10ο ΕΤΗΣΙΟ ΠΑΝΕΛΛΗΝΙΟ ΕΠΙΣΤΗΜΟΝΙΚΟ ΣΥΝΕΔΡΙΟ ΕΠΕΜΥ

27/04 01/05 2018

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Συζήτηση περιστατικών «Οστικές Μεταβολικές Παθήσεις»

Ιωάννης Π. Σταθόπουλος

Ορθοπαιδικός Χειρουργός, MSc στα «Μεταβολικά Νοσήματα των Οστών»

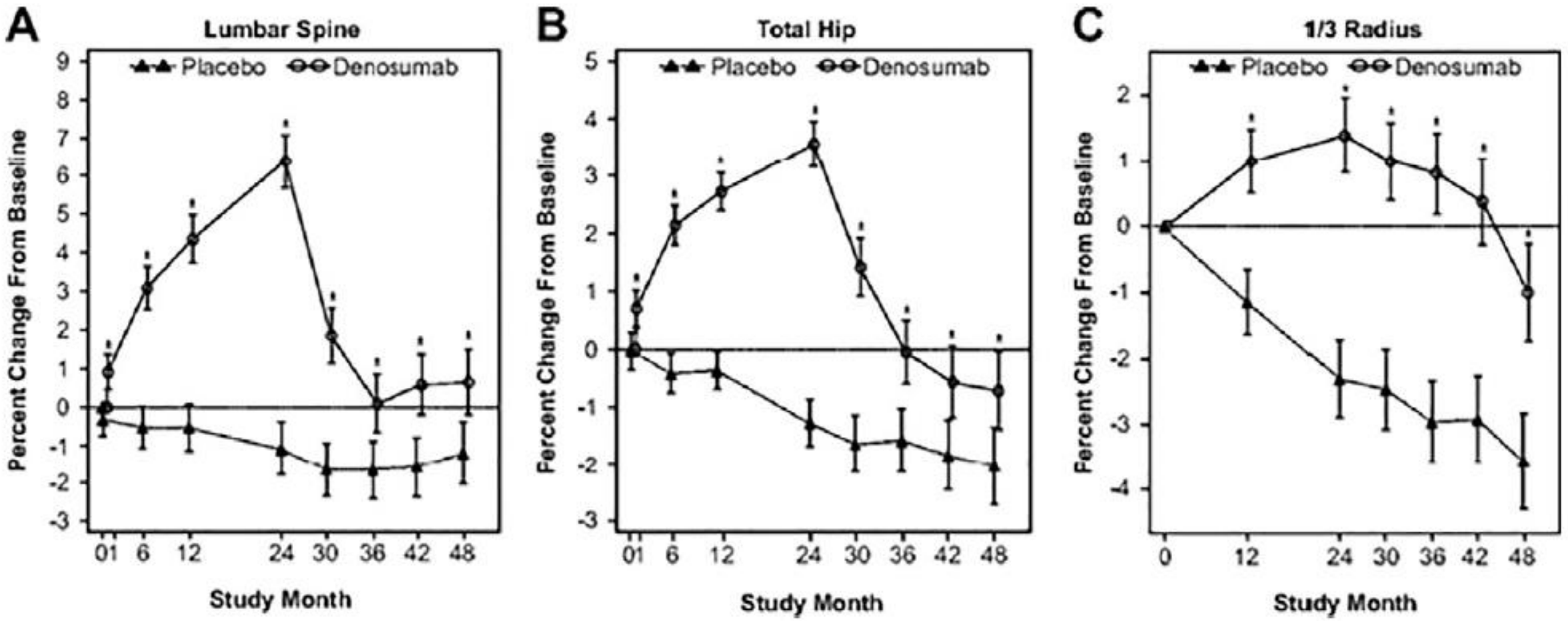
ΠΕΡΙΠΤΩΣΗ 3η

- Γυναίκα 72 ετών
- Β = 59kg, Υ = 158cm, BMI = 23.6kg/cm^2
- Ιστορικό κατάγματος ΑΡ ισχίου 2013
- Έναρξη Denosumab σε συνδυασμό με Ca+D από το 2014 λόγω χαμηλής ΟΠ μέχρι τέλους 2015
- Το 2016 σταμάτησε την αγωγή για προσωπικούς της λόγους και τον 2/2017 παρουσίασε πολλαπλά κατάγματα στη ΣΣ (7)

