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FLS Bone Health ECHO® TeleECHO Clinic

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By participating in this clinic you are consenting to be recorded.

- If you do not wish to be recorded, please email andrea.medeiros@nof.org at least one week prior to the TeleECHO Clinic you wish to attend.
- Please type in your name, location, and email address in the chat.

Some helpful tips:

- Please mute your microphone when not speaking
- Position webcam effectively
- Communicate clearly during clinic:
  - Speak clearly
  - Use chat function

Project ECHO's goal is to protect patient privacy

To help Project ECHO accomplish that goal, please only display or say information that doesn't identify a patient or that cannot be linked to a patient.

References:

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Common HIPAA Identifier Slip-Ups and Easy Ways to Protect Patient Privacy

- 1st – **Names:** Please do not refer to a patient's *first/middle/last name* or use any *initials*, etc. Instead please use the *ECHO ID*.
- 2nd – **Locations:** Please do not identify a patient's *county, city or town*. Instead please use only the patient's *state* if you must or the *ECHO ID*.
- 3rd – **Dates:** Please do not use any dates (like *birthdates*, etc.) that are linked to a patient. Instead please use only the patient's *age* (unless > 89)
- 4th – **Employment:** Please do not identify a patient's *employer*, work *location* or *occupation*. Instead please use the *ECHO ID*.
- 5th – **Other Common Identifiers:** Do not identify patient's *family* members, *friends, co-workers, numbers, e-mails*, etc.

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as *of 10-10-19*

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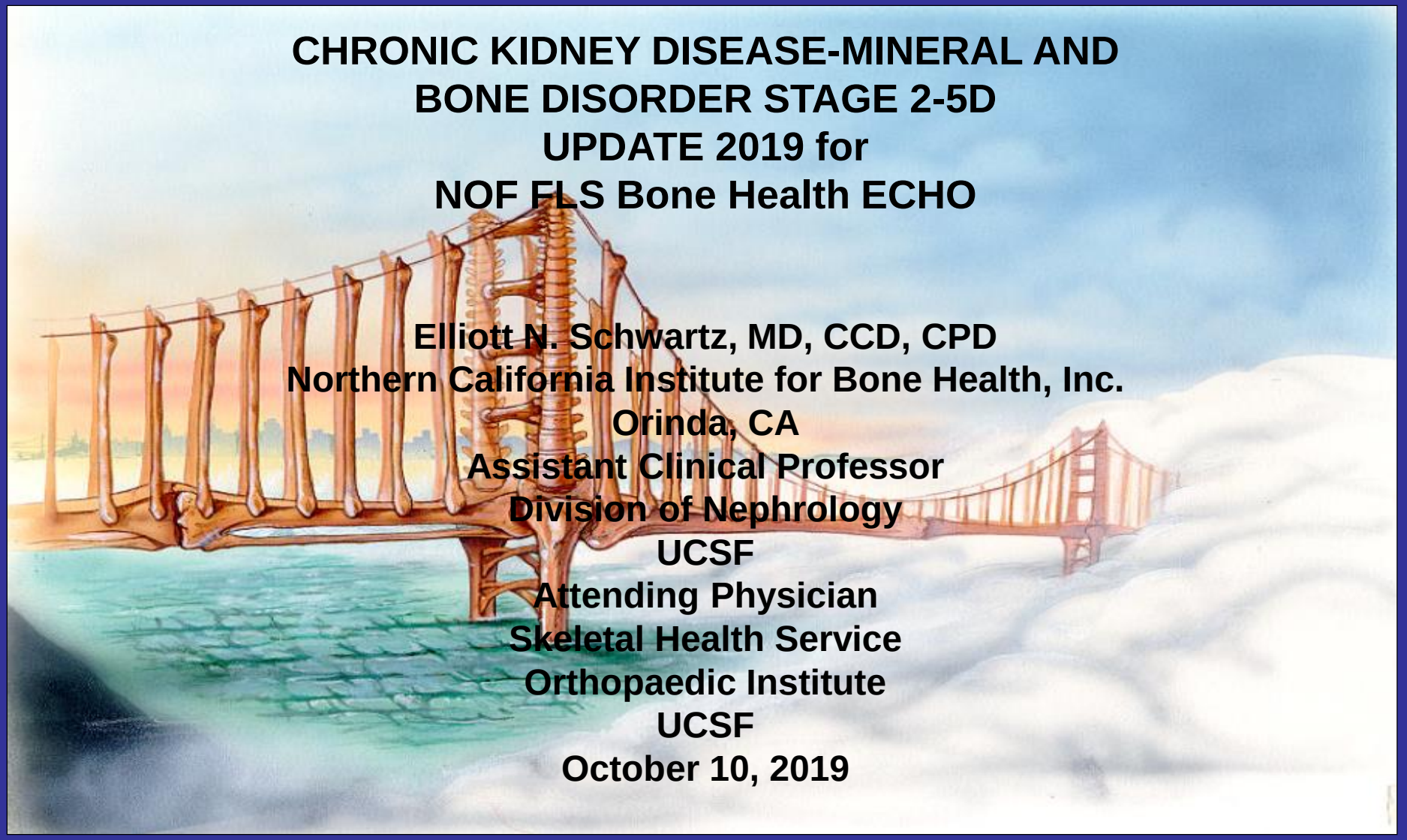
- **Off label uses of some products may be discussed; such uses relate to the topics presented and unsolicited questions asked by the audience; please see all product labels and PIs for indications, contraindications and warnings etc.**
- **Investigational Agents, such as cathepsin K inhibitors, PTHrP analogs and sclerostin antibodies, may be addressed in the course of some discussions, such as bone formation or resorption or anti-fracture efficacy.**



CHRONIC KIDNEY DISEASE-MINERAL AND BONE DISORDER STAGE 2-5D UPDATE 2019 for NOF FLS Bone Health ECHO

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October 10, 2019

Objectives

After attending this conference, the listener will be able to:

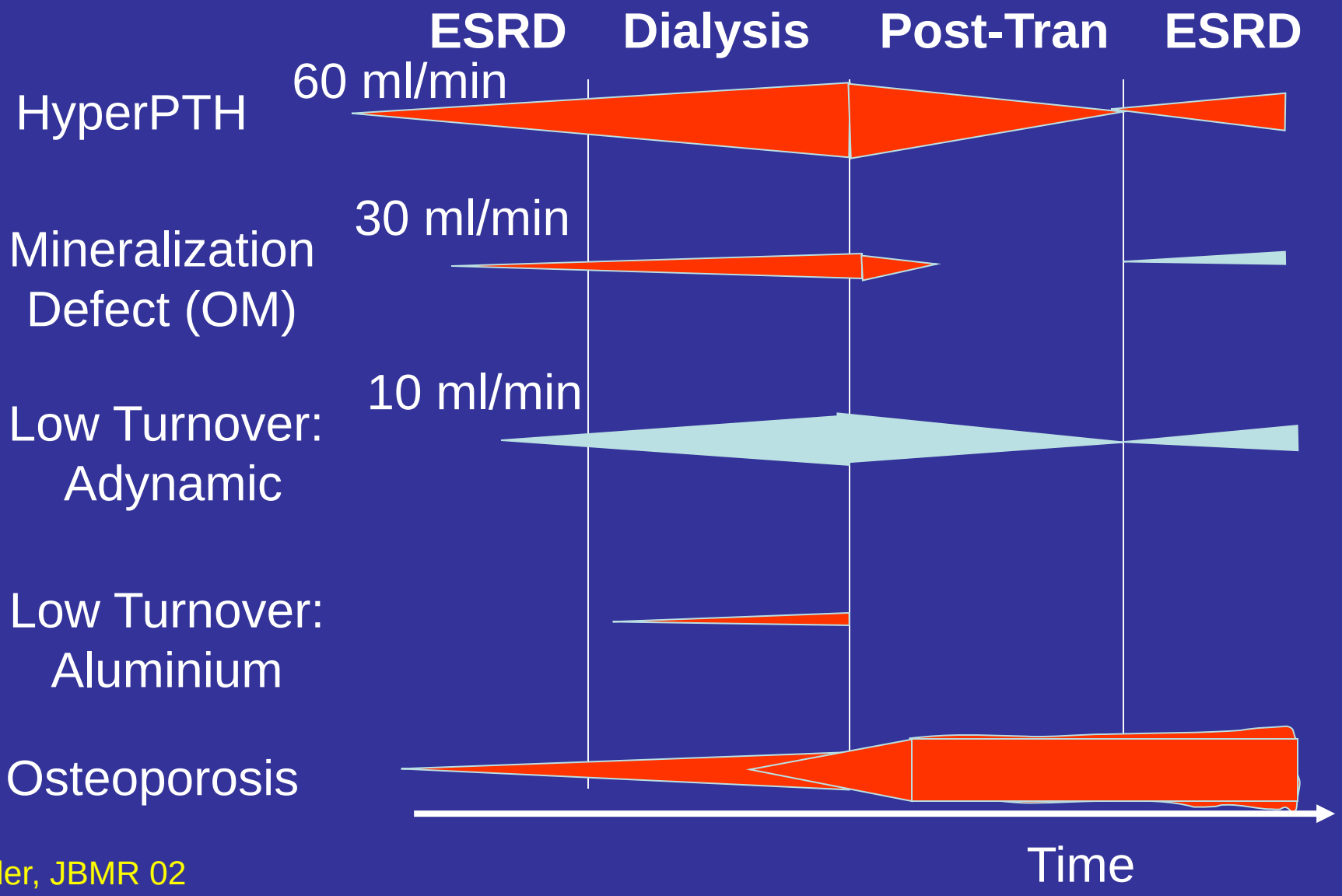
1. Understand the pathophysiology of Chronic Kidney Disease-Mineral Bone Disorder (CKD-MBD)
2. Will be able to describe the role of bone densitometry in the evaluation of the patient with CKD-MBD
3. Will understand the limitations of the available therapies for CKD-MBD

What are the Stages of Chronic Kidney Disease (CKD)?

Stage	Description	(GFR)
At increased risk	**Risk factors** for kidney disease (e.g., diabetes, high blood pressure, family history, older age, ethnic group)	More than 90
1	Kidney damage with normal kidney function	90 or above
2	Kidney damage with mild loss of kidney function	89 to 60
3a	Mild to moderate loss of kidney function	59 to 44
3b	Moderate to severe loss of kidney function	44 to 30
4	Severe loss of kidney function	29 to 15
5	Kidney failure	Less than 15

Your GFR number tells you how much kidney function you have.
As kidney disease gets worse, the GFR number goes down.

