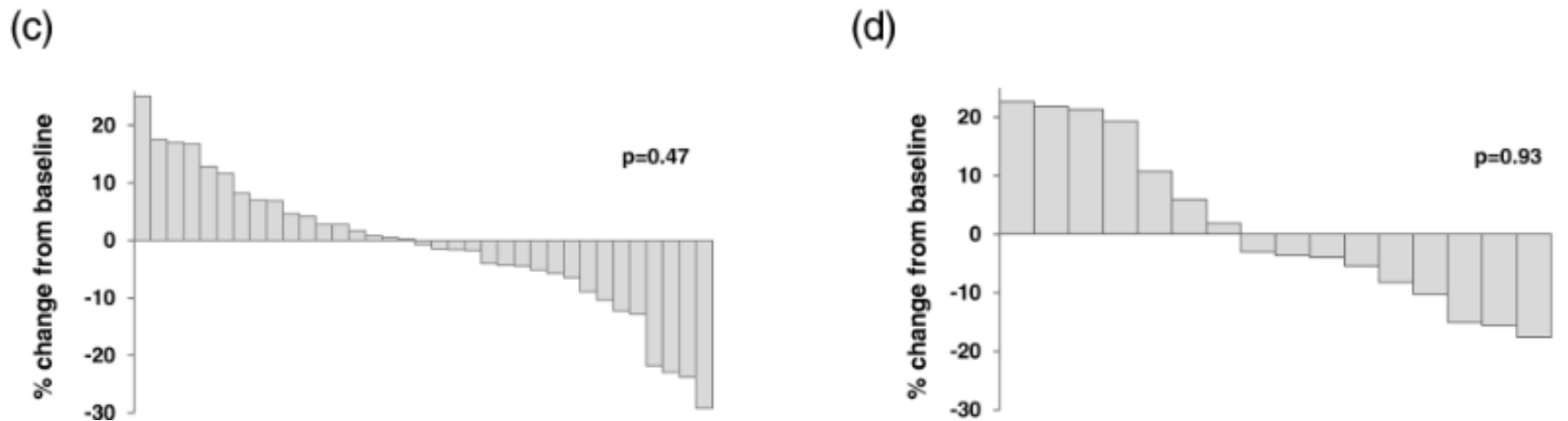
Vertebral fracture prevalence stratified according to body composition in AI-naïve and AI-treated patients



Influence of abiraterone and enzalutamide on body composition in patients with metastatic castration resistant prostate cancer

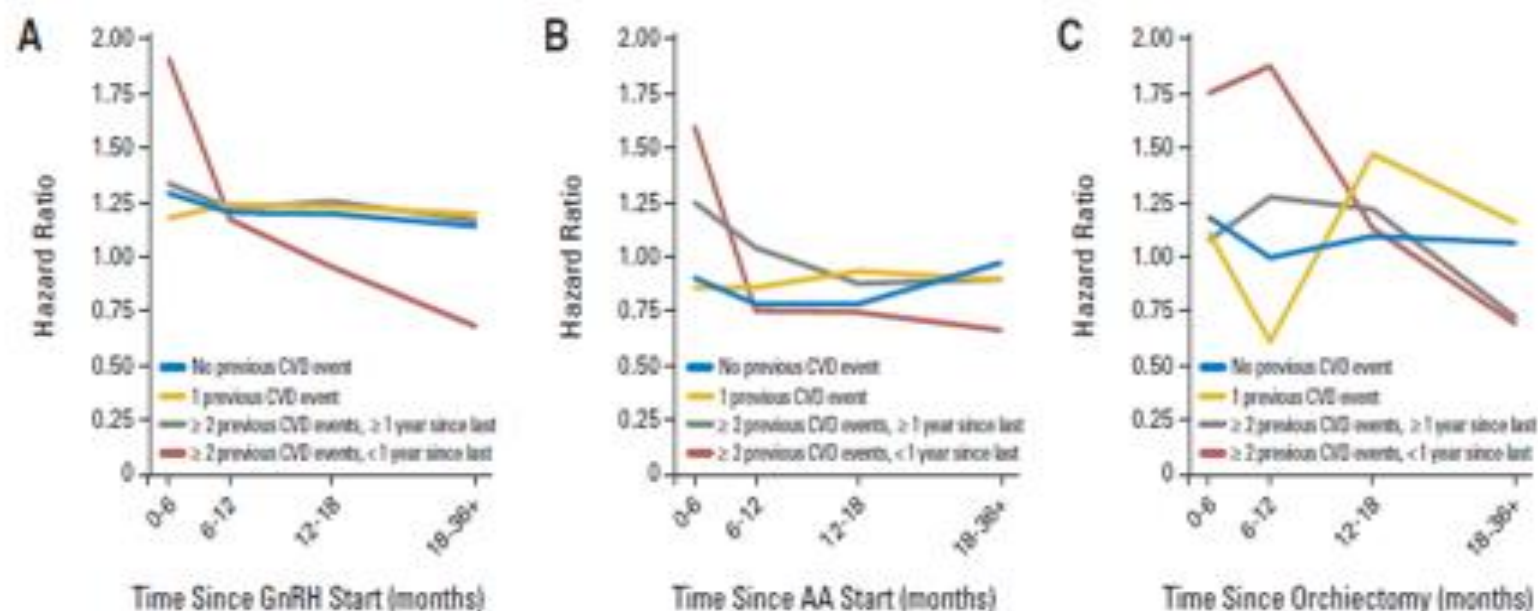


MUSCLE MASS




SUBCUT. FAT MASS

Risk and Timing of Cardiovascular Disease After Androgen-Deprivation Therapy in Men With Prostate Cancer

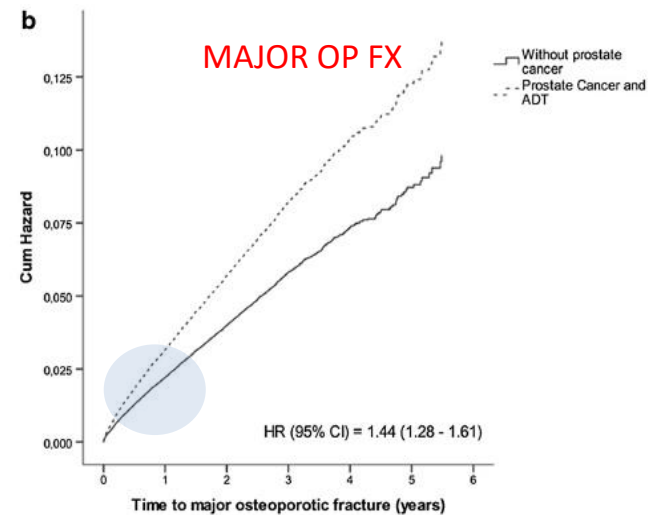
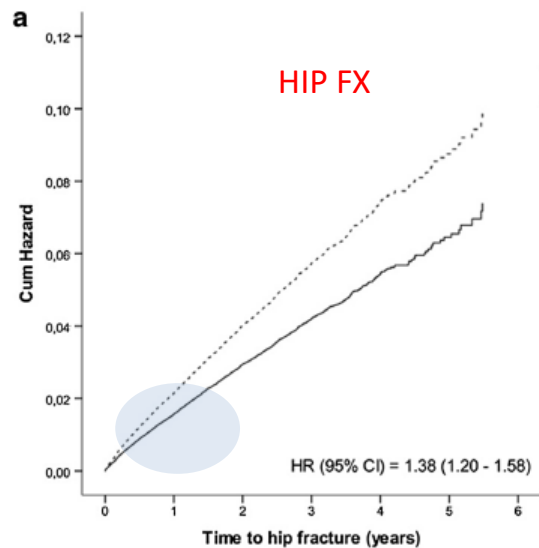


Sean O'Farrell, Hans Garmo, Lars Holmberg, Jan Adolfsson, Pär Stattin, and Mieke Van Hemelrijck

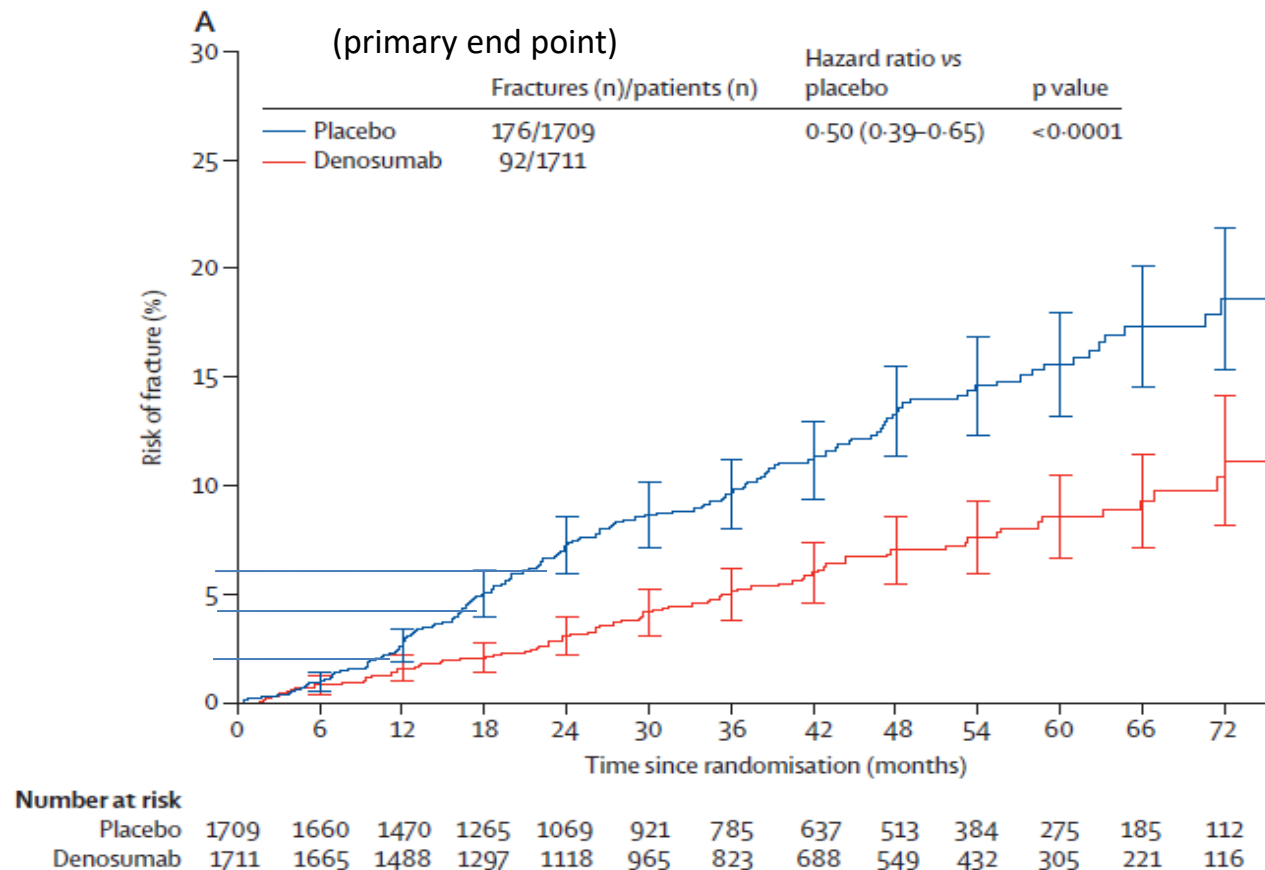
Patients with prostate cancer and androgen deprivation therapy have increased risk of fractures—a study from the fractures and fall injuries in the elderly cohort (FRAILCO)

M. Wallander^{1,2} • K. F. Axelsson^{2,3} • D. Lundh⁴ • M. Lorentzon^{2,5} 

179,744 men (79.1 ± 7.9 years (mean \pm SD))



Adjuvant denosumab in breast cancer (ABCSCG-18): a multicentre, randomised, double-blind, placebo- controlled trial





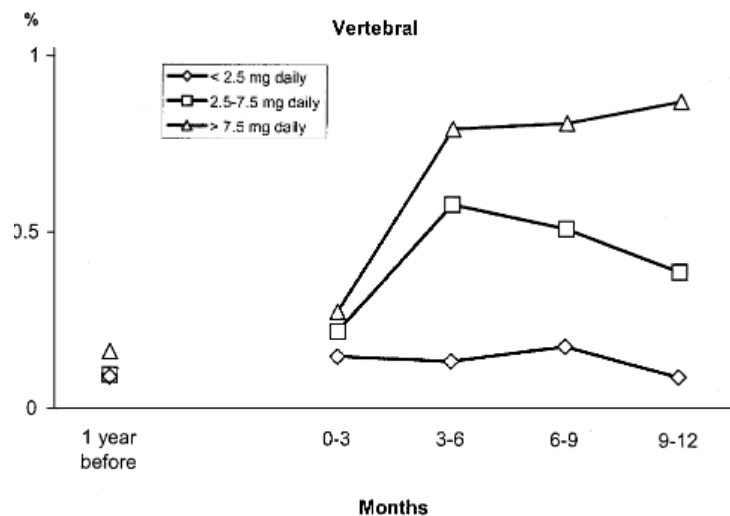
- Prevenzione primaria in donne in menopausa o uomini di età ≥ 50 anni a rischio elevato di frattura a causa di almeno una delle condizioni sottoelencate:

Condizione	I scelta ^a	II scelta	III scelta
Trattamento in atto o previsto per >3 mesi con prednisone equivalente ≥ 5 mg/die	Alendronato (\pm vit.D), Risedronato, Zoledronato ^d	Denosumab ^e	_____
Trattamento in corso di blocco ormonale adiuvante in donne con carcinoma mammario o uomini con carcinoma prostatico	Alendronato (\pm vit.D), Risedronato, Zoledronato ^d Denosumab ^e	_____	_____
T-score colonna o femore ^c ≤ -4	Alendronato (\pm vit.D), Risedronato	Denosumab ^e Zoledronato ^d Ibandronato, Raloxifene, Bazedoxifene	
T-score colonna o femore ^c ≤ -3 + almeno una delle seguenti condizioni: 1) Familiarità per fratture di vertebre o femore 2) Comorbidità a rischio di frattura (artrite reumatoide o altre connettiviti, diabete,			

Linee Guida AIOM 2015-2022
Linee Guida SIOMMMS 2015

IMMINENT RISK

Risk of non-vertebral and vertebral fracture
before and during
first year of CS therapy stratified by dose



Van Staa et al. Osteoporos Int (2002) 13:777-787

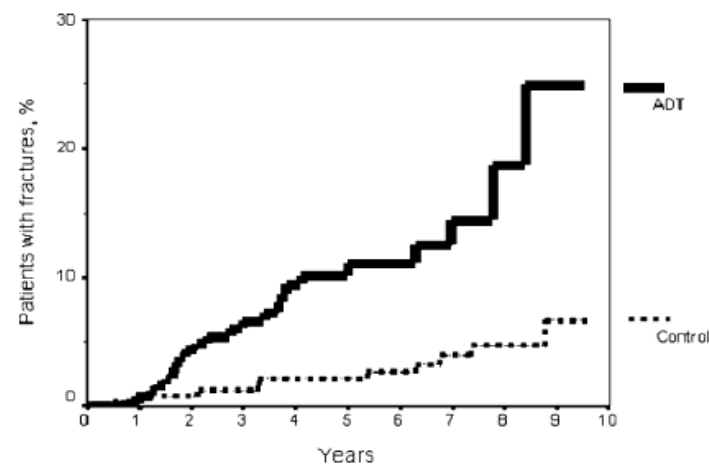
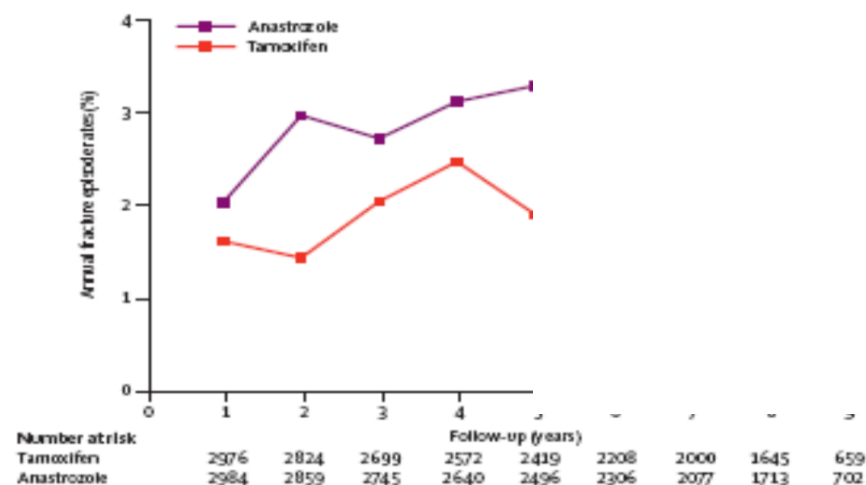