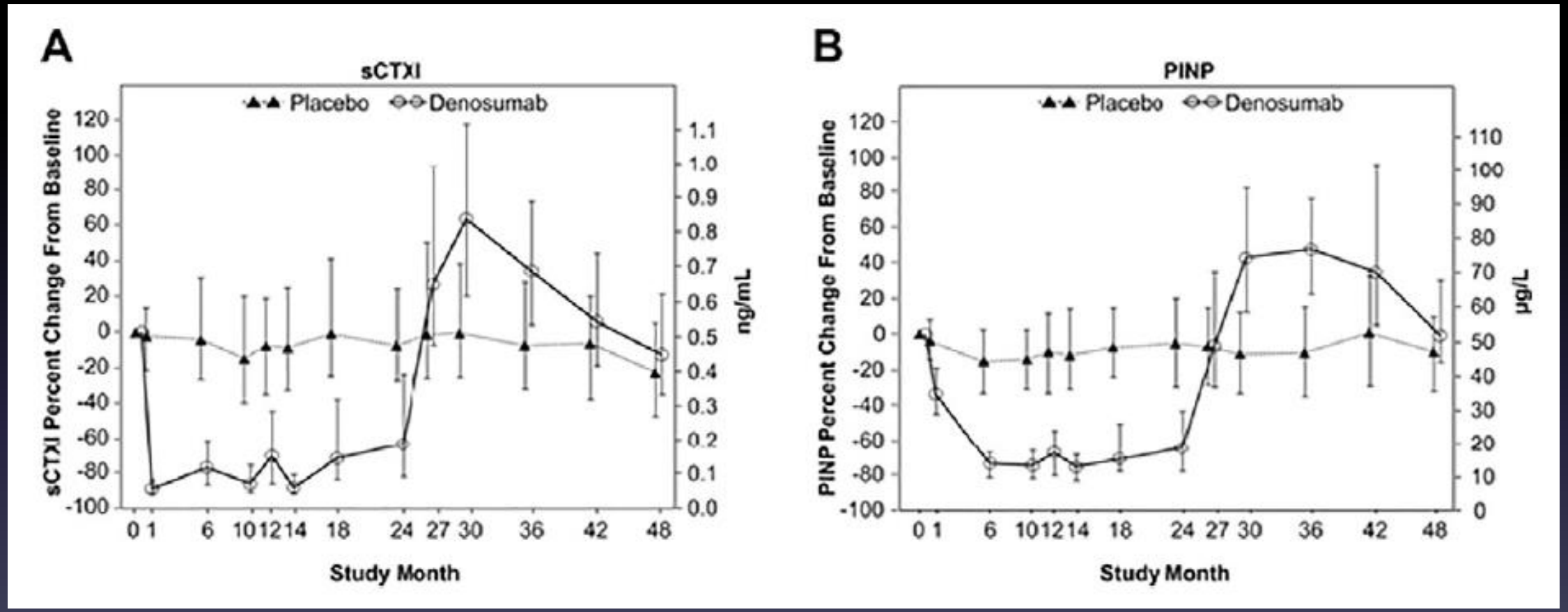
- Αναφέρει από το ιστορικό της:
  - ✓ήπιο μυελοδυσπλαστικό σύνδρομο
  - ✓σύνδρομο Sjogren’s χωρίς αγωγή

Ποιά είναι τα επόμενα βήματα;

- Ορθοπαιδική αντιμετώπιση
- Εργαστηριακός έλεγχος
  - Ο εργαστηριακός έλεγχος μετά τα κατάγματα ήταν χωρίς ιδιαίτερα ευρήματα εκτός από μια εξέταση
- ΜΟΠ



P.D. Miller, R.B. Wagman, M. Peacock, et al., Effect of denosumab on bone mineral density and biochemical markers of bone turnover: six-year results of a phase 2 clinical trial, J Clin Endocrinol Metab 96 (2) (2011) 394–402.
H.G. Bone,M.A. Bolognese, C.K. Yuen, et al., Effects of denosumab treatment and discontinuation on bone mineral density and bone turnover markers in postmenopausal women with low bonemass, J Clin Endocrinol Metab 96 (4) (2011) 972–980.



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Journal of Bone and Mineral Research
JBMR
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The American Society for Bone and Mineral Research

Short Report | Full Access

Clinical Features of 24 Patients With Rebound-Associated Vertebral Fractures After Denosumab Discontinuation: Systematic Review and Additional Cases

Athanasios D Anastasilakis, Stergios A Polyzos, Polyzois Makras, Berengere Aubry-Rozier, Stella Kaouri, Olivier Lamy

First published: 27 February 2017 | https://doi.org/10.1002/jbmr.3110 | Cited by:20

- 24 μετεμμηνοπαυσιακές γυναίκες
- 8 – 16 μήνες μετά την τελευταία δόση denosumab
- 4,7 κατάγματα/ασθενή
- 83% χωρίς προηγούμενη θεραπεία
- 33% με προηγούμενο σπονδυλικό κάταγμα
- Αποτυχία κυφοπλαστικής (5 ασθενείς)

Bone 105 (2017) 11–17

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Bone

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

Review Article

Discontinuation of Denosumab therapy for osteoporosis: A systematic review and position statement by ECTS

Elena Tsourdi [a,b], Bente Langdahl [c], Martine Cohen-Solal [d], Bérengere Aubry-Rozier [e], Erik Fink Eriksen [f], Nuria Guañabens [g], Barbara Obermayer-Pietsch [h,i], Stuart H. Ralston [j], Richard Eastell [k], M. Carola Zillikens [l,*]

Position statement ECTS

- Ισχυρότερος προγνωστικός παράγοντας: σπονδυλικά # προ ή κατά τη διάρκεια της θεραπείας

- Μικρότερη αύξηση ΒΔΟΜ σε ασθενείς με προηγούμενη αγωγή με ΔΦ

B. Uebelhart, R. Rizzoli, S.L. Ferrari, Retrospective evaluation of serum CTX levels after denosumab discontinuation in patients with or without prior exposure tobisphosphonates, Osteoporos Int (2017) epub ahead of print http://dx.doi.org/10.1007/s00198-017-4080-6

- Διατήρηση της αύξησης της BMD σε ασθενείς που συνέχιζαν με ΔΦ

B.Z. Leder, J.N. Tsai, L.A. Jiang, H. Lee, Importance of prompt antiresorptive therapy in postmenopausal women discontinuing teriparatide or denosumab: the denosumab and teriparatide follow-up study (DATA-Follow-Up), Bone 98 (2017) 54–58.