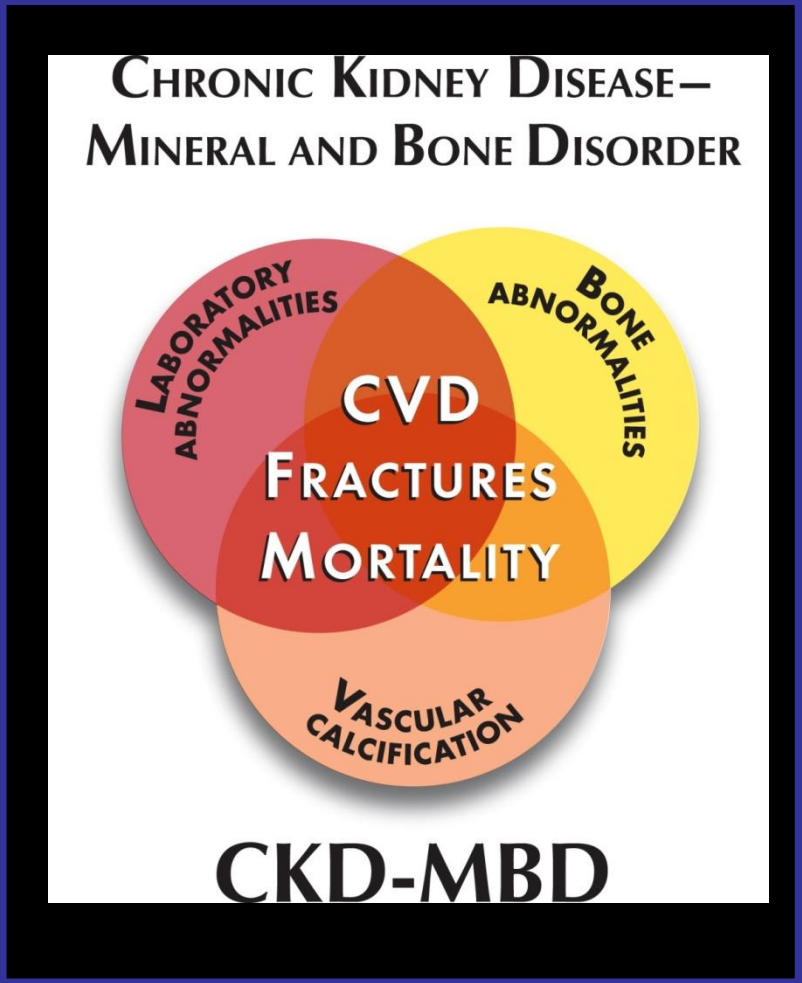
Bone and Mineral Disorders in ESRD and After Transplantation



Elder, JBMR 02

Fracture Risk is Very High In Stage 5 CKD

- ~ 50 % prevalence of fractures
- ~ 50% excess mortality as compared to age-matched controls without stage 5 CKD
- Fractures occur ~ 10 years earlier than age-matched, BMD matched patients without CKD
- Hip fractures risk 17X higher than age-matched patients without stage 5 CKD



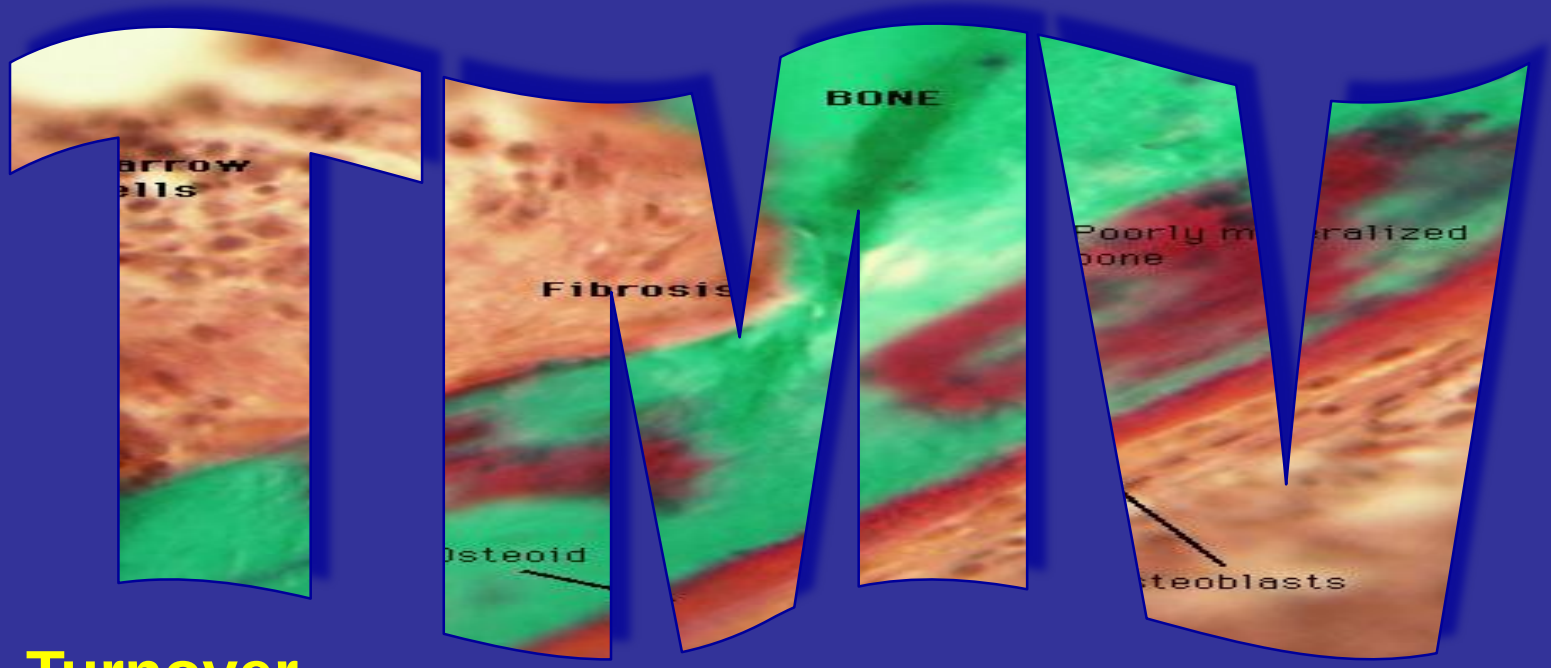
A systemic disorder of mineral and bone metabolism due to chronic kidney disease manifested by either one or a combination of the following:

- Abnormalities of calcium, phosphorus, PTH or vitamin D metabolism
- Abnormalities in bone turnover, mineralization, volume, linear growth or strength
- Vascular or other soft tissue calcification

Renal osteodystrophy is an alteration of bone morphology in patients with CKD. It is one measure of the systemic disorder of CKD that is quantifiable by histomorphometry of bone biopsy