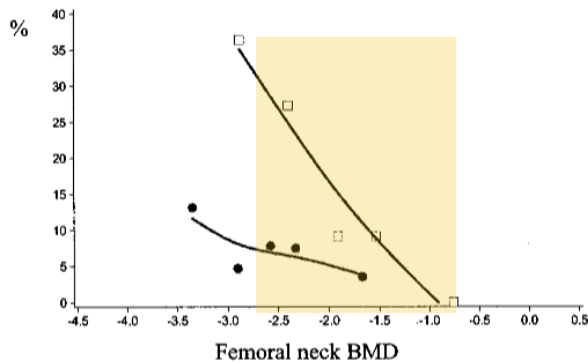
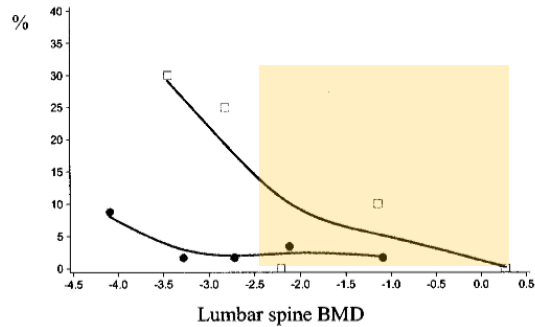
Fig. 1 Kaplan-Meier plots of patients with fractures after ADT (patient group) or diagnosis (control group)



Lancet Oncol 2008

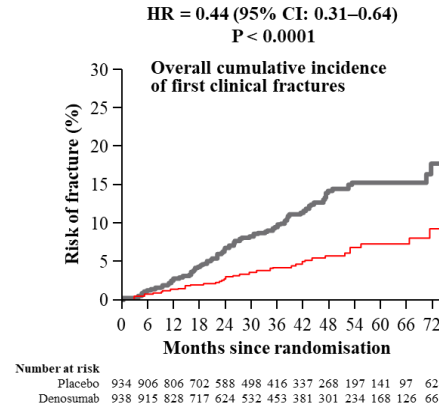
ABCSG-18: denosumab significantly reduced the incidence of clinical fractures vs placebo regardless of baseline BMD

Bone Density Threshold and Other Predictors of Vertebral Fracture in Patients Receiving Oral Glucocorticoid Therapy

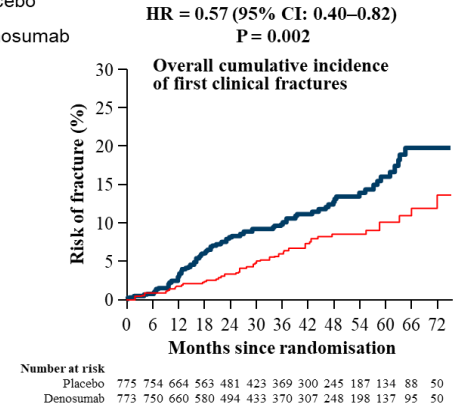


ARTHRITIS & RHEUMATISM
Vol. 48, No. 11, November 2003, pp 3224–3229

Normal BMD (baseline T-score ≥ -1.0)

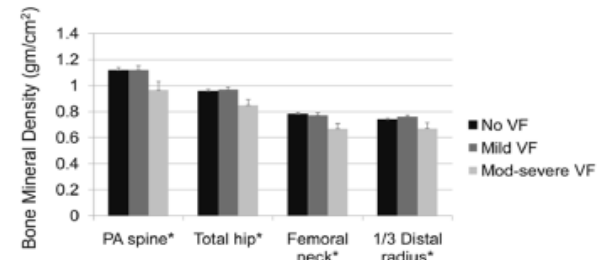
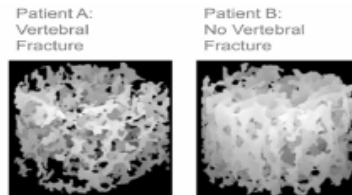


Osteopenia (baseline T-score < -1.0)



Vertebral Fractures and Trabecular Microstructure in Men with Prostate Cancer on Androgen Deprivation Therapy

Susan L. Greenspan, MD¹, Julie Wagner, PA-C¹, Joel B. Nelson, MD², Subashan Perera, PhD³, Cynthia Britton, MD⁴, and Neil M. Resnick, MD⁵



PC + ADT



AOUI Verona

centro per le Malattie del Metabolismo Minerale e Osteonologia
Responsabile : Prof. F. Bertoldo

11/04/2019 - 69 anni - Uomo - 83Kg - 174cm

XXXX - XXXX

Storia familiare frattura femore e vertebre: No

Pregresse fratture vertebrali o di femore: No

Altre pregresse fratture osteoporotiche: No

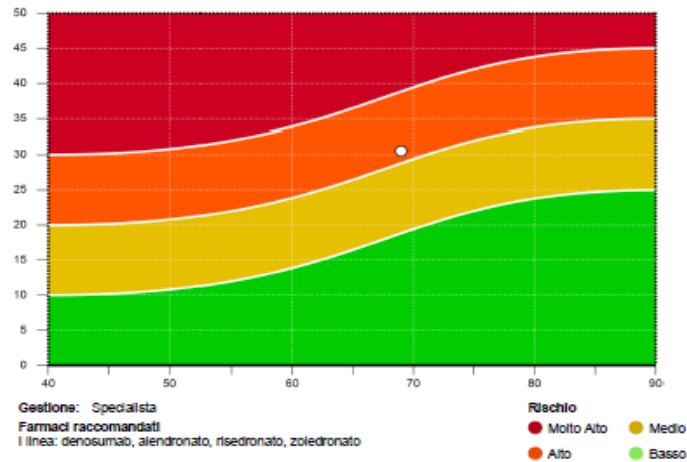
Comorbidità che aumentano il rischio di frattura: No

Farmaci che aumentano il rischio di frattura: Blocco ormonale adiuvante

TScore: -0,80 (colonna)

Nota 79: Si

Rischio di fratture maggiori a 10 anni: 31%



Terapia prescritta: denosumab

La prescrizione va fatta nel rispetto delle indicazioni e avvertenze delle note 79 e delle schede tecniche dei singoli farmaci

BMD T-score: -0.8

OSTEOPOROTIC MAN



AOUI Verona

centro per le Malattie del Metabolismo Minerale e Osteonologia
Responsabile : Prof. F. Bertoldo

11/04/2019 - 68 anni - Uomo - 83Kg - 174cm

XX

Storia familiare frattura femore e vertebre: No

Pregresse fratture vertebrali o di femore: No

Altre pregresse fratture osteoporotiche: No

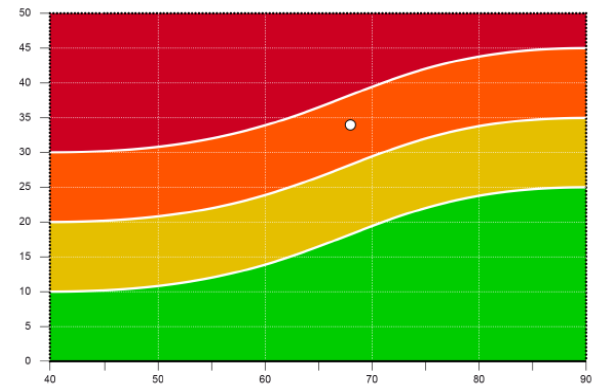
Comorbidità che aumentano il rischio di frattura: No

Farmaci che aumentano il rischio di frattura: No

TScore: -5,00 (colonna)

Nota 79: Si

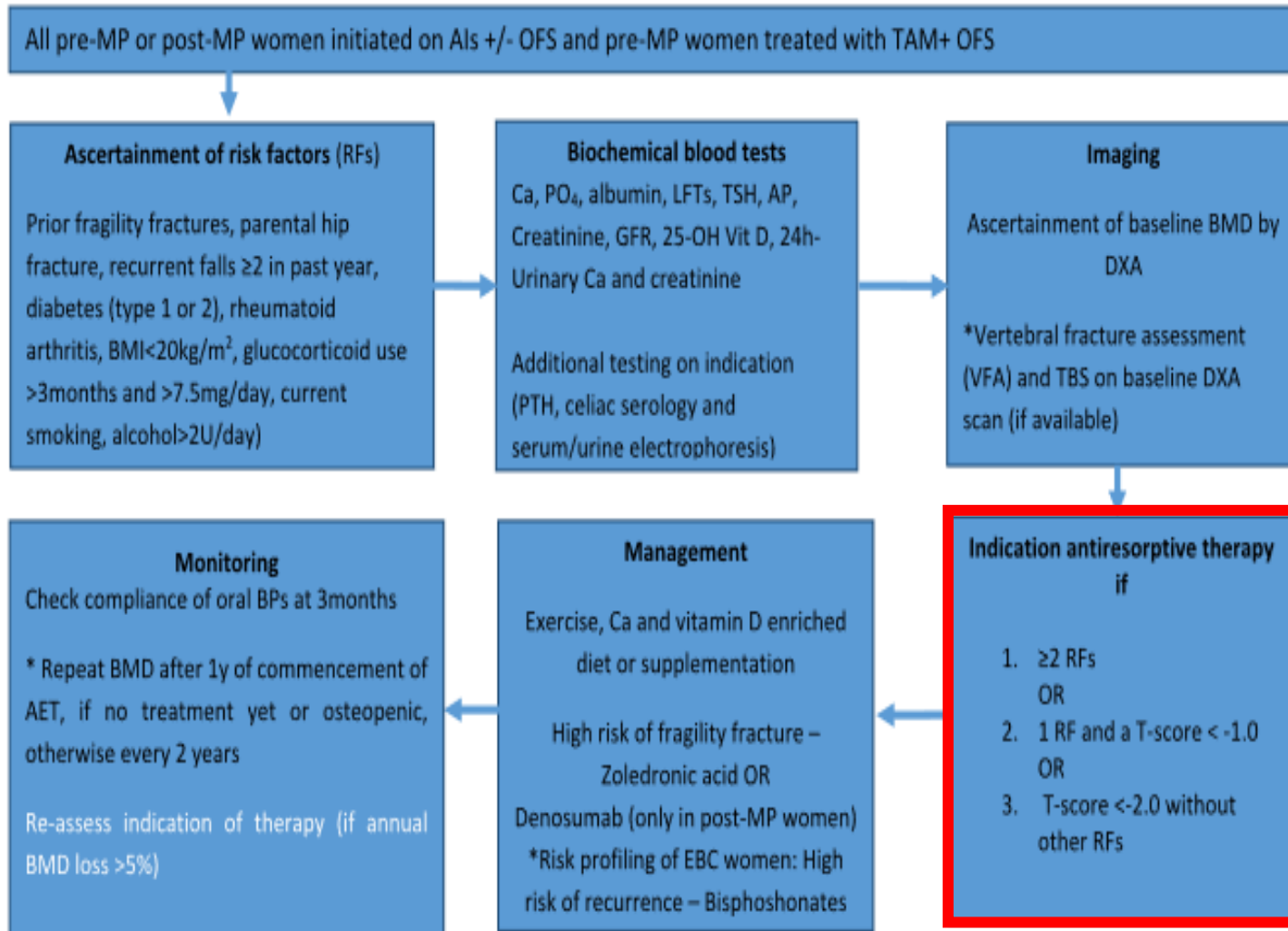
Rischio di fratture maggiori a 10 anni: 34%



BMD T-score -5

<https://defracalc>

Management algorithm for EBC women on adjuvant endocrine therapy



Evaluation of bone fragility in endocrine disorders

Eller-Vainicher C, Falchetti A, Gennari L, Cairoli E, Bertoldo F, Vescini F, Scillitani A, Chiodini I

Table 3 Fragility fracture risk and most frequent findings in the evaluation of bone mineral density and bone quality in the endocrine-related forms of osteoporosis.

Disorder	VFx risk	Hip Fx risk	DXA	TBS	Available data from other imaging tools
Obesity	↑	N.A.	N/High	Reduced	MRS for BMF estimates
Type 2 diabetes	↑	↑	N/High	Reduced	QUS, HSA, QUS, QCT, HR-pQCT, MRI, MRS for BMF estimates
Type 1 diabetes	↑↑	↑↑↑	↓↓	Reduced	QUS, QCT, HR-pQCT
Acromegaly	↑↑	N.A.	N	Reduced	HR-pQCT
Overt hyperthyroidism	↑	↑	↓↓	NA	NA
Subclinical Hyperthyroidism	↑*	↑	↓↓	Reduced	QCT, HR-pQCT, HAS
Primary Hyperparathyroidism	↑	↑	↓	Reduced	QUS
Overt Hypercortisolism	↑↑↑	↑	↓↓	Reduced	QUS, QCT
Subclinical hypercortisolism	↑↑	N.A.	↓/N	Reduced	QUS, QCT
Hypogonadism in CTIBL	↑↑	↑↑	↓/N	Reduced	MRI, QCT, MDCT

AZIENDA OSPEDALIERA INTEGRATA VERONA
UOC di Radiologia BR - UOC Medicina Generale e Malattie Aterotrombotiche e Degenerative

Telefono: USF Malattie del Metabolismo Minerale e Scheletrico

Nome: XXXXXXXXXX FLAVIA
ID paziente: V050N7
Data di nascita: 13 giugno 1948

Sesso: Femmina
Etnia: Bianca

Height: 152.0 cm
Peso: 64.0 kg
Età: 73

Medico di riferimento:

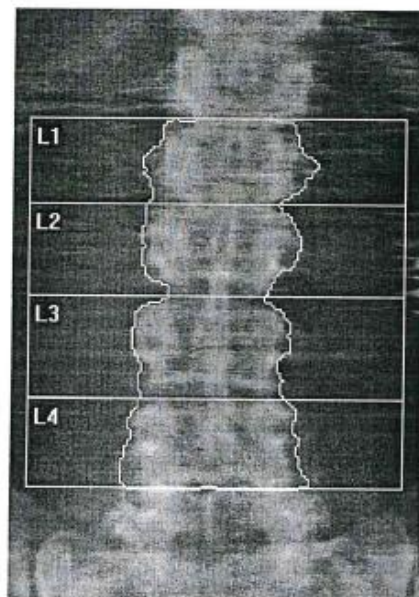
Informazioni sulla scansione:

Data scansione: 28 Aprile 2022 ID: A0428220R
Tipo di scansione: a Lombare
Analisi: 28 aprile 2022 11:33 Versione 13.6.1:7
Col. T
Operatore:
Modello: Horizon W (S/N 300201M)
Commento:

Riepilogo risultati DXA:

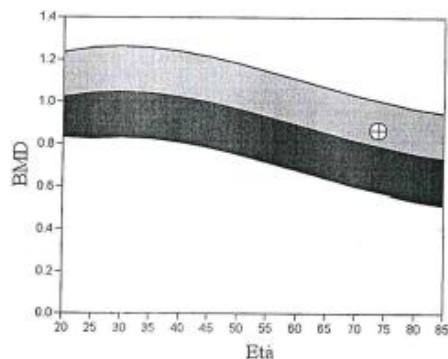
Regione	Area (cm ²)	BMC (g)	BMD (g/cm ²)	T - score	Z - score
L1	12.43	11.18	0.900	-0.8	1.3
L2	12.77	11.44	0.896	-1.2	1.1
L3	14.36	10.82	0.753	-3.0	-0.6
L4	15.41	14.23	0.923	-1.3	1.2
Totale	54.97	47.67	0.867	-1.6	0.7

Totale BMD CV 1.0%, ACF = 1.027, BCF = 1.009, TH = 7.052

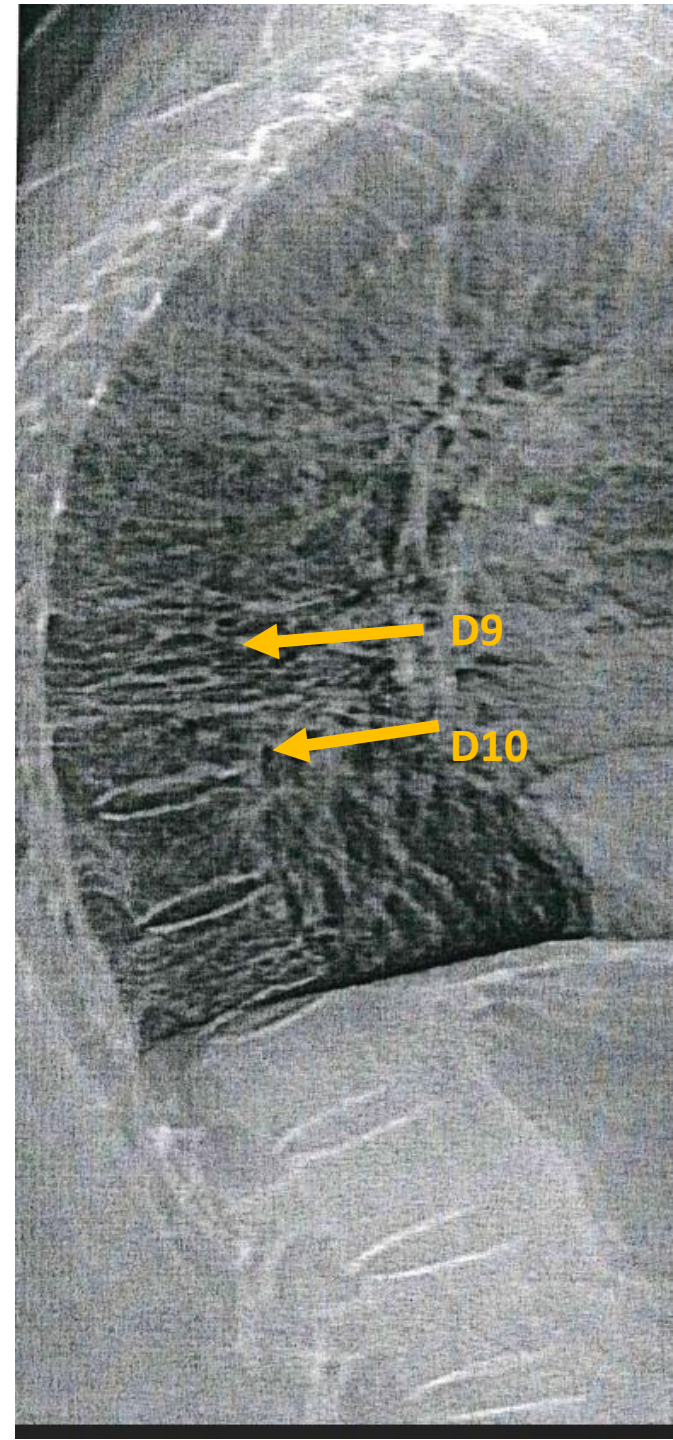


k = 1.134, d0 = 46.1
116 x 117

Totale



Commento:



