

Sistema Socio Sanitario



Regione  
Lombardia

ASST Spedali Civili

ASST Spedali Civili di Brescia  
Dott. Alberto Dalla Volta



## VII sessione

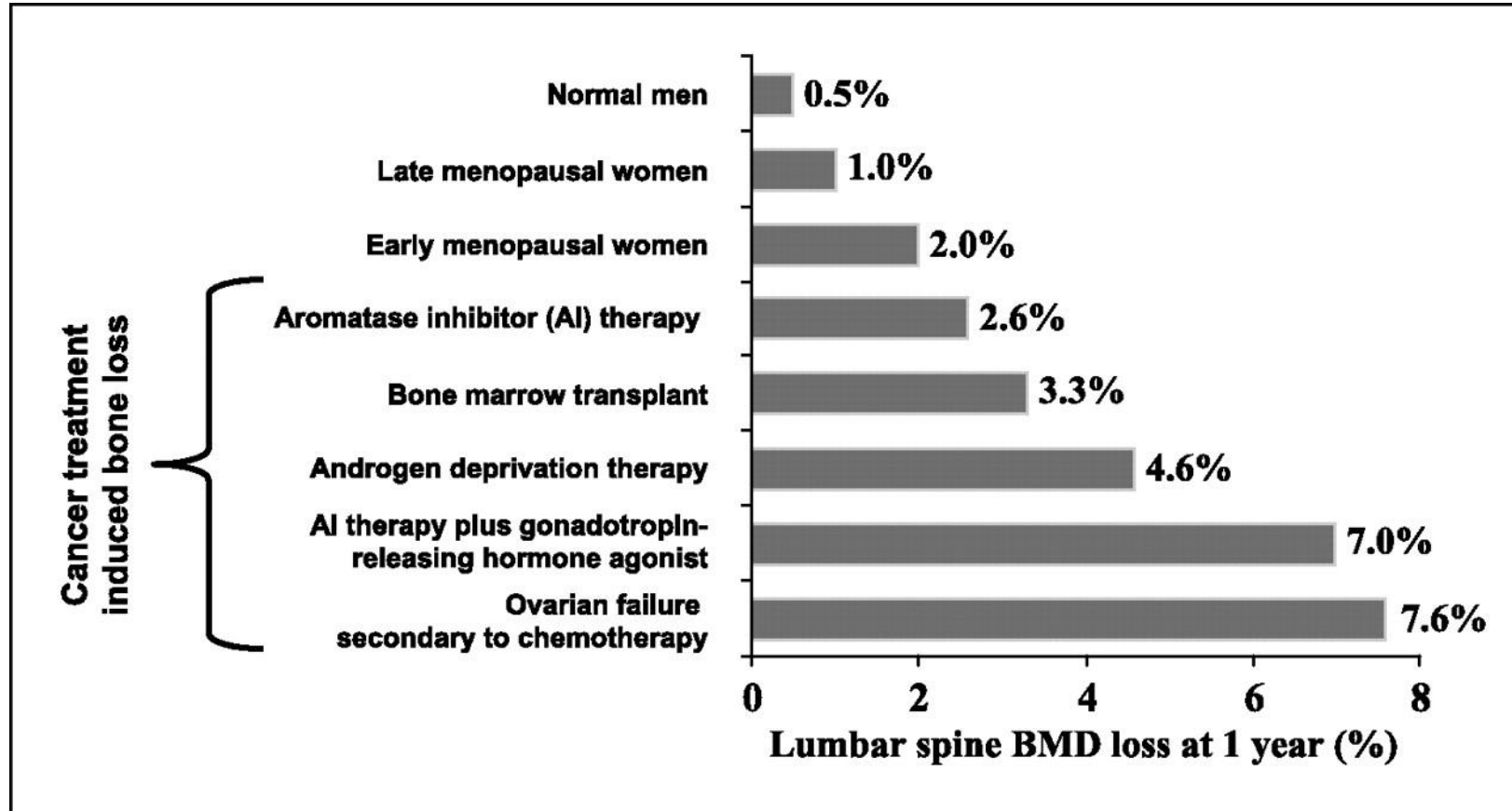
*«Utilizzo precoce dei nuovi farmaci inibenti il recettore degli androgeni e relativo impatto sulla salute dell'osso nel carcinoma prostatico»*







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



# BONE LOSS AND CANCER THERAPY



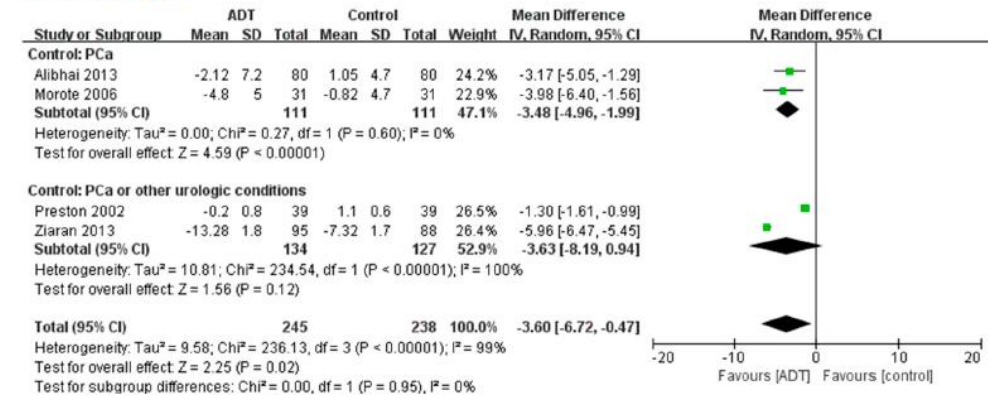
# Effect of Androgen-Deprivation Therapy on Bone Mineral Density in Patients with Prostate Cancer: A Systematic Review and Meta-Analysis

Do Kyung Kim <sup>1</sup> , Joo Yong Lee <sup>2</sup> , Kwang Joon Kim <sup>3</sup>, Namki Hong <sup>4</sup>, Jong Won Kim <sup>2</sup>, Yoon Soo Hah <sup>1</sup> , Kyo Chul Koo <sup>1</sup>, Jae Heon Kim <sup>5</sup> and Kang Su Cho <sup>1,\*</sup> 

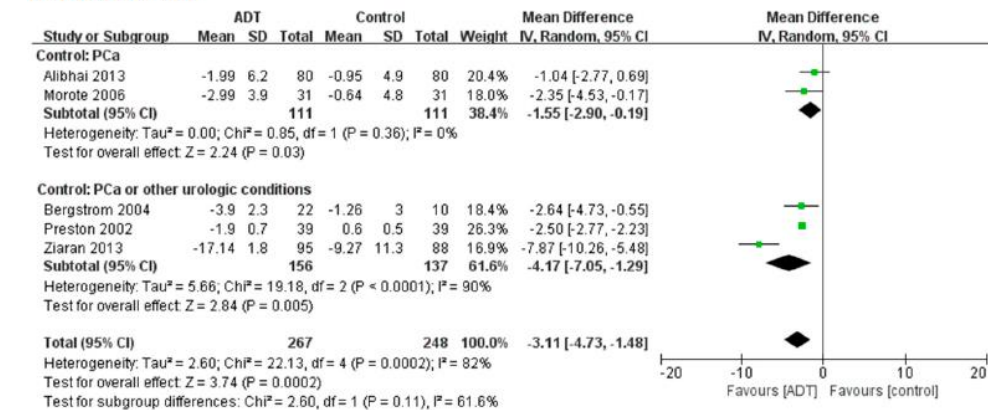
- Prima metanalisi di dati prospettici su:
  1. *PCa trattati con ADT vs PCa o altre condizioni urologiche senza ADT*
  2. *ADT almeno 6 mesi (med 12 mesi)*
  3. *Follow-up almeno 12 mesi*
  4. *Disponibilità di dati BMD*
- Risultati (% change BMD se ADT):
  - *Lumbar spine: -3,6%*
  - *Femoral neck: -3,11%*
  - *Total hip: -1,59%*

- Tratto lombare più esposto all'azione di ADT poiché a maggiore composizione di osso trabecolare vs corticale (quindi metabolicamente più attivo)?