Moe et al. *Kidney Int* 2006;69:1945–1953

Classification of Renal Osteodystrophy



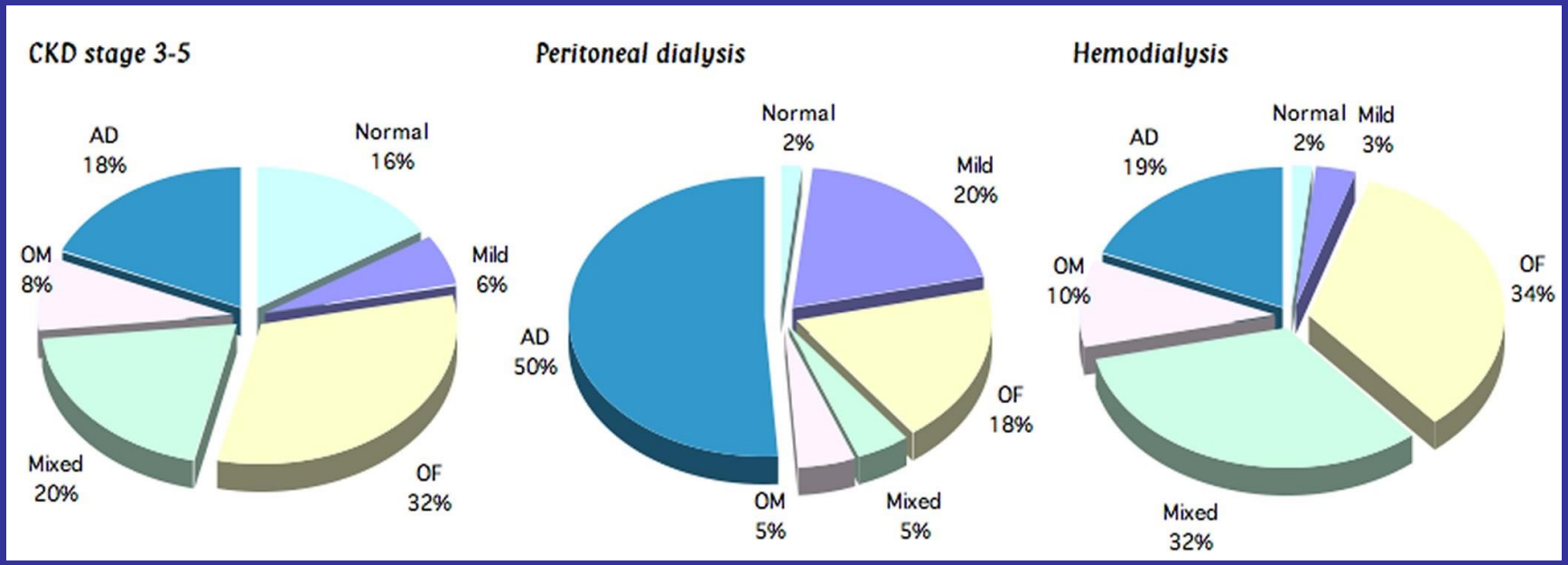
Turnover
High
Normal
Low

Mineralization
Normal
Abnormal

Volume
High
Normal
Low

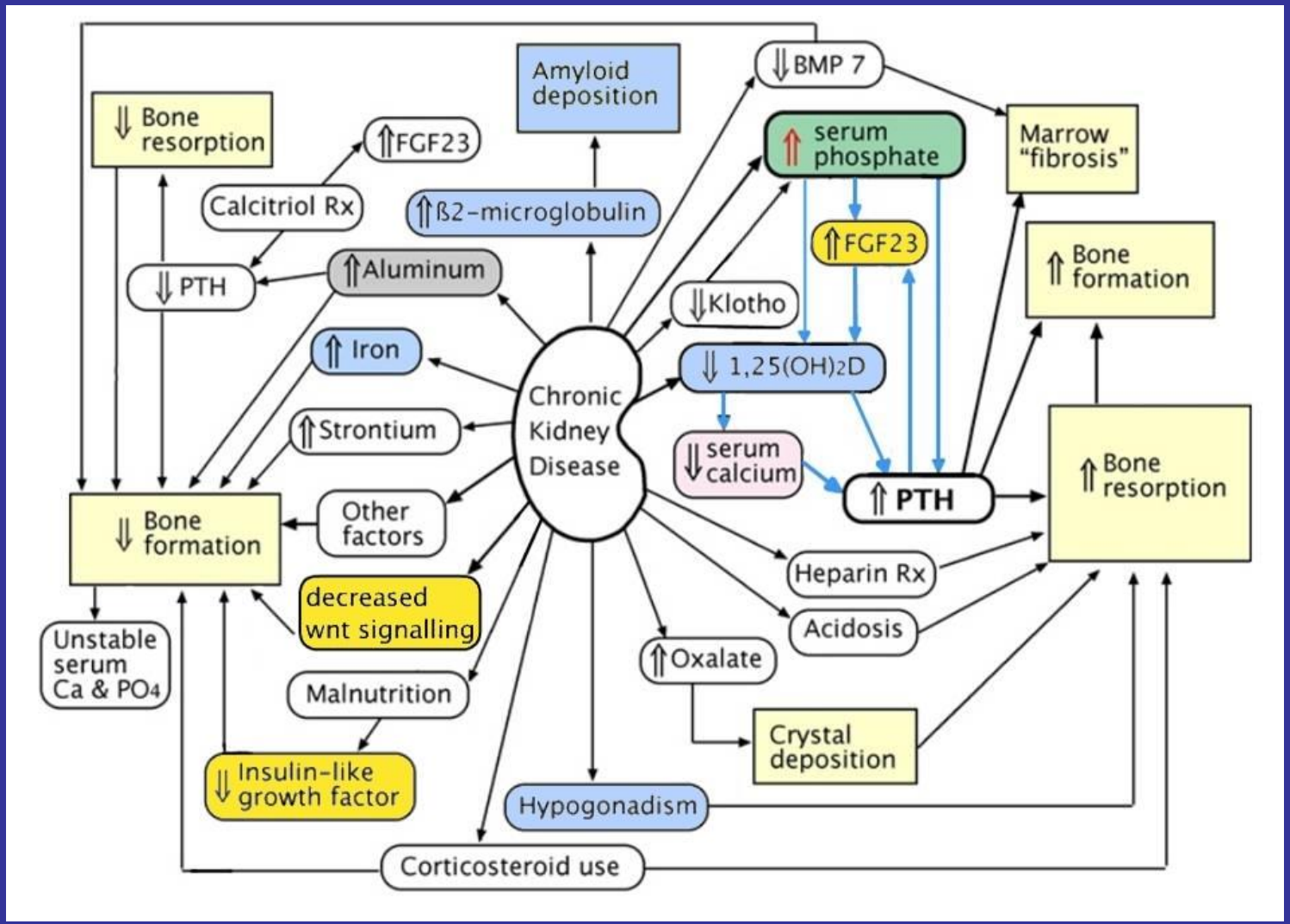
BONE HISTOLOGY IN CKD

Prevalence of types of bone disease as determined by bone biopsy in patients with CKD-MBD



AD, adynamic bone; OF, osteitis fibrosa, OM, osteomalacia

CKD-MBD Pathophysiology Pathways



Courtesy of Susan M. Ott, M.D.

Several studies have evaluated the FRAX Tool's performance in CKD

- In a cross-sectional study of patients with CKD Stages 3-5 (no dialysis) FRAX did not perform better than BMD at discriminating fractures[1]
- [illegible] only 1 had CKD Stage 4[2]
- In a cohort of 485 Japanese patients on hemodialysis FRAX did not predict either major osteoporotic or hip fractures[3]

These studies suggest that the performance accuracy of the FRAX Tool is decreased in patients with kidney disease

Nickolas, et al., J Bone Miner Res, 2015, 30 (S1): S46, Abs 1138

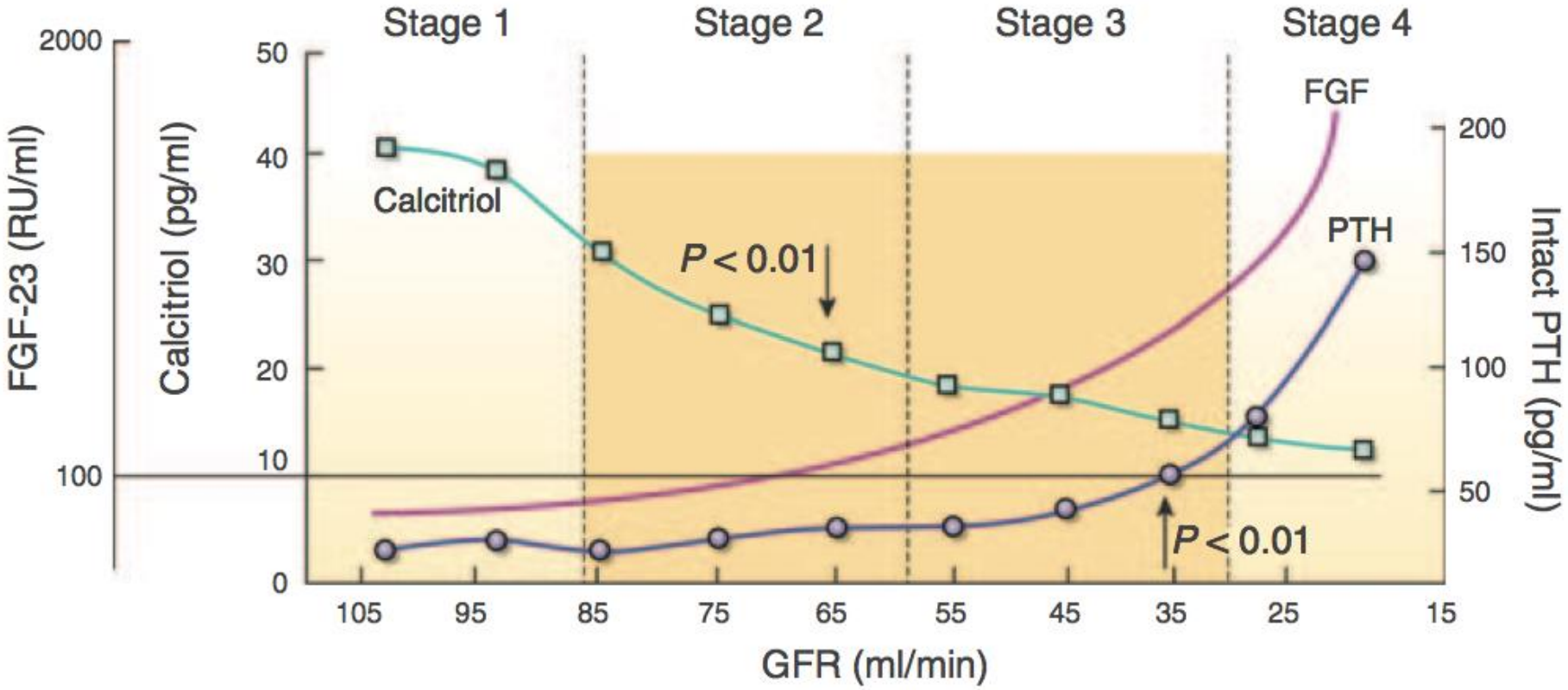
1. Jamal/Nickolas el al OI 2014 2. Naylor et al CJASN 2015 3. Limori et al NDT 2012

Additional Lab Studies: Risk Factors for Fracture Independent of BMD[1-5] (or important in CKD)

- Homocysteine level[1]
- hs CRP[2]
- Vitamin B12[3]
- Ferritin level[4]
- Vitamin A[5]
- Hemoglobin A1c
- Celiac panel
- Estradiol (and FSH)
- Carotene
- SPEP
- Beta-2-microglobulin
- Total/free testosterone level
- SPEP
- TSH/free T4
- FGF-23
- Sclerostin[6]
- RANKL[7]
- Dkk1[8]
- IGF-1[9]

[1]van Meurs, NEJM,, 2004,350:2033-40;[2]Schett, Arch Intern Med,2006, 166:2495-2501;[3]Clemens, NEJM, 2014, 371:963-4;[4] Kim, Osteoporos Int, 2013, 10:2627-37;[5]Michaelsson, NEJM, 2003,348:287-94;[6]Clarke, BoneKEy Rep, 2013, Art 361; [7]Schett, JAMA, 2004, 291:1108-13; [8]Pinzone, Blood, 2009, 113:517-525; [9]Garnero, Lancet, 2000, 355:898-899

FGF23 in CKD



Gal-Moscovici, KI 2010

Clinical Roundtable/Case Conference- Treating Osteoporosis Associated with CKD

-Keith Hruska, MD: Use of FGF-23 as a powerful biomarker that can be used to gauge the onset and severity of CKD-MBD

-Early in CKD stage 2, after a few nephrons are lost, a signal is sent ? from the kidney to the skeleton to the osteocyte that an “osteodystrophy” exists

-In response, the osteocyte secretes FGF-23

-A normal FGF-23 indicates that CKD-MBD has not started

-An elevated FGF-23 indicates that CKD-MBD has started and that all the other changes start: reduction in 24 α hydroxylase, reduction in 1α hydroxylase, loss of phosphate homeostasis, calcitriol deficiency

Diagnosis of “Osteoporosis” in Stage 4-5 CKD

Is a diagnosis of exclusion

Biochemical and Histomorphometry

PTH and BSAP combining the best of both worlds

- 1. PTH “extremes” (< 100 pg/ml) or (> 600pg/ml) high specificity for adynamic/OFC.
- 2. Bone specific alkaline phosphatase (< 20 IU/L) has a high PPV (80%) for low bone turnover .
- 3. BSAP correlate with PTH values in stage 5D CKD: both are increased on bone biopsy in established high bone turnover.
- 4. Combining the lower quartile BSAP and PTH < 100-150 have a high PPV (90%) for adynamic bone disease.