- A study addressing the question of whether a single infusion of zoledronic acid can prevent the increase in bone turnover and decrease BMD after discontinuation of denosumab is currently ongoing (NCT02499237).

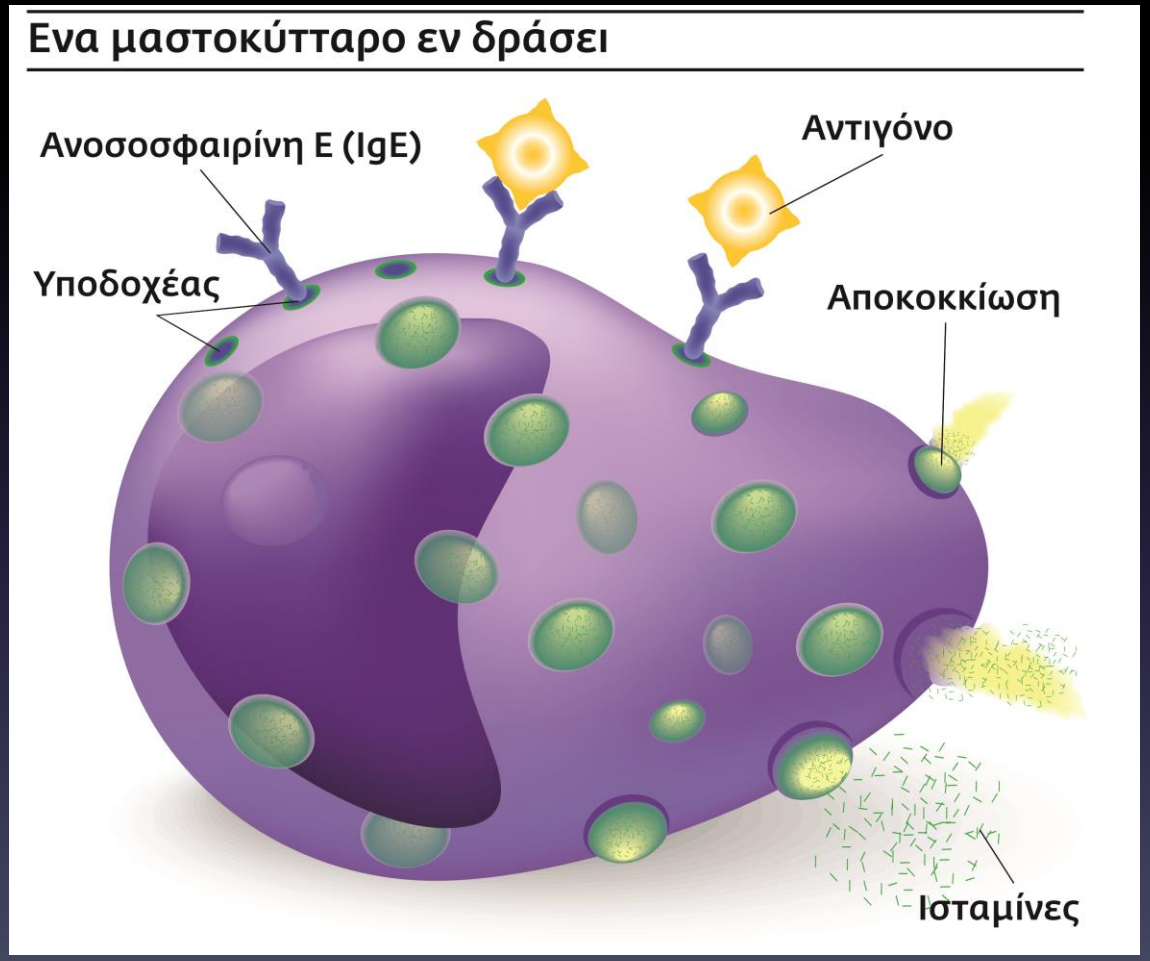
DENOSUMAB για πόσο καιρό και μετά τι;

- 5 έτη
  - High-risk (…):
    1. >>> 10 έτη
    2. Teriparatide (όμως… DATA-switch study)
    3. 5 years of oral or 3 years of intravenous bisphosphonates should be considered
  - Low-risk:
    1. BPs
    2. >>> 10 έτη

…Patients and physicians should be advised against discontinuing denosumab without evaluation and consideration of an alternative therapy, especially in those patients considered at high fracture risk…

ΓΙΑ ΤΗΝ ΙΣΤΟΡΙΑ…

- Αυξημένη τρυπτάση ορού



ΠΕΡΙΠΤΩΣΗ 4η

- Άνδρας 60 ετών, τρόφιμος του ψυχιατρείου (Δαφνί)
- εμφάνισε αιφνίδιο άλγος στη οσφύ
- έγινε ορθοπαιδική εξέταση
- Α/α Θ/ΟΜΣΣ: σοβαρού βαθμού παραμορφώσεις Θ12-Ο1 σπονδύλων

- Ο ασθενής πάσχει από ΧΝΑ υπό αιμοκάθαρση και ήπιο ΣΔ2 χωρίς αγωγή
- Λαμβάνει πολλαπλά μείζονα νευροληπτικά και αγχολυτικά φάρμακα
- Β = 78kg, Υ = 1.73cm, BMI = 26kg/cm^2
- Επικοινωνία μέσω νοσηλεύτριας