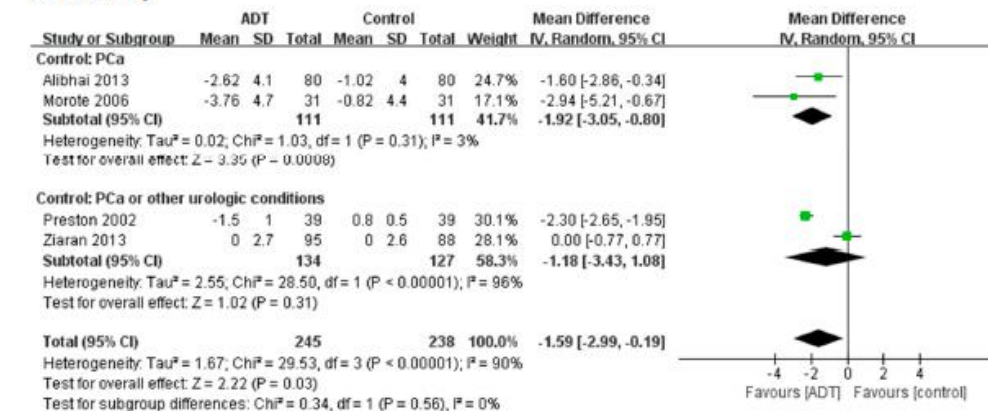
## A. Lumbar spine



## B. Femoral neck

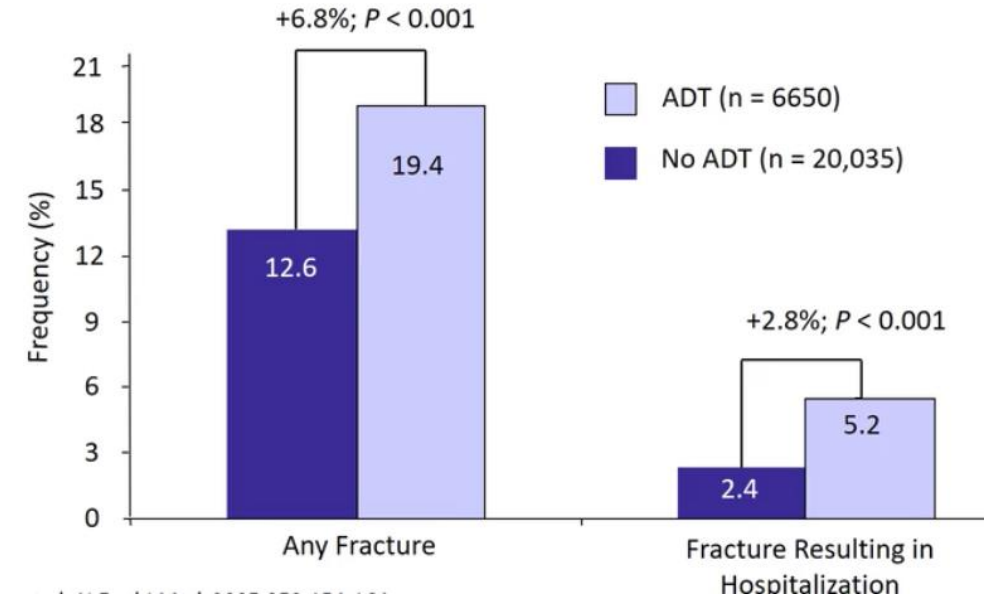
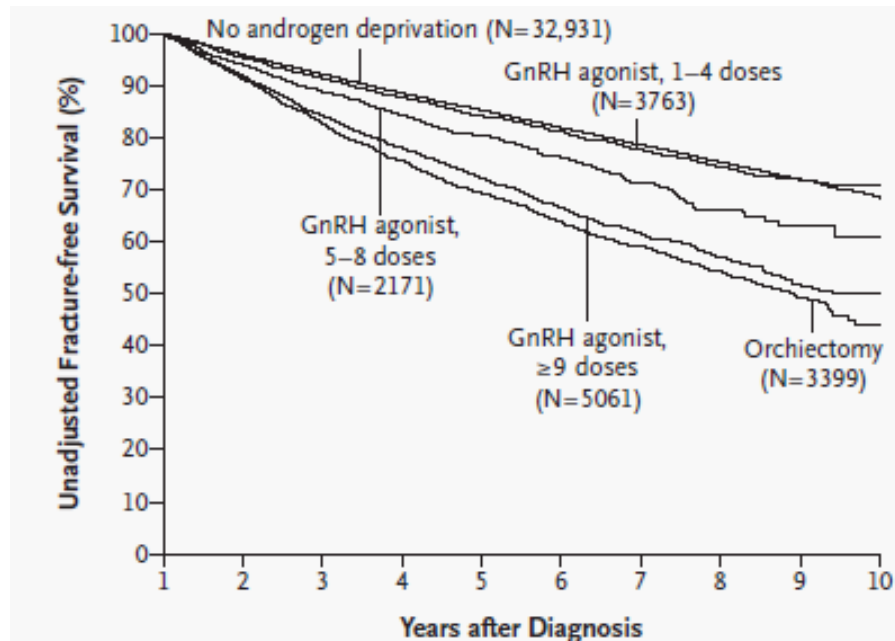


## C. Total hip





## Risk of Fracture after Androgen Deprivation for Prostate Cancer

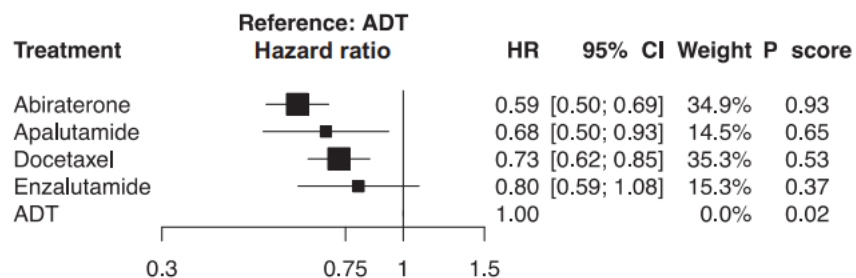


- **SEER database:** 1 uomo su 5 in trattamento con ADT per PCa si frattura (*1 su 8 coetanei con Pca non ADT*)
- **Fattori di rischio:** età, numero di somministrazioni (dato raccolto solo per i primi 12 mesi di terapia)
- $N^{\circ}$  needed to harm (median) = 28 (range 12-74)

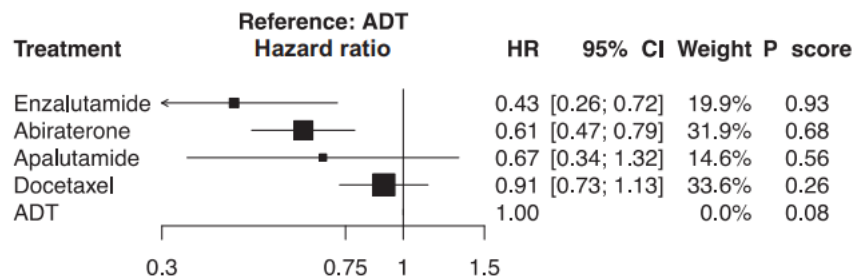
Age	Gonadotropin-Releasing Hormone Agonist			Orchiectomy
	1–4 doses	5–8 doses	$\geq 9$ doses	
	no. needed to harm (95% CI)			
66–69 yr	74 (50–146)	42 (29–73)	18 (16–24)	15 (13–18)
70–74 yr	69 (46–146)	39 (27–71)	17 (15–20)	14 (12–17)
75–79 yr	61 (41–125)	34 (24–61)	15 (14–17)	13 (11–15)
$\geq 80$ yr	46 (32–91)	26 (19–45)	12 (11–13)	10 (9–11)

# Overall Survival e nuovi agenti ormonali

## High Volume



## Low Volume



Comparison and study	Median overall survival, mo (95% confidence interval)					
	Treatment arm	Control arm	High-volume mHSPC		Low-volume mHSPC	
			Treatment arm	Control arm	Treatment arm	Control arm
Docetaxel vs ADT						
CHAARTED [24]	57.6 (52.0–63.9)	47.2 (41.8–52.8)	51.2 (45.2–58.1)	51.2 (45.2–58.1)	22.7 (18.9–29.1)	31.0 (23.1–51.1)
STAMPEDE arm C [19]	58.5 (NA–NA)	43.8 (NA–NA)	40.1 (NA–NA)	40.1 (NA–NA)	61.0 (NA–NA)	76.0 (NA–NA)
GETUG-AFU 15 [25]	62.1 (49.5–73.7)	48.6 (40.9–60.6)	39.8 (28.0–53.4)	39.8 (28.0–53.4)	83.4 (61.8–NR)	NR (69.5–NR)
Abiraterone vs ADT						
LATITUDE [20]	53.3 (48.2–NR)	36.5 (33.5–40.0)	49.7 (NA–NA) <sup>a</sup>	49.7 (NA–NA) <sup>a</sup>	NR	NR
STAMPEDE arm G [22]	79.2 (NA–NA) <sup>b</sup>	45.6 (NA–NA) <sup>b</sup>	–	–	–	–
STAMPEDE arm G [26]	–	–	51.0 (NA–NA)	51.0 (NA–NA)	NR	NR
ADT = androgen deprivation therapy; mHSPC = metastatic hormone-sensitive prostate cancer; NA = not available; NR = not reached.						
<sup>a</sup> According to the LATITUDE update [15].						
<sup>b</sup> According to the STAMPEDE arm G update [17].						

Wenzel M. Eur Urol Focus 2021

I Pazienti con carcinoma prostatico avanzato vivono oggi mediamente 4-5 anni, larga parte dei quali è trascorsa durante un trattamento ormonale combinato (ADT + inibitore del segnale mediato da AR).

## Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

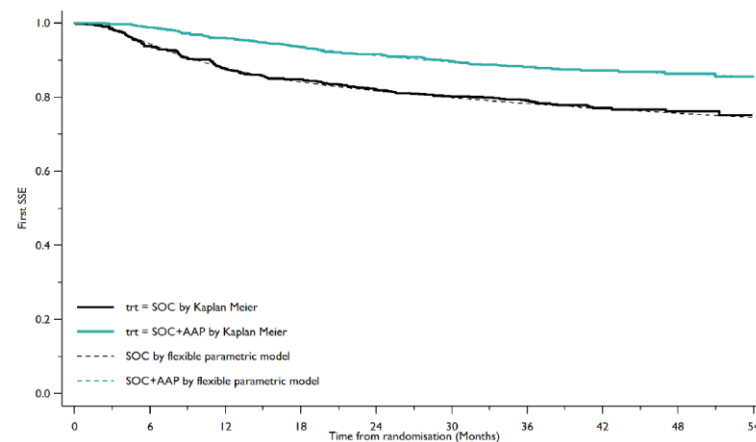
Karim Fizazi, M.D., Ph.D., NamPhuong Tran, M.D., Luis Fein, M.D.,

**Table 1. Prespecified Secondary and Exploratory Efficacy End Points.\***

End Point	Abiraterone Group (N = 597)	Placebo Group (N = 602)	Hazard Ratio (95% CI)	P Value†
<b>Secondary end points</b>				
Median time to pain progression (mo)	NR	16.6	0.70 (0.58–0.83)	<0.001
Median time to PSA progression (mo)	33.2	7.4	0.30 (0.26–0.35)	<0.001
Median time to next symptomatic skeletal event (mo)	NR	NR	0.70 (0.54–0.92)	0.009
Median time to chemotherapy (mo)	NR	38.9	0.44 (0.35–0.56)	<0.001
Median time to subsequent prostate cancer therapy (mo)	NR	21.6	0.42 (0.35–0.50)	<0.001

Fizazi et al, NEJM 2017

Figure S4A: Time to first Symptomatic Skeletal Event



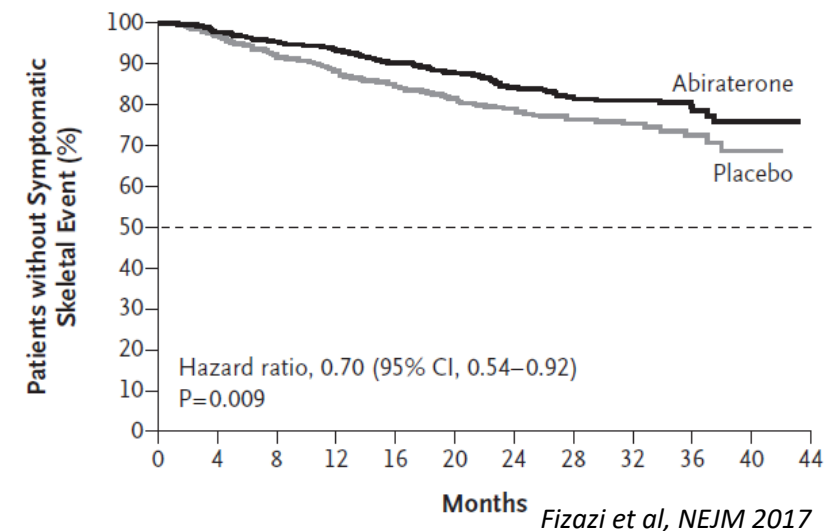
James et al, NEJM 2017

## Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy

N.D. James, J.S. de Bono, M.R. Spears, N.W. Clarke, M.D. Mason,

- ❖ Abiraterone mostra un significativo effetto protettivo sul rischio di sviluppare eventi scheletrici sintomatici
- ❖ Tuttavia l'evento «frattura non patologica» non è stato scorporato dai SSEs
- ❖ L'effetto antitumorale di abiraterone sulla malattia ossea può aver nascosto un incremento del rischio di fratture da fragilità?

C Symptomatic Skeletal Event



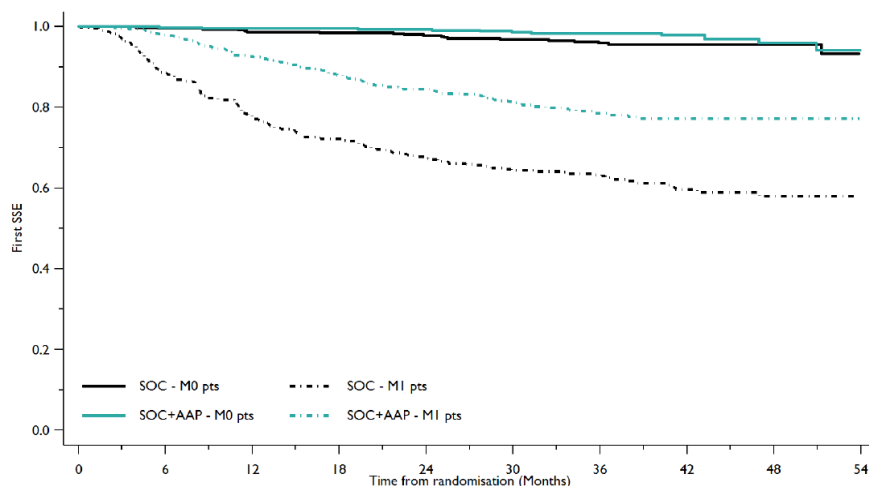
Fizazi et al, NEJM 2017

# mHSPC – abiraterone (2)

## Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy

N.D. James, J.S. de Bono, M.R. Spears, N.W. Clarke, M.D. Mason,

Figure S4B: Time to first Symptomatic Skeletal Event by baseline metastasis



James et al, NEJM 2017

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
Fracture	0	331	100%	458	100%
	1	0	0%	0	0%
	2	0	0%	0	0%
	3	0	0%	0	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	629	n/a	489	n/a
Osteoporosis (G1-3)	0	331	100%	458	100%
	1	0	0%	0	0%
	2	0	0%	0	0%
	3	0	0%	0	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	629	n/a	489	n/a

Studio STAMPEDE (suppl mat), l'aggiunta di abiraterone non sembra incrementare il rischio di fratture da fragilità, stando ai seguenti punti:

- ❖ Curve SSE M1 vs M0
- ❖ 0% fratture e osteoporosi (ma 50% di pazienti non valutati...)

## ORIGINAL ARTICLE

## Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer

Kim N. Chi, M.D., Neeraj Agarwal, M.D., Anders Bjartell, M.D.,

## mHSPC – ARSI (1)

## Apalutamide

## Adverse events of special interest

Rash†	142 (27.1)	33 (6.3)	45 (8.5)	3 (0.6)
Fall	39 (7.4)	4 (0.8)	37 (7.0)	4 (0.8)
Fracture‡	33 (6.3)	7 (1.3)	24 (4.6)	4 (0.8)

Chi et al, NEJM 2019

❖ Apalutamide mostra un modesto incremento del rischio fratturativo (+1.7%)

❖ L'evento «frattura» anche in questo caso è aggregato e non è noto se individuato su base clinica o morfometrica, né se comprensivo delle fratture patologiche

## Enzalutamide

Fall	21 (3.7)	2 (0.3)	15 (2.6)	1 (0.2)
Fractures	37 (6.5)	6 (1.0)	24 (4.2)	6 (1.0)

Armstrong et al, J Clin Oncol 2019

❖ Enzalutamide mostra un notevole incremento del rischio fratturativo solo in uno dei due studi di fase III (non sponsorizzato...)

❖ Quale ruolo della modalità di rilevazione di fratture/osteoporosi e della definizione di frattura?

## ORIGINAL ARTICLE

Enzalutamide with Standard First-Line Therapy in Metastatic Prostate Cancer

I.D. Davis, A.J. Martin, M.R. Stockler, S. Begbie, K.N. Chi, S. Chowdhury,

ARCHES: A Randomized, Phase III Study of Androgen Deprivation Therapy With Enzalutamide or Placebo in Men With Metastatic Hormone-Sensitive Prostate Cancer

Andrew J. Armstrong, MD, ScM<sup>1</sup>; Russell Z. Szmulowitz, MD<sup>2</sup>; Daniel P. Petrylak, MD<sup>3</sup>; Jeffrey Holznerlein, MD<sup>4</sup>; Anasud Vilars, MD<sup>5</sup>

	Anti-androgen						Enzalutamide						
	Worst grade						Worst grade						
	1	2	3	4	5	N	1	2	3	4	5	N	TOTAL
Osteonecrosis of jaw	2	3	—	—	—	5	—	2	—	—	—	2	7
Osteoporosis	2	3	—	—	—	5	6	6	—	—	—	12	17

	Anti-androgen						Enzalutamide						
	Worst grade						Worst grade						
	1	2	3	4	5	N	1	2	3	4	5	N	TOTAL
Fall	10	8	2	—	—	20	20	28	6	—	—	54	74
Fracture	2	5	3	—	—	10	2	11	8	1	—	22	32
Hip fracture	—	—	1	—	—	1	—	1	2	—	—	3	4