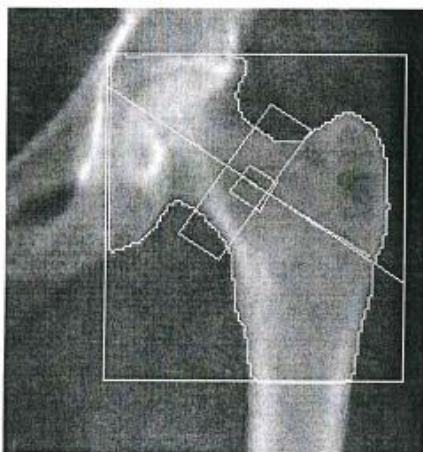
Telefono: USF Malattie del Metabolismo Minerale e Scheletrico

Nome: XXXXXXXXXX FLAVIA
ID paziente: V036N7
Data di nascita: 13 giugno 1948

Sesso: Femmina
Etnia: Bianca

Height: 152.0 cm
Peso: 64.0 kg
Età: 73

Medico di riferimento:



k = 1.140, d0 = 47.9
90 x 102
COLLO: 49 x 15

Informazioni sulla scansione:

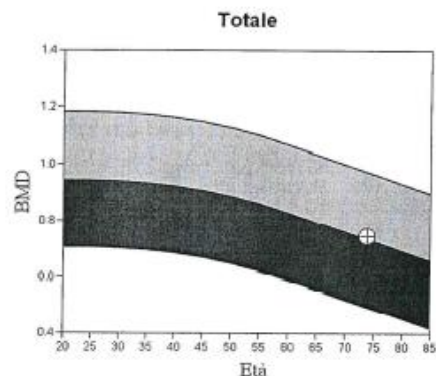
Data scansione: 28 Aprile 2022 ID: A0428220S
Tipo di scansione: x anca sinistra
Analisi: 28 aprile 2022 11:32 Versione 13.6.1:7
Anca

Operatore:
Modello: Horizon W (S/N 300201M)
Commento:

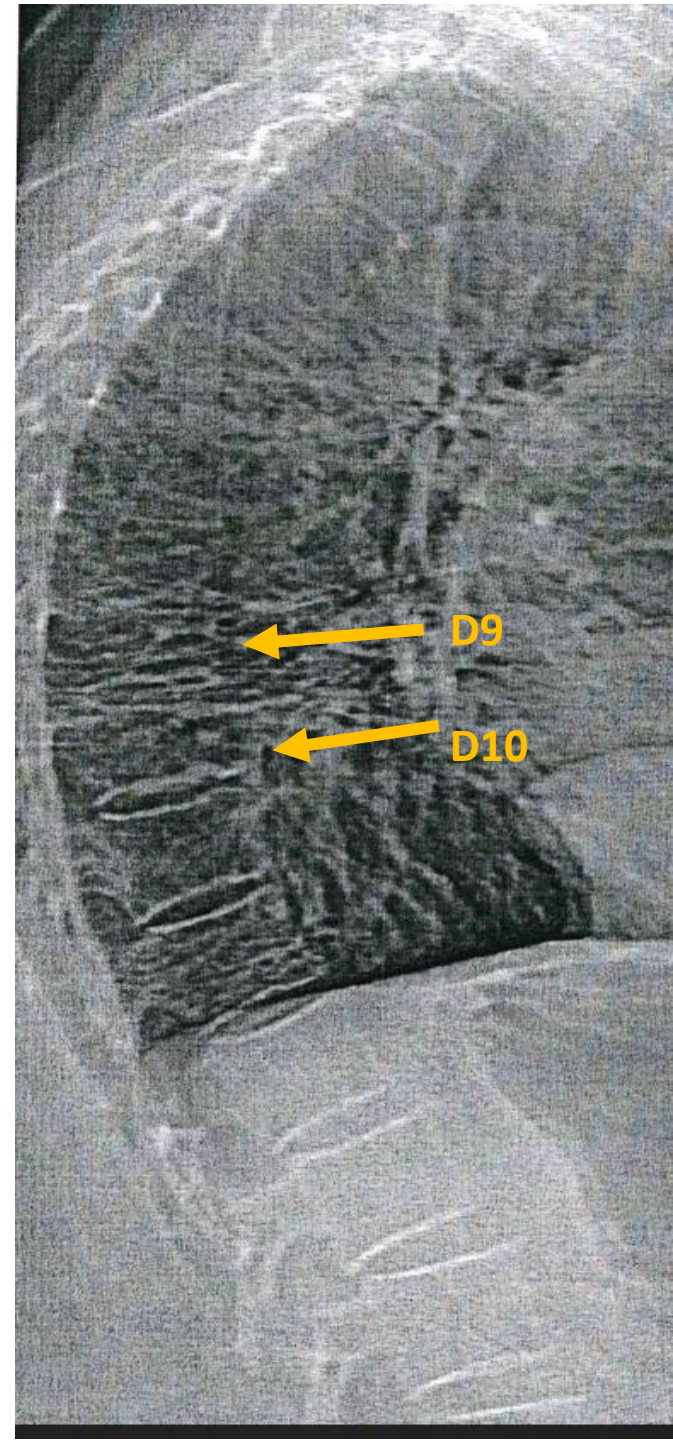
Riepilogo risultati DXA:

Regione	Area (cm ²)	BMC (g)	BMD (g/cm ²)	T-score	Z-score
Collo	5.09	3.28	0.643	-1.9	0.2
Totale	34.05	25.33	0.744	-1.6	0.1

Totale BMD CV 1.0%, ACF = 1.027, BCF = 1.009, TH = 6.403



Commento:



Paziente: XXXXXXXXXX FLAVIA

Data di nascita: 06/13/1948 73.9 anni

Altezza / Peso: 152.0 cm / 64.0 kg

Sesso / Etnia: Donna / Bianca

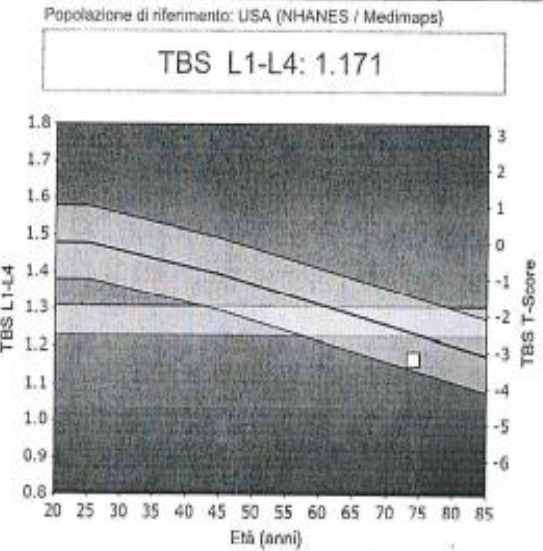
Id paziente: V036N7

Data di acquisizione: 04/28/2022

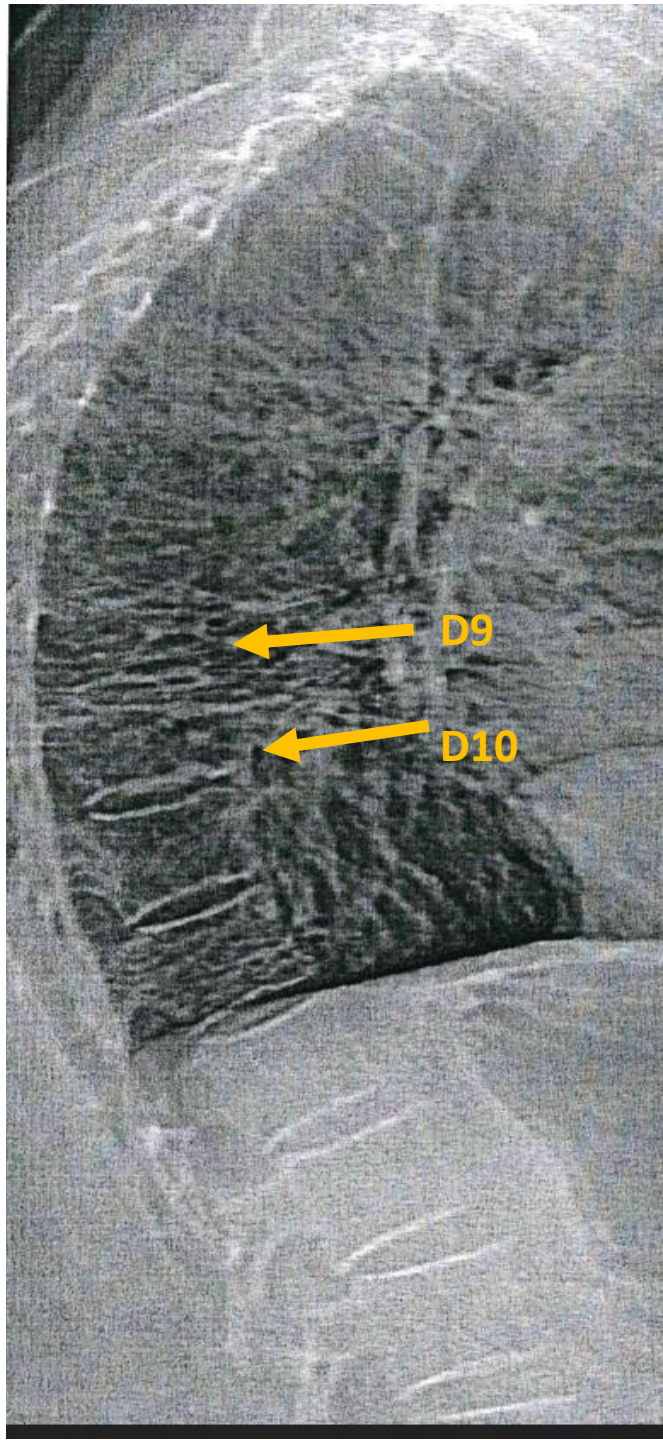
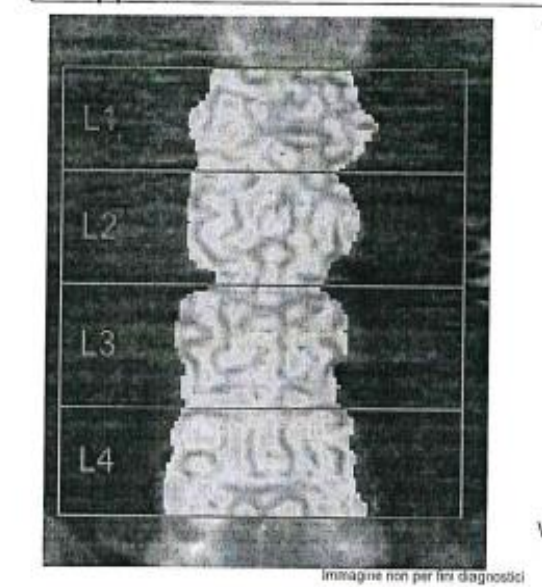
Medico Prescrivente:

REFERTO ESAME TBS COLONNA AP

Grafico di riferimento TBS



Mappatura TBS



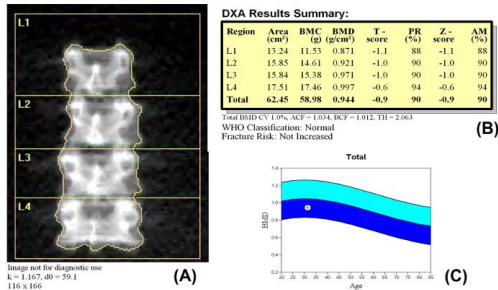
Risultati aggiuntivi

Regione	TBS	TBS T-score	TBS Z-score	BMD
L1	1.093	---	---	0.900
L2	1.186	---	---	0.896
L3	1.074	---	---	0.753
L4	1.333	---	---	0.923
L1-L4	1.171	-3.2	-0.7	0.867
L1-L3	1.118	-3.9	-1.3	0.845
L1-L2	1.139	-3.7	-0.9	0.898
L2-L3	1.130	-4.0	-1.3	0.821
L2-L4	1.198	-3.0	-0.5	0.858
L3-L4	1.204	-2.6	-0.4	0.841

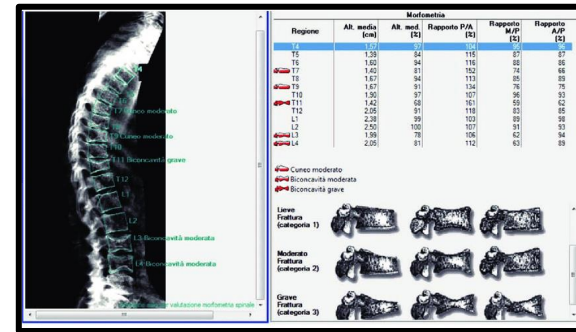
Commenti

RUOLO DELL' ANALISI DEXA NEL PAZIENTE CON CTIBL NEL CORSO DELLE VARIE FASI DELLA SUA MALATTIA

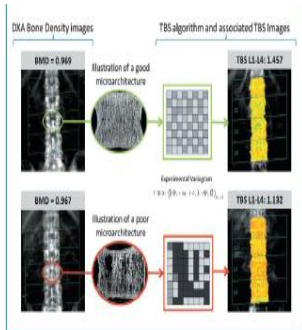
BMD



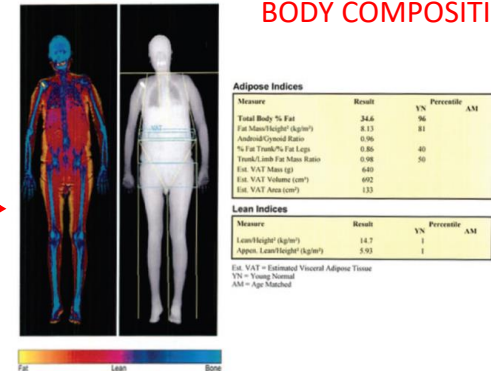
FRATTURE



TBS BONE QUALITY



BODY COMPOSITION



DEXA Results Summary:

Region	BMC (g)	Fat Mass (g)	Lean Mass (g)	Lean + BMC (g)	Total Mass (g)	% Fat
L Arm	98.02	1199.7	1775.1	1873.1	3072.8	39.0
R Arm	201.61	1156.5	1837.7	2039.3	3195.8	36.2
Trunk	342.71	9856.5	19720.6	19720.6	29620.8	33.5
L Leg	280.47	3799.0	5834.4	6114.9	9913.9	28.3
R Leg	300.80	3930.0	5739.8	6040.6	9970.6	39.4
Subtotal	1223.62	19941.6	34417.7	35641.3	55582.9	35.9
Head	346.56	668.2	3356.0	3662.6	4550.8	19.1
Total	1570.18	20809.7	37753.7	39323.9	60133.7	34.6



- Prevenzione primaria in donne in menopausa o uomini di età ≥ 50 anni a rischio elevato di frattura a causa di almeno una delle condizioni sottoelencate:

Condizione	I scelta ^a	II scelta	III scelta
Trattamento in atto o previsto per >3 mesi con prednisone equivalente ≥ 5 mg/die	Alendronato (\pm vit.D), Risedronato, Zoledronato ^d	Denosumab ^e	_____
Trattamento in corso di blocco ormonale adiuvante in donne con carcinoma mammario o uomini con carcinoma prostatico	Alendronato (\pm vit.D), Risedronato, Zoledronato ^d Denosumab ^e	_____	_____
T-score colonna o femore ^c ≤ -4	Alendronato (\pm vit.D), Risedronato	Denosumab ^e Zoledronato ^d Ibandronato, Raloxifene, Bazedoxifene	
T-score colonna o femore ^c ≤ -3 + almeno una delle seguenti condizioni: 1) Familiarità per fratture di vertebre o femore 2) Comorbidità a rischio di frattura (artrite reumatoide o altre connettiviti, diabete,			

Linee Guida AIOM 2015-2022
Linee Guida SIOMMMS 2015

IMMINENT RISK

Definition, Assessment, and Management of Vitamin D Inadequacy: Suggestions, Recommendations, and Warnings from the Italian Society for Osteoporosis, Mineral Metabolism and Bone Diseases (SIOMMMS)

Bertoldo F , Cianferotti L , Di Monaco M , Falchetti A , Fassio A , Gatti D , Minisola S,et al.