Εργαστηριακός Έλεγχος

- Οστική Πυκνότητα:

✓αυχ. μηριαίου: 0.642g/cm^2, T-score=-3.3

✓ολικό ισχίο: 0.730g/cm^2, T-score=-2.8

- HT=38%, ΤΚΕ=28/mm,
- Glu=130g/dL, HbAc1=6.9

- Ηλεκτροφόρηση λευκωμάτων = χωρίς ευρήματα
- TSH=2.3, Ca=8.8, P=4.9, PTH=180, ALP=80 (35-104), OC=20 (14-45), 25(OH)D_3=21ng/ml

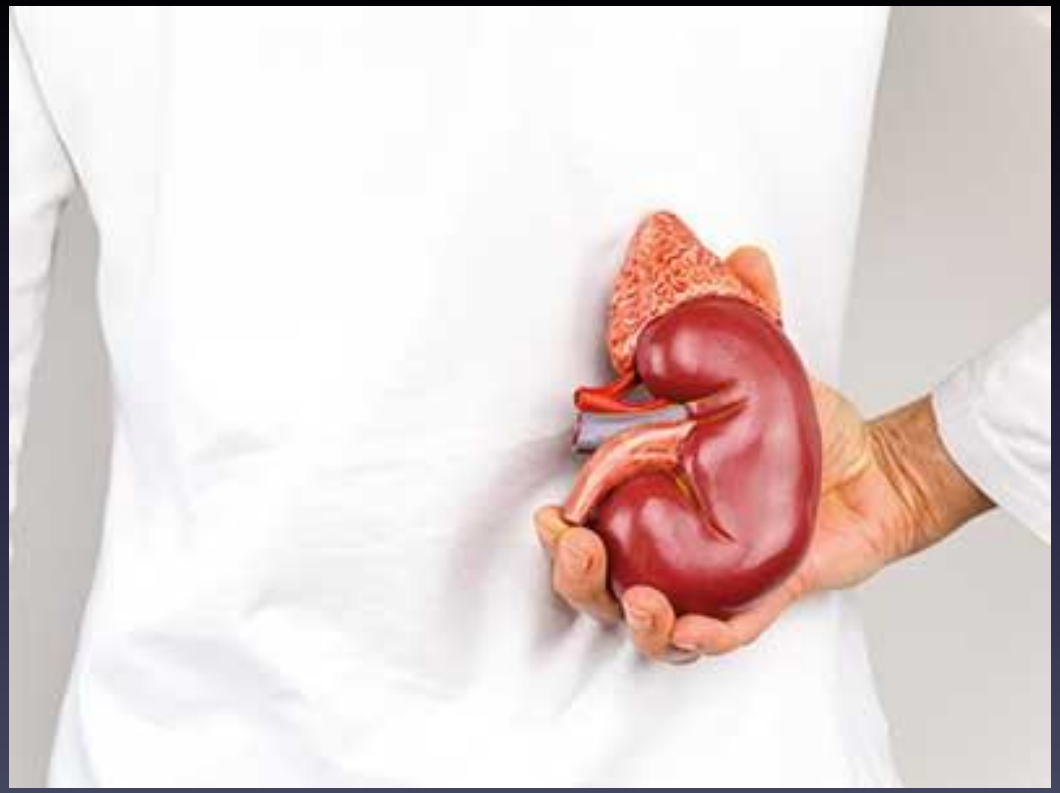
ΠΟΙΑ ΕΙΝΑΙ Η ΠΡΟΣΕΓΓΙΣΗ;


5
1
6
7
8
9
0

Πάσχει ο ασθενής από Οστεοπόρωση;