Davis et al, NEJM 2019



# mHSPC – ARSI (2)

The NEW ENGLAND JOURNAL of MEDICINE

## ORIGINAL ARTICLE

### Darolutamide and Survival in Metastatic, Hormone-Sensitive Prostate Cancer

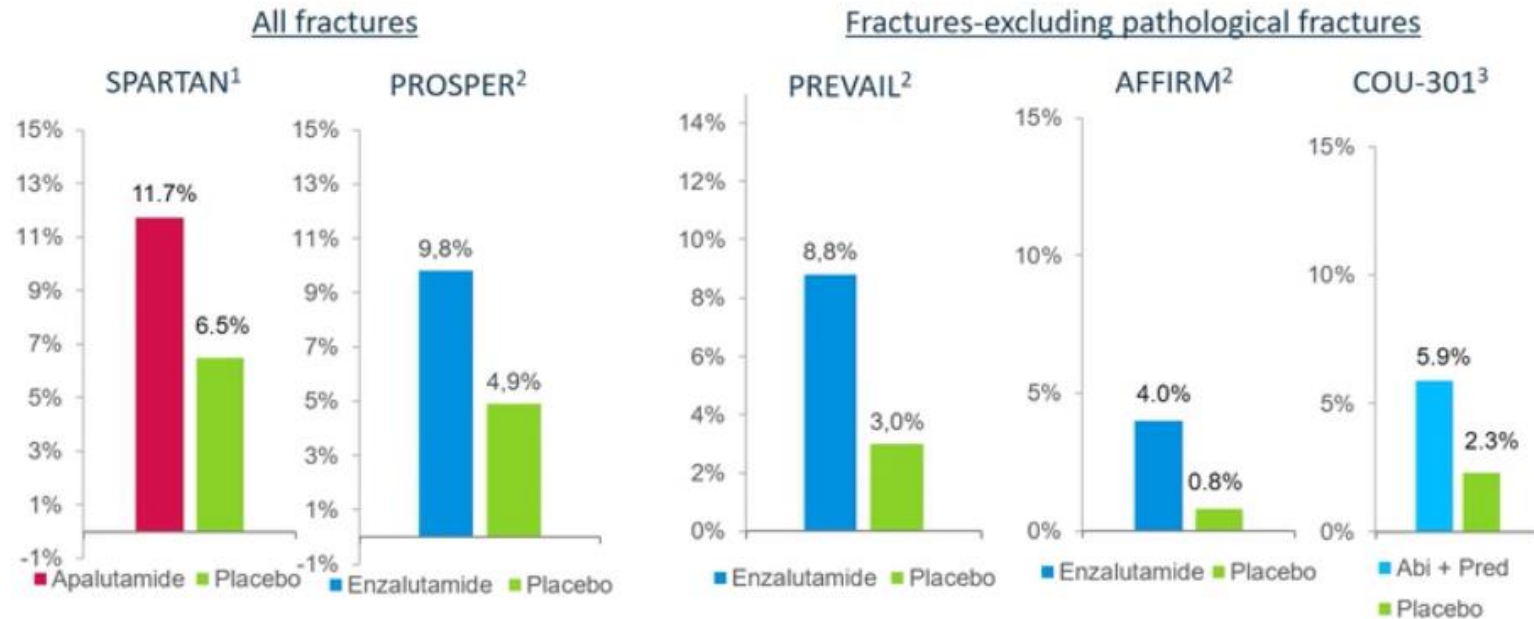
Matthew R. Smith, M.D., Ph.D., Maha Hussain, M.D., Fred Saad, M.D.,

- ❖ Darolutamide è associata ad un incremento degli eventi fratturativi (+2,4%): significativo?
- ❖ Nello studio ARAMIS l'evento di speciale interesse «frattura» è stato scorporato dall'evento «frattura patologica»
- ❖ Non è chiaro se l'evento «frattura» tuttavia sia stato valutato a livello morfometrico o clinico-sintomatico

Table S6. Adverse Events of Special Interest (Safety Analysis Set)

Adverse Event	Darolutamide + ADT + Docetaxel (N = 652*)		Placebo + ADT + Docetaxel (N = 650*)	
	No. of patients (%)	EAIR/ 100 PY†	No. of patients (%)	EAIR/ 100 PY†
Events commonly associated with ADT or androgen receptor pathway inhibitor therapy				
Fatigue	216 (33.1)	12.5	214 (32.9)	17.8
Vasodilatation and flushing	133 (20.4)	7.7	141 (21.7)	11.7
Rash‡	108 (16.6)	6.2	88 (13.5)	7.3
Diabetes mellitus and hyperglycemia	99 (15.2)	5.7	93 (14.3)	7.7
Hypertension§	89 (13.7)	5.1	60 (9.2)	5.0
Cardiac disorder	71 (10.9)	4.1	76 (11.7)	6.3
Cardiac arrhythmia§	52 (8.0)	3.0	55 (8.5)	4.6
Coronary artery disorder§	19 (2.9)	1.1	13 (2.0)	1.1
Heart failure§	4 (0.6)	0.2	13 (2.0)	1.1
Bone fracture¶	49 (7.5)	2.8	33 (5.1)	2.7
Falls, including accident	43 (6.6)	2.5	30 (4.6)	2.5
Mental-impairment disorder§	23 (3.5)	1.3	15 (2.3)	1.2
Weight decreased	22 (3.4)	1.3	35 (5.4)	2.9
Depressed-mood disorder§	21 (3.2)	1.2	24 (3.7)	2.0

# nmCRPC / mCRPC



1. Smith MR, et al. *N Engl J Med* 2018; doi:10.1056/NEJMoa1715546. 2. Xtandi (enzalutamide) [prescribing information]. Northbrook, IL: Astellas Pharma US, Inc; July 2017. 3. Zytiga (abiraterone acetate) [prescribing information]. Horsham, PA: Janssen Biotech, Inc; February 2018. 4. Erleada (apalutamide) [prescribing information]. Horsham, PA: Janssen Products, LP; February 2018. 5. Hussain M, et al. *N Engl J Med*. 2018;378(26):2465–2474.

Presented by Smith MR at ESMO 2018 meeting

I farmaci ormonali di nuova generazione incrementano ulteriormente il rischio fratturativo

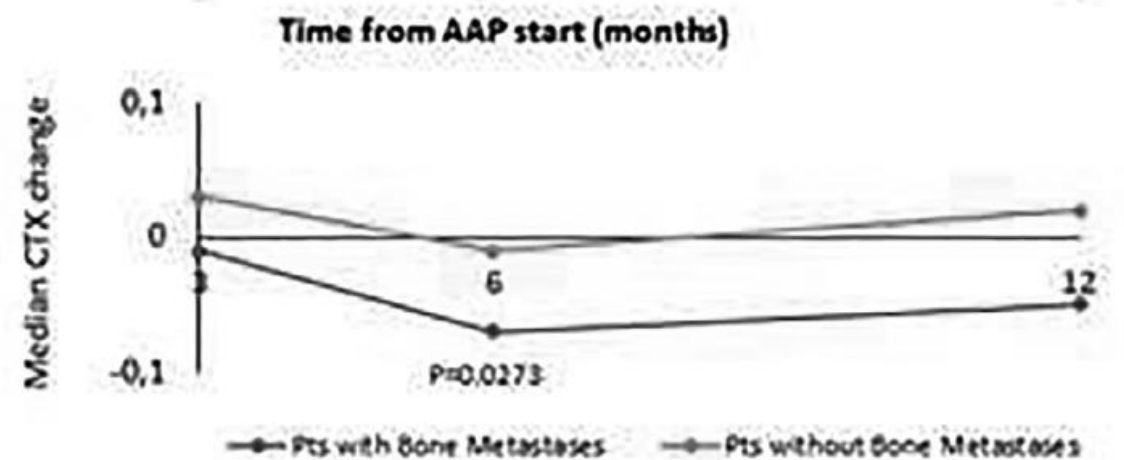
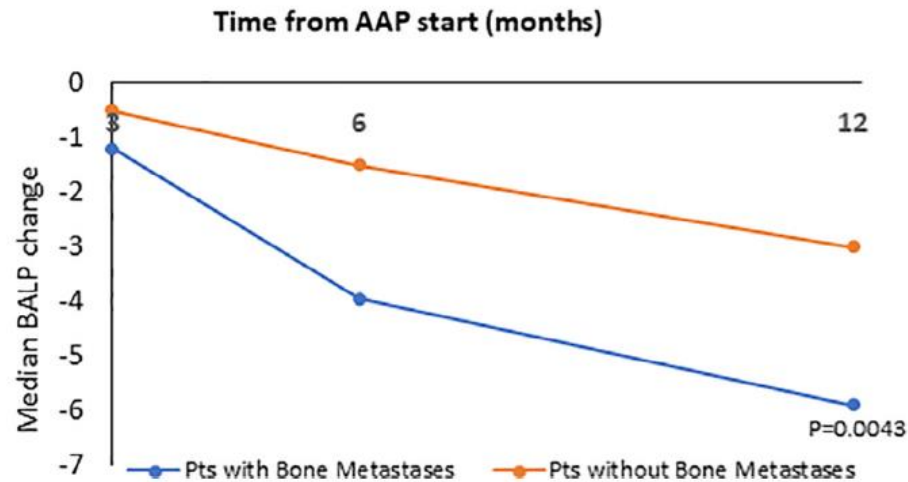
# nmCRPC

Preferred Terms	PROSPER				SPARTAN				ARAMIS			
	Enzalutamide (N=930)		Placebo (N=465)		Apalutamide (N=803)		Placebo (N=398)		Darolutamide (N=954)		Placebo (N=554)	
	All	3-4	All	3-4	All	3-4	All	3-4	All	3-4	All	3-4
Fatigue	32.6	2.9	13.8	0.6	30.4	0.9	21.1	0.3	12.1	0.4	8.7	0.9
Hypertension	11.9	4.6	5.2	2.2	24.8	14.3	19.8	11.8	6.6	3.1	5.2	2.2
Rash	2.3	0.0	2.2	0.2	23.8	5.2	5.5	0.3	2.9	0.1	0.9	0.0
Diarrhea	9.8	0.3	9.8	0.4	20.3	1.0	15.1	0.5	6.9	0.0	5.6	0.0
Nausea	11.4	0.3	8.6	0.0	18.1	0.0	15.8	0.0	5.0	0.2	5.8	0.0
Weight decreased	5.9	0.2	1.5	0.0	16.1	1.1	6.3	0.3	3.6	0.0	2.2	0.0
Arthralgia	8.4	0.1	6.9	0.2	15.9	0.0	7.5	0.0	8.1	0.3	9.2	0.4
Fall	11.4	1.3	4.1	0.6	15.6	1.7	9.0	0.8	4.2	0.8	4.7	0.7
Fracture	11.2	2.4	5.6	1.9	11.7	2.7	6.5	0.8	4.2	0.9	3.6	0.9
Dizziness	9.8	0.4	4.3	0.4	9.3	0.6	6.3	0.0	4.5	0.2	4.0	0.2
Hypothyroidism	0.6	0.0	0.6	0.0	8.1	0.0	2.0	0.0	0.2	0.0	0.0	0.0
Seizure	0.3	0.2	0.0	0.0	0.2	0.0	0.0	0.0	0.2	0.0	0.2	0.0
Mental impairm dis	5.0	0.5	2.0	0.0	5.1	0.0	3.0	0.0	0.4	0.0	0.2	0.0
SAE	24.0	0.0	18.0	0.0	24.8	0.0	23.1	0.0	24.8	15.8	20.0	12.6
AE discontinuation	9.0	0.0	6.0	0.0	10.6	0.0	7.0	0.0	8.9	3.4	8.7	4.3



