

Uso dei farmaci anti-riassorbitivi e anabolizzanti nell'osteoporosi del paziente con malattia renale cronica

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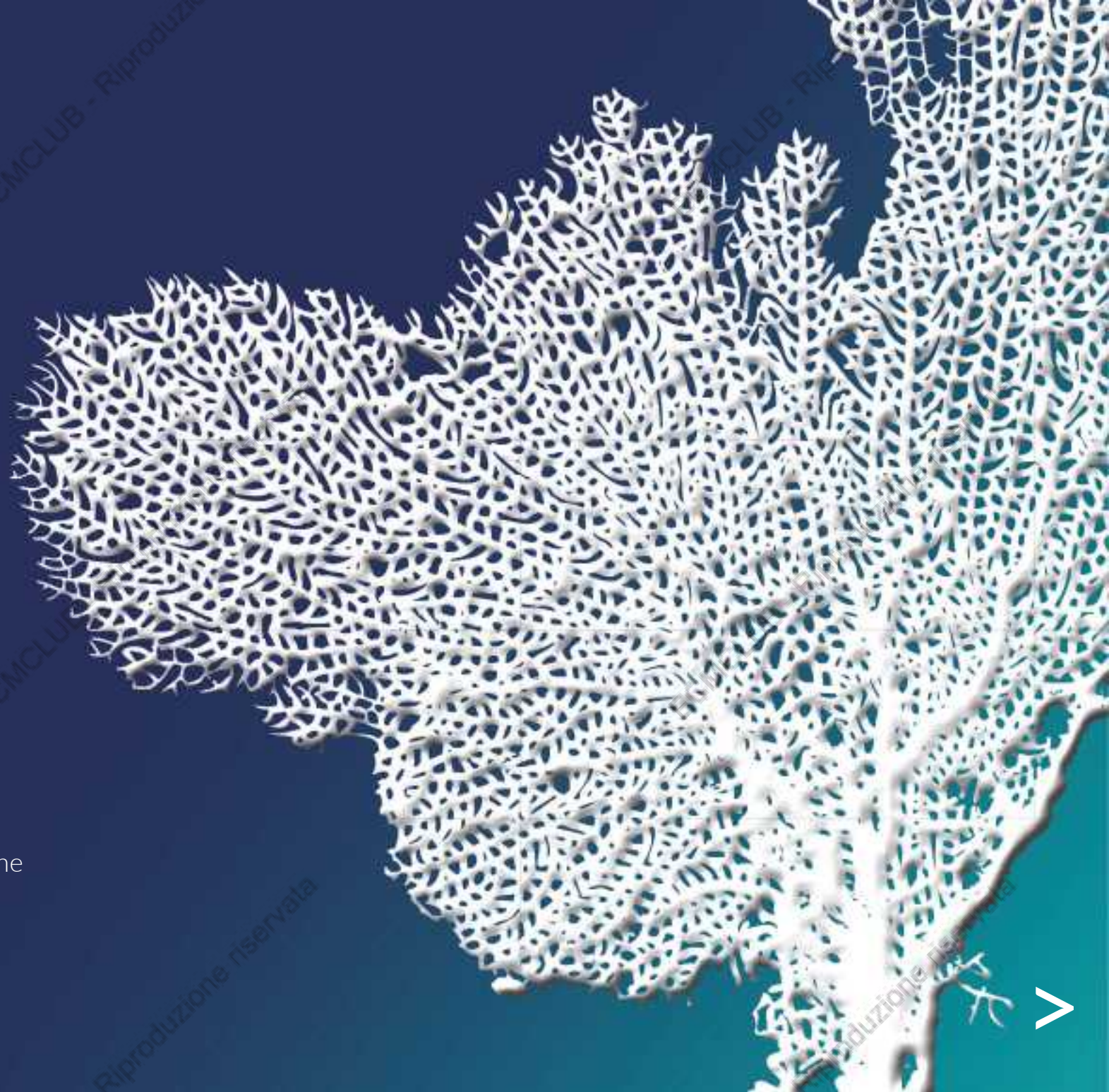
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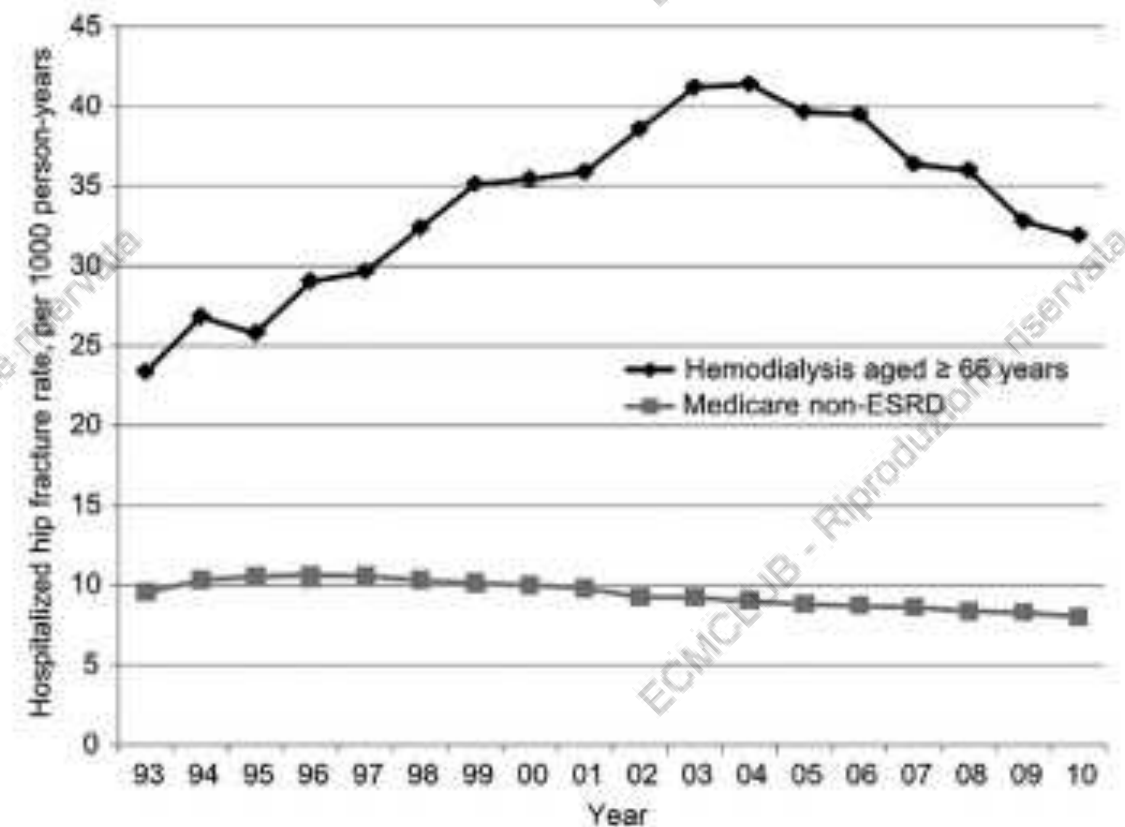
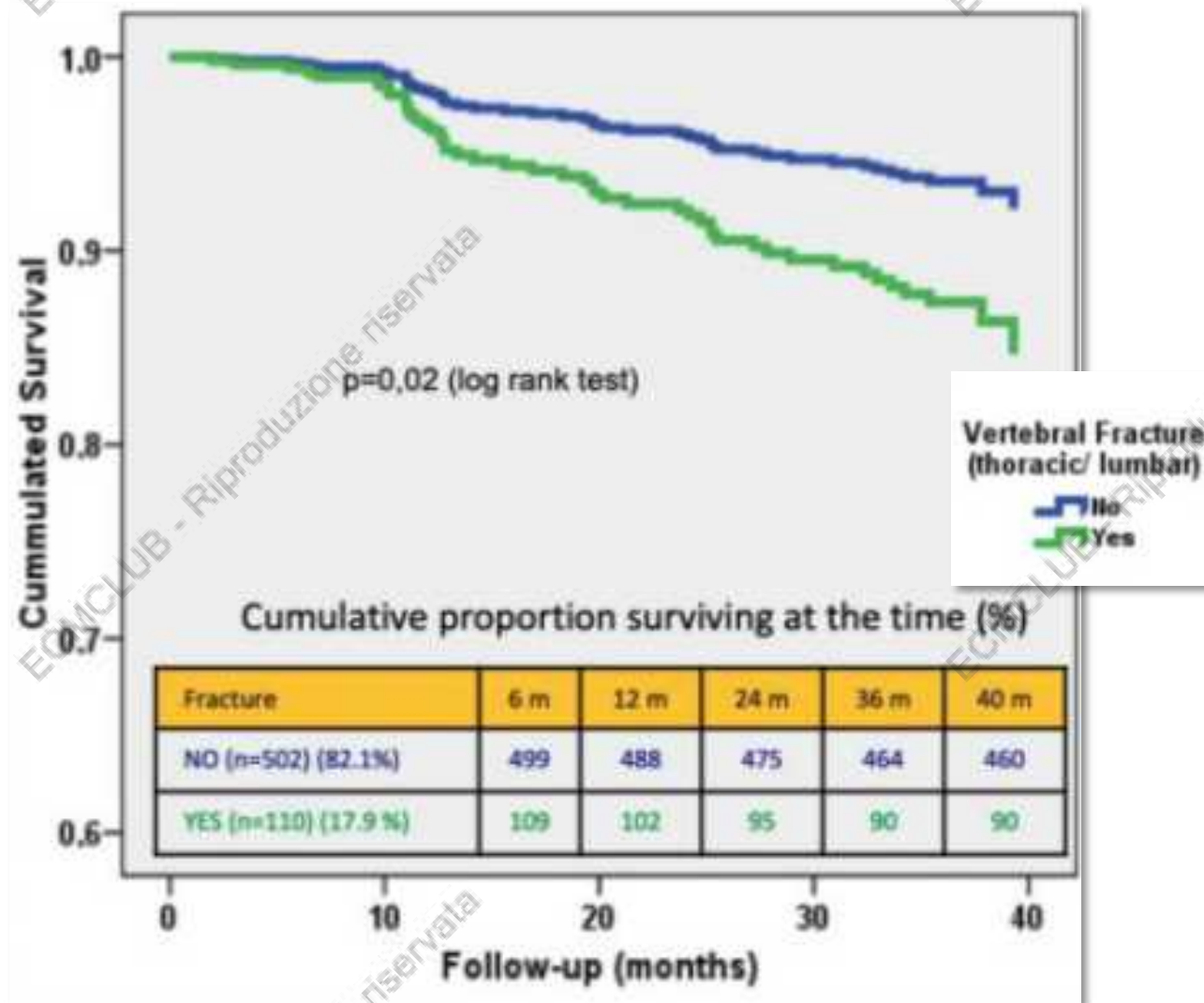