Table 2. Population/condition at risk of hypovitaminosis D.

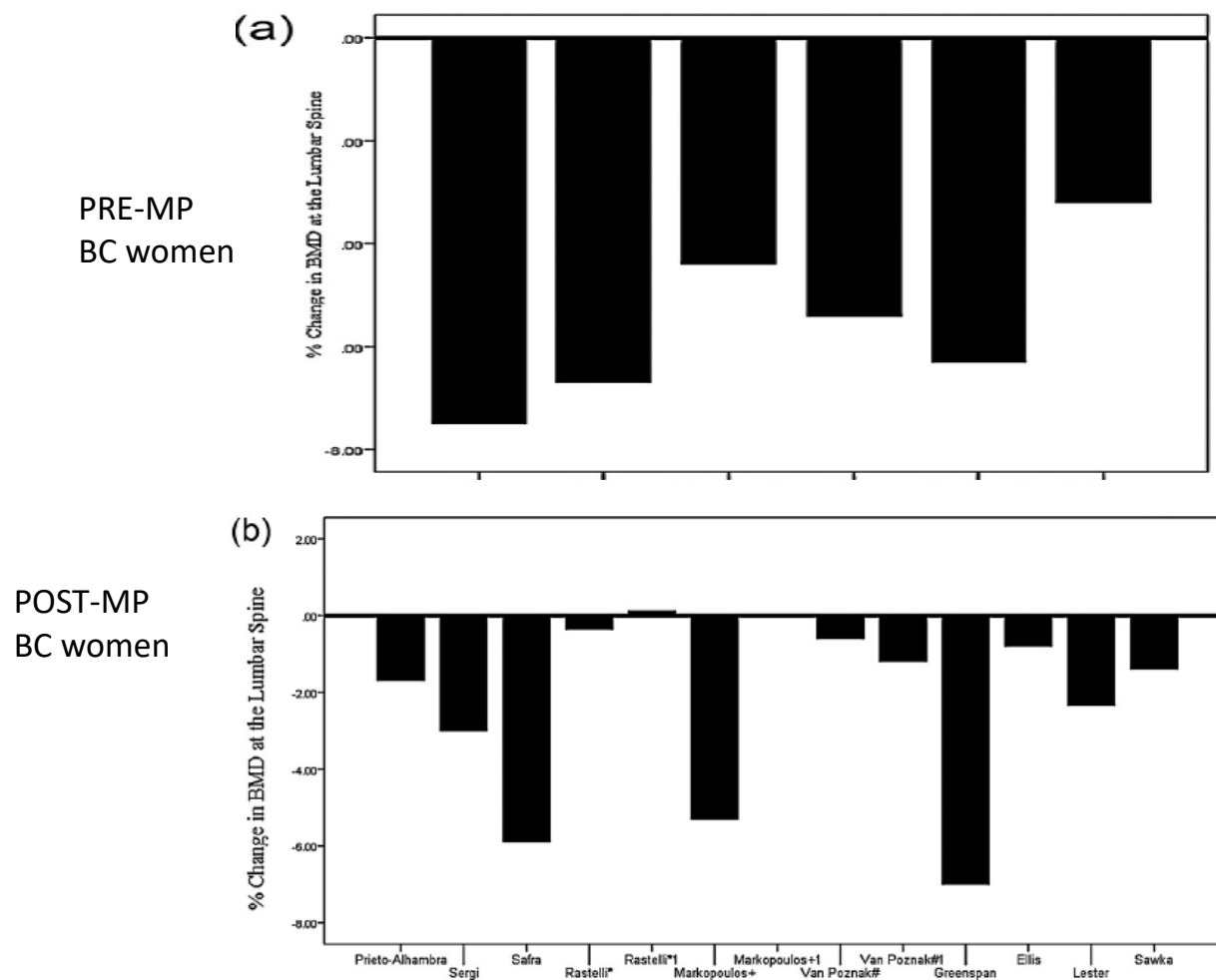
- Old people (≥ 75 years)
- Institutionalized subjects or conditions associated with inadequate solar exposure
- Obesity
- Pregnancy and breast-feeding
- Metabolic bone diseases and other skeletal disorders
- Vegan diet
- Anorexia nervosa
- Chronic renal failure
- Cancer (in particular breast, prostate, and colon)
- Type 2 diabetes mellitus
- Intestinal malabsorption and bariatric surgery
- Drugs that interfere with the absorption or hepatic metabolism of vitamin D (antiepileptic glucocorticoids, antiviral AIDS, antifungal agents, cholestyramine)
- Cystic fibrosis

Table 6. Suggestions and recommendations concerning vitamin D supplementation in subjects with hypovitaminosis D or candidates to receive anti-fracture drugs.

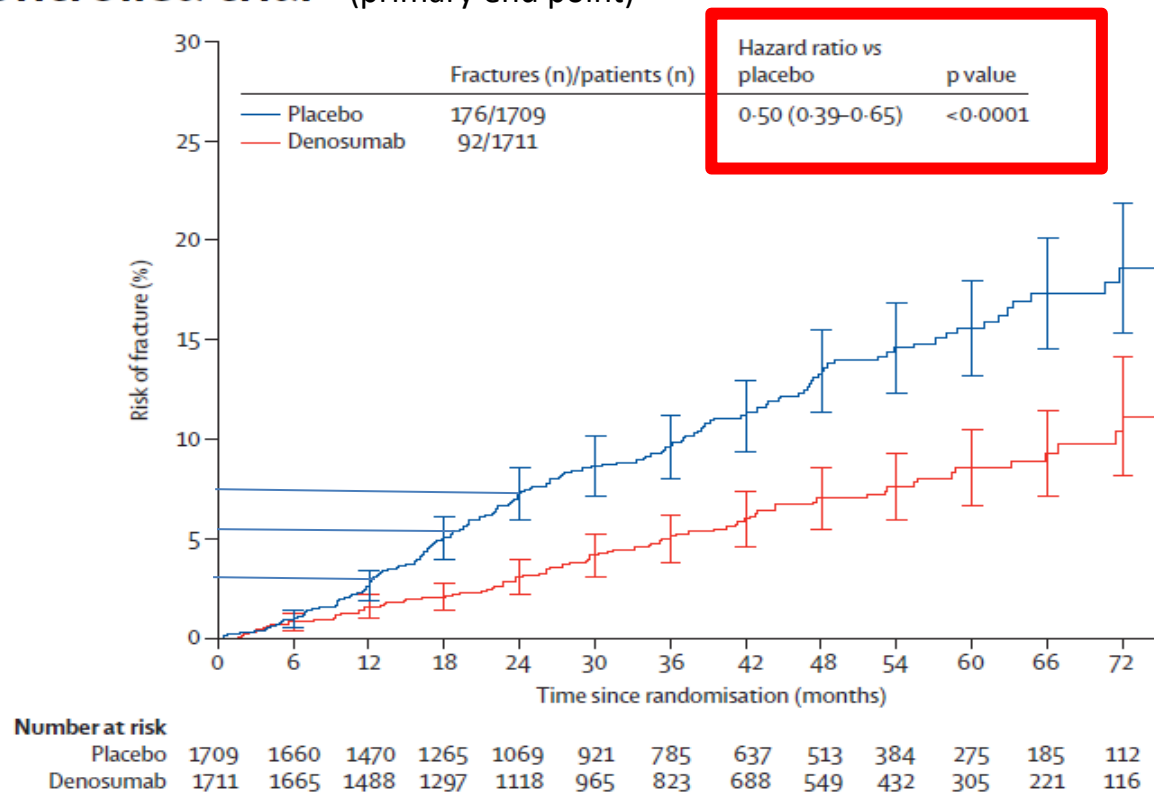
In Subjects with Hypovitaminosis D, or Candidates for Bone Active Agents for Osteoporosis:	Evidence Levels
We suggest a dose of cholecalciferol supplementation between 800 IU/day and 2000 IU/day. There is no single, fixed dose for all subjects that needs to be supplemented.	⊕
We suggest a daily, weekly, monthly schedule based on the dose administered. In these settings, the maximum single daily dose to be administered should not exceed 100,000 IU. An adequate calcium intake (800–1000 mg/day) must always be ensured.	⊕
We recommend the use of an initial loading dose, followed by the maintenance dose in patients with symptomatic osteomalacia and/or serum 25(OH)D < 10 ng/mL, or in patients starting bone anti-resorptive therapy with intravenous bisphosphonates or denosumab with serum 25(OH)D < 20 ng/mL.	⊕⊕⊕
We recommend , as loading dose, cholecalciferol 3000–10,000 IU/day (average 5000 IU/day) for 1–2 months, or cholecalciferol in a single dose of 60,000 to 150,000 IU followed by the maintenance dose (2000 IU/day). Alternatively, we suggested calcifediol 20–40 mcg/day (4–8 gtt/day) for 20–30 days, before switching to maintenance dose *.	⊕⊕⊕

* With a limited recommendation for a faster normalization of serum levels of 25(OH)D only.

Calcium and vitamin D supplementation and loss of bone mineral density in women undergoing breast cancer therapy



Adjuvant denosumab in breast cancer (ABCSG-18): a multicentre, randomised, double-blind, placebo- controlled trial (primary end point)



Real-World Effectiveness of Denosumab and Bisphosphonates on Risk of Vertebral Fractures in Women with Breast Cancer Undergoing Treatment with Aromatase Inhibitors

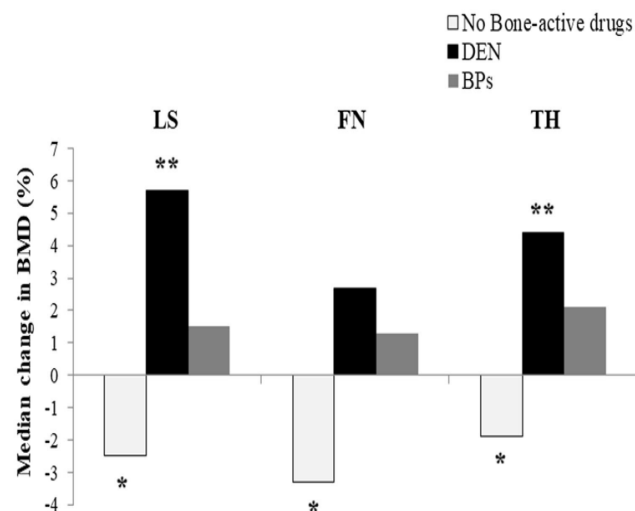
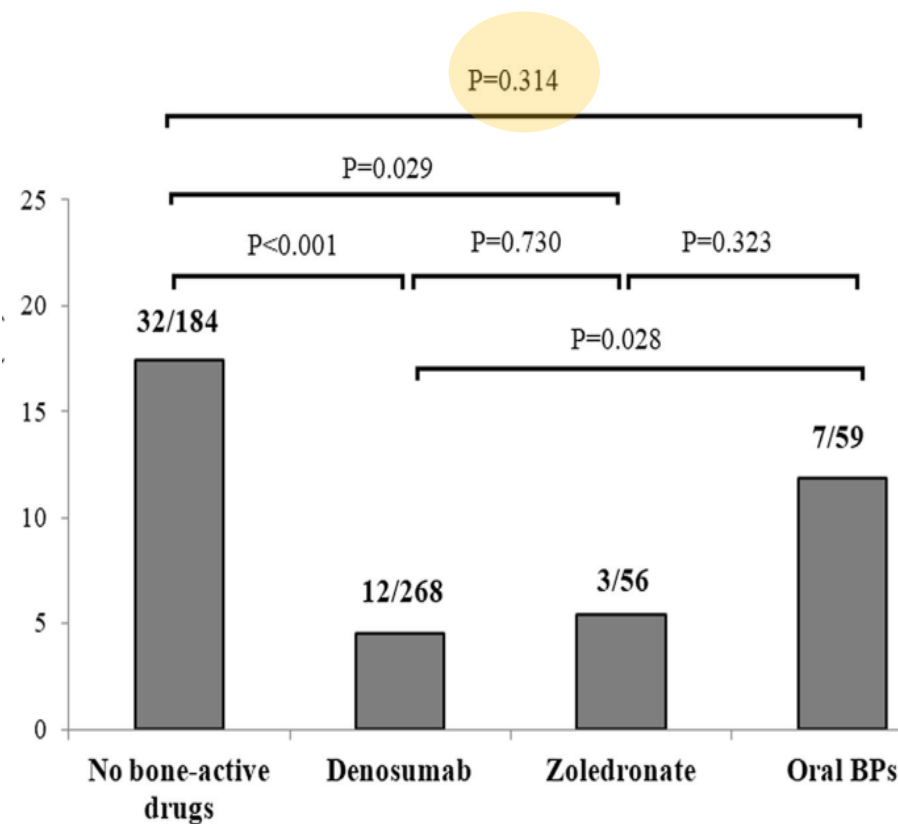


Table 4 Multivariate logistic regression analysis evaluating the determinants of incident VFs in women under treatment with AIs

	Odds ratio	95% CI	P-values
Age	1.05	1.01–1.10	0.031
Baseline FRAX major fracture score	1.03	0.88–1.22	0.515
Baseline FRAX hip fracture score	1.04	0.82–1.32	0.744
Prevalent VFs	2.76	1.21–6.30	0.016
Denosumab therapy	0.32	0.13–0.77	0.010
BPs therapy	0.68	0.28–1.63	0.383
Change in LS BMD	0.97	0.92–1.02	0.659
Change in FN BMD	0.99	0.94–1.04	0.127
Change in TH BMD	0.95	0.89–1.00	0.060



The prevention of fragility fractures in patients with non-metastatic prostate cancer: a position statement by the international osteoporosis foundation

Cianferotti L, Bertoldo F, et al Oncotarget 2017

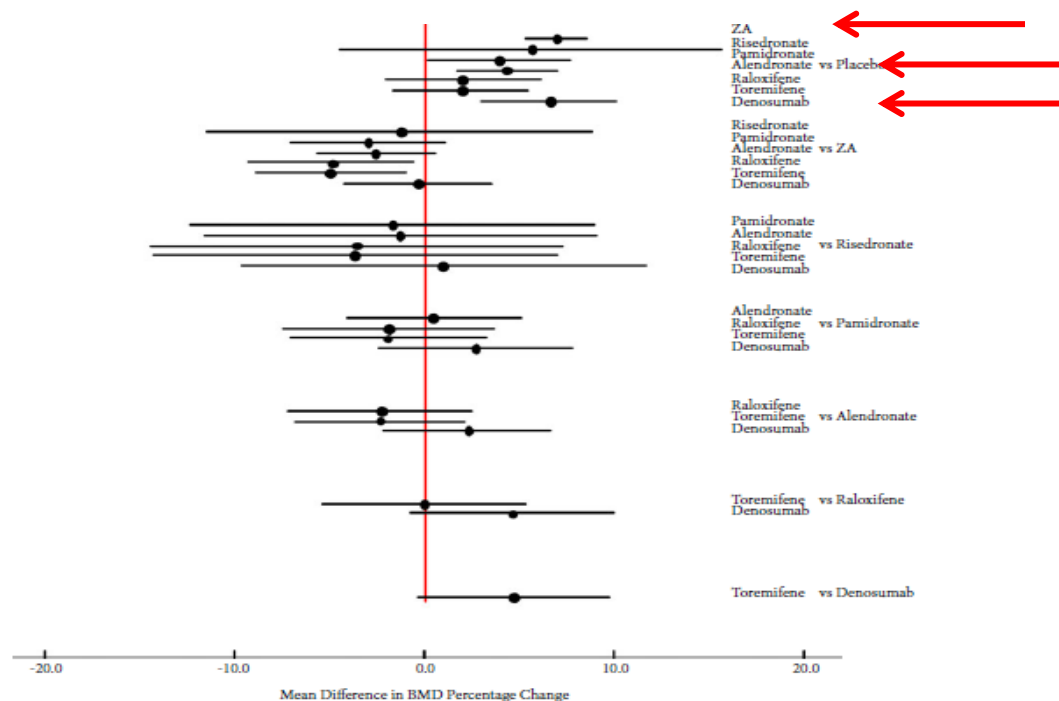
1b. Men with prostate cancer without bone metastases (M0) under ADT

Study	Treatment period	Patients	Drug tested in the treatment group	Drug regimen	Prevention of reduction/increase in BMD	Reduction of fracture risk
Smith et al. [70]	48 weeks	n. 47 men with locally advanced, lymph-node positive or recurrent prostate cancer (M0) starting ADT (leuprolide)	pamidronate	60 mg/12 weeks, i.v.	Yes (spine and hip)	No
Greenspan et al. [80] Greenspan et al. [81]	12–24 months	n. 112 men with prostate cancer (M0) on ADT (GnRH agonists or antiandrogen or combination therapy)	alendronate	70 mg/week, oral	Yes (spine and hip)	No
Klotz et al. [82]	12 months	n. 191 men with prostate cancer (M0) starting ADT (leuprolide acetate)	alendronate	70 mg/week, oral	Yes (spine and hip)	No
Choo et al. [85]	24 months	n. with locally advanced prostate cancer (N0 M0)	risedronate	35 mg/week, oral	Yes (spine and hip)	No
Smith et al. [71]	12 months	n. 106 men with prostate cancer (M0), beginning ADT (GnRH analog with or without antiandrogen)	zoledronate	4 mg/3 months, i.v.	Yes (spine and hip)	No
Israeli et al. [73]	48 weeks	n. 215 men with locally advanced prostate cancer (M0) on ADT (LHRH agonist with or without antiandrogen) for < 12 months	zoledronate	4 mg/3 months i.v.	Yes (spine and hip)	No
Kapoor et al. [75]	12 months	n. 41 men with prostate cancer (M0) on ADT (LHRH agonist or orchidectomy) for < 12 months	zoledronate	4 mg/3 months i.v.	Yes (spine and hip)	No
Michaelson et al. [76]	12 months	n. 40 men with prostate cancer (M0) receiving GnRH analogs and with T-score > -2.5	zoledronate	4 mg/year i.v.	Yes (spine and hip)	No
Casey et al. [77]	24 months	n. 200 men with prostate cancer (M0) starting ADT (< 30 days of goserelin acetate)	zoledronate	4 mg/3 months i.v.	Yes (spine and hip)	No
Denham et al. [78]	36 months	n. 1071 men with locally advanced prostate cancer (M0) starting ADT (leuporelin)	zoledronate	4 mg/3 months i.v.	Yes (spine and hip)	No
Smith et al. [88]	36 months	n. 1468 men with prostate cancer (M0) on ADT (GnRH agonist or orchidectomy)	denosumab	60 mg/6 months s.c.	Yes (spine and hip)	Yes (vertebral)

Systematic review and network meta-analysis on the relative efficacy of osteoporotic medications: men with prostate cancer on continuous androgen-deprivation therapy to reduce risk of fragility fractures

SOLO BMD !