## Effects of abiraterone acetate plus prednisone on bone turnover markers in chemotherapy-naïve mCRPC patients after ADT failure: A prospective analysis of the italian real-world study ABITUDE

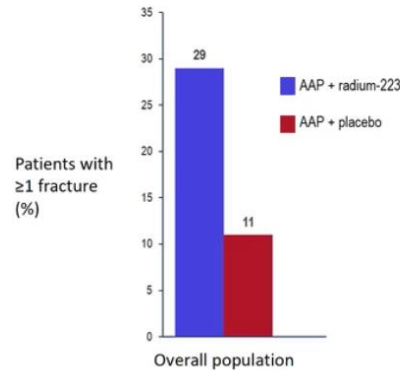
Daniele Santini<sup>a,\*</sup>, Saverio Cinieri<sup>b</sup>, Donatello Gasparro<sup>c</sup>, Roberto Bordonaro<sup>d</sup>, Pamela Francesca Guglielmini<sup>e</sup>, Vincenzo Emanuele Chiuri<sup>f</sup>, Rolando M D'Angelillo<sup>g</sup>, Giovanni Luca Ceresoli<sup>h</sup>, Daniele Fagnani<sup>i</sup>, Mirko Acquati<sup>j</sup>, Manlio Mencoboni<sup>k</sup>, Gaetano Lanzetta<sup>l</sup>, Donata Sartori<sup>m</sup>, Paolo Carlini<sup>n</sup>, Fabiana Panebianco<sup>o</sup>, Patrizia Beccaglia<sup>o</sup>, Giuseppe Procopio<sup>p</sup>



- ❖ L'impiego di AA+P come 1<sup>a</sup> linea mCRPC si associa al calo dei marcatori di metabolismo osseo (bALP e CTX-1)
- ❖ Il contributo dato alla riduzione dei marcatori di metabolismo osseo è largamente dovuto ai pazienti con malattia ossea metastatica
- ❖ Quale effetto netto sull'osso sano?

# Perchè è necessario studiare separatamente l'osso "sano"...

## Radium-223 Increases Fractures in Men Receiving Abiraterone Acetate +Prednisone/Prednisolone for mCRPC



### Independent Review of Fracture Events\*

	AAP + radium-223	AAP + placebo
Patients with ≥1 fracture, n	76	23
No bone metastasis at site of fracture, n	60	17
Type of fracture, n		
Pathological	19	6
Traumatic	27	13
Osteoporotic	37	4
Indeterminate	1	0

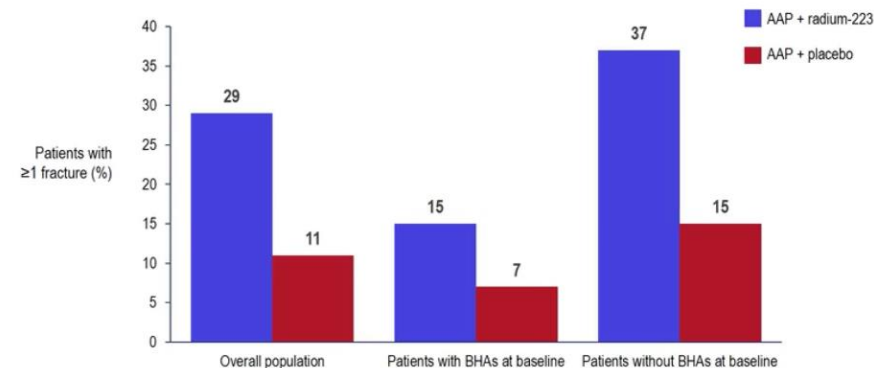
\*Independent review of patients with fractures and available images:  
n=80 in AAP + radium-223 group, n=27 in AAP + placebo group.

Lo studio di combinazione tra Radium223 ed Abiraterone ha mostrato un eccesso di fratture osteoporotiche per la combinazione dei due farmaci

Smith MR *et al* (2018) ESMO Annual Meeting, LBA30

## Post-Hoc Subgroup Analysis of Fractures by Baseline BHA Use

I pazienti che assumono agenti ossei antiriassorbitivi presentano una minore incidenza di fratture osteoporotiche





# Management of Osteoporosis in Survivors of Adult Cancers With Nonmetastatic Disease: ASCO Clinical Practice Guideline

Charles L. Shapiro, MD<sup>1</sup>; Catherine Van Poznak, MD<sup>2</sup>; Christina Lacchetti, MHS<sup>3</sup>; Jeffrey Kirshner, MD<sup>4</sup>; Richard Eastell, MD<sup>5</sup>; Robert Gagel, MD<sup>6</sup>; Sean Smith, MD<sup>2</sup>; Beatrice J. Edwards, MD, MPH<sup>7</sup>; Elizabeth Frank, EdM<sup>8</sup>; Gary H. Lyman, MD, MPH<sup>9</sup>; Matthew R. Smith, MD, PhD<sup>10</sup>; Rahul Mhaskar, PhD, MPH<sup>11</sup>; Tara Henderson, MD, MPH<sup>12</sup>; and Joan Neuner, MD, MPH<sup>13</sup>

## THE BOTTOM LINE

### Management of Osteoporosis in Survivors of Adult Cancers With Nonmetastatic Disease: ASCO Clinical Practice Guideline

#### Guideline Questions

1. Which patients with nonmetastatic cancer are at increased risk for developing osteoporotic fractures?
2. How should patients with nonmetastatic cancer who are at an elevated risk for osteoporotic fractures be screened?
3. Which patients with nonmetastatic cancer should be treated and which interventions are effective in reducing the risk of osteoporotic fractures?

**Recommendation 1.3.** Clinicians may use a **risk assessment tool** (eg, the WHO Fracture Risk Assessment Tool (FRAX)) to quantify the risk estimates for osteoporotic fracture in adult patients with nonmetastatic cancer. To date, existing risk assessment tools have **not been validated in patients with cancer** and clinical judgment is necessary in interpreting results from these tools (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

**Recommendation 2.1.** Patients with nonmetastatic cancer with one or more risk factors for osteoporotic fracture, as per Recommendation 1, should be offered bone mineral density (BMD) testing with central/axial dual-energy x-ray absorptiometry (DXA). In settings in which DXA is not available or technically feasible, other BMD testing (eg, quantitative ultrasound or calcaneal DXA) should be offered (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

**Recommendation 2.2.** Patients with nonmetastatic cancer who are prescribed a **drug that causes bone loss** or whose baseline or subsequent **BMD is near the threshold** of treatment using FRAX **should be offered BMD testing every 2 years**, or more frequently if deemed medically necessary, based on the results of BMD testing and expected bone loss. Testing should generally not be conducted more than annually (Type: expert panel consensus, relative balance of benefits and harms; Evidence quality: insufficient).

## Linee guida ASCO 2019: punti in sospeso

- Prevenzione dell'osteoporosi soltanto in pazienti non metastatici e guariti?
- Impiego routinario della BMD come «*gate-keeper*» per la prescrivibilità dei *bone-protecting agents* (vs linee guida AIOM...)
- Impiego del FRAX score, non validato per i pazienti oncologici in trattamento ormonale...
- Necessità di ulteriori parametri!

# Fratture: oltre la BMD

Journal of Bone Oncology 33 (2022) 100421

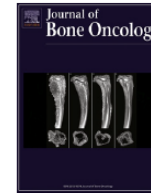


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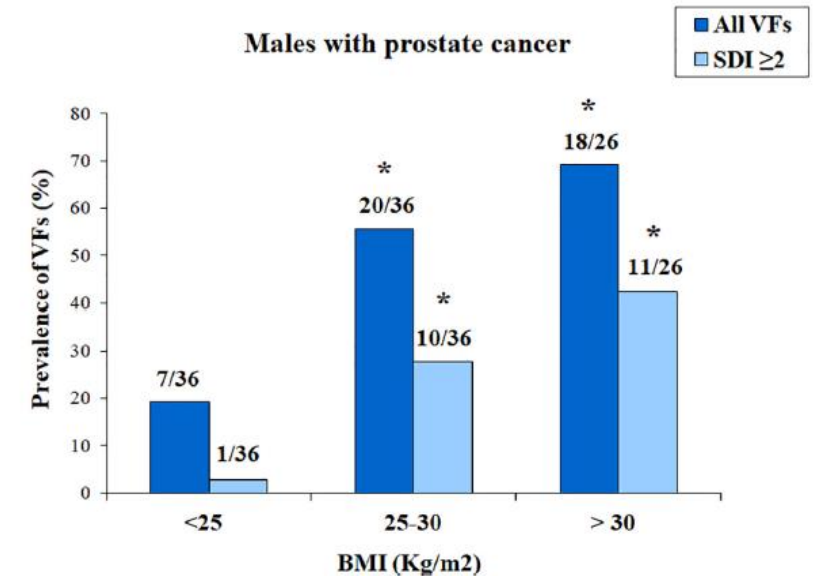
journal homepage: [www.elsevier.com/locate/jbo](http://www.elsevier.com/locate/jbo)