Fig. 1. Adjusted hospitalized fracture rates per 1000 person-years in Medicare point-prevalent hemodialysis and non-ESKD patients aged 66 years or older. Reprinted with permission from Arneson et al.⁽⁷³⁾

Alendronate use in older patients with reduced renal function: challenges and opportunities in clinical practice

N. Naganathar¹ • W. -P. Yau² • Z. H. Mok¹ • Z. Y. F. Tan¹ • S. T. H. Chew³

Table 3 Comparisons of incidence of osteoporotic fractures and adverse events between groups

Outcomes	Group A (n=98)	Group B (n=96)	Group C (n=96)	Group A vs group B		Group A vs group C	
				Relative risk	p value	Relative risk	p value
Incidence of osteoporotic fractures	12 (12.2%)	5 (5.2%)	11 (11.4%)	2.02 ^a (0.64–6.37)	0.232 ^a	1.15 ^b (0.46–2.89)	0.768 ^b
Incidence of AKI or AoCKD	8 (8.2%)	17 (17.7%)	1 (1.0%)	0.48 ^c (0.20–1.12)	0.090 ^c	7.84 ^d (0.98–62.66)	0.052 ^d
Incidence of GI bleeding	2 (2.0%)	-	3 (3.1%)	-	-	0.65 ^d (0.11–3.91)	0.641 ^d
Incidence of esophageal irritation or dyspepsia	6 (6.1%)	-	3 (3.1%)	-	-	1.96 ^d (0.49–7.83)	0.342 ^d

AKI, acute kidney disease; AoCKD, acute on chronic kidney disease; GI, gastrointestinal

Group A, treated with alendronate 70 mg/week; Group B, not treated; Group C, treated with alendronate and CrCl > 35 ml/min

Among patients with CrCl <35ml/min, **alendronate therapy** was not associated with significant deterioration in renal function from baseline.

Although not powered for secondary outcomes, there were no statistically significant differences in osteoporotic fracture or AKI incidence between the groups.

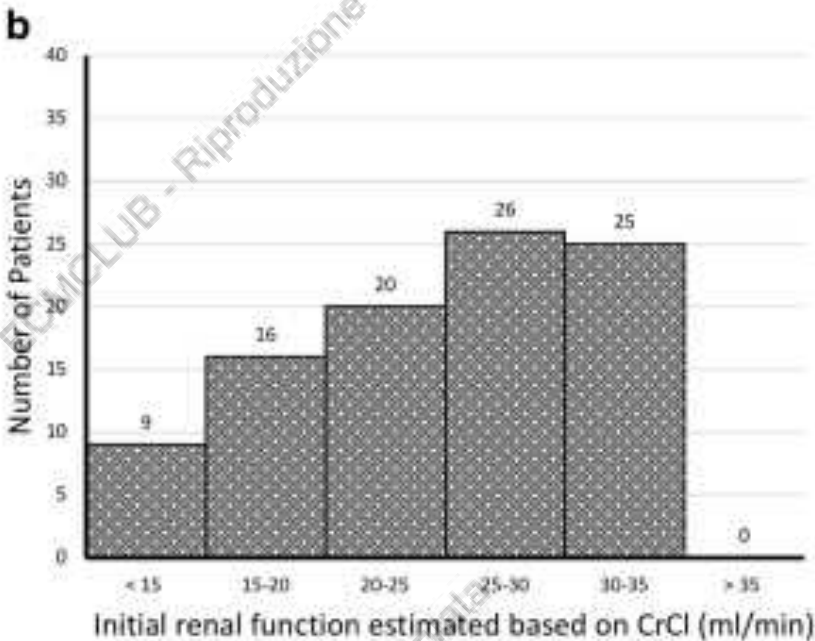
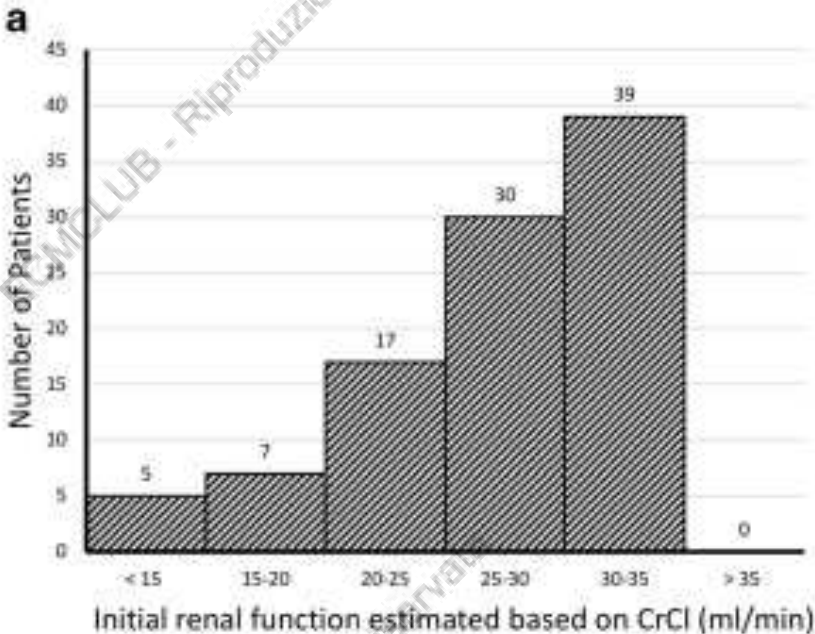