Garrett G et al CJASN 2013
Couttenye C et al Nephrol Dialysis Transpl 2009

Biomarkers in Stage 4-5 CKD: Update 2015

- Bone remodeling can be assessed with reasonable accuracy by measurement of bone turnover markers (BTOMs) in patients with normal renal function
- Osteocalcin and serum C-telopeptide are renally excreted
- Bone-specific alkaline phosphatase (BSAP), procollagen type-1N-terminal propeptide (P1NP) [procollagen peptide], and tartrate-resistant acid phosphatase 5b (Trap 5b) are metabolized by non-renal mechanisms
- BTOMs are higher in patients with more severe CKD and are associated with lower aBMD by DXA
- 60% of fracture patients had FN T-scores <-2 and serum OC, P1NP and Trap 5b in upper 2 tertiles of CKD patients

Nickolas, J Am Soc Nephrol, 2011, 22:1560-1572

DXA Issues in CKD

- Diagnostic criteria for osteoporosis (T-scores) were set by the WHO in 1994[1]
- CKD patients were excluded in the development of these criteria although DXA is frequently used in CKD patients to give them a diagnosis of “osteoporosis”[2]
- DXA AP Spine image includes trabecular bone of the vertebral body + cortical bone of the posterior elements
- DXA hip image includes both trabecular and cortical bone in different proportions dep on region of interest
- DXA 1/3 Forearm (Radius) is 99% cortical bone
- Hyperparathyroidism (1º or 2º) is anabolic to trabecular bone and catabolic to cortical bone and may make qualitative not quantitative changes[3]
- Therefore, looking at trabecular bone sites is likely to not be helpful or be problematic

[1]WHO Tech Rep Ser, 1994,843:1-129;[2]Amerling, Blood Purif, 2010;29:293-9; [3]Parfitt, J Bone Miner Res, 1998, 13:1213-20

DXA Issues: Update 2015

- In longitudinal studies[1], T-scores at the TF and UDR decreased significantly per year; those with most severe kidney disease had bone loss rates twice normal; bone loss associated with higher PTH and higher BTOM
- More patients with fracture had osteoporosis (T-score <-2.5) at TF (16 v 3%) and UDR (38 v 16%) than patients without fracture; low UDR aBMD was associated with the highest risk with >2 fold increased odds of fracture[2]
- For every 1 SD decrease in AP Spine BMD by DXA, there is a 1.5 fold increase in fracture risk[3] in CKD 3-5
- For every 1 SD decrease in TF BMD by DXA, there is a 2 fold increase in fracture risk[3] in CKD 3-5
- ? Treatment decisions should be based on the Z-score not the T-score[4]

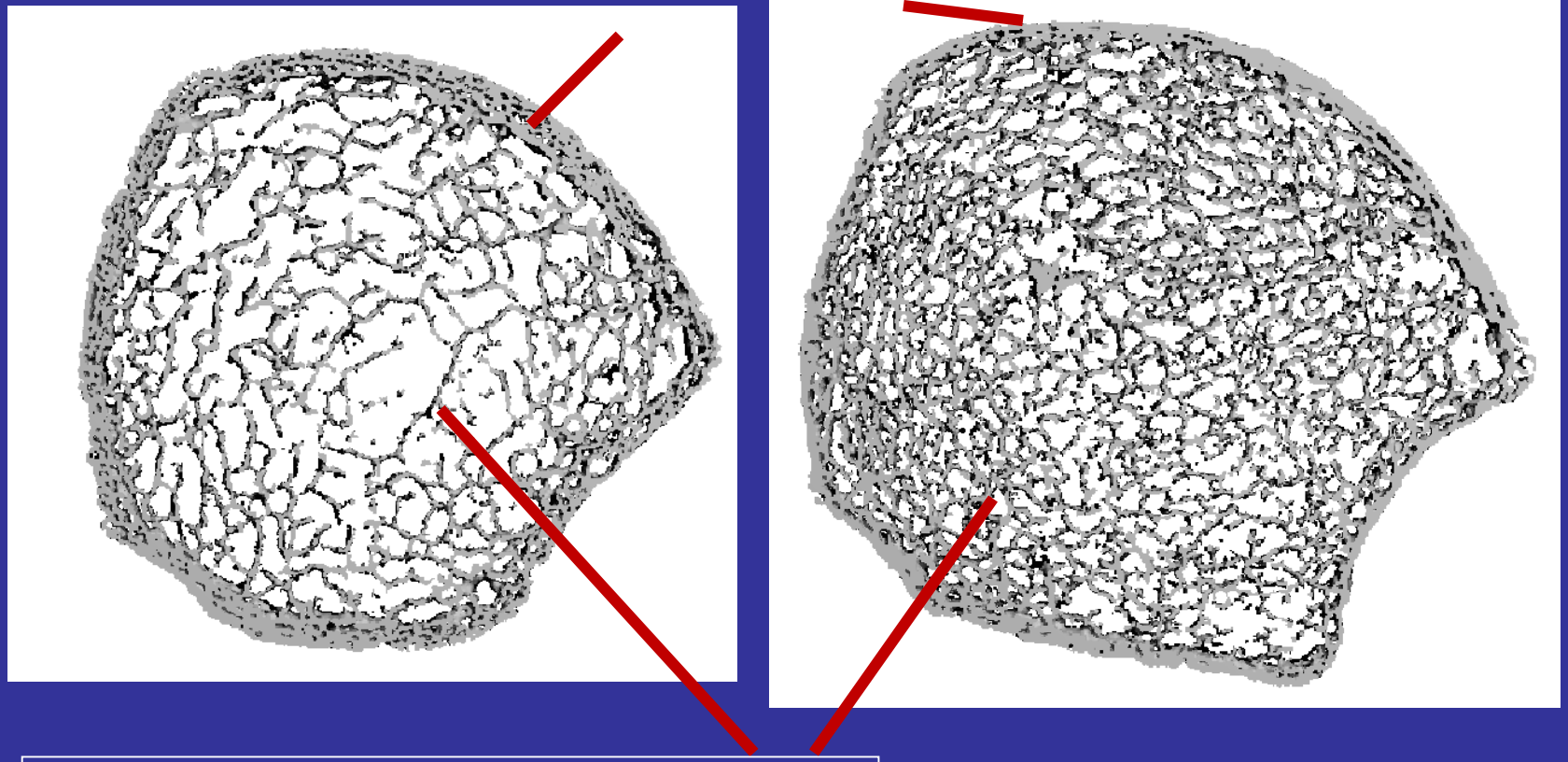
[1]Nickolas, J Bone Miner Res, 2013, 28:1811-20;[2]Nickolas, J Am Soc Nephrol, 2010, 21:1371-80;[3]West, J Bone Miner Res, 2015, 30:913-9;[4] Amerling, Blood Purif,2013, 29:293-9;

Tibia for 2 Age-, and FN T-Score Matched PMO Women

Control 64 yo Female T-Score -2.7: Tibia

PMO 62 yo CKD Pt T-Score -2.5

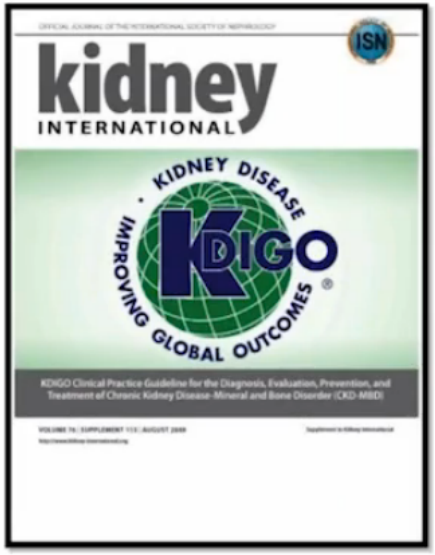
Thicker Ct vs CKD pt



Increased Tb Separation vs CKD pt

Nickolas T et al CJASN 2010

KDIGO CKD-MBD Guideline update



August 2009

In press May 2017

Topic 1: Bone Quality

OLD 3.2.2 In patients with CKD stages 3–5D with evidence of CKD–MBD, we suggest that BMD testing not be performed routinely, because BMD does not predict fracture risk as it does in the general population, and BMD does not predict the type of renal osteodystrophy **(2B).**

NEW 3.2.1: In patients with CKD Stages 3a–5D 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. *(2B)*

Ms SB TBS: 8-25-15

Northern California Institute For Bone Health, Inc.

Elliott N. Schwartz, MD, CCD, CPD
50 Vashell Way, Suite 400
- Orinda - CA 94563

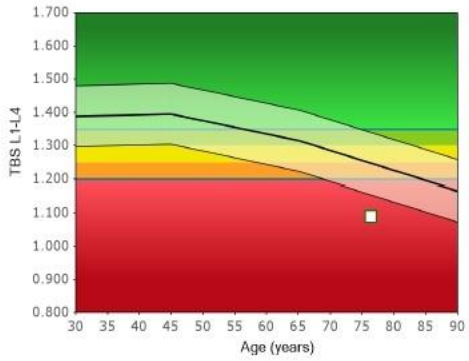
Patient :	[redacted]	Patient ID:	
Date of birth:	04/07/1939 76.4 years	Acquisition date:	08/25/2015
Height / Weight:	5.0 ft / 174.0 lb	Prescribing doctor:	ELLIOTT N. SCHWARTZ, MD
Gender / Ethnicity:	Female / White		

SPINE TBS REPORT

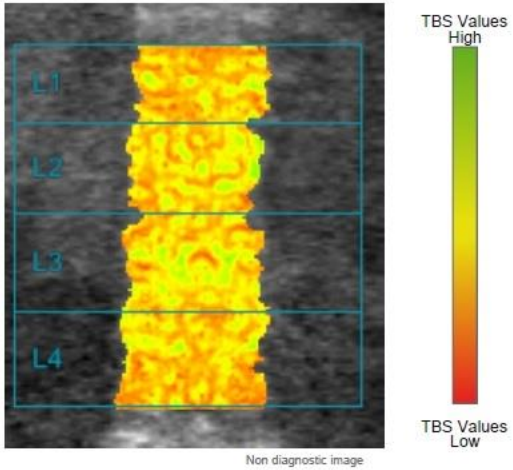
TBS reference graph

Reference population: USA

TBS L1-L4:1.092



TBS Mapping



Non diagnostic image

Additional results

Region	TBS	BMD
L1	0.984	0.676
L2	1.182	0.749
L3	1.211	0.882
L4	0.992	0.602
L1-L4	1.092	0.728
L1-L3	1.126	0.778
L1-L2	1.083	0.715
L2-L4	1.129	0.742
L2-L3	1.197	0.820
L3-L4	1.102	0.738