Research Paper

Prediction of vertebral fractures in cancer patients undergoing hormone deprivation therapies: Reliability of who fracture risk assessment tool (frax) and bone mineral density in real-life clinical practice

Gherardo Mazziotti<sup>a,b</sup>, Walter Vena<sup>b</sup>, Rebecca Pedersini<sup>f</sup>, Sara Piccini<sup>a,b</sup>, Emanuela Morengi<sup>a,c</sup>, Deborah Cosentini<sup>f</sup>, Paolo Zucali<sup>a,d</sup>, Rosalba Torrisi<sup>d</sup>, Silvio Sporeni<sup>b</sup>, Edda L. Simoncini<sup>f</sup>, Roberto Maroldi<sup>g,h</sup>, Luca Balzarini<sup>e</sup>, Andrea G. Lania<sup>a,b,\*</sup>, Alfredo Berruti<sup>f,h</sup>



**Table 2**

Determinants of vertebral fractures in prostate cancer patients treated with androgen deprivation therapies. Results of univariate and multivariate logistic regression analyses. \*, the lowest BMD value at lumbar spine, femoral neck or total hip was considered.

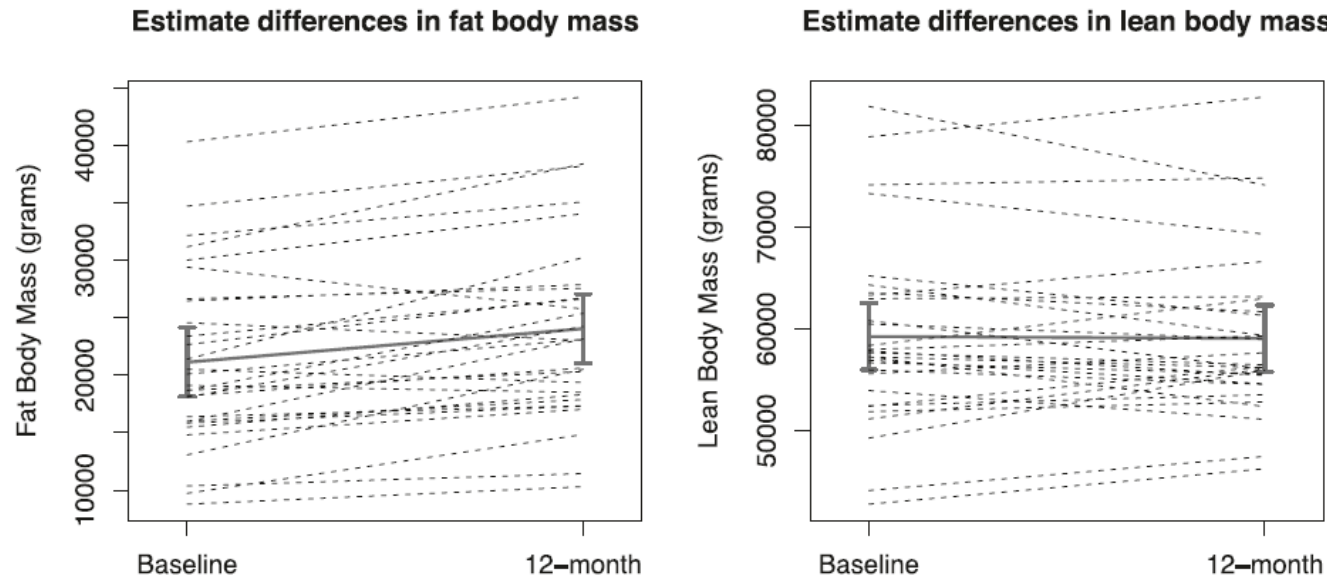
	UNIVARIATE ANALYSIS			MULTIVARIATE ANALYSIS		
	OR	95% C.I.	P	OR	95% C.I.	P value
N = 98						
Age	1.05	1.00–1.10	0.072			0.168
BMI ≥ 25 Kg/m2	6.56	2.49–17.32	<0.001	17.63	4.88–63.73	<0.001
BMD T-score < -1.0 SD at any skeletal site*	4.36	1.82–10.42	0.001	7.79	2.48–24.50	<0.001
FRAX score for major fractures	1.07	1.00–1.45	0.038			
GnRHa plus abiraterone	4.38	1.62–11.84	0.004	11.51	2.78–47.69	0.001
Duration of HDTs	1.01	1.00–1.02	0.182			

BMD, bone mineral density; BMI, body mass index; C.I., confidence interval; FRAX, WHO Fracture Risk Assessment Tool; GnRHa, gonadotropin-releasing hormone agonists; HDT, hormone deprivation therapies; OR, odds ratio, SD, standard deviation.



## Changes in body composition and lipid profile in prostate cancer patients without bone metastases given Degarelix treatment: the BLADE prospective cohort study

Carlotta Palumbo<sup>1,2</sup> · Alessandro Antonelli<sup>2,3</sup> · Luca Triggiani<sup>4</sup> · Alberto Dalla Volta<sup>5</sup> · Filippo Maffezzoni<sup>6</sup> · Stefania Zamboni<sup>2</sup> · Paolo Borghetti<sup>4</sup> · Luca Rinaudo<sup>7</sup> · Francesca Valcamonico<sup>5</sup> · Roberto Maroldi<sup>6</sup> · Stefano Maria Magrini<sup>4</sup> · Claudio Simeone<sup>2</sup> · Alfredo Berruti<sup>5</sup> · Collaborators

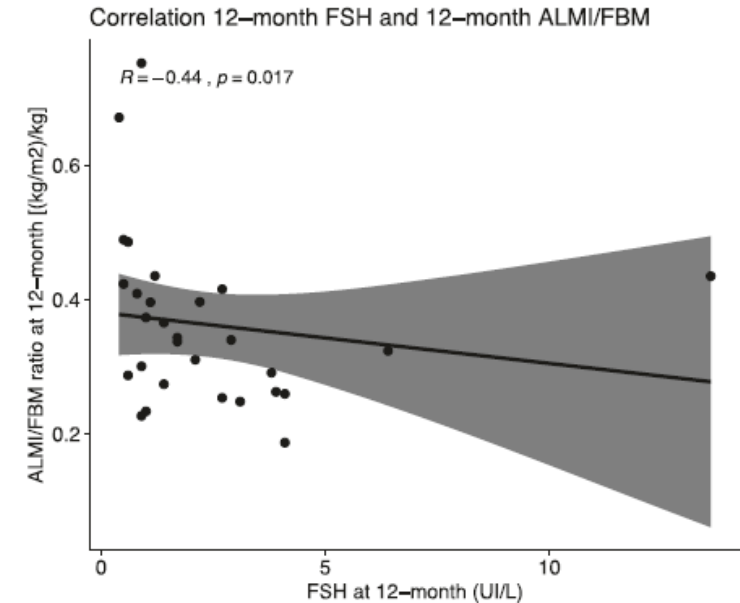


Analisi dopo 12 mesi di trattamento con degarelix:

- FBM incrementata: +13,8%
- LBM stabile: - 0,3%
- Correlazione inversa tra FSH e il rapporto ALMI/FBM

## Studio BLADE

### 1) Body composition



Palumbo C, Prostate Can Prostatic Dis, 2021

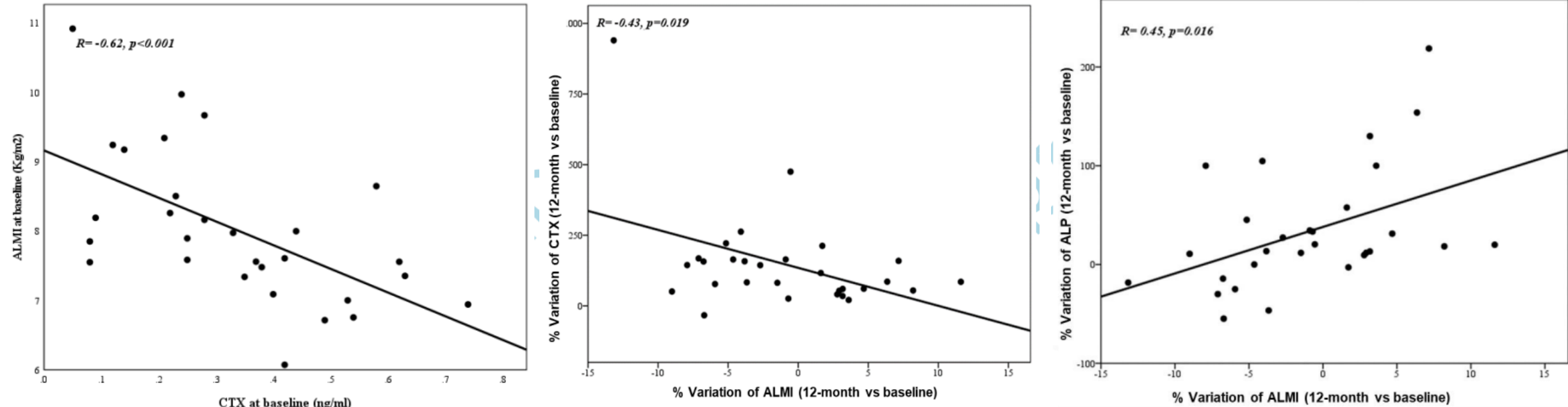
# Effect of Degarelix administration on bone health in prostate cancer patients without bone metastases.