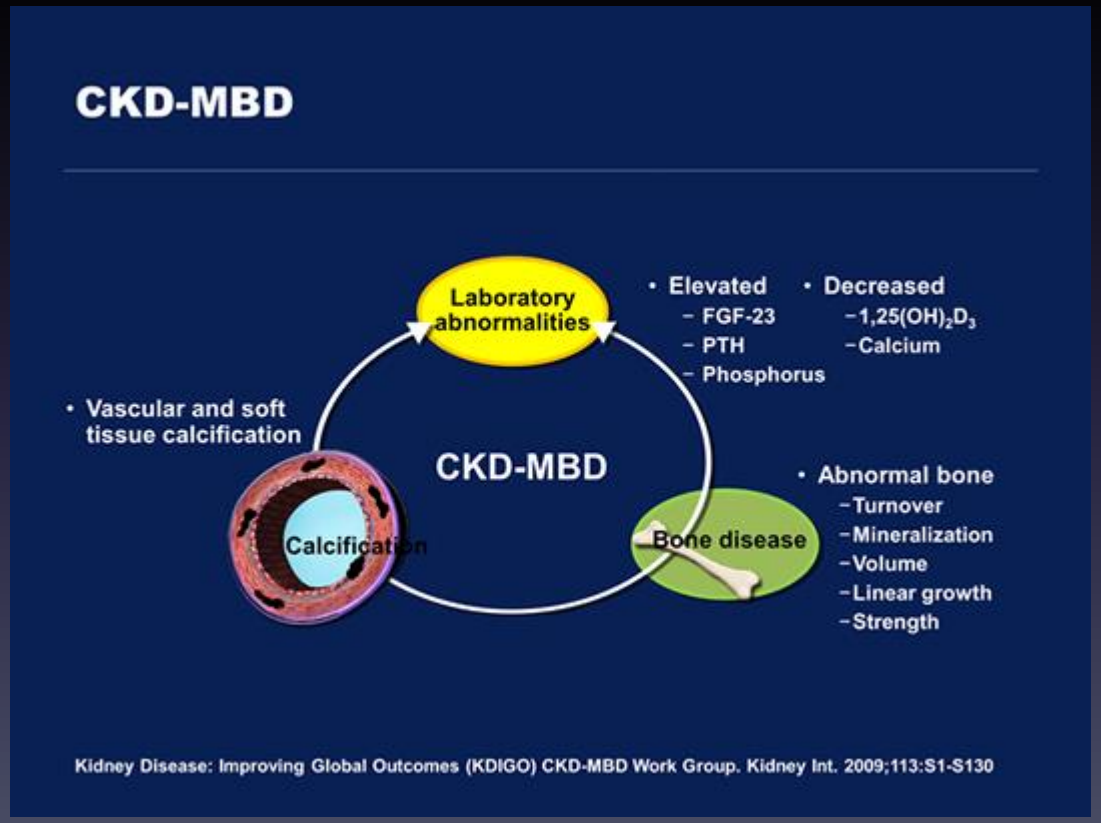
Οστική νόσος στη ΧΝΑ

- **ΝΕΦΡΙΚΗ ΟΣΤΕΟΔΥΣΤΡΟΦΙΑ**
  - Β’παθής υπερπαραθυρεοειδισμός (ινώδης οστείτιδα)
  - Αδυναμική οστική νόσος
  - Μικτή νόσος
  - Οστεομαλακία
  - Αγγειακές επασβεστώσεις
  - Διαταραχές μετάλλων



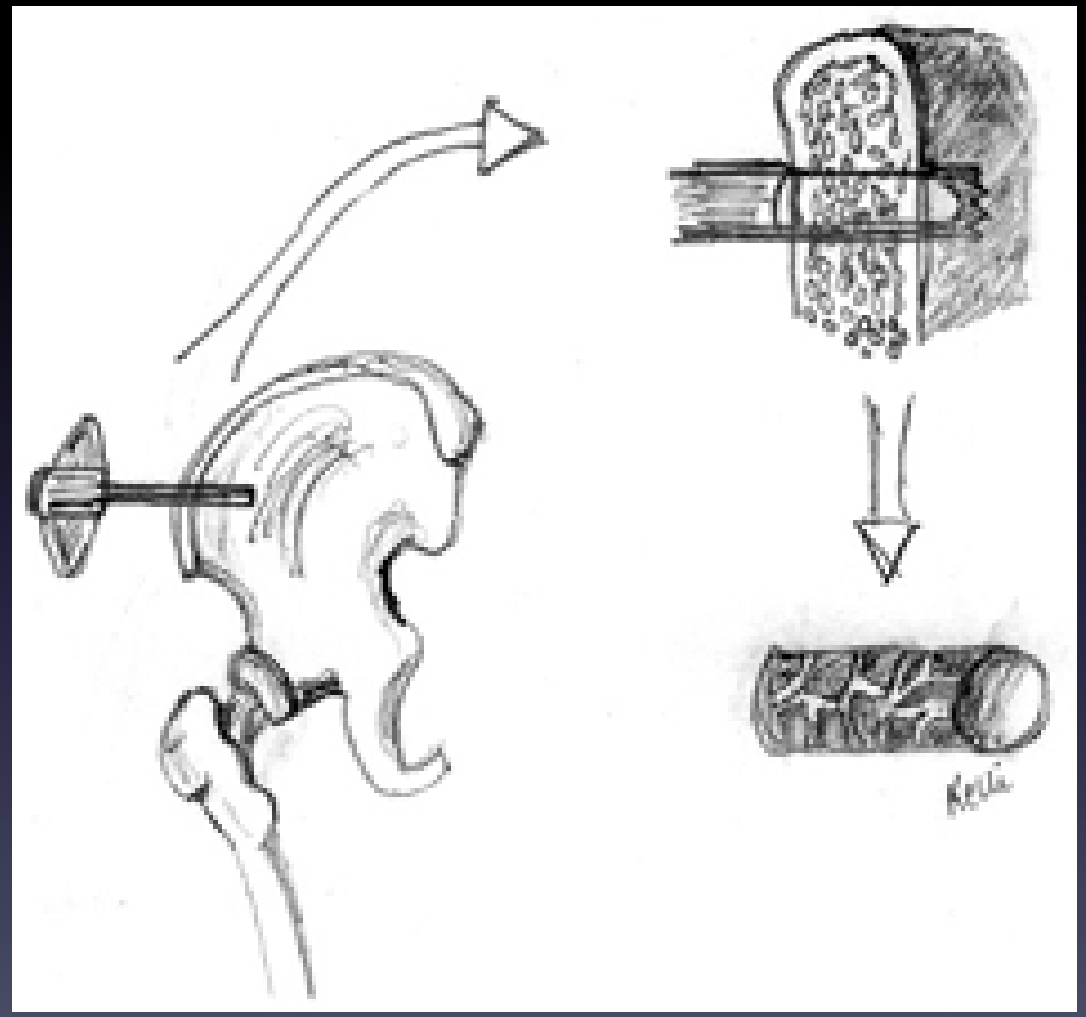
Οστική νόσος στη ΧΝΑ

- **Chronic Kidney Disease–Mineral and Bone Disorder (CKD–MBD)**
  - Διαταραχές Ca, P, PTH, vitD
  - Διαταραχές οστικής εναλλαγής, επιμετάλλωσης, όγκου και οστικής αντοχής
  - Επασβεστώσεις
    - ❖ T(bone turnover)
    - ❖ M(mineralization)
    - ❖ V(bone volume)