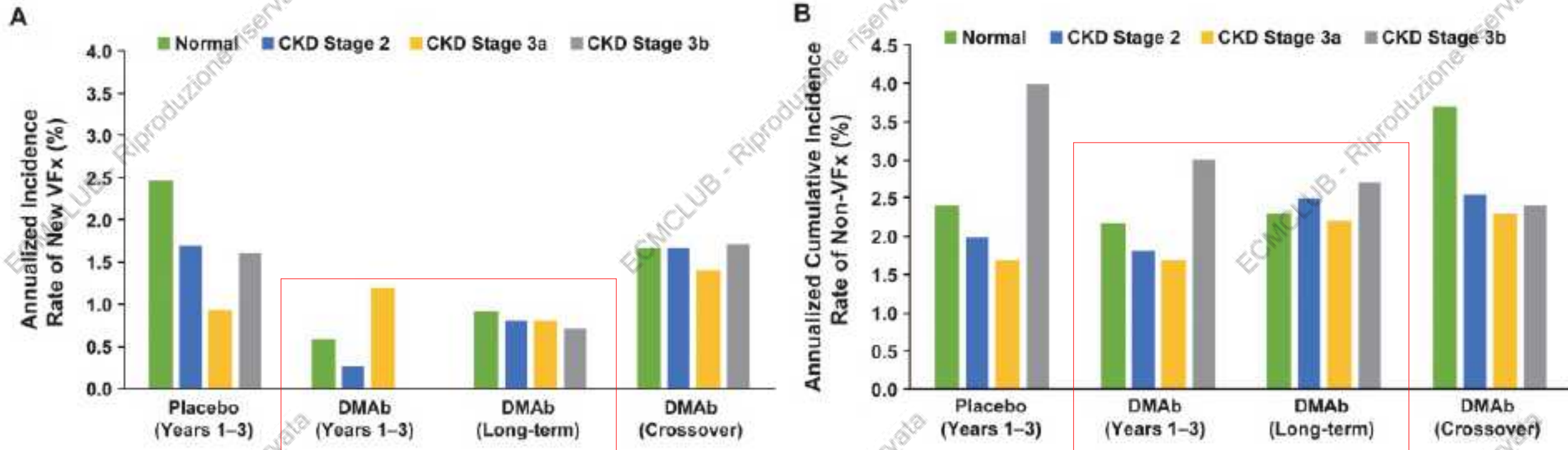
Fig. 1 Distribution of initial creatinine clearance (CrCl) among patients in group A (a) and group B (b). Groups included patients with CrCl <25ml/min as opposed to the previous post hoc analysis of the Fracture Intervention Trial assessing alendronate use in patients with reduced renal function, which defined reduced renal function as CrCl <45ml/min, and had few patients with CrCl < 35ml/min, and none with CrCl <25ml/min

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

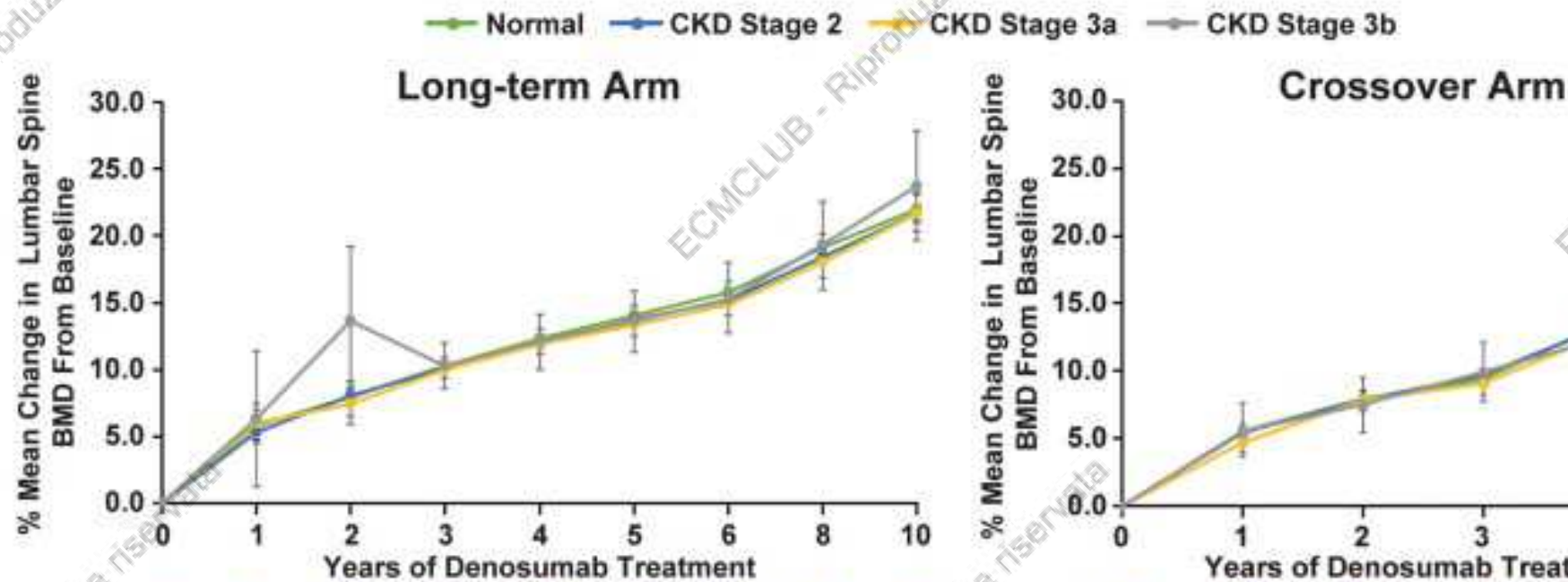
Aaron Broadwell,¹ Arkadi Chines,² Peter R. Ebeling,³ Edward Franek,⁴ Shuang Huang,² Shawna Smith,² David Kendler,⁵ Osvaldo Messina,⁶ and Paul D. Miller⁷