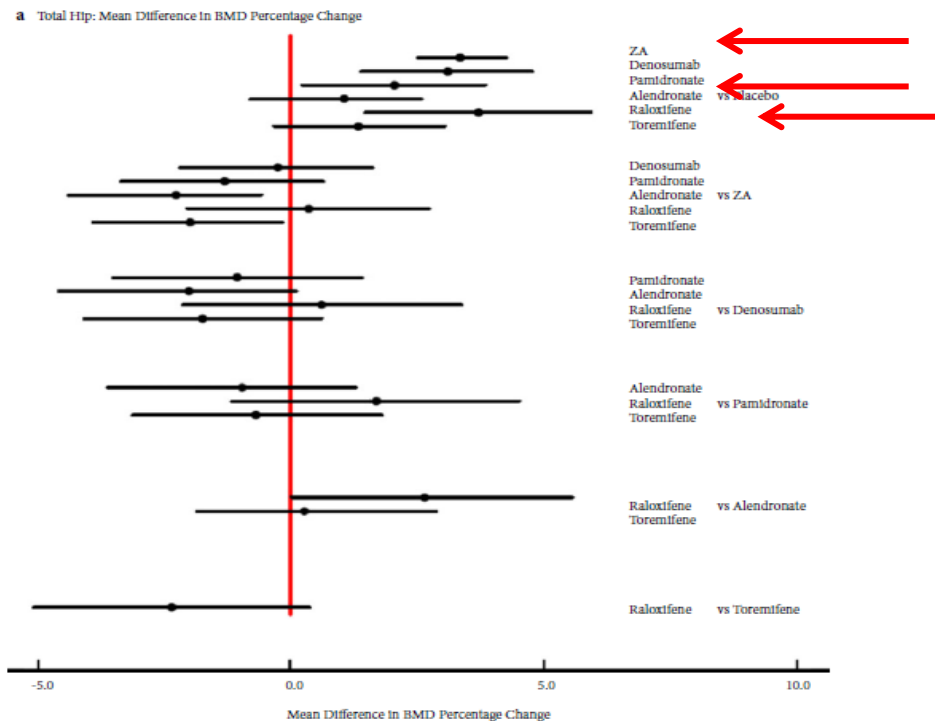
The BMD percentage change compared to other treatments for TH (a), LS (b), and FN (c).



Systematic review and network meta-analysis on the relative efficacy of osteoporotic medications: men with prostate cancer on continuous androgen-deprivation therapy to reduce risk of fragility fractures

SOLO BMD !

The BMD percentage change compared to other treatments for TH (a), LS (b), and FN (c).



Effects of once-yearly zoledronic acid on bone density and incident vertebral fractures in nonmetastatic castration-sensitive prostate cancer patients with osteoporosis

Table 2 Changes in clinical parameters from baseline to 12 months after ADT for MOCSPC patients with osteoporosis

	ZOL 5 mg group (n = 26)			Control group (n = 16)		
	Baseline	12 months	% Change	Baseline	12 months	% Change
BMD (g/cm ²)						
Lumbar spine	1.06 ± 0.21	1.11 ± 0.25	+ 4.02 ± 3.61 ^{d, f}	1.06 ± 0.16	1.03 ± 0.16	−3.72 ± 3.91 ^b
Femoral neck	0.73 ± 0.09	0.73 ± 0.10	+ 0.99 ± 4.41 ^e	0.78 ± 0.11	0.76 ± 0.09	−1.52 ± 2.14 ^a
Serum biochemistry						
Creatinine (mg/dl)	0.84 ± 0.16	0.81 ± 0.15	− 2.65 ± 11.1	0.99 ± 0.27	0.97 ± 0.24	+ 1.22 ± 10.0
eGFR (ml/min/1.73 m ²)	71.4 ± 16.0	73.5 ± 14.9	+ 4.21 ± 13.9	61.5 ± 15.3	61.5 ± 13.4	−0.57 ± 10.8
TRACP-5b (mU/dl)	560.5 ± 198.6	247.2 ± 75.5	−52.1 ± 19.0 ^{d, f}	390.9 ± 227.9	545.4 ± 286.8	+ 36.4 ± 34.9 ^c

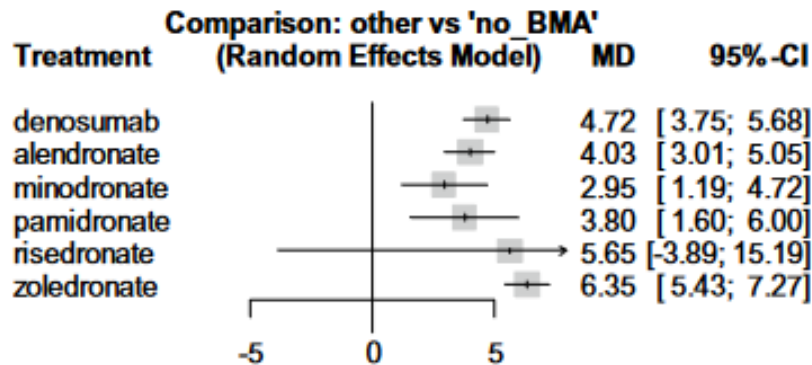
Table 3 Association between ZOL 5 mg and presence of incident VFs evaluated by a logistic regression analysis

Parameter	Presence of incident VFs		
	OR	95%CI	p
Administration of ZOL 5 mg	2.10	0.37–11.9	0.4033
Adjusted for age	2.19	0.37–12.9	0.3683
Adjusted for age, BMI	4.49	0.56–36.2	0.1279
Adjusted for age, BMI, Δ LS-BMD	0.66	0.04–11.3	0.7774

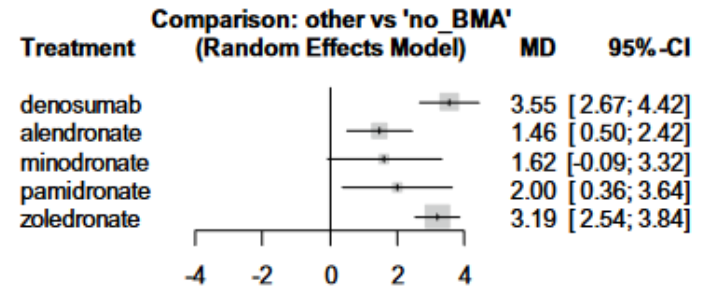
BMD bone mineral density, *BMI* body mass index, *CI* confidence interval, *LS* lumbar spine, *VFs* vertebral fractures, *Δ* percent changes

Bone-modifying agents for bone loss in patients with prostate cancer receiving androgen deprivation therapy; insights from a network meta-analysis

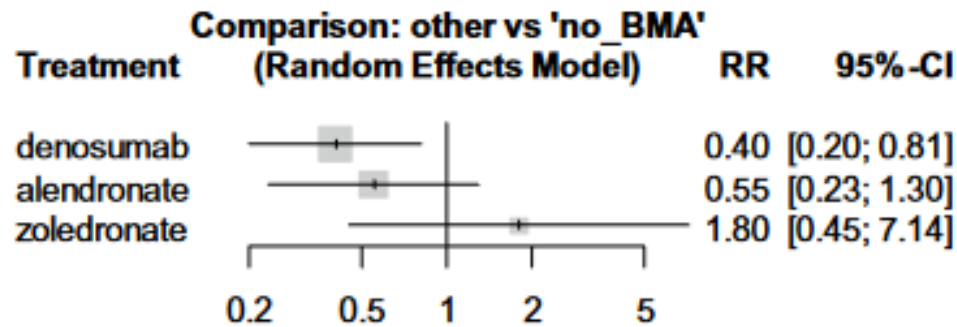
%Lumbar BMD



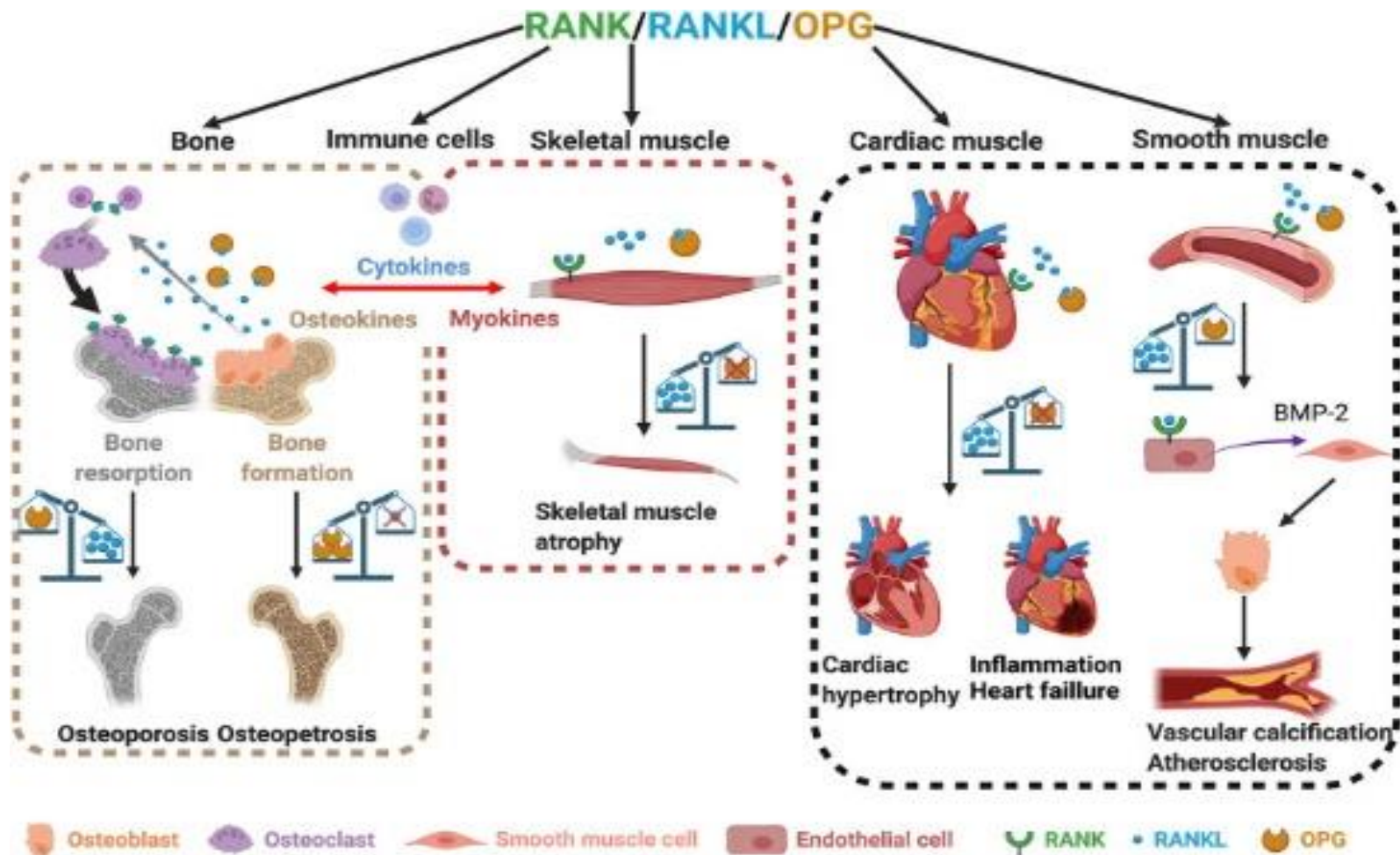
%HIP BMD



VFX

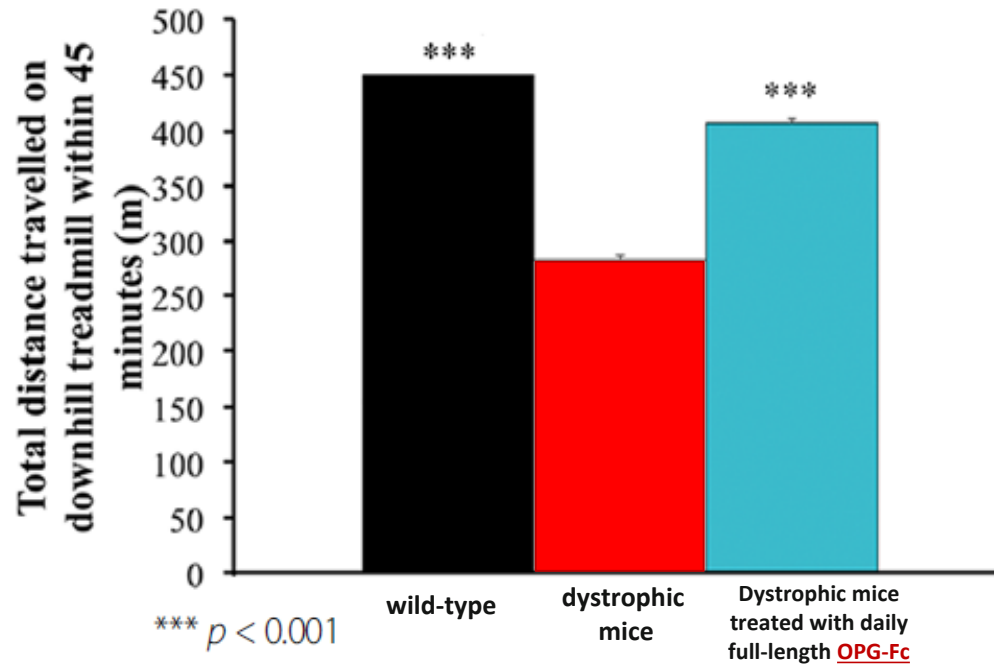
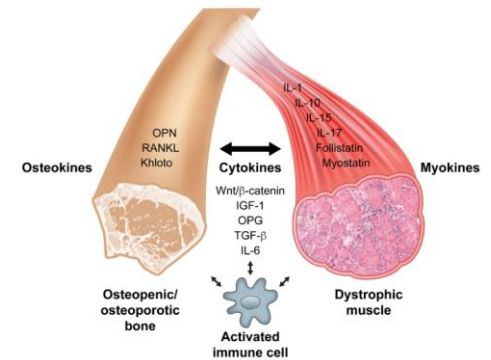


The roles of the RANK/RANKL/OPG triad in bone and skeletal, cardiac, and smooth muscles