Comments

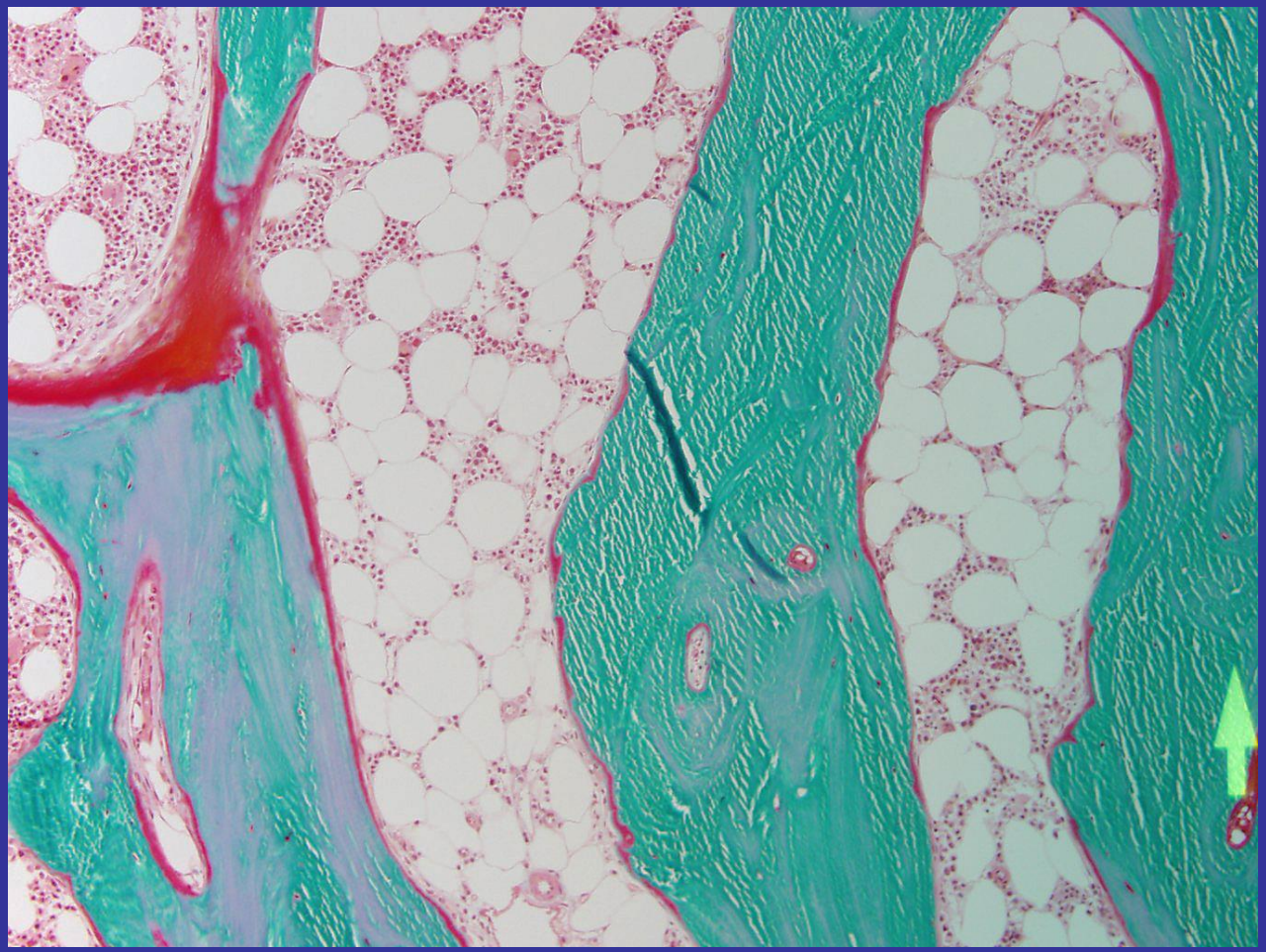
The Spinal Trabecular Bone Score (TBS) is 1.092. This value is less than 1.200 and is classified as "degraded" compared to a normal female Caucasian database.

Topic 1: Bone Quality

OLD 3.2.1 In patients with CKD stages 3–5D, it is reasonable to perform a bone biopsy in various settings including, but not limited to: unexplained fractures, persistent bone pain, unexplained hypercalcemia, unexplained hypophosphatemia, possible aluminum toxicity, and prior to therapy with bisphosphonates in patients with CKD–MBD **(not graded)**

NEW 3.2.2: In patients with CKD Stages 3a–5, it is reasonable to perform a bone biopsy if knowledge of the type of renal osteodystrophy will impact treatment decisions. **(Not Graded)**

Ms SB Bone Biopsy 9-18-15



Bone biopsy 9-18-15

Double Tetracycline Labelled Left Anterior Iliac Crest

- Hyperosteoidosis: osteoid surface is 33% (normal: 14)
- No mineralization defect
- Eroded surfaces are markedly diminished; 0.98% (normal: 4%)
- Dramatically low bone formation rate (BFR); 0.1 (normal: 35)
- Conclusion: markedly diminished osteoclastic activity; hyperosteoidosis indicates functioning osteoblasts but low bone formation indicates only “weakly” functioning; not adynamic but diminished osteoclast activity means would not be responsive to anti-resorptive; “Forteo might help to stimulate increased osteoblastic activity”

Alendronate Treatment in Women with Normal to Severely Impaired Renal Function

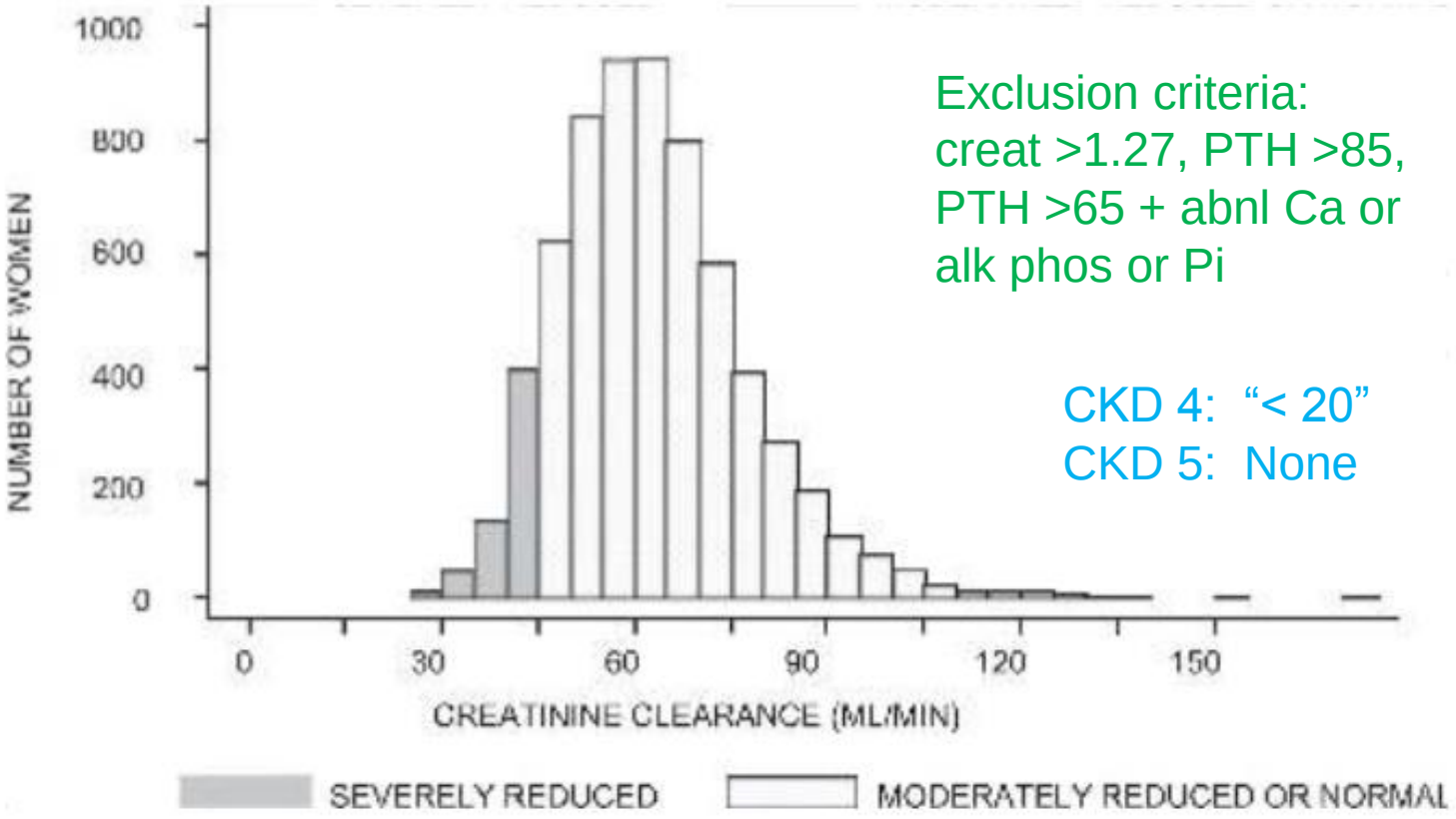


FIG. 1. Proportion of women with severely reduced (<45 ml/minute), moderately reduced, or normal estimated GFR.

Jamal, et al., J Bone Miner Res, 2007;22:503-508

Bisphosphonate Use in CKD: Association with Adynamic Bone Disease in a Bone Histology Series

Pt.	Age/Sex	Dx	GFR	PTH	Ca x P	Alk phos	Agent(s)	Months Rx	DEXA	Bone bx date	Results
1	67/F	NC	53	30	35	73	alend, acton	>60	osteopenia	5/5/2004	Low turnover
2	74/M	IF	49	39	32	81	alendronate	>12	osteoporosis	6/15/2005	Low turnover
3	64/F	DM	20	47.5	27	138	risendronate	>15	osteopenia	8/10/2005	Low turnover
4	47/M	IN v FSGS	29	60.2	50	46	alendronate	>3	osteopenia	8/17/2005	Low turnover
5	52/F	NC	39	30	26	176	alend, acton	>12	osteopenia	9/28/2005	Low turnover
6	74/F	?	54	22	31		actonel	>13	osteopenia	10/12/2005	

Amerling, et al., Blood Purification, 2010, 29(3):293-9

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

Table 2 Glomerular filtration rate (GFR), incident fracture, bone mineral density (BMD) response, and treatment-emergent and renal-related adverse event (AE) data for women with severe renal impairment (GFR <30 ml/min) (*TPTD20* teriparatide 20 mcg/day, *TPTD40* teriparatide 40 mcg/day, *NA* data not available)

Patients	GFR (ml/min)	Number of fractures		Percent change in lumbar spine BMD	Percent change in femoral neck BMD	Number of AEs	Number of renal-related AEs	Serum calcium >10.6 mg/dl	Serum uric acid >8.3 mg/dl
		Vertebral	Nonvertebral						
TPTD20									
A	26.50	0	0	8.33	1.27	3	0	No	Yes
TPTD40									
A	29.30	NA	1	NA	NA	3	0	No	No
B	26.75	NA	0	9.37	NA	10	0	No	Yes
Placebo									
A	22.09	NA	0	2.14	−1.15	0	0	No	No
B	28.64	0	0	−0.59	−6.48	7	0	No	No

Miller, P, Schwartz, EN et al. Osteoporos Int, 2007, 18:59-68

Teriparatide and Bone Turnover and Formation in a Hemodialysis Patient with Low-Turnover Bone Disease: A Case Report

- 41 yo W male, 1979 MPGN, started PD
- 1980 cadaveric transplant; failed 1982; 2nd cadaveric transplant 1983; failed 1985; initiate HD
- 1998, fall led to wrist fracture; iPTH 23.5 (0.6-7.2); rx'd calcium, calcitriol, cholecalciferol, CaCo3
- 2003 fall led to hip fracture: calcium 2.67 (2.10-2.60), P 1.70 (0.81-1.45), iPTH 27.5
- 2010 decreasing BMD + bilateral non-displaced pelvic fractures, "several" low-trauma fractures,
- Bone biopsy: hypodynamic low turnover
- Rx: teriparatide 20 mcg subcut daily in AM and after dialysis on dialysis days for 2 years; no hypercalcemia, no further fractures
- Repeat bone biopsy: improved static and dynamic parameters;