Women age 60 to 90 years with a BMD T-score of less than -2.5 to greater than -4.0 at the total hip or lumbar spine

The Journal of Clinical Endocrinology & Metabolism, 2021, Vol. 106, No. 2, 397–409

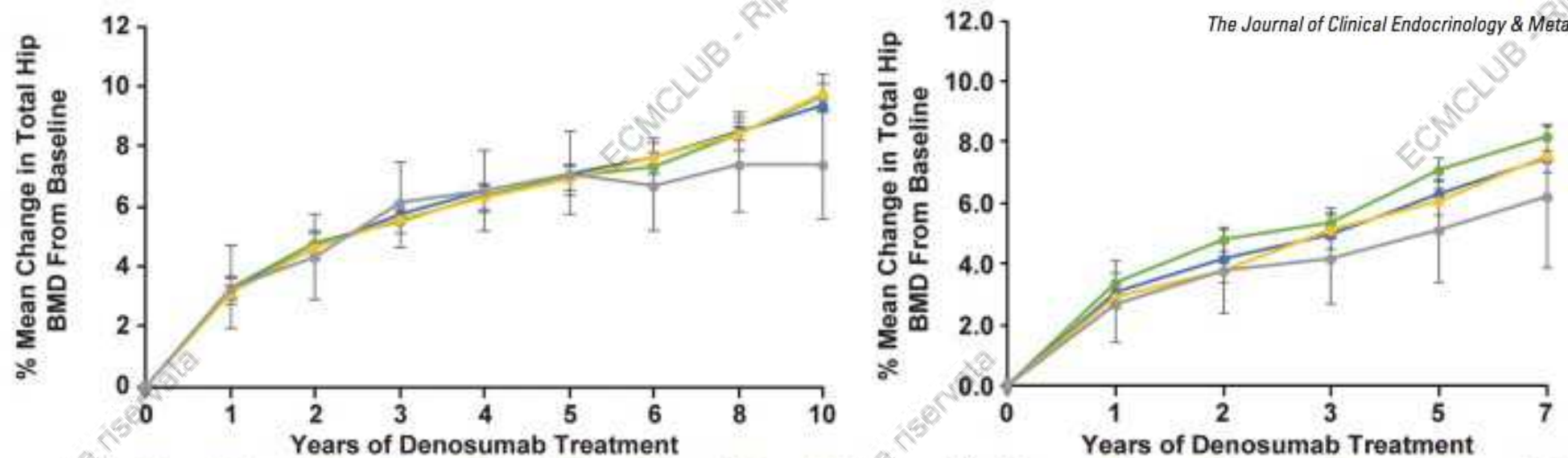


Lumbar spine



Long-term Arm				Crossover Arm			
N = 369	n = 17	18	325	N = 414	n = 376	381	274
1644	108	108	1496	1495	1394	1324	1038
292	14	14	258	253	232	214	168
33	1	1	30	33	28	26	20
			30				13
			29				6
			21				
			20				
			14				

Total hip



Long-term Arm				Crossover Arm			
N = 369	n = 336	329	322	N = 414	n = 370	353	269
1644	1518	1504	1493	1495	1393	1319	1024
292	262	258	258	253	230	210	156
33	29	29	27	33	26	26	20
			29				13
			28				6
			20				
			19				
			12				

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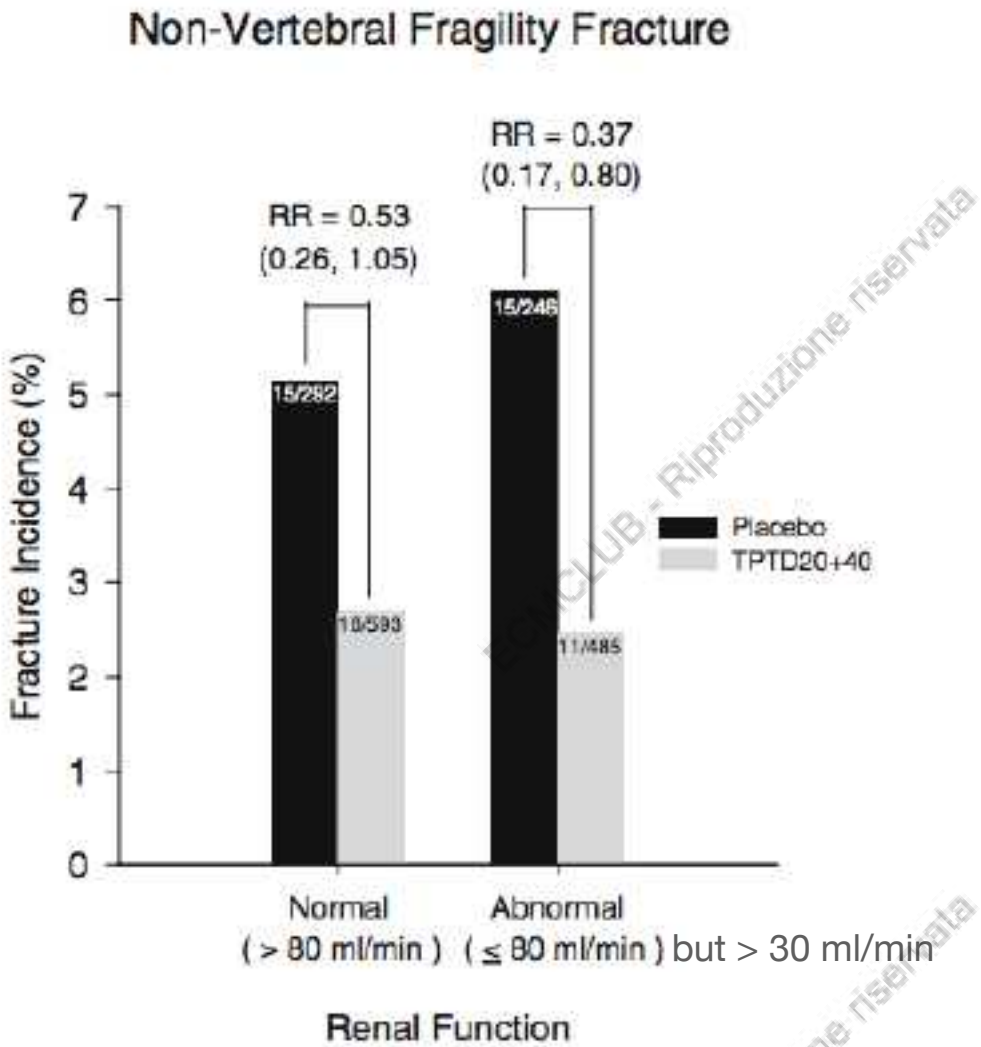
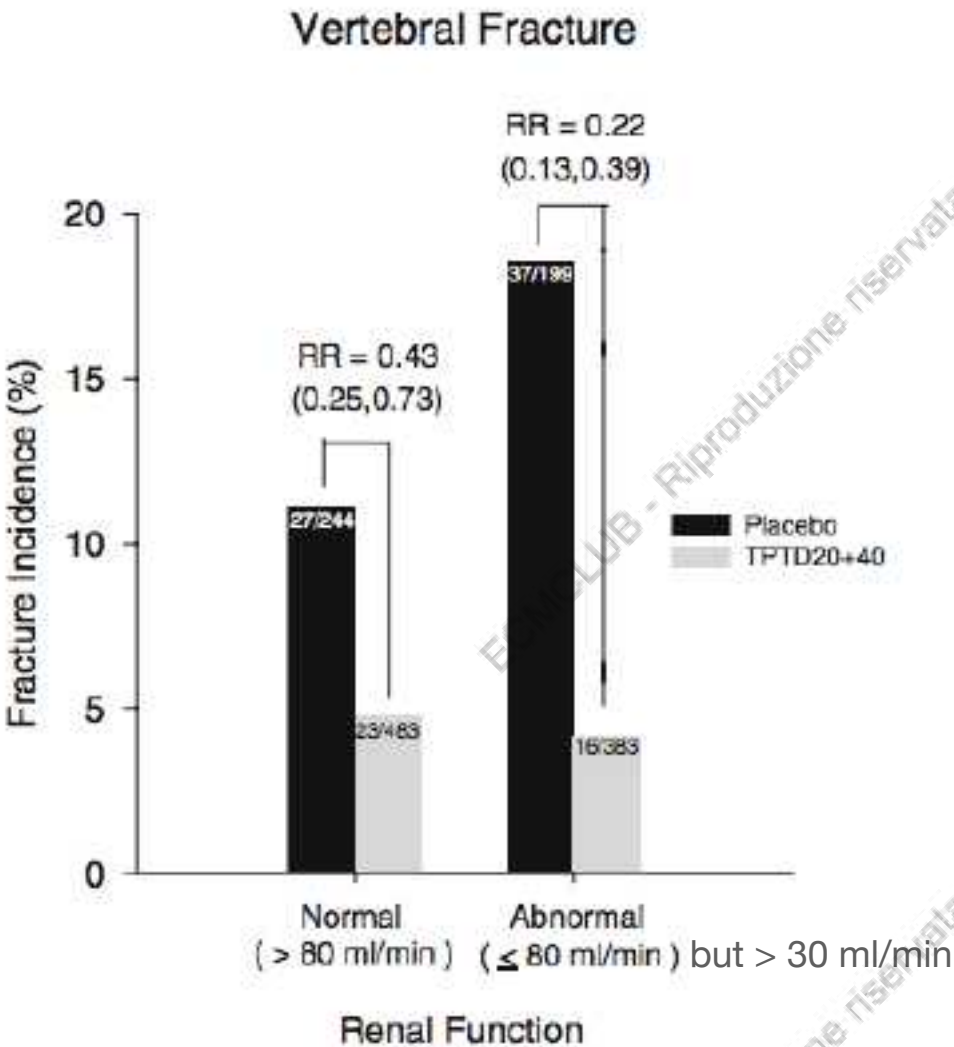
Teriparatide in postmenopausal women with osteoporosis and mild or moderate renal impairment