Πάσχει ο ασθενής από Οστεοπόρωση;

- ΧΝΝ I-II >>> οστεοπόρωση
- ΧΝΝ III >>> ???
- ΧΝΝ IV-V >>> CKD–MBD



CLINICAL GUIDELINE

Annals of Internal Medicine

Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder: Synopsis of the Kidney Disease: Improving Global Outcomes 2017 Clinical Practice Guideline Update

Markus Ketteler, MD; Geoffrey A. Block, MD; Pieter Evenepoel, MD, PhD; Masafumi Fukagawa, MD, PhD; Charles A. Herzog, MD; Linda McCann, RD, CSR; Sharon M. Moe, MD; Rukshana Shroff, MD, PhD; Marcello A. Tonelli, MD, SM, MSc; Nigel D. Toussaint, MBBS, PhD; Marc G. Vervloet, MD, PhD; and Mary B. Leonard, MD, MSCE

Ann Intern Med. 2018;168:422-430. doi:10.7326/M17-2640

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

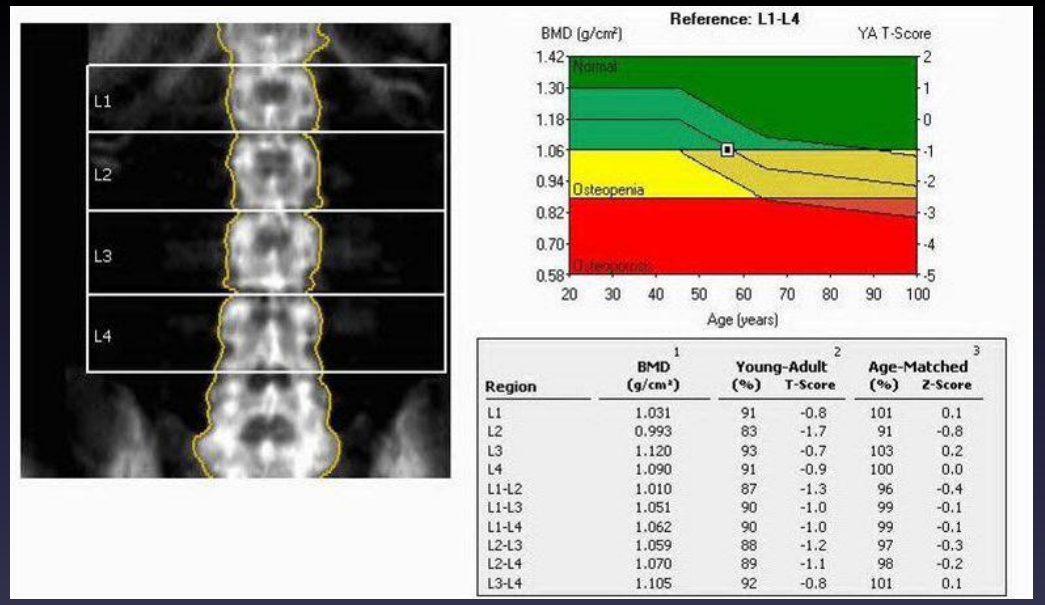
GFR categories (ml/min/ 1.73 m²) Description and range				Persistent albuminuria categories description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30mg/g <3mg/mmol	30–300mg/g 3–30mg/mmol	>300mg/g >30mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to mederately decreased	45–59			
	G3b	Mederately to severely decreased	30–44			
	G4	severely decreased	15–29			
	G5	Kidney failure	<15			

Diagnosis of CKD–MBD: Biochemical Abnormalities

- Monitoring serum levels of Ca, P, PTH, and ALP beginning in CKD G3a
- 25(OH)D levels might be measured, and repeated testing determined by baseline values and therapeutic interventions

Diagnosis of CKD–MBD: Bone Abnormalities

- **CKD G3a to G5D with evidence of CKD–MBD and/or risk factors for osteoporosis:**
  - we suggest **BMD testing** to assess fracture risk if results will impact treatment decisions
  - perform a **bone biopsy** if knowledge of the type of renal osteodystrophy will impact treatment decisions
  - we suggest that measurements of **sPTH or bALP** can be used to evaluate bone disease because markedly high or low values predict underlying bone turnover
  - we suggest **not to routinely measure bone-derived turnover markers**