Palcu, et al, AmJ Kid Dis, 2015, 65:933-936

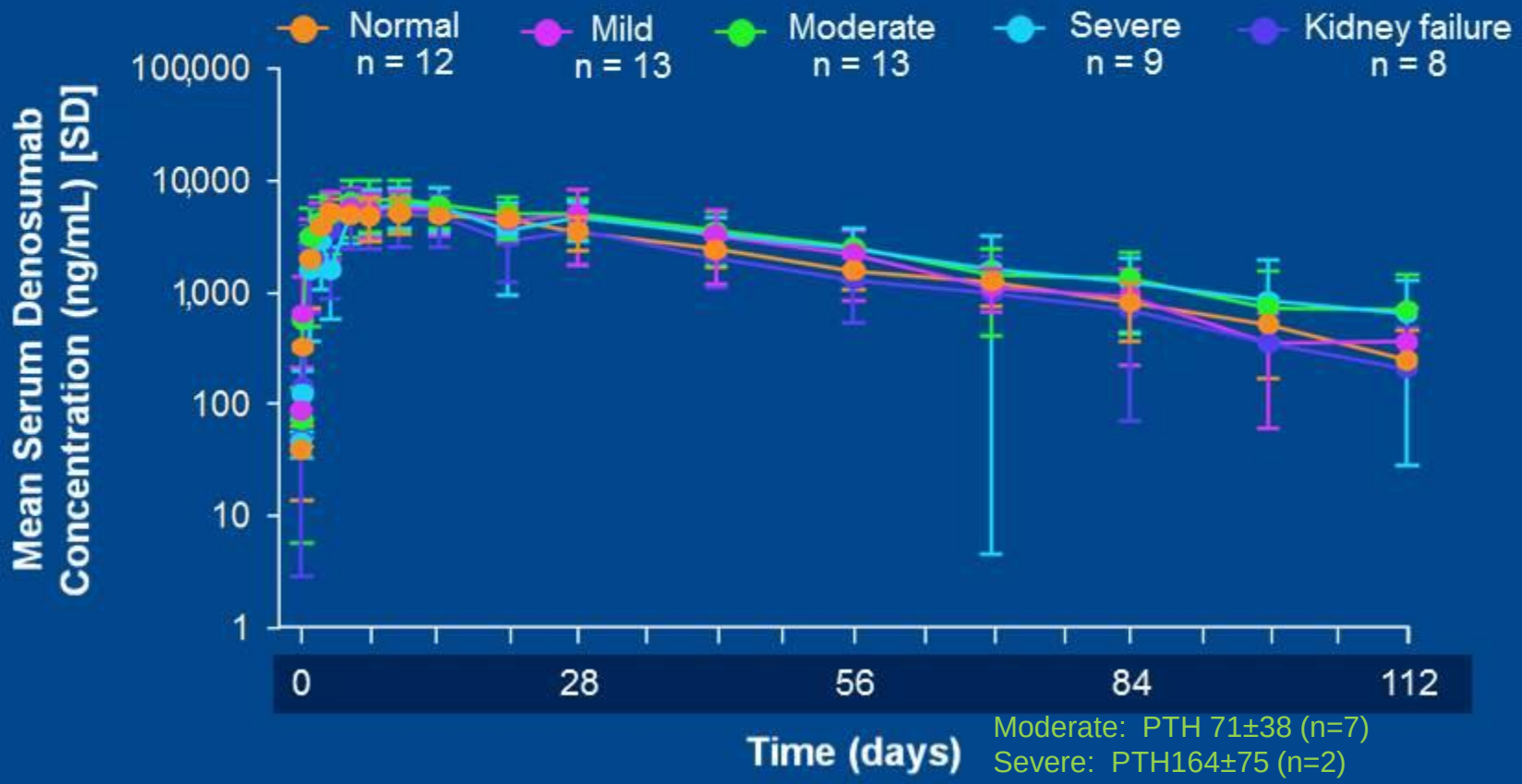
Renal Impairment Data From the Prolia® (denosumab) US Prescribing Information

- No dose adjustment of Prolia® is necessary in patients with renal impairment
- In clinical studies, patients with severe renal impairment (CrCl < 30 mL/min) or receiving dialysis were at greater risk of developing hypocalcemia
  - Prolia® is contraindicated in patients with hypocalcemia
  - Consider the benefit-risk profile when administering Prolia® to patients with severe renal impairment or receiving dialysis
  - Pre-existing hypocalcemia must be corrected prior to initiating Prolia®
  - Adequately supplement all patients with calcium and vitamin D
  - Clinical monitoring of calcium, phosphorus, and magnesium is highly recommended

US = United States; CrCl = creatinine clearance
Prolia® (denosumab) prescribing information, Amgen.

Effect of Renal Impairment on Denosumab Pharmacokinetics

Denosumab Concentration–Time Profiles Following a Single SC Dose of 60 mg Denosumab to Healthy and Renally Insufficient Subjects

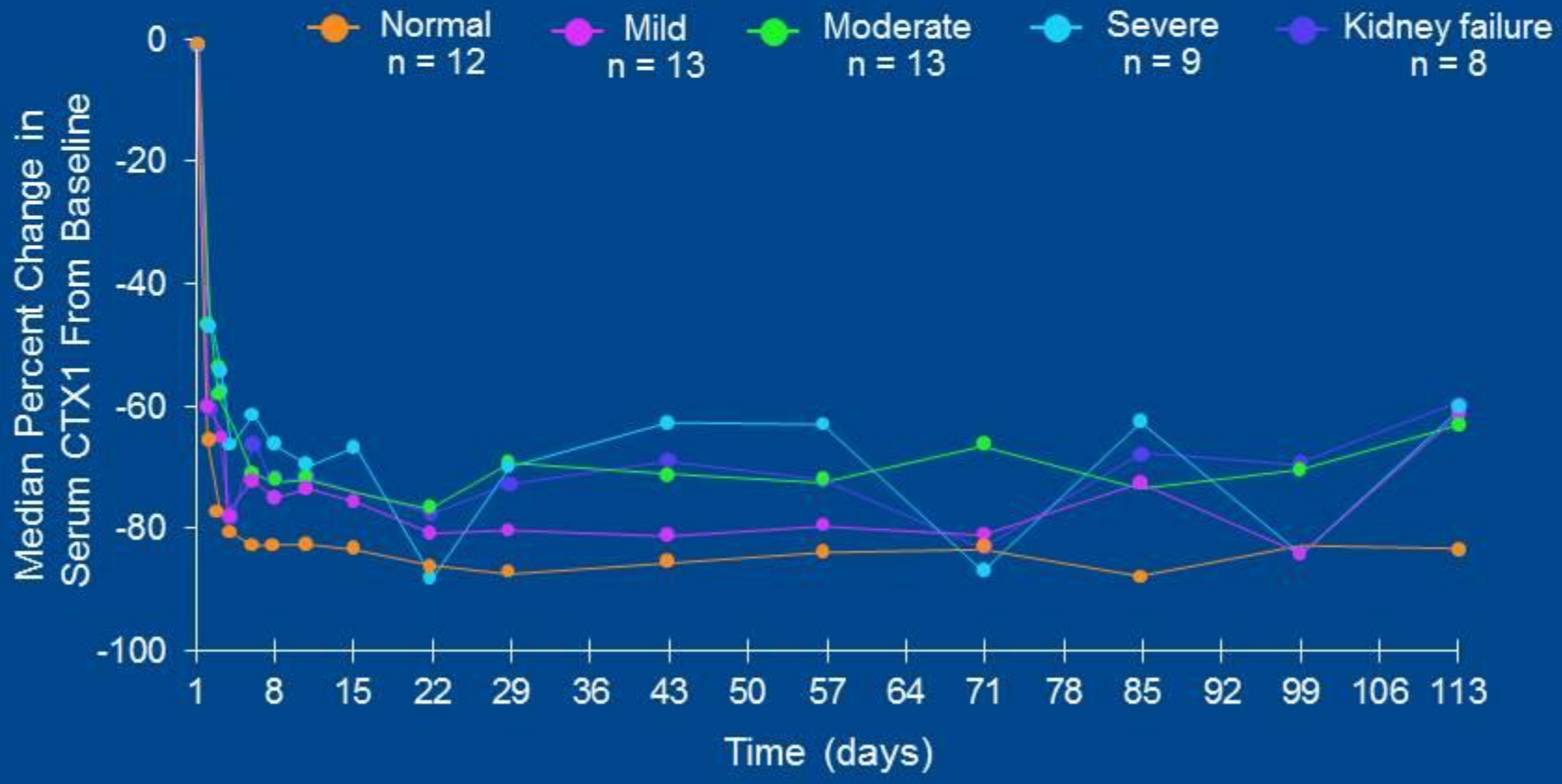


Moderate: PTH 71±38 (n=7)
Severe: PTH164±75 (n=2)
Kidney Failure: PTH (n=0)* study amend excl pts w high PTH or low 1,25 D

SC = subcutaneous; SD = standard deviation
Adapted from: Block GA, et al. *J Bone Miner Res*. 2012;27:1471-1479.