Osteoporos Int (2007) 18:59–68

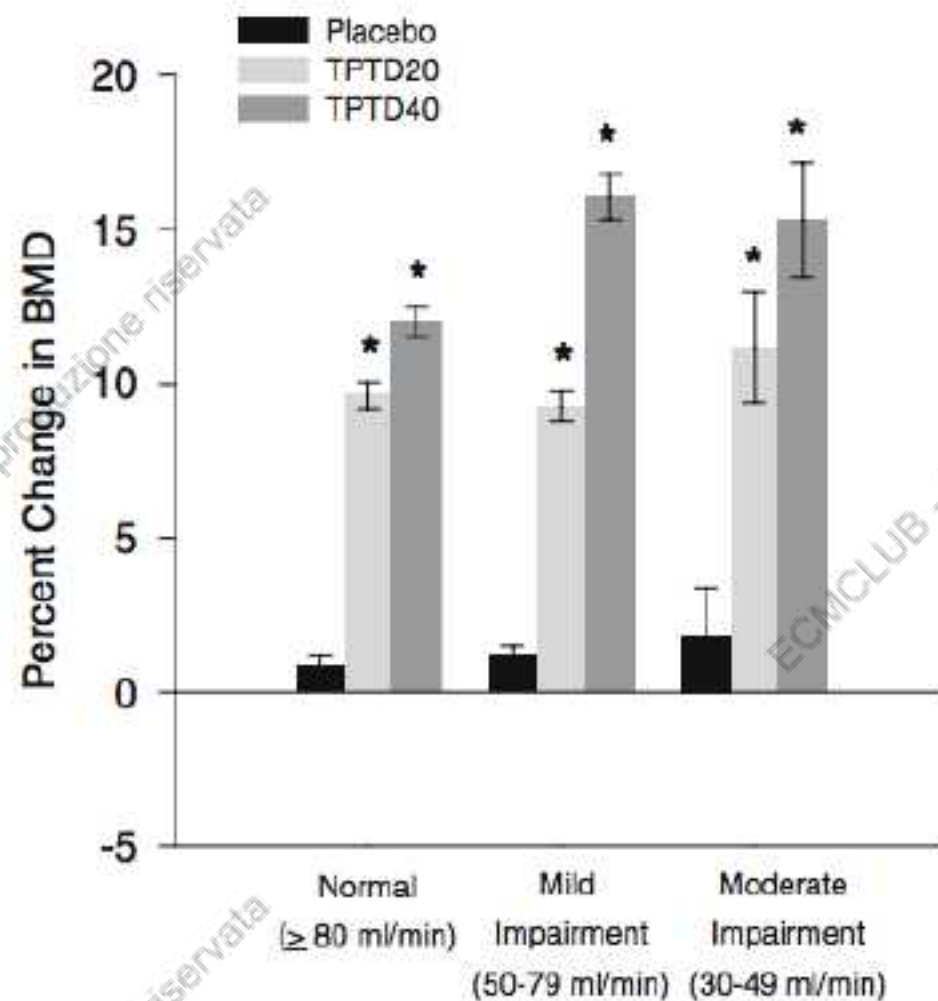
P. D. Miller • E. N. Schwartz • P. Chen • D. A. Misurski • J. H. Kregge

Data from the Fracture Prevention Trial

Patients were required to have serum creatinine ≤ 2.0 mg/dl and normal serum PTH levels



Lumbar Spine BMD (18 months)



Femoral Neck BMD (12 months)