## The Blade study [Get access >](#)

Carlotta Palumbo, Alberto Dalla Volta, Stefania Zamboni, Gherardo Mazziotti, Manuel Zamparini, Luca Triggiani, Paolo Borghetti, Filippo Maffezzoni, Roberto Bresciani, Luca Rinaudo, Francesca Valcamonico, Davide Farina, Stefano Maria Magrini, Alessandro Antonelli, Claudio Simeone, Alfredo Berruti ✉

## Studio BLADE

### 2) Metabolismo osseo



Analisi dopo 12 mesi di trattamento con degarelix:

- BMD lombare ridotta: -2,5%
- CTX incrementato: +99%
- Correlazione inversa tra  $\Delta$ ALMI e  $\Delta$ CTX
- Correlazione diretta tra  $\Delta$ ALMI e  $\Delta$ ALP

## Long-Term Antitumor Activity and Safety of Enzalutamide Monotherapy in Hormone Naïve Prostate Cancer: 3-Year Open Label Followup Results

Bertrand Tombal,<sup>\*,†</sup> Michael Borre, Per Rathenborg, Patrick Werbrouck, Hendrik Van Poppel, Axel Heidenreich,<sup>‡</sup> Peter Iversen,<sup>‡</sup> Johan Braeckman, Jiri Heracek, Benoit Baron,<sup>‡</sup> Andrew Krivoshik,<sup>‡</sup> Mohammad Hirmand<sup>§</sup> and Matthew R. Smith

J Urol 199: 459-464, 2018

	No. Pts	Mean ± SD % Change from Baseline	
Bone mineral density (gm/cm <sup>2</sup> ):			
Total	26	−0.2 ±	3.5
Femoral neck	30	−2.4 ±	3.2
Trochanter	30	−2.7 ±	4.4
Spine L1-L4	30	−0.1 ±	4.8
Forearm, radius 33%	29	−2.0 ±	4.7
Body mass (kg):			
Fat	26	16.5 ±	13.4
Lean	26	−6.5 ±	4.2





**BonEnza**

**VALUTAZIONE DELLA RISPOSTA OSSEA DOPO LHRH-ANALOGO  
IN ASSOCIAZIONE AD ENZALUTAMIDE CON O SENZA ACIDO  
ZOLEDRONICO IN PAZIENTI CON METASTASI OSSEE DA  
CARCINOMA PROSTATICO ORMONO-SENSIBILE: STUDIO  
PROSPETTICO DI FASE II RANDOMIZZATO MULTICENTRICO**

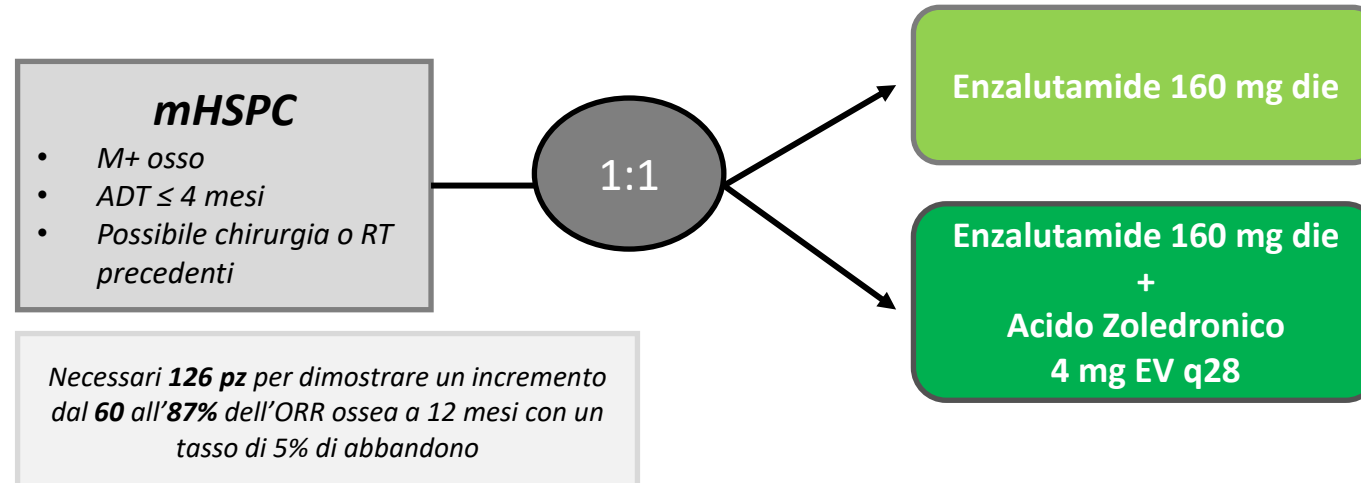
**Centro Promotore: ASST Spedali Civili di Brescia**

**EudraCT: 2017-000305-21**

**ID: ASCB-ONCO-2336-2017**

# Disegno

- Carcinoma prostatico ormono-sensibile avanzato (M+ osso)
- Randomizzazione 1:1 Enzalutamide vs Enzalutamide + Acido Zoledronico (*open label*)
- Rivalutazione strumentale ogni 6 mesi (*periodo di studio = 18 mesi + follow-up*)
- **Obiettivo primario**
  - *ORR ossea secondo WB-DW-MRI a 12 mesi*
- **Obiettivi secondari**
  - *Variazione della BMD e della composizione corporea secondo DEXA scan*
  - *Variazione dei markers di metabolismo osseo*
  - *QoL mediante questionari validati*
  - *PFS, OS*



# BonEnza – body composition

Analisi aggregata dei primi 40 pazienti arruolati (*unpublished data*)

	Baseline	18-month	P*
<b>Fat body mass (grams)</b>	19390.8 (6196.2)	27510.3 (7245.2)	<0.001
<b>Lean body mass (grams)</b>	56935.3 (6870.2)	52345.8 (7112.4)	0.011
<b>Bone mineral density COLONNA (grams/cm<sup>2</sup>)</b>	1.06 (0.22)	1.00 (0.24)	0.297
<b>Bone mineral density FEMORE (grams/cm<sup>2</sup>)</b>	0.80 (0.18)	0.75 (0.13)	0.212
<b>BMI (kg/m<sup>2</sup>)</b>	25.63 (3.69)	26.85 (3.93)	0.190
<b>ALP</b>	282.8 (498.2)	93.7 (42.5)	0.027
<b>TBS</b>	1.30 (0.12)	1.25 (0.14)	0.161
<b>T-score COLONNA</b>	-0.13 (2.19)	-0.81 (2.23)	0.212
<b>T-score FEMORE</b>	-0.83 (1.40)	-1.33 (1.03)	0.107
<b>LBM/FBM</b>	3.14 (1.27)	2.08 (0.79)	0.001



Dopo 18 mesi:

1. **FBM +34,3%; p 0,001**
2. **LBM -11,95%; p 0,011**
3. BMI +2,6%; p 0,190
4. **LBM/FBM -38%; p 0,001**

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

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[www.nrjournal.com](http://www.nrjournal.com)

## Review Article

## Obesity is a concern for bone health with aging

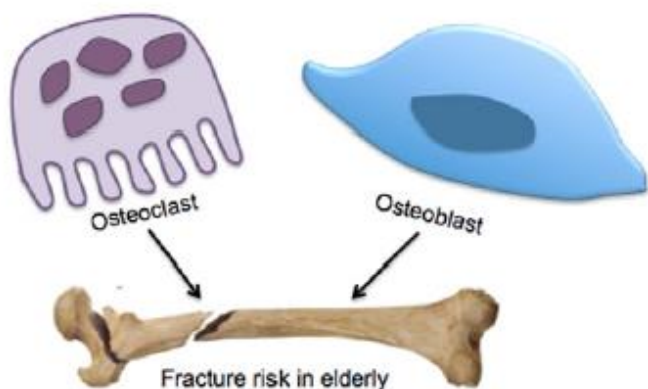
Sue A. Shapses\*, L. Claudia Pop, Yang Wang

Department of Nutritional Sciences, Rutgers University, New Brunswick, NJ



- SFA (+), PUFA (-)
- Calcium (-)
- PTH, PGE2 (+)
- ↑Oxidative stress (+)
- ↑Inflammation(+)
- Cytokines: IL1 $\beta$ , IL6, TNF $\alpha$
- RANKL

- PUFA (+)
- Protein (+)
- ↑GH, IGF-1 (+)
- ↓25OHD (-)
- FGF23 + insulin (+)