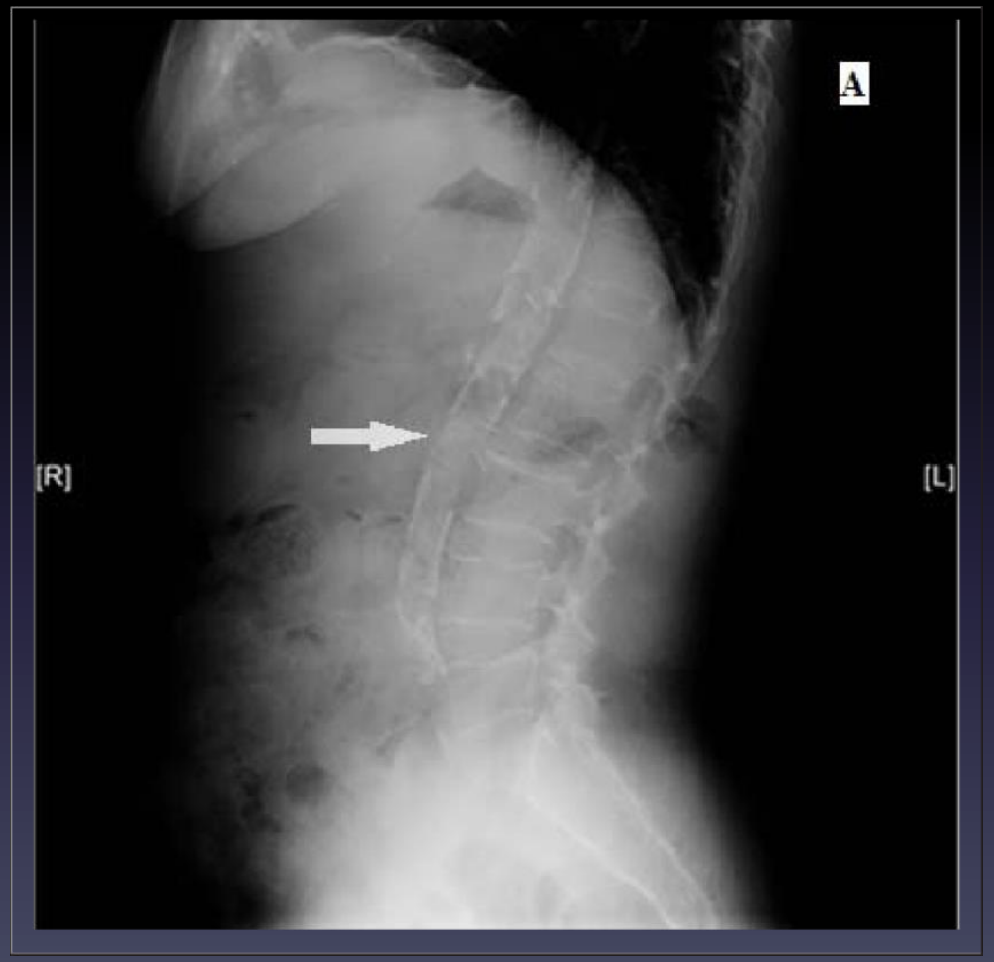


Region	1 BMD (g/cm²)	2 Young-Adult (%)	2 Young-Adult T-Score	3 Age-Matched (%)	3 Age-Matched Z-Score
L1	1.031	91	-0.8	101	0.1
L2	0.993	83	-1.7	91	-0.8
L3	1.120	93	-0.7	103	0.2
L4	1.090	91	-0.9	100	0.0
L1-L2	1.010	87	-1.3	96	-0.4
L1-L3	1.051	90	-1.0	99	-0.1
L1-L4	1.062	90	-1.0	99	-0.1
L2-L3	1.059	88	-1.2	97	-0.3
L2-L4	1.070	89	-1.1	98	-0.2
L3-L4	1.105	92	-0.8	101	0.1

Diagnosis of CKD–MBD: Vascular Calcification

- **lateral abdominal radiograph** (presence or absence of vascular calcification)
- **echocardiogram** (presence or absence of valvular calcification)
- **computed tomography**

- We suggest that patients with CKD G3a to G5D with known vascular or valvular calcification be considered at **highest cardiovascular risk**. It is reasonable to use this information to guide the management of CKD–MBD



Treatment of CKD–MBD: Targeted at Lowering High Serum Phosphate and Maintaining Serum Calcium

Treatment of CKD–MBD Targeted at Lowering High Serum Phosphate and Maintaining Serum Calcium

- treatments should be based on **serial assessments** of P, Ca, and PTH
- we suggest lowering elevated **P levels toward the normal range**
- we suggest **avoiding hypercalcemia**
- In patients receiving phosphate-lowering treatment, we suggest **restricting the dose of calcium-based phosphate binders**
- we recommend **avoiding the long-term use of aluminum-containing phosphate binders** and, in patients with CKD G5D, avoiding dialysate aluminum contamination to prevent aluminum intoxication
- we suggest **limiting dietary phosphate intake** in the treatment of hyperphosphatemia alone or in combination with other treatments
- In **CKD G5D**, we suggest **increasing dialytic phosphate removal** in the treatment of persistent hyperphosphatemia

Treatment of Abnormal PTH Levels in CKD–MBD

- In CKD G3a to G5 not on dialysis, **the optimal PTH level is not known**. However, we suggest that patients with levels of intact PTH progressively rising or persistently above the upper normal limit for the assay be evaluated for **modifiable factors**, including hyperphosphatemia, hypocalcemia, high phosphate intake, and vitamin D deficiency
- In CKD G3a to G5 not on dialysis, we suggest that **calcitriol and vitamin D analogues not be routinely used**. It is reasonable to reserve the use of calcitriol and vitamin D analogues for patients with CKD G4 to G5 with severe and progressive hyperparathyroidism
- In **CKD G5D**, we suggest maintaining iPTH levels in the range of approximately **two to nine times the upper normal limit** for the assay. We suggest that marked changes in PTH levels in either direction within this range prompt an initiation or change in therapy to avoid progression to levels outside of this range.