Effect of Renal Impairment on Denosumab Pharmacodynamics

Change From Baseline for Serum CTX1 Following SC Administration of 60 mg Denosumab to Subjects with Varying Degrees of Renal Function



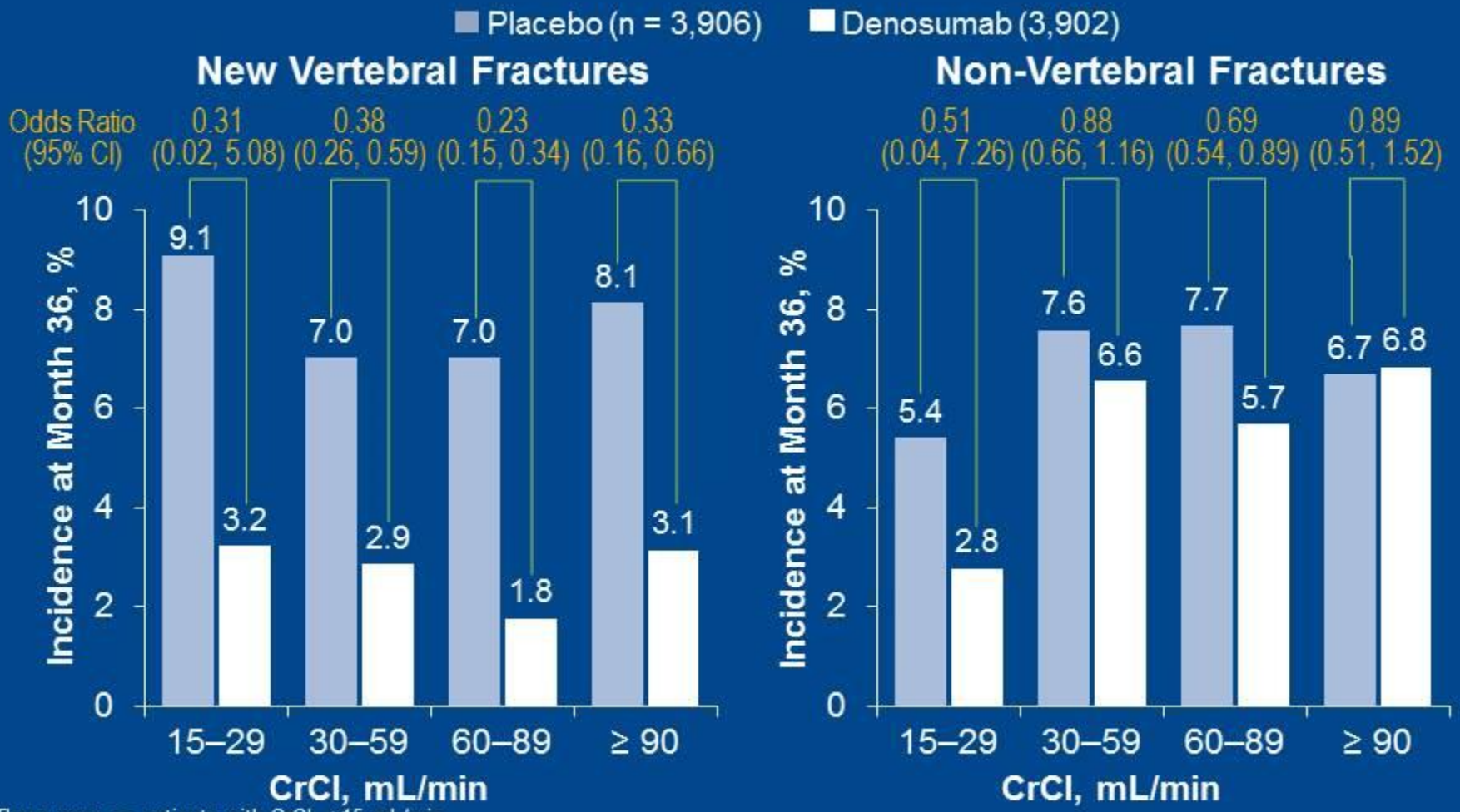
CTX1 = type 1 C-telopeptide

Adapted from: Block GA, et al. *J Bone Miner Res*. 2012;27:1471-1479.

Incidence of Fractures Through Month 36 by Baseline CrCl

Pivotal Phase 3 Trial

CKD 4: 73 by CG, 17 by MDRD; CKD 5: None



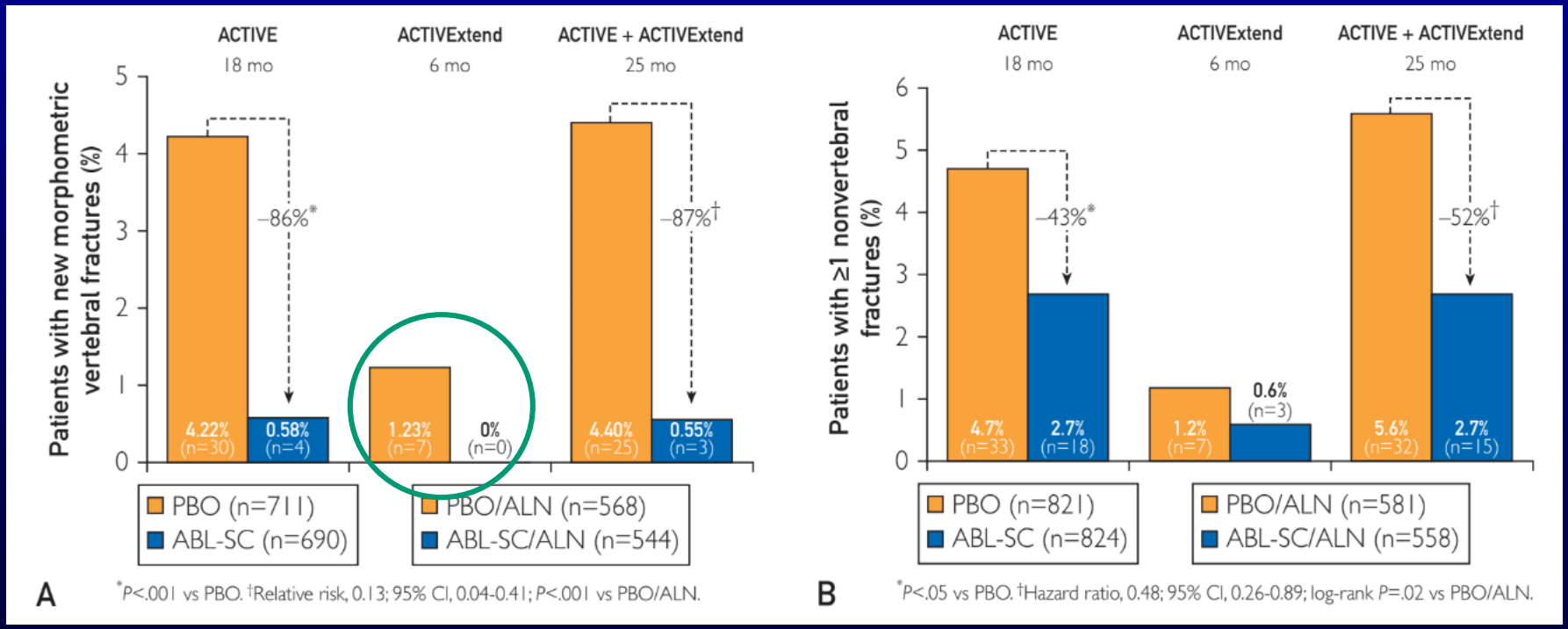
There were no patients with CrCl < 15 mL/min.
CI = confidence interval

Jamal SA, et al. *J Bone Miner Res.* 2011;26:1829-1835.

Abaloparatide

Phase 3 ACTIVE Extension

Fracture protection is sustained during 6 months of alendronate therapy



OOC

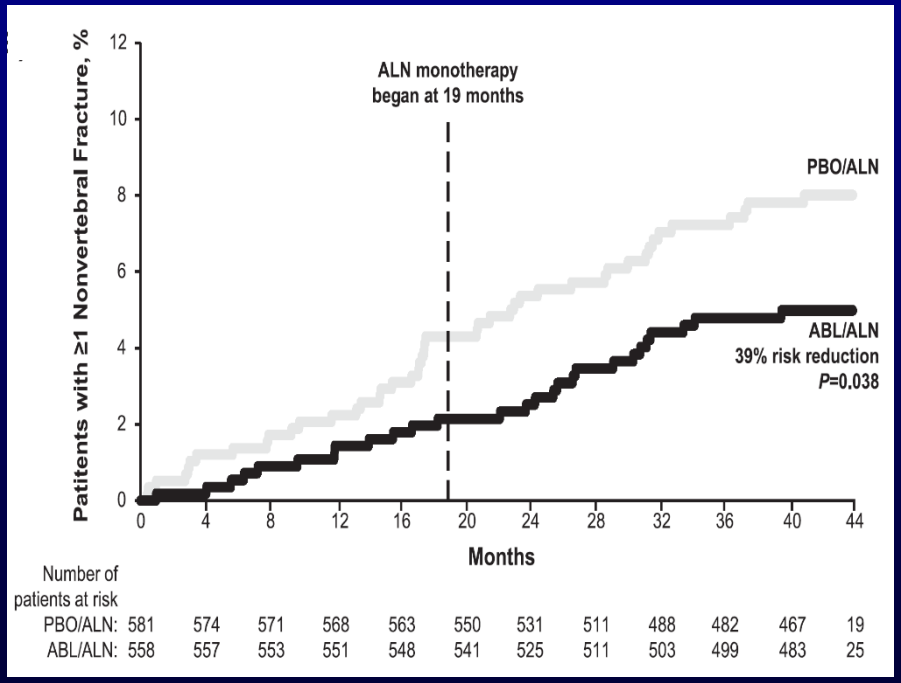
Cosman F et al. *Mayo Clin Proc.* 2017;92:200-10

Abaloparatide

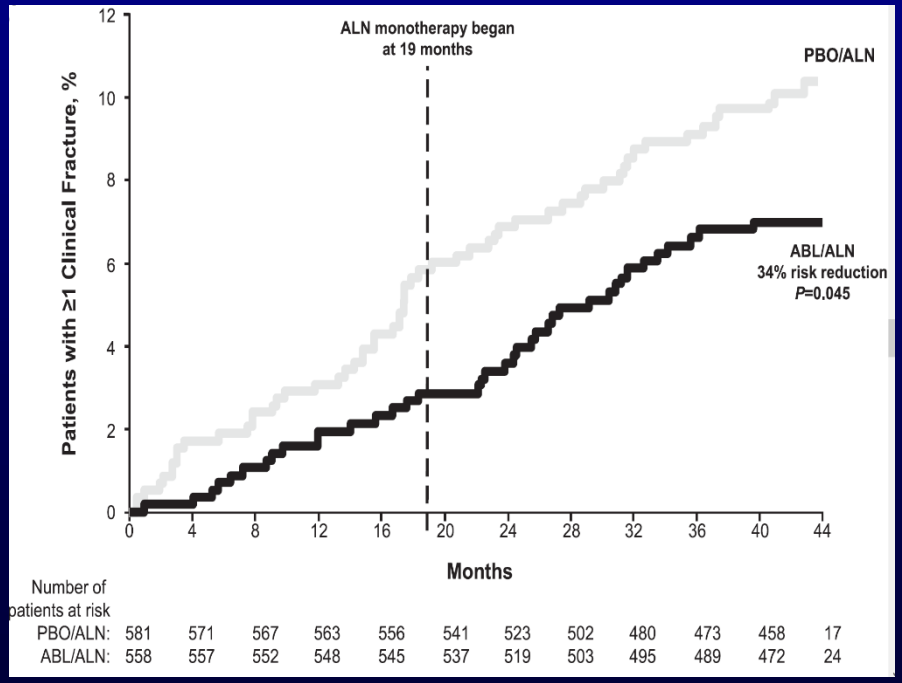
Phase 3 ACTIVE Extension

- **The non-vertebral and clinical fracture protection benefit of abaloparatide is preserved upon transitioning to alendronate**

Non-vertebral fracture



Clinical fracture (non-vertebral + painful vertebral fractures)