- Sedentary Lifestyle
- Immobility
- Falls

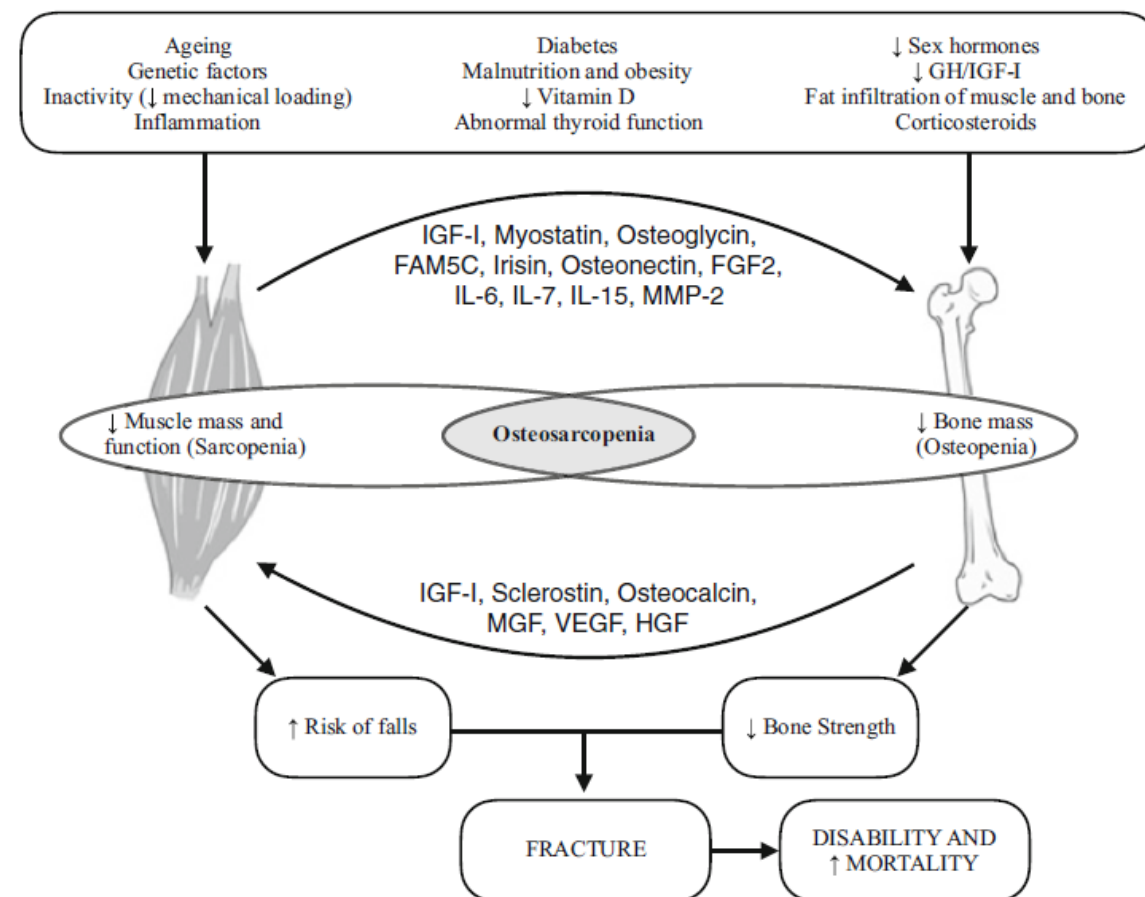
- Body composition
- ↑Adipogenesis
- Muscle loss
- Bone
- ↓Ct. vBMD

Osteoporos Int (2017) 28:2781–2790

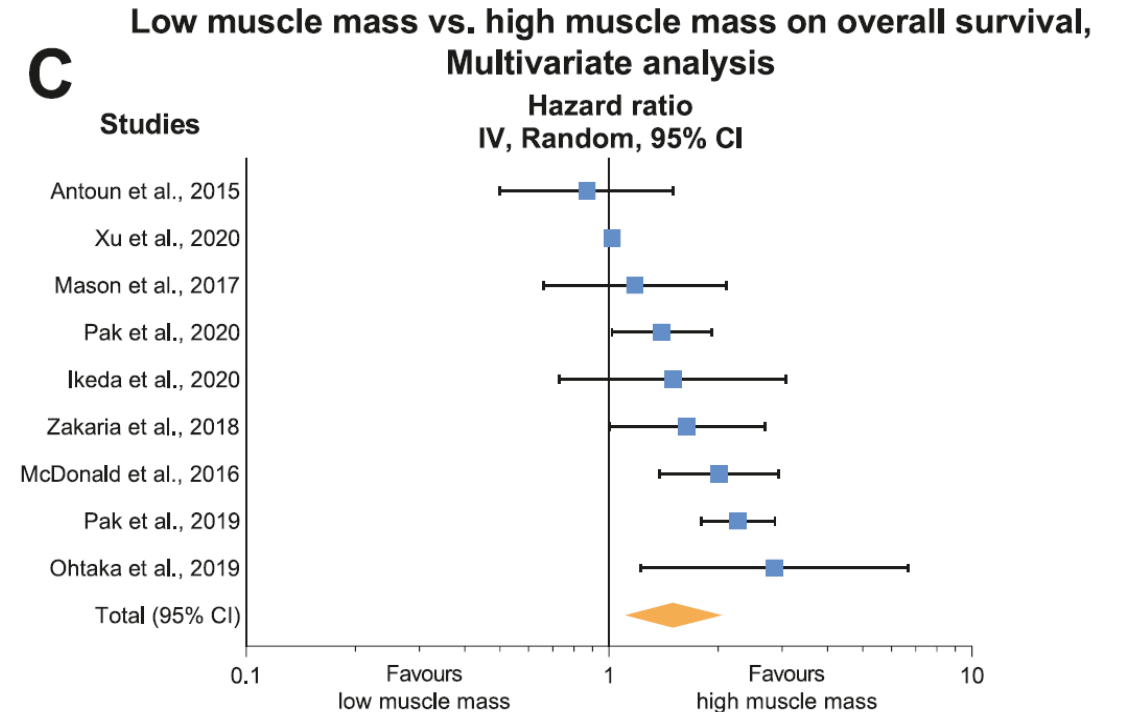
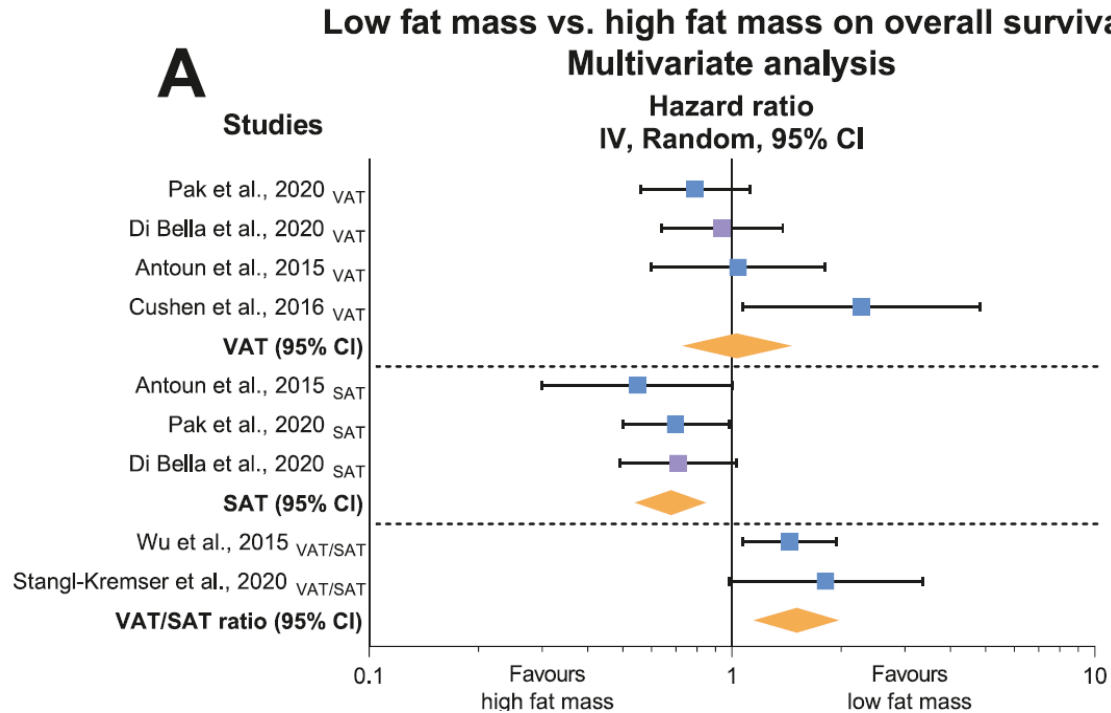
DOI 10.1007/s00198-017-4151-8

## REVIEW

## Osteosarcopenia: where bone, muscle, and fat collide

H. P. Hirschfeld<sup>1</sup> · R. Kinsella<sup>2</sup> · G. Duque<sup>2,3</sup> 

# Body composition e prognosi



- Rapporto grasso viscerale / grasso sottocutaneo correlato a peggior prognosi.
- Sarcopenia correlata a peggior prognosi.

Lopez P, Prostate Can Prostatic Dis, 2021

Quale ruolo della prognosi metabolica vs cancro-correlata?



# Conclusioni

- I pazienti con carcinoma prostatico metastatico ormono-sensibile e non metastatico resistente alla castrazione ricevono terapia ormonale di nuova generazione per 3-4 anni
- Unmet needs negli studi clinici registrativi dei nuovi agenti ormonali:
  1. definizione di fratture (*patologiche vs fragilità*)
  2. modalità di registrazione dell'evento (*cliniche vs morfometriche*)
  3. sistematicità nella registrazione (*tutti i pazienti, in tempi precisi*)
- Oltre alla BMD sono da valutare BMI (meglio, body composition, ma ancora sperimentale) ed «intensità» del trattamento ormonale (aggiunta di nuovi agenti ormonali) nella definizione del rischio fratturativo



**ARRIVEDERCI A BRESCIA...!**

## **LE NEOPLASIE GENITOURINARIE**

TRA PRATICA CLINICA E INNOVAZIONE



**V edizione**  
**18 Novembre 2022**