Treatment of Abnormal PTH Levels in CKD–MBD

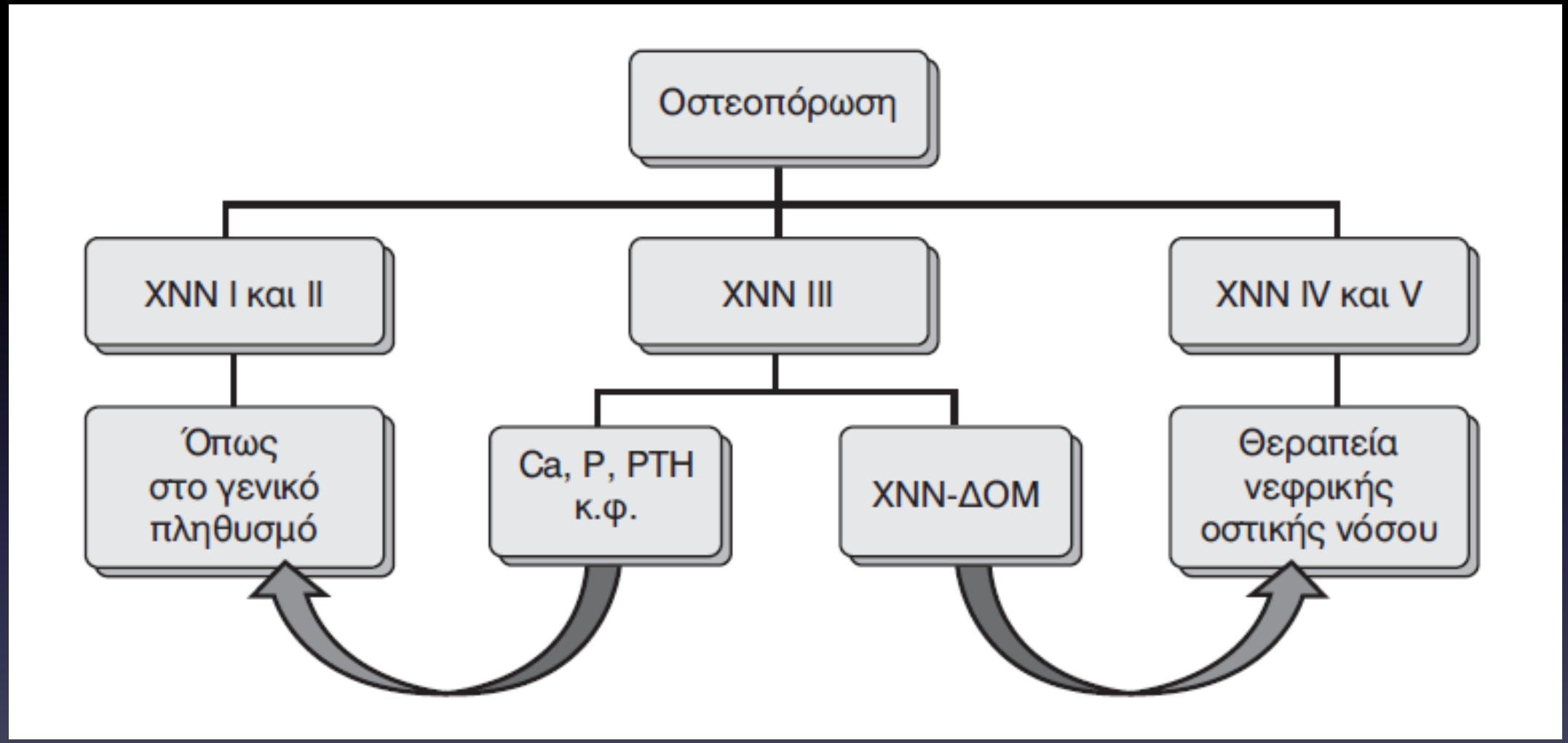
- In patients with **CKD G5D** requiring PTH-lowering therapy, we suggest **calcimimetics, calcitriol, or vitamin D analogues, or a combination** of calcimimetics with calcitriol or vitamin D Analogues

- In patients with CKD G3a to G5D with severe hyperparathyroidism (HPT) who fail to respond to medical or pharmacological therapy, we suggest **parathyroidectomy**

Treatment of Bone With Bisphosphonates, Other Osteoporosis Medications, and Growth Hormone

- In CKD **G3a to G3b** with **PTH in the normal** range and **osteoporosis and/or high risk of fracture**, we suggest **treatment as for the general population**

- In CKD **G3a to G5D** with **biochemical abnormalities of CKD–MBD** and **low BMD and/or fragility fractures**, we suggest that treatment choices take into account the **magnitude and reversibility** of the biochemical abnormalities and the **progression** of CKD, with consideration of a **bone biopsy**.


Οστεοπόρωση
ΧΝΝ I και II
ΧΝΝ III
ΧΝΝ IV και V
Όπως στο γενικό πληθυσμό
Ca, P, PTH κ.φ.
ΧΝΝ-ΔΟΜ
Θεραπεία νεφρικής οστικής νόσου

Για τον ασθενή μας…

- ΜΟΠ όχι απαραίτητη
- Μείωση πρόσληψης P
- Ανάλογα vitD
- Τακτική παρακολούθηση Ca, P, PTH, vitD

ΕΥΧΑΡΙΣΤΩ ΓΙΑ ΤΗΝ ΠΡΟΣΟΧΗ ΣΑΣ!!!