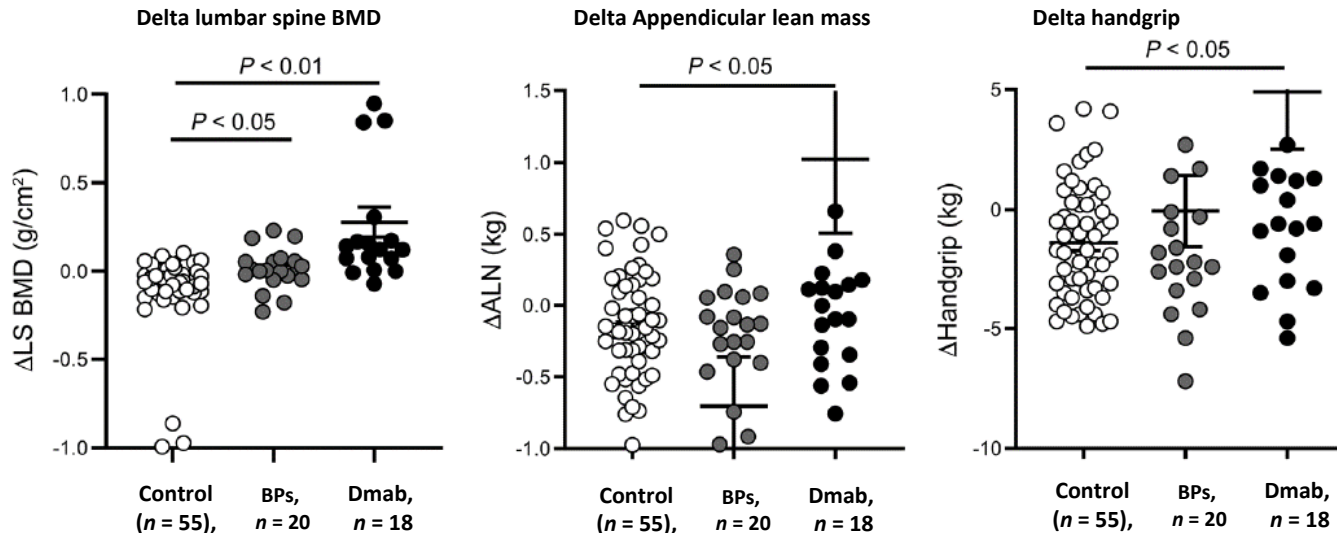
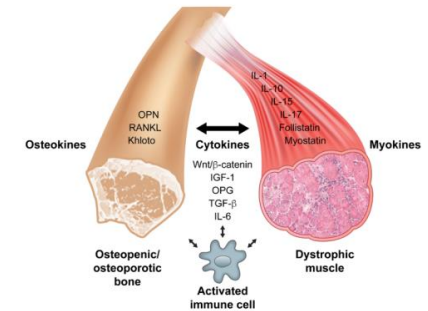
Genetic deletion of muscle RANK or selective inhibition of RANKL is not as effective as full-length OPG-fc in mitigating muscular dystrophy

Sébastien S. Dufresne¹, Antoine Boulanger-Piette¹, Sabrina Bossé¹, Anteneh Argaw¹, Dounia Hamoudi¹, Laetitia Marcadet¹, Daniel Gamu², Val A. Fajardo², Hideo Yagita³, Josef M. Penninger⁴, A. Russell Tupling² and Jérôme Frenette^{1,5*}



RANKL inhibition improves muscle strength and insulin sensitivity and restores bone mass

Nicolas Bonnet,¹ Lucie Bourgoignie,¹ Emmanuel Biver,¹ Eleni Douni,^{2,3} and Serge Ferrari¹





In women, taking denosumab for more than 3 years improved appendicular lean mass and handgrip strength compared with no treatment, whereas bisphosphonate did not

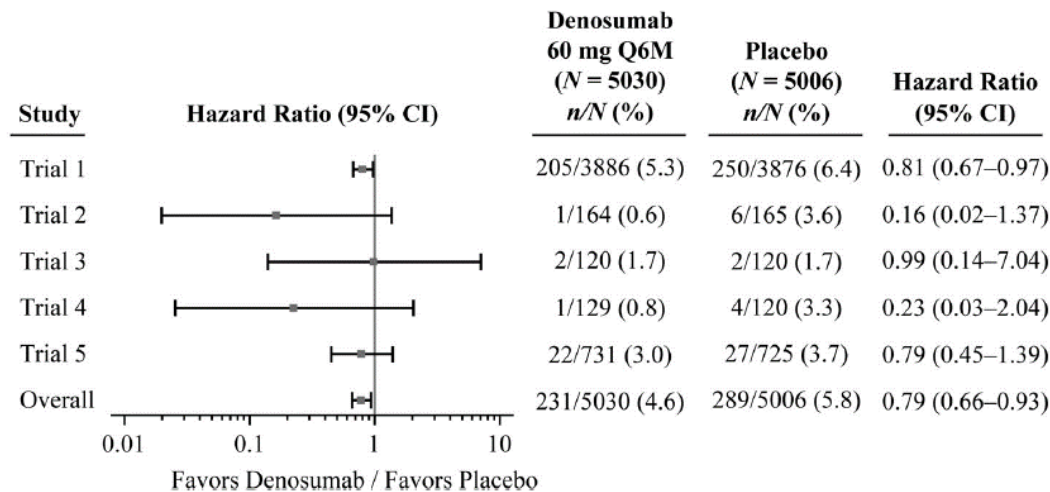
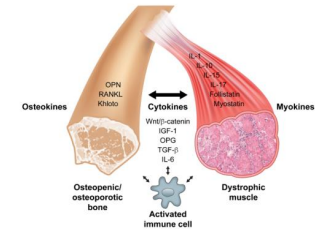
Comparison between Post-treatment measures of Dmab, Zol, and Aln therapy, stratified according to the patients' sex

		Females					Males				
		<i>N</i>	Mean	SD	<i>F</i>	Sig	<i>N</i>	Mean	SD	<i>F</i>	Sig
DXA spine	Aln	101	-1.5406	4.12512	.000	1.000	35	-2.2543	.18684	.051	.950
	Zol	101	-1.5436	4.12556			35	-2.2686	.19519		
	Dmab	101	-1.5436	4.12556			34	-2.2647	.19677		
DXA hip	Aln	101	-2.2683	.14692	.002	.998	35	-2.2343	.14337	.409	.665
	Zol	101	-2.2693	.14611			35	-2.2514	.13799		
	Dmab	101	-2.2693	.14611			34	-2.2647	.13901		
Calcium	Aln	101	2.2036	.07021	.000	1.000	35	2.1974	.00505	.164	.849
	Zol	101	2.2036	.07021			35	2.1969	.00530		
	Dmab	101	2.2036	.07021			34	2.1968	.00535		
Vitamin D	Aln	101	57.5644	5.75919	.000	1.000	35	61.3714	6.76099	.081	.922
	Zol	101	57.5644	5.75919			35	61.1143	6.54744		
	Dmab	101	57.5644	5.75919			34	60.7353	6.43527		
FRAS	Aln	101	2.941	.92002	47.706	.000	35	2.9714	.74698	23.720	.000
	Zol	101	2.90	.92002			35	2.917	.80570		
	Dmab	101	1.9158	.72825			34	1.9265	.55230		
FRAX Major	Aln	101	12.1485	1.53223	.001	.999	35	12.1429	1.28665	.016	.984
	Zol	101	12.1584	1.50155			35	12.1714	1.22440		
	Dmab	101	12.1584	1.50155			34	12.1176	1.20012		
FRAX Hip	Aln	101	2.6010	.24678	.001	.999	35	2.5400	.21989	.137	.872
	Zol	101	2.6050	.24915			35	2.5571	.22134		
	Dmab	101	2.6079	.24400			34	2.5676	.22391		
Grip strength	Aln	101	23.5198	3.25297	14.964	.000	35	27.3343	4.65466	13.805	.000
	Zol	101	23.5297	3.25228			35	27.8200	4.64776		
	Dmab	101	25.666	3.13018			34	31.315	4.74534		
TUG	Aln	101	9.462	1.20847	11.021	.000	35	9.198	1.60662	10.005	.000
	Zol	100	9.588	1.21812			35	9.204	1.61715		
	Dmab	101	8.772	1.04241			34	8.500	1.68990		
4-m walk	Aln	101	1.066	.09484	9.046	.00	35	1.267	.10140	11.013	.00
	Zol	100	1.0710	.09684			35	1.257	.10090		
	Dmab	101	1.2695	.09752			34	1.5935	.09319		

*SD standard deviation

A Pooled Analysis of Fall Incidence From Placebo-Controlled Trials of Denosumab

Pojchong Chotiyarnwong,^{1,2*} Eugene McCloskey,^{2*}  Richard Eastell,² Michael R McClung,³ Evelien Gielen,⁴ John Gostage,² Michele McDermott,⁵ Arkadi Chines,⁵ Shuang Huang,⁵ and Steven R Cummings⁶ 



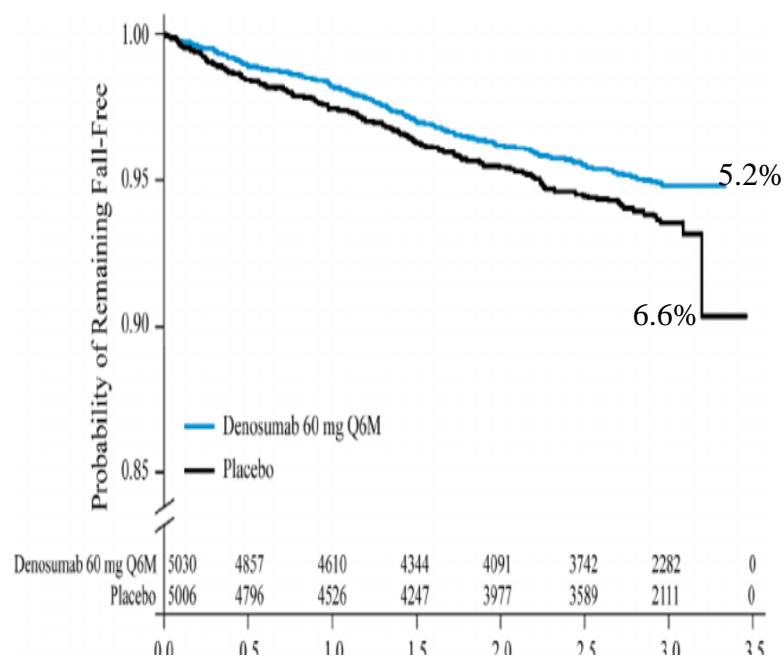
Calo Rischio Medio = 21%

Calo Rischio Minimo= 7%

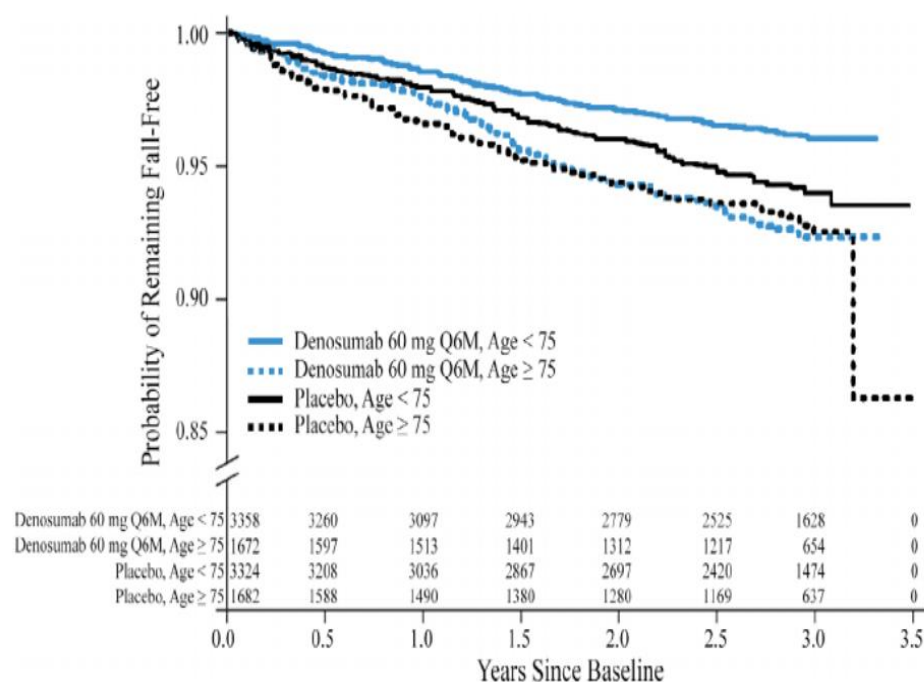
Calo Rischio Massimo= 34%

A Pooled Analysis of Fall Incidence From Placebo-Controlled Trials of Denosumab

HR of 0.79 (95% CI
0.66–0.93; $p = 0.0061$).



(HR = 0.65, 95% CI 0.52–0.82)



Management of Osteoporosis in Chronic Kidney Disease

Kosaku Nitta¹, Aiji Yajima¹ and Ken Tsuchiya²

Caution in the Use of Therapeutic Agents for Osteoporosis in CKD Patients.

Drug	Renal insufficiency of preservation period		Dialysis (CKD-5D)
	eGFR \geq 35 mL/min/1.73 m ²	eGFR<35 mL/min/1.73 m ²	
Calcium L-aspartate	Contraindication (C)	Contraindication (C)	Careful administration (B) (Check the calcium concentration)
Alfacalcidol, calcitriol	Change dose depending on the condition of a patient (A)		
Eldecacitol	Careful about rises in serum calcium concentration (B)		
SERM (Raloxifene, bazedoxifene)	Careful administration (B)		
Bisphosphonate	Alendronate	Careful administration (B)	Contraindication (C)
	Risedronate	Careful administration (B)	Contraindication (C)
	Minodronic acid	Careful administration (B)	Contraindication (C)
	Ibandronate	Careful administration (B)	Contraindication (C)
	Etidronate	Contraindication (C)	Contraindication (C)
Elcatonin	Normal dose possibility (for osteoporotic pain) (A)		
Denosumab	Careful administration (B) (Hypocalcemia should be watched for in patients with severe renal dysfunction)		
Teriparatide	Careful administration (B)		

A: Normal dose possibility, B: Careful administration, C: Contraindication. CKD: chronic kidney disease

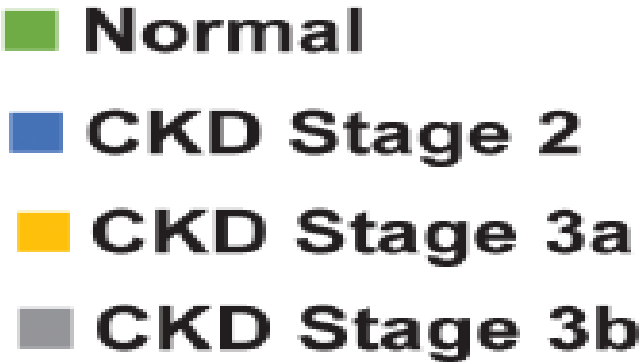
Intravenous ibandronate injection in postmenopausal women with osteoporosis showed comparable safety levels to that of alendronate

Intravenous zoledronic acid is contraindicated for CKD patients with eGFR <35 mL/min/1.73 m².

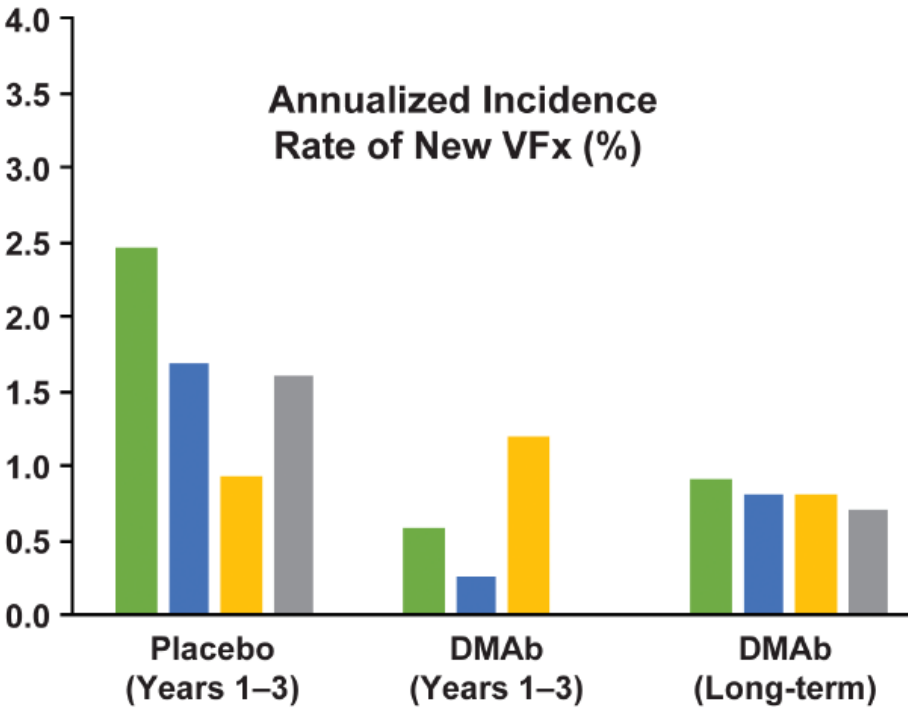
Denosumab Safety and Efficacy Among Participants in the FREEDOM Extension Study With Mild to Moderate Chronic Kidney Disease

Aaron Broadwell,¹ Arkadi Chines,² Peter R. Ebeling,³ Edward Franek,⁴ Shuang Huang,² Shawna Smith,² David Kendler,⁵ Osvaldo Messina,⁶ and Paul D. Miller⁷

7-year extension



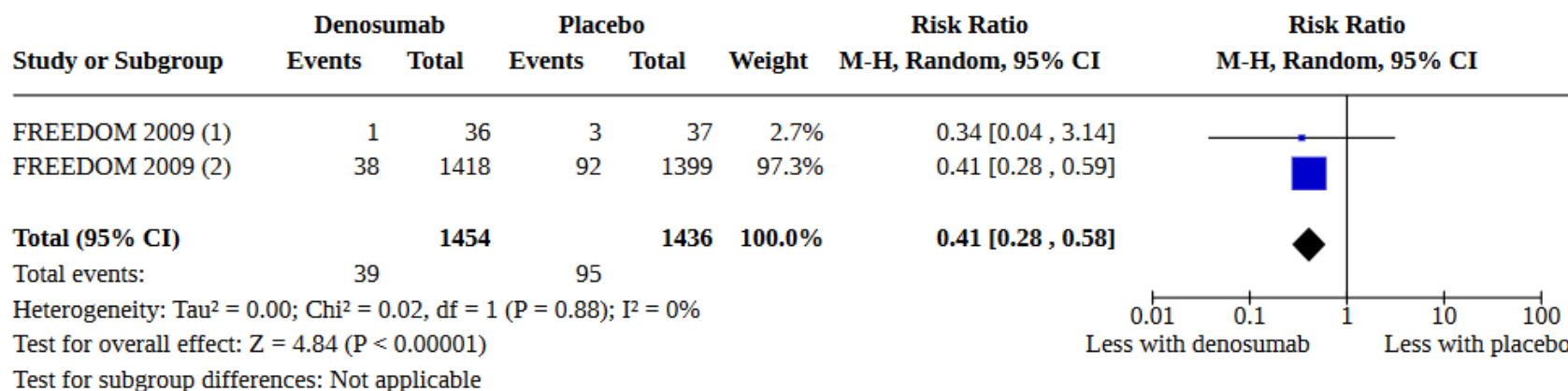
Most participants (1259/1969 [64%]) with baseline CKD stage 2 or 3 remained within the same CKD subgroup at study completion; less than 3% progressed to CKD stage 4.