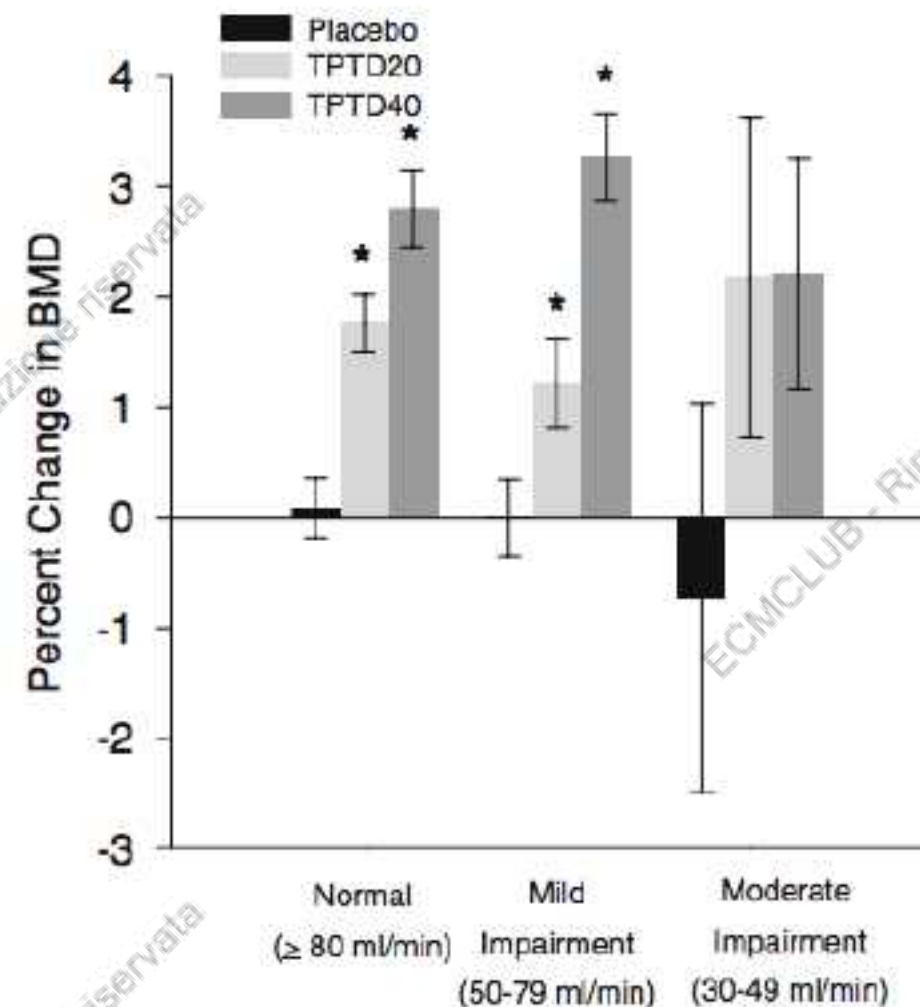
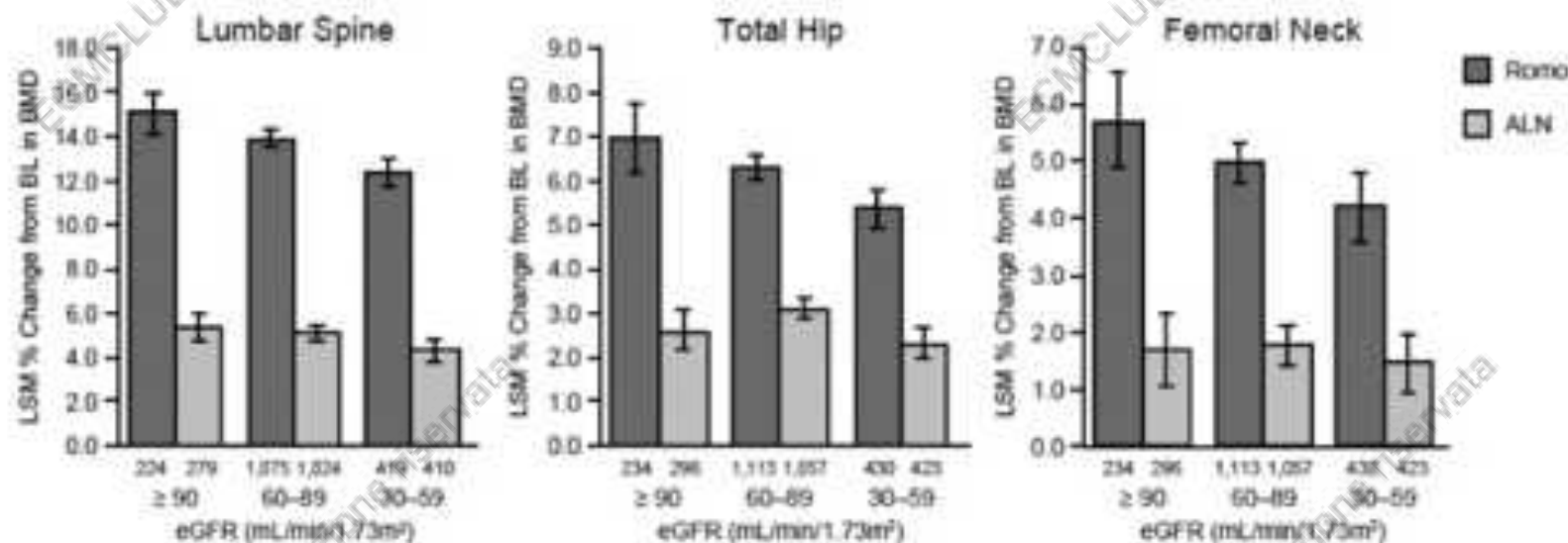
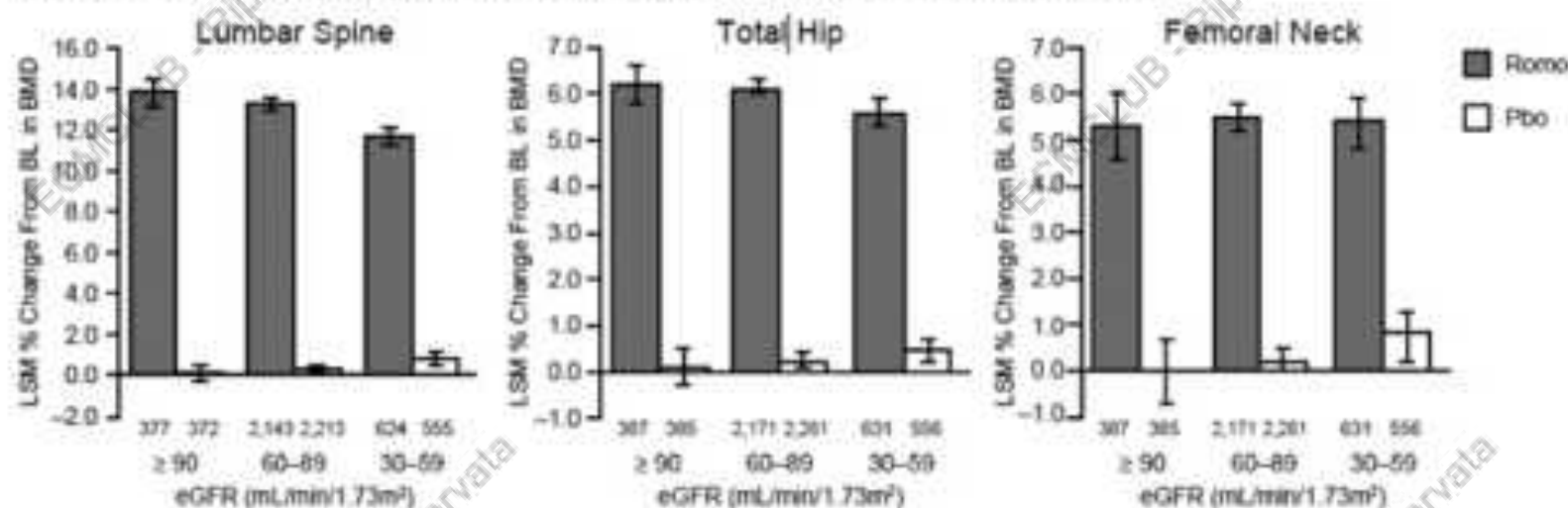


Figure. LSM (95% CI) % Change in BMD From Baseline to Month 12

ARCH Treatment-by-subgroup interaction: LS, $P = 0.006$; TH, $P = 0.006$; FN, $P = 0.12$



FRAME Treatment-by-subgroup interaction: LS, $P < 0.001$; TH, $P = 0.009$; FN, $P = 0.13$



Number of pts are shown below each bar. Error bars represent 95% CIs.