Pharmacological interventions versus placebo, no treatment or usual care for osteoporosis in people with Chronic kidney disease stages 3-4

Analysis 5.1. Comparison 5: Denosumab versus placebo for patients with osteoporosis and CKD stages 3-4, Outcome 1: Vertebral fracture by radiography



Footnotes

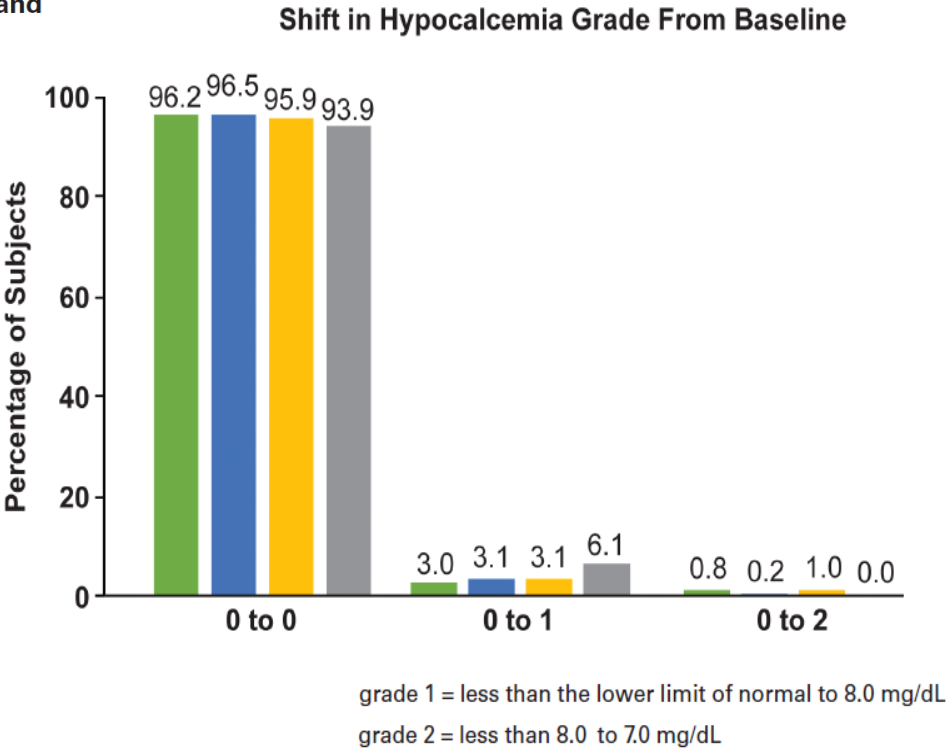
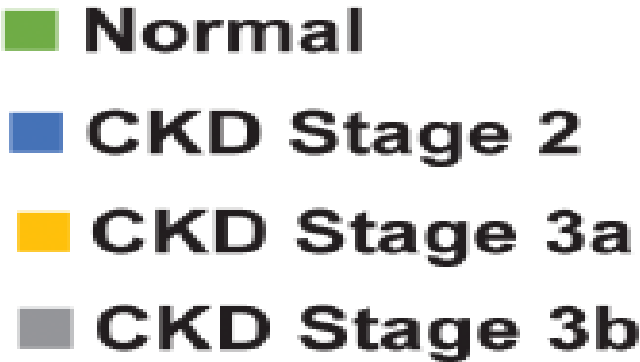
(1) CKD stage 4

(2) CKD stage 3

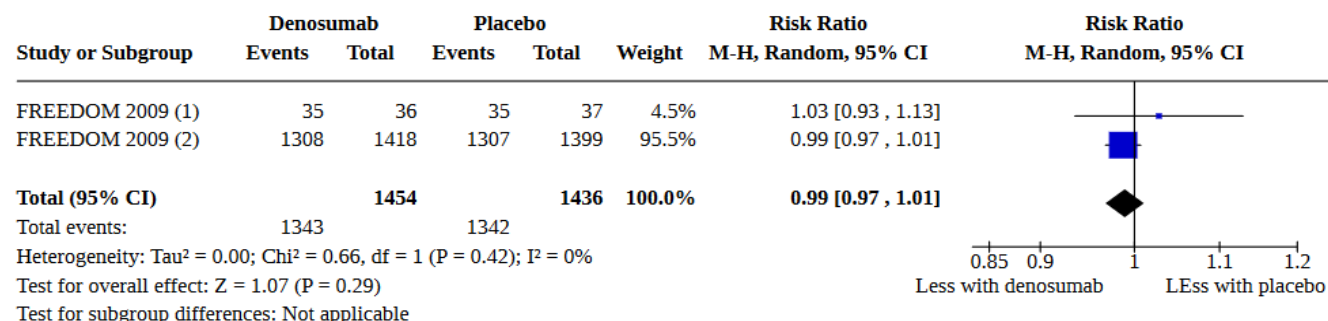
Denosumab Safety and Efficacy Among Participants in the FREEDOM Extension Study With Mild to Moderate Chronic Kidney Disease

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7-year extension



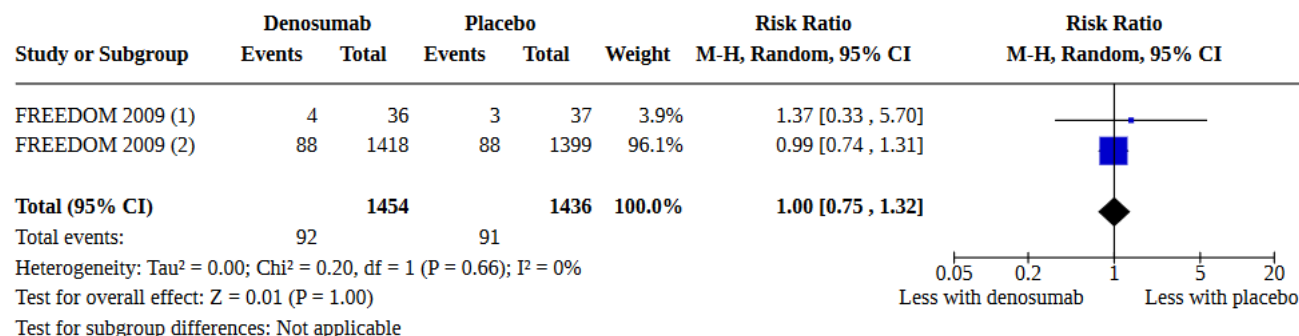
Analysis 5.6. Comparison 5: Denosumab versus placebo for patients with osteoporosis and CKD stages 3-4, Outcome 6: Adverse events



Footnotes

- (1) CKD stage 4
(2) CKD stage 3

Analysis 5.7. Comparison 5: Denosumab versus placebo for patients with osteoporosis and CKD stages 3-4, Outcome 7: Cardiovascular and cerebrovascular morbidity



Footnotes

- (1) CKD stage 4
(2) CKD stage 3



- **Prevenzione primaria in donne in menopausa o uomini di età ≥ 50 anni a rischio elevato di frattura a causa di almeno una delle condizioni sottoelencate:**

Condizione	I scelta ^a	II scelta	III scelta
Trattamento in atto o previsto per >3 mesi con prednisone equivalente ≥ 5 mg/die	Alendronato (\pm vit.D), Risedronato, Zoledronato ^d	Denosumab ^e	_____
Trattamento in corso di blocco ormonale adiuvante in donne con carcinoma mammario o uomini con carcinoma prostatico	Alendronato (\pm vit.D), Risedronato, Zoledronato ^d Denosumab ^e	_____	_____
T-score colonna o femore ^c ≤ -4	Alendronato (\pm vit.D), Risedronato	Denosumab ^e Zoledronato ^d Ibandronato, Raloxifene, Bazedoxifene	
T-score colonna o femore ^c ≤ -3 + almeno una delle seguenti condizioni: 1) Familiarità per fratture di vertebre o femore 2) Comorbidità a rischio di frattura (artrite reumatoide o altre connettiviti, diabete,			

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Bone health management in the continuum of prostate cancer disease: a review of the evidence with an expert panel opinion

Daniele Santini D, Berruti A, Di Maio M, Procopio G, Bracarda S, Ibrahim T and Bertoldo F

Experts' advices on treatment modalities by setting

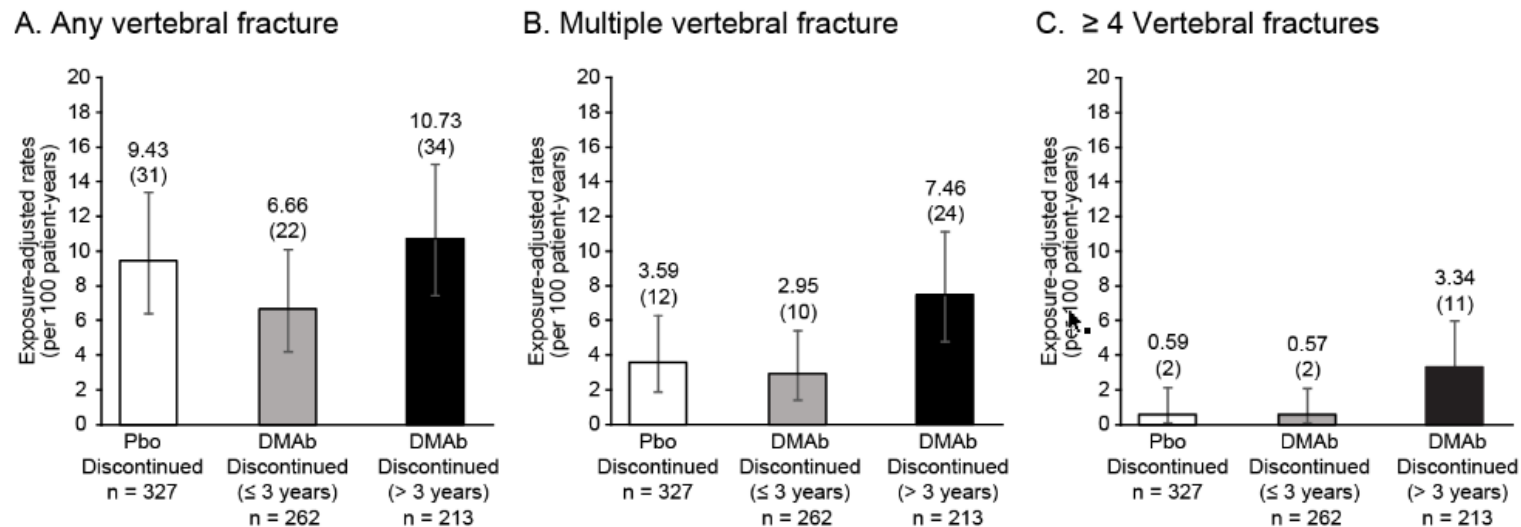
• Non-metastatic disease

Therapeutic thresholds and modalities are the same for M0 HSPC and M0 CRPC

Metastatic disease

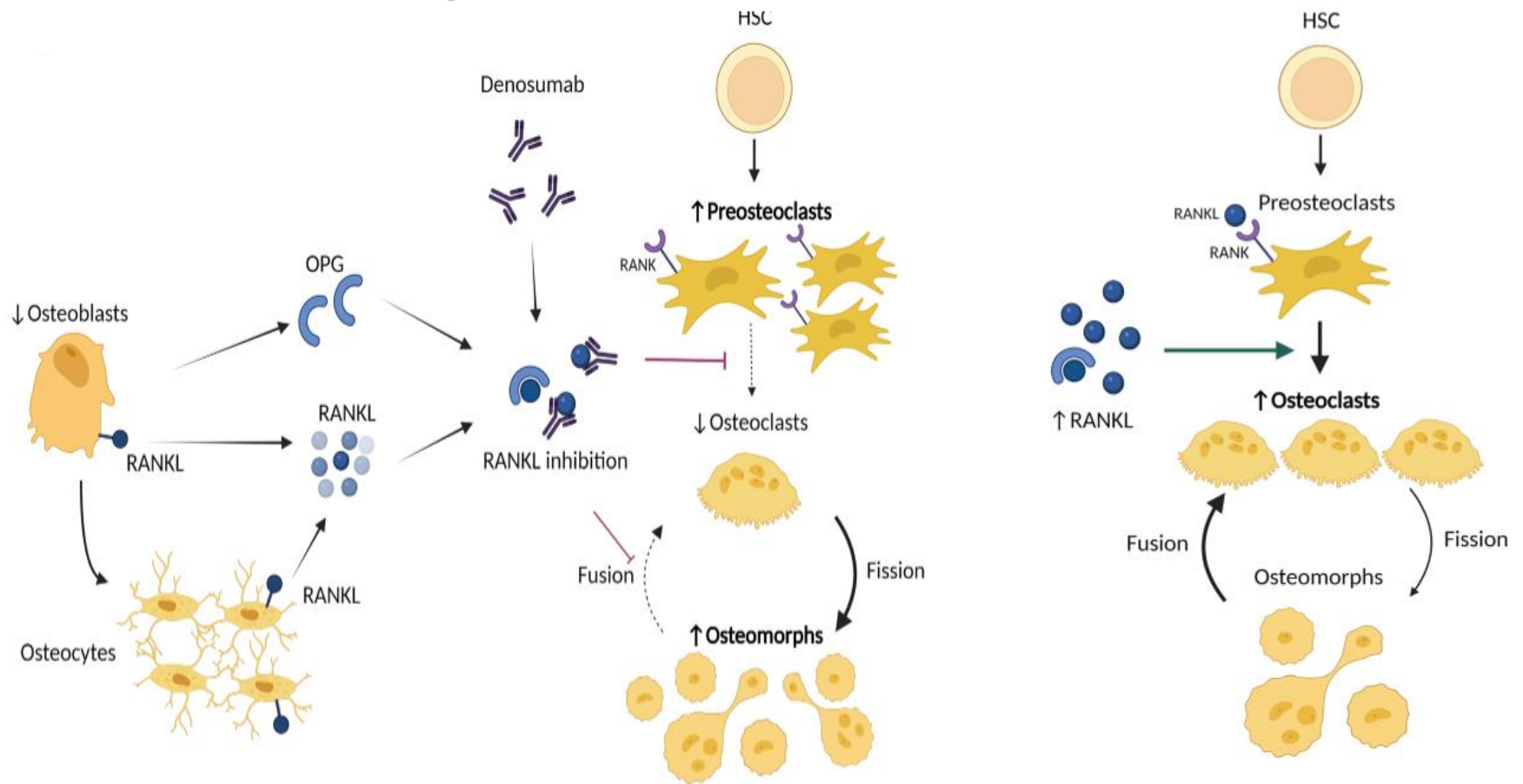
In the setting of **M1 HSPC**, the therapeutic schedule of BTTs is that **used for osteoporosis** (the same of M0 CRPC), not for metastases

Multiple Vertebral Fractures After Denosumab Discontinuation: FREEDOM and FREEDOM Extension Trials Additional Post Hoc Analyses



Patients with off-treatment x-ray N = 736 ^a	
Significant covariates	Odds ratio (95% CI)
Prior VF ^b (Yes vs No)	3.14 (1.54, 6.39)
Off-treatment duration (per year)	1.35 (1.08, 1.68)
On-treatment duration (per year)	1.20 (1.03, 1.40)
Off-treatment annualized total hip BMD loss ^c (per 1%)	1.19 (1.08, 1.32)

Osteoclast Recycling and the Rebound Phenomenon Following Denosumab Discontinuation



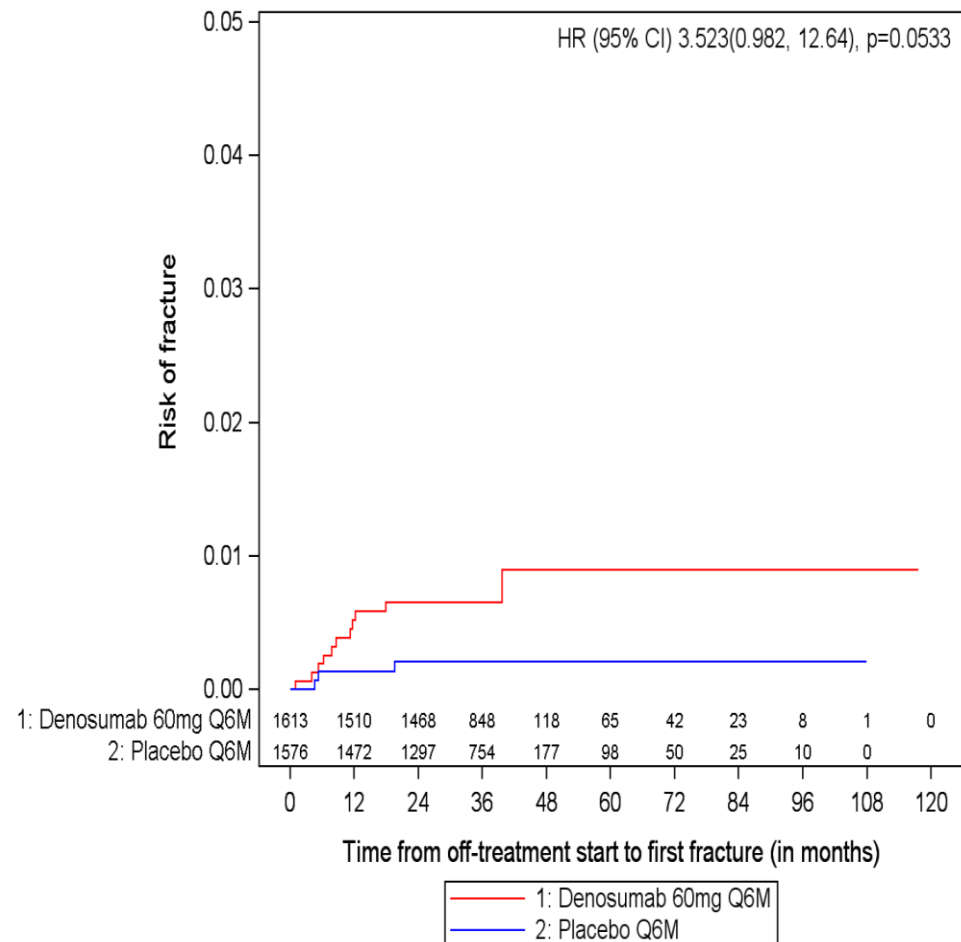
Results Clinical Multiple Vertebral Off Treatment Fracture Risk

Denosumab: 28 Fractures

Subjects with Fractures: 11 (0.7%)

Placebo: 8 Fractures

Subjects with Fractures: 3 (0.2%)



Results Clinical Vertebral Off Treatment Fractures according to AI End

		Clinical Vertebral Fractures		Clinical Multiple Vertebral Fractures	
		Denosumab	Placebo	Denosumab	Placebo
AI end > 6 months <u>after</u> last DNB dose	n Subjects in %	29 (0.9%)	11 (0.4%)	22 (0.5%)	7 (0.1%)
AI end within 6 months of last DNB dose	n Subjects in %	3 (0.2%)	1 (0.1%)	0 (0%)	1 (0.1%)



MANAGEMENT TERAPIA ANTIRIASSORBITIVA IN CTIBL

FINE TERAPIA ORMONALE ADIUVANTE

RISCHIO FRATTURATIVO
ALTO

**NON SOSPENDERE
QUALSIASI TERAPIA**
Proseguire in nota 79

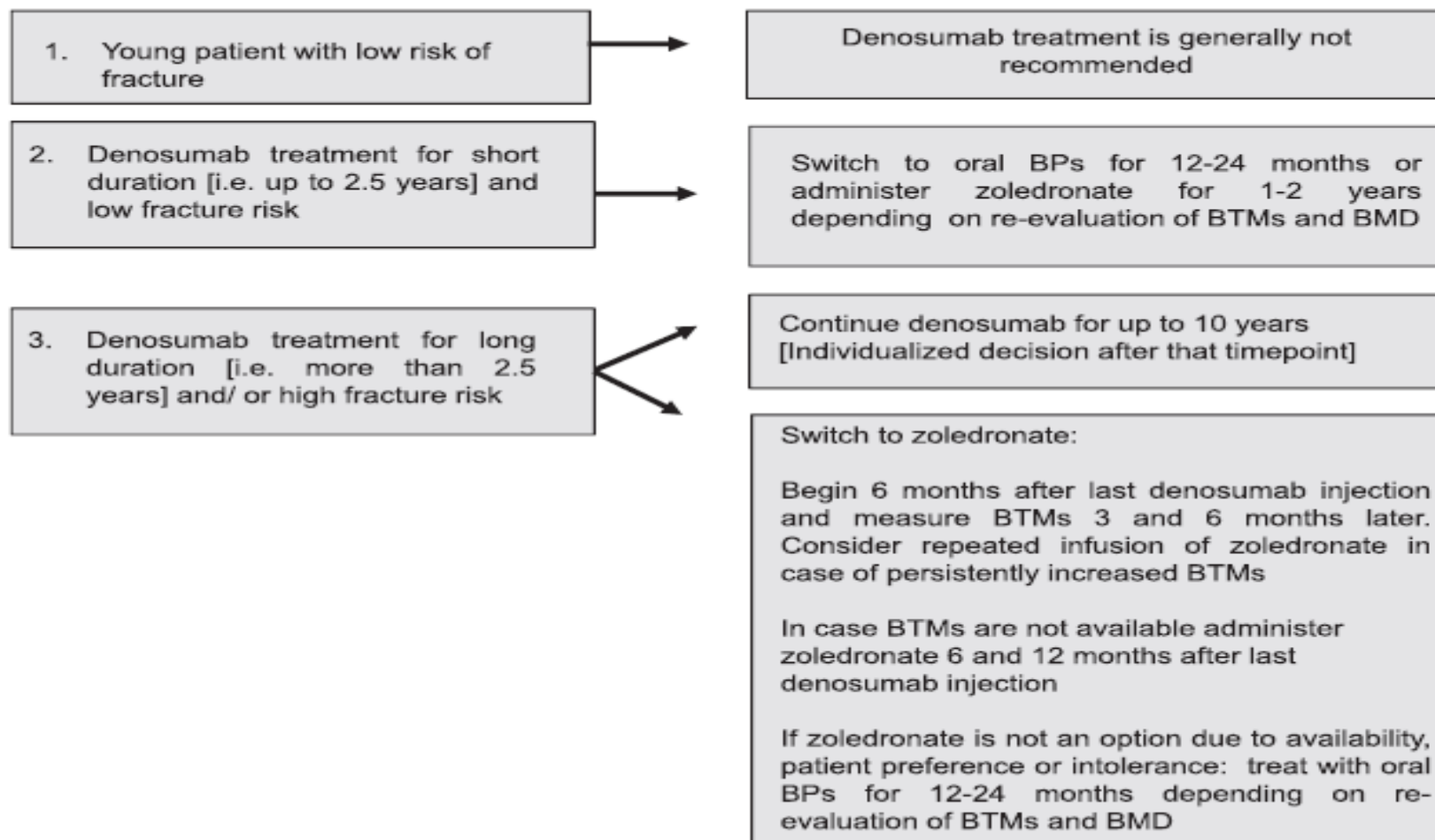
RISCHIO FRATTURATIVO
BASSO *

VERA PREVENZIONE PRIMARIA

STOP QUALSIASI TERAPIA per
La prevenzione delle fratture



Fracture Risk and Management of Discontinuation of Denosumab Therapy: A Systematic Review and Position Statement by ECTS





Conference Report

Medication-Related Osteonecrosis of Jaws (MRONJ) Prevention and Diagnosis: Italian Consensus Update 2020

Giuseppina Campisi ^{1,2}, Rodolfo Mauceri ^{1,2,3,*}, Francesco Bertoldo ^{2,4},
Giordana Bettini ^{2,5}, Matteo Biasotto ⁶, Giuseppe Colella ⁷, Ugo Consolo ⁸, Olga Di Fede ^{1,2},
Gianfranco Favia ⁹, Vittorio Fusco ^{2,10}, Mario Gabriele ¹¹, Antonio Lo Casto ^{1,2},
Lorenzo Lo Muzio ¹², Antonia Marciano ³, Marco Mascitti ¹³, Marco Meleti ¹⁴,
Michele D. Mignogna ¹⁵, Giacomo Oteri ³, Vera Panzarella ^{1,2}, Umberto Romeo ¹⁶,
Andrea Santarelli ¹³, Paolo Vescovi ^{2,14}, Claudio Marchetti ^{2,17} and Alberto Bedogni ^{2,5}

Raccomandazioni clinico-terapeutiche sull'osteonecrosi delle ossa mascellari
(ONJ) farmaco-relata e sua prevenzione

Versione 2.0 - Marzo 2020

(aggiornamento delle Raccomandazioni clinico-terapeutiche sull'osteonecrosi
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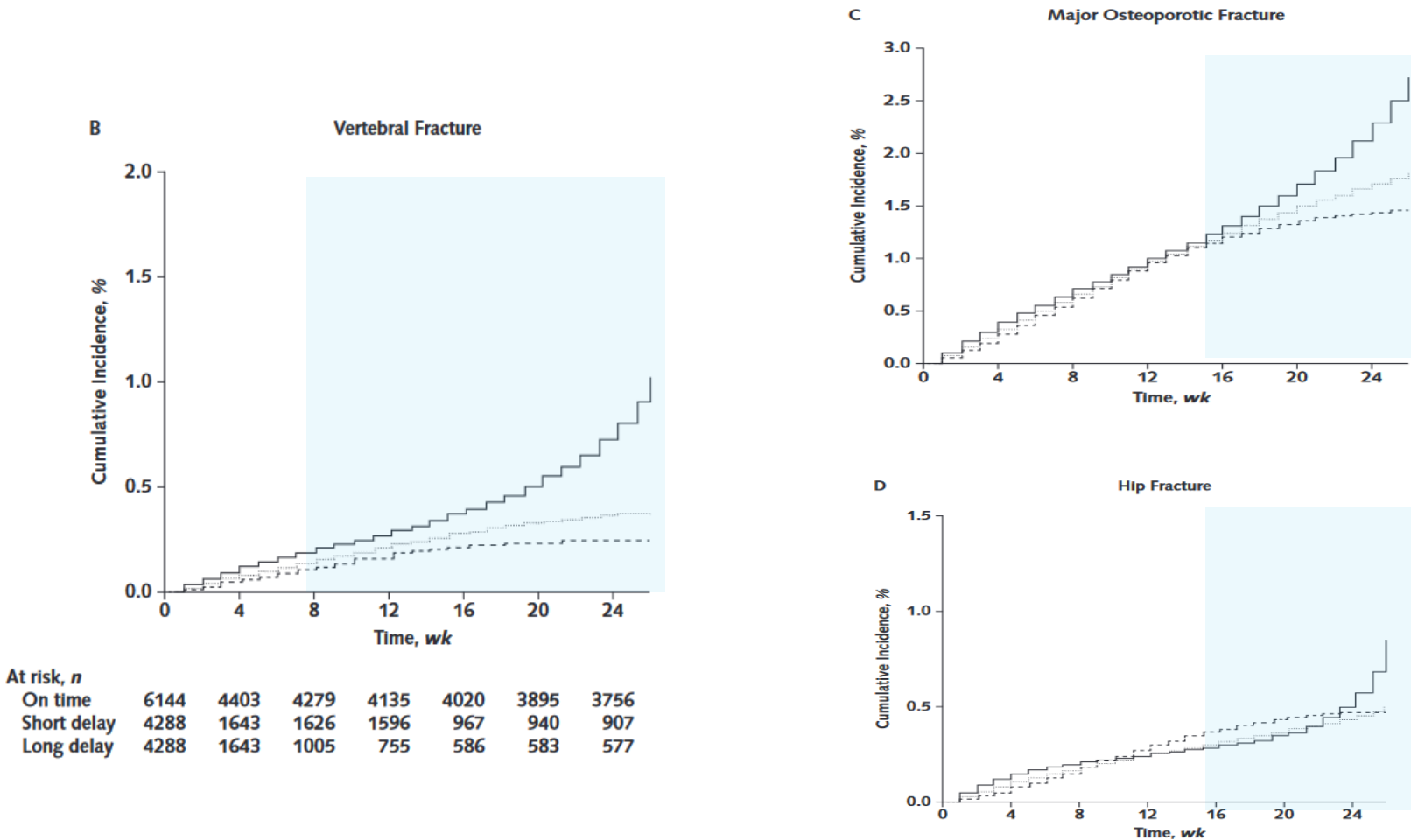


Società Italiana
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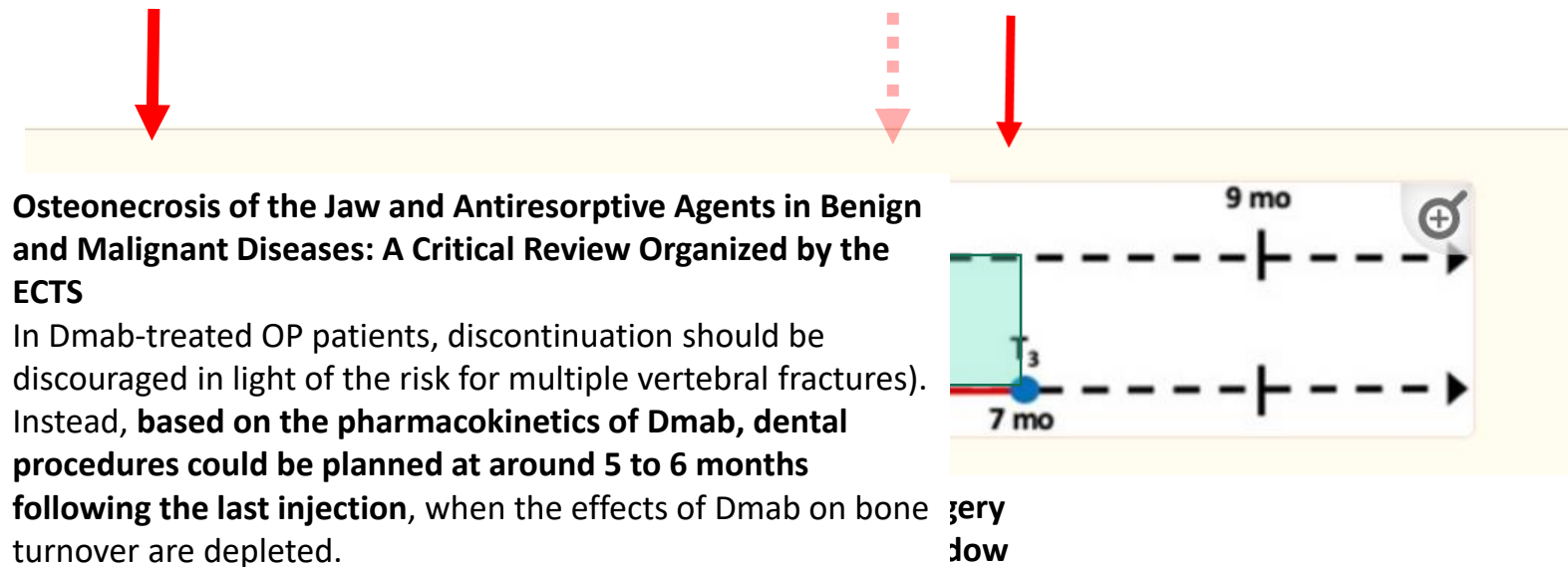
Società Italiana
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Delayed Denosumab Injections and Fracture Risk Among Patients With Osteoporosis



A pragmatic window of opportunity to minimise the risk of MRONJ development in individuals with osteoporosis on Denosumab therapy

Campisi G, Mauceri R, Fusco V, Bedogni A, Bertoldo F



[J Clin Endocrinol Metab.](#) 2022 May; 107(5): 1441–1460.

Take Home Message

CHI E' A RISCHIO DI FRATTURA	QUANDO COMINCIARE IL TRATTAMENTO	IN BASE A COSA SCEGLIERE IL TRATTAMENTO	QUANDO SOSPENDERE IL TRATTAMENTO?	BODY COMPOSITION
<p>Maschi in qualsunque tipo di terapia ormonale adiuvante (TOA) in corso , a prescindere dalla loro massa ossea o altri fattori.</p> <p>Il rischio di frattura è intrinseco alla terapia ormonale di per se</p>	<p>Il rischio di frattura è a breve tempo dall'inizio della TOA</p> <p>Va iniziato il prima possibile</p>	<p>in base all'evidenza il denosumab è l'unico farmaco che ha dimostrazione di ridurre il rischio frattura</p>	<p>Si può valutare se sospendere La terapia con antirassorbitivi alla fine della terapia ormonale.</p> <p>NON E' UN AUTOMATISMO</p> <p>Va valutato il rischio fratturativo</p>	<p>Preservare la Lean Mass</p> <p>Ridurre Fat Mass (?)</p> <p>Dieta (?) Attività Fisica Denosumab (?) (Non EBM)</p>