In FRAME, change in BMD from baseline for the eGFR 15-29 mL/min/1.73m² subgroup is not reported: there were only 7 patients in the placebo group for each of the measured sites and only 7, 8, and 8 patients in the romosozumab group for LS, TH, and FN, respectively.

Abbreviations: ALN, alendronate; BL, baseline; BMD, bone mineral density; CI, confidence interval; eGFR, estimated glomerular filtration rate; FN, femoral neck; LS, lumbar spine; LSM, least squares mean; Pbo, placebo; Romo, romosozumab; TH, total hip.

OP0297

EFFICACY AND SAFETY OF ROMOSUZUMAB AMONG POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS AND MILD-TO-MODERATE CHRONIC KIDNEY DISEASE

USE OF ROMOSUZUMAB FOR OSTEOPOROSIS IN HEMODIALYSIS PATIENTS

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²SEKISHINKAI SAYAMA RENAL CLINIC, department of nephrology, Saitama, Japan

Results: At 6 months after the start of treatment, no change was seen in bone density of the proximal femur compared to the pre-dosing value. In contrast, lumbar spine bone density YAM value (%) was significantly improved, from $63.8\% \pm 9.4\%$ to $70.9\% \pm 5.2\%$ ($P = 0.012$). Regarding bone metabolism markers, mean value of bone resorption marker TRACP-5b after the start of administration did not significantly differ from that at the start of observation. BAP value increased significantly from 16.2 ± 8.7 to 25.2 ± 11.0 ($p < 0.01$) while whole-PTH significantly increased from 103.5 ± 52.8 to 236.1 ± 100.8 ($p < 0.01$). In addition, serial time changes for each bone metabolic marker, whole-PTH value, and corrected Ca value during the observation period are also reported.

Conclusion: Romosozumab may improve bone density in dialysis patients with osteoporosis.

Strategy to evaluate bone fragility in CKD

Clinical risk factors

- Age, Gender
- History of fracture
- Glucocorticoids
- Diabetes and cardiovascular diseases
- Frax analysis with or without BMD

Serum biomarkers

- Mineral tests :
 - calcium - Phosphate
 - PTH – 25OH Vitamin D
- Bone turnover:
 - bone specific alkaline phosphatase - CTX

Bone imaging

- Standard X-Rays for the evaluation of vertebral or long bone fractures
- BMD measured by DEXA < 2.5 T-score
- HRpQCT to measure the bone microarchitecture for research purposes



Endocrine
CONNECTIONS

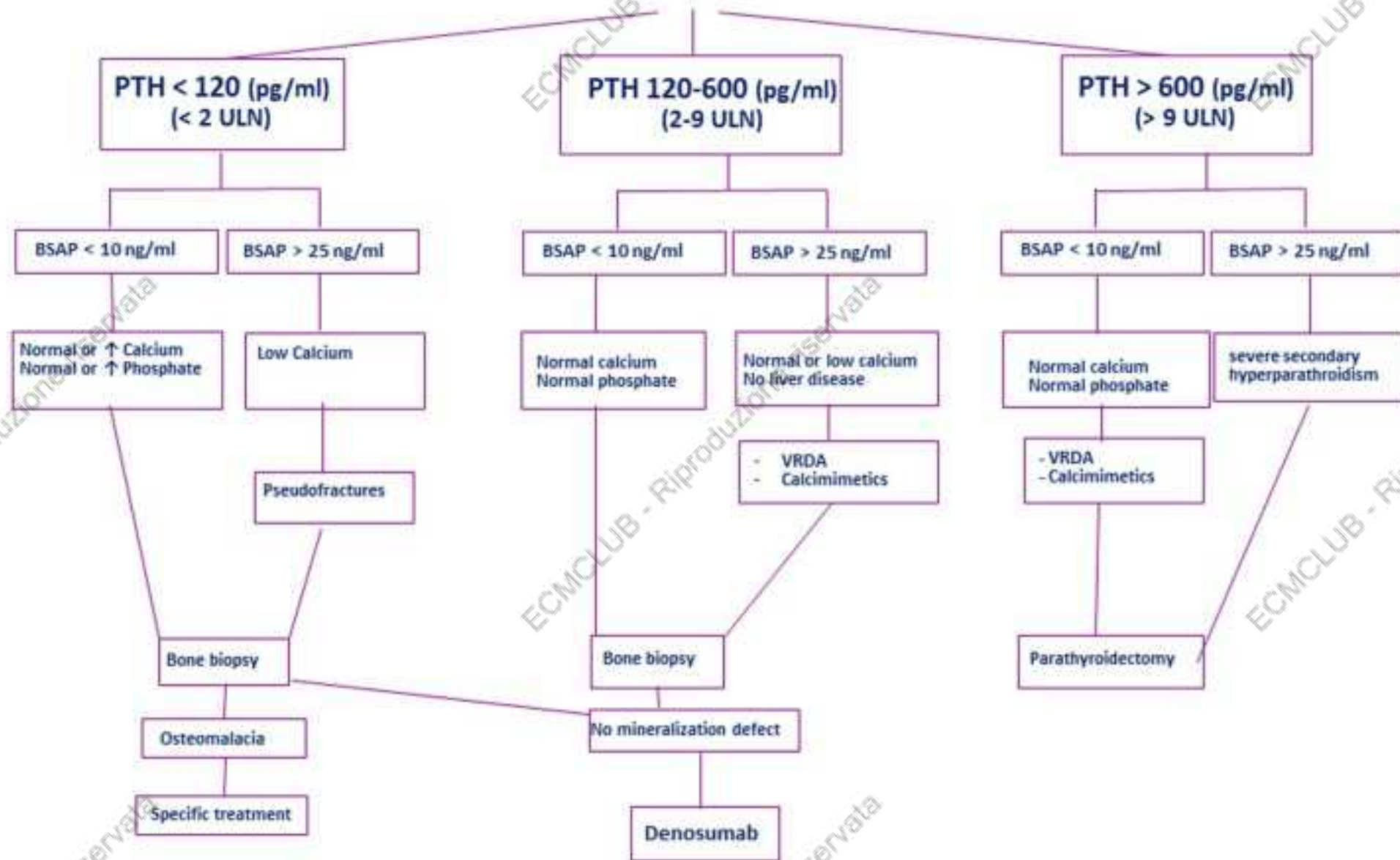
M Cohen-Solal *et al.*

Bone fragility in chronic kidney
diseases

9/4

R93–R101

CKD stage 4 – 5 – 5D and severe fractures (vertebrae, femur, humerus, pelvis)



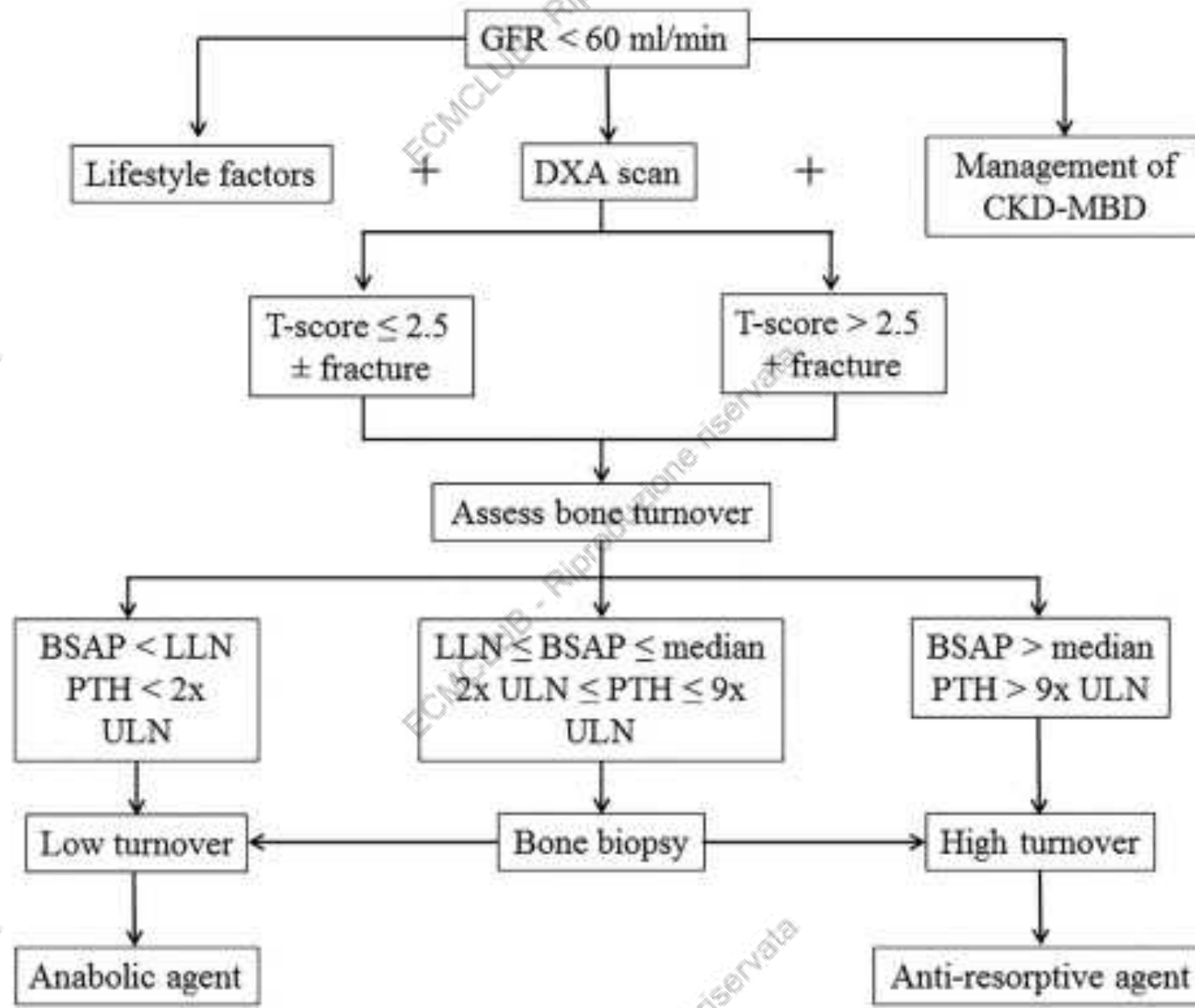


Tabella 1. Indicazione alla biopsia ossea in base ai livelli di PTH e ALP ossea.

Parametri biochimici	Turn-over	Opzione decisionale
ALP ossea > valore medio del range di normalità + PTH > 9x limite sup del range di normalità (> 600 pg/ml)	Alta probabilità di patologia ad ALTO turn-over	Procedere con terapia anti-riassorbitiva
ALP ossea < limite inf del range di normalità + PTH < 2x limite sup del range di normalità (< 120 pg/ml)	Alta probabilità di patologia a BASSO turn-over	Procedere con terapia anabolica
ALP compresa fra limite inf del range e il valore medio del range + PTH compreso fra 2 e 9x limite sup del range	Assente capacità dei BTM di discriminare fra alto e basso turn-over	Indicazione a biopsia ossea , per valutare sottotipo istologico: -alto/N turn-over: tp anti-riassorbitiva -basso turn-over: tp anabolica

Pharmacological interventions versus placebo, no treatment or usual care for osteoporosis in people with chronic kidney disease stages 3-5D (Review)

Hara T, Hijikata Y, Matsubara Y, Watanabe N



**Cochrane
Library**

Cochrane Database of Systematic Reviews

Cochrane library, 2021-07-07, Vol.2021 (7)

Implications for practice

Among patients with **CKD stages 3-4**, anti-osteoporotic drugs may reduce the risk of vertebral fracture in low certainty evidence. Anti-osteoporotic drugs probably make little or no difference to the risk of clinical fracture and adverse events in moderate certainty evidence.

In low certainty evidence, patients with **CKD stages 5 and 5D**, it is uncertain whether anti-osteoporotic drug reduces the risk of clinical fracture and death because the certainty of this evidence is very low. Anti-osteoporotic drug may slightly improve the BMD at the lumbar spine in low certainty evidence. It is uncertain whether anti-osteoporotic drug improves the BMD at the femoral neck because the certainty of this evidence was very low.



Table 1. Bone Turnover, Mineralization, and Volume (TMV) Classification System for Renal Osteodystrophy^a

Turnover	Mineralization	Volume
Low	Normal	Low
Normal		Normal
High	Abnormal	High

Reprinted with permission from ^aMoe et al.^[4]

Table 2. Bone Changes Associated With Hormonal and Metabolic Changes of End-Stage Kidney Disease

Decreased bone density

Alterations in bone microarchitecture

- Cortical porosity
- Cortical thinning and trabecularization
- Trabecular thinning and dropout
- Disruption in balance and orientation of newly formed and mature bone

Decreased bone quality

- Mineralization (osteomalacia)
- Abnormal remodeling (loss of normal repair processes)
 - Adynamic bone disease
 - Low turnover
 - High turnover
- Microdamage accumulation
 - Reduced resistance to impact
- Advanced glycation end products cross-linking
 - Loss of elasticity and tissue embrittlement

Table 3. General and CKD-Specific Risk Factors for Bone Loss and Fractures

General risk factors	CKD-specific
Patient-related (non-modifiable) • Age • Sex • Ethnicity • Past history of fracture General (modifiable) • Low physical activity • Smoking • Alcohol • Medications (eg, steroids) • Diabetes • Sarcopenia • Chronic inflammatory disorders	• Hyperparathyroidism • Low nutritional and activated vitamin D • Disordered mineral metabolism • Chronic inflammation • Metabolic acidosis • Premature hypogonadism • Medications ◦ Steroids ◦ Phosphate binders (eg, aluminium) ◦ CNI • Dietary restriction • Dialysis-related amyloidosis • Higher prevalence of general risk factors for osteoporosis

CKD = chronic kidney disease; CNI = calcineurin inhibitor.

Damasiewicz MJ, Nickolas TL.
JBMR Plus 2018;2:309-322.

Gestione integrata della salute dell'osso in specifici setting clinici