OOC

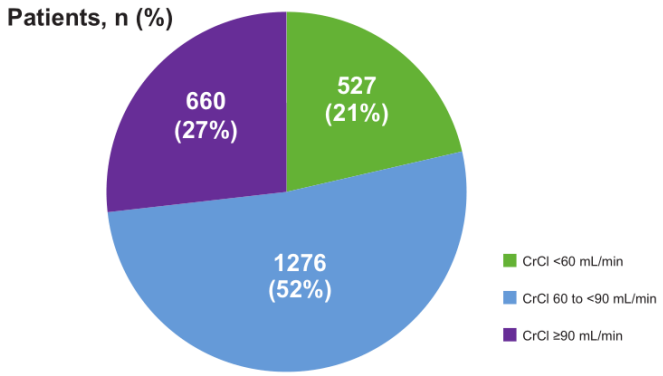
Bone HG et al. *J Clin Endocrinol Metab* 2018;103:2949–57

Abaloparatide in CKD

RENAL IMPAIRMENT SUBGROUP ANALYSIS

- Patients with significantly impaired renal function (creatinine >2.0 mg/dL [177 µmol/L] or creatinine clearance [CrCl] by Cockcroft-Gault calculation <37 mL/min) were excluded from the ACTIVE trial
- A post hoc analysis evaluated the effect of renal function on safety and efficacy endpoints
- There were 527 subjects with baseline CrCl <60 mL/min, 1276 with CrCl 60 to <90 mL/min, and 660 with CrCl of ≥90 mL/min

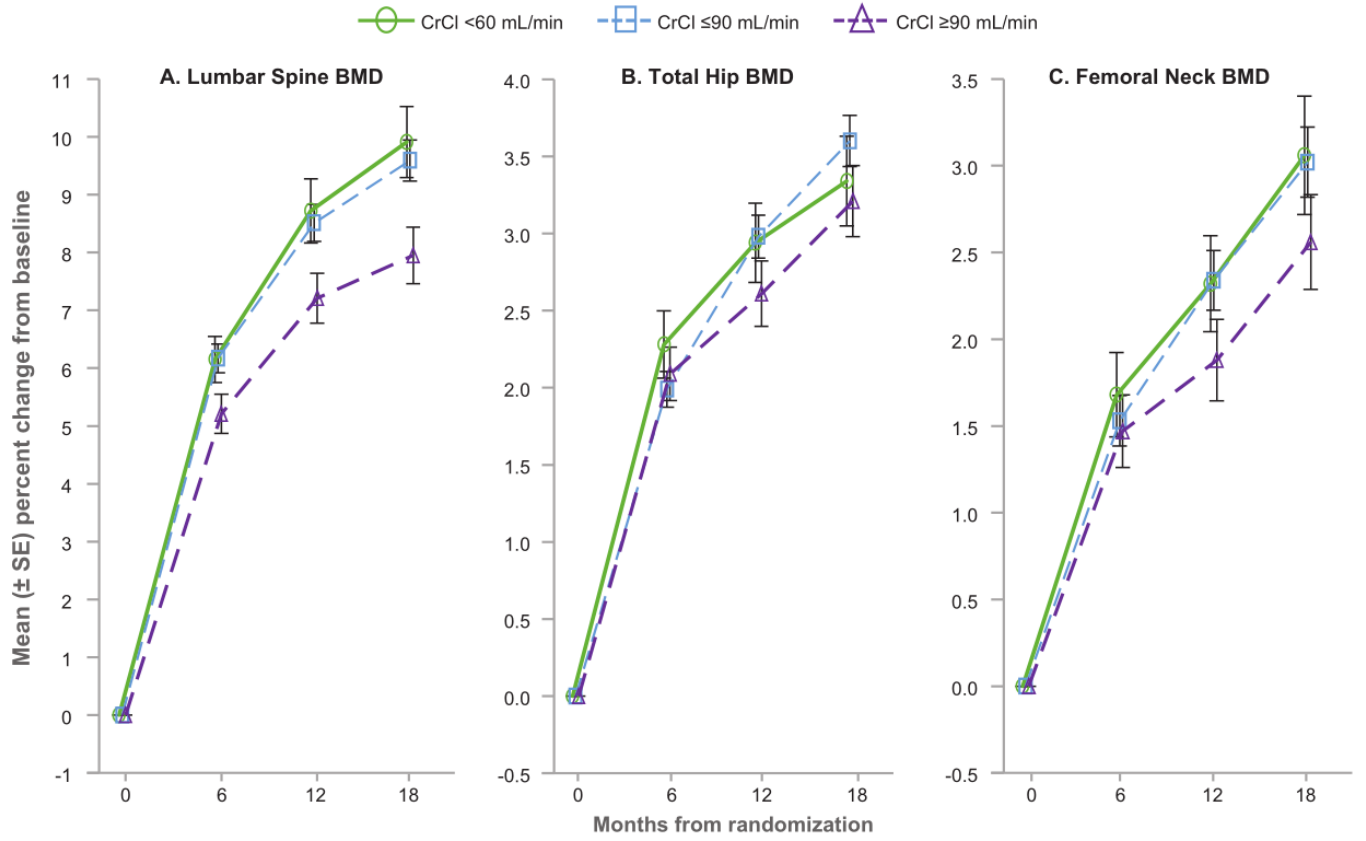
Figure 3. Renal Impairment Subgroups, Prespecified by Baseline CrCl



Presented at ASBMR; Atlanta, Georgia; Sunday, September 18, 2016

Courtesy of JP Bilezikian MD

Figure 4. BMD Changes, by Renal Function (ITT Population in Abaloparatide-SC Treatment Group using LOCF)



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Courtesy of JP Bilezikian MD

Table 3. Treatment-Emergent Adverse Events by Baseline Renal Function Group (Safety Population)

Preferred Term Renal status*	Placebo n/N (%)	Abaloparatide-SC n/N (%)	Teriparatide n/N (%)
Anemia			
<60 mL/min	5/167 (3.0)	13/168 (7.7)	7/192 (3.6)
60 to <90 mL/min	7/435 (1.6)	8/428 (1.9)	16/413 (3.9)
≥90 mL/min	3/218 (1.4)	2/226 (0.9)	0/213 (0.0)
Hypercalcemia			
<60 mL/min	1/167 (0.6)	3/168 (1.8)	14/192 (7.3)
60 to <90 mL/min	1/435 (0.2)	7/428 (1.6)	13/413 (3.1)
≥90 mL/min	1/218 (0.5)	1/226 (0.4)	2/213 (0.9)
Nausea			
<60 mL/min	5/167 (3.0)	16/168 (9.5)	11/192 (5.7)
60 to <90 mL/min	13/435(3.0)	36/428 (8.4)	20/413 (4.8)
≥90 mL/min	7/218 (3.2)	16/226 (7.1)	11/213 (5.2)
Orthostatic hypotension			
<60 mL/min	1/167 (0.6)	2/168 (1.2)	1/192 (0.5)
60 to <90 mL/min	3/435 (0.7)	4/428 (0.9)	2/413 (0.5)
≥90 mL/min	0/218 (0.0)	1/226 (0.4)	0/213 (0.0)

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In None of the PMO Clinical Trials

Did any patients in whom baseline PTH was measured have an elevated baseline PTH

Other Anabolic Agents (BMP 7, monoclonal antibody to sclerostin, PTHrp analogues, etc)

May offer more targeted therapy and robust data for patients with CKD and low bone turnover

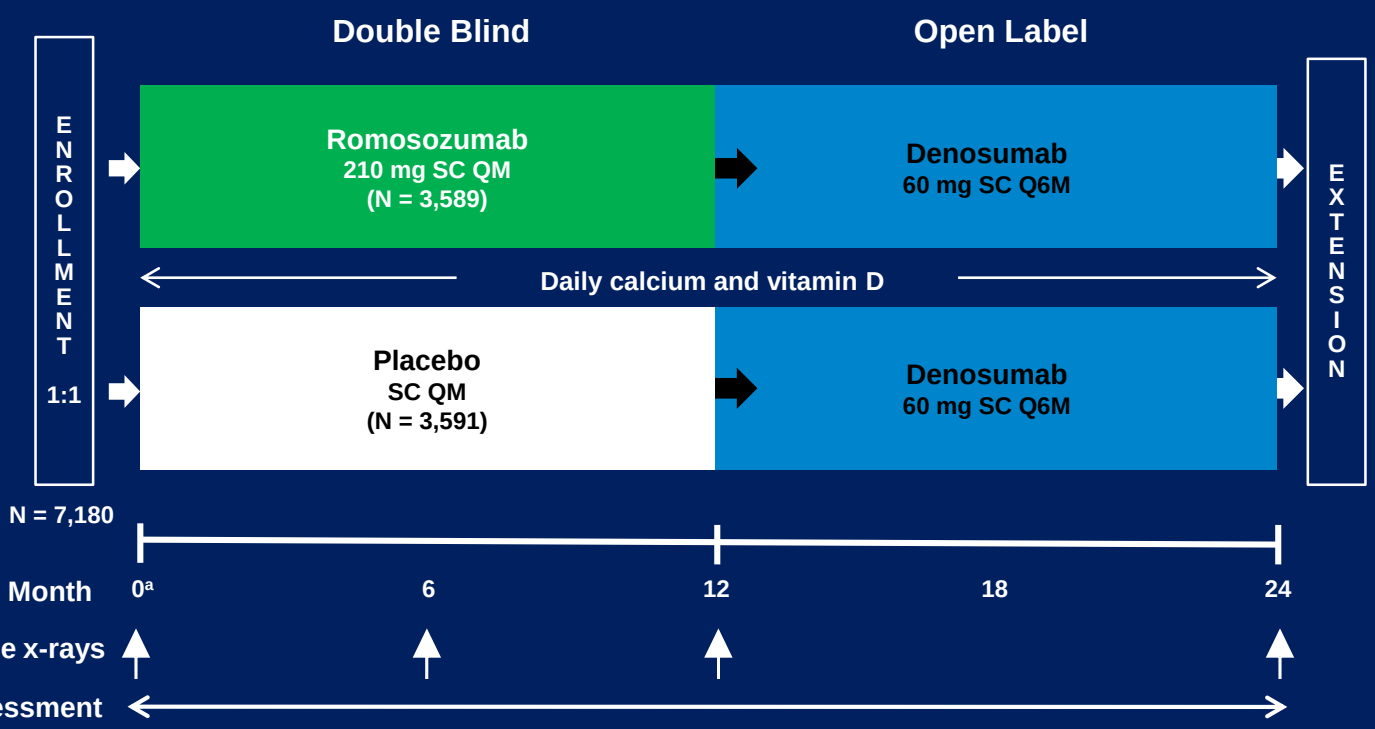
FRActure study in postmenopausal woMen with osteoporosis (FRAME) Study Design

Inclusion criteria

- Postmenopausal women age 55–90 years
- BMD T-score ≤ –2.5 at the total hip or femoral neck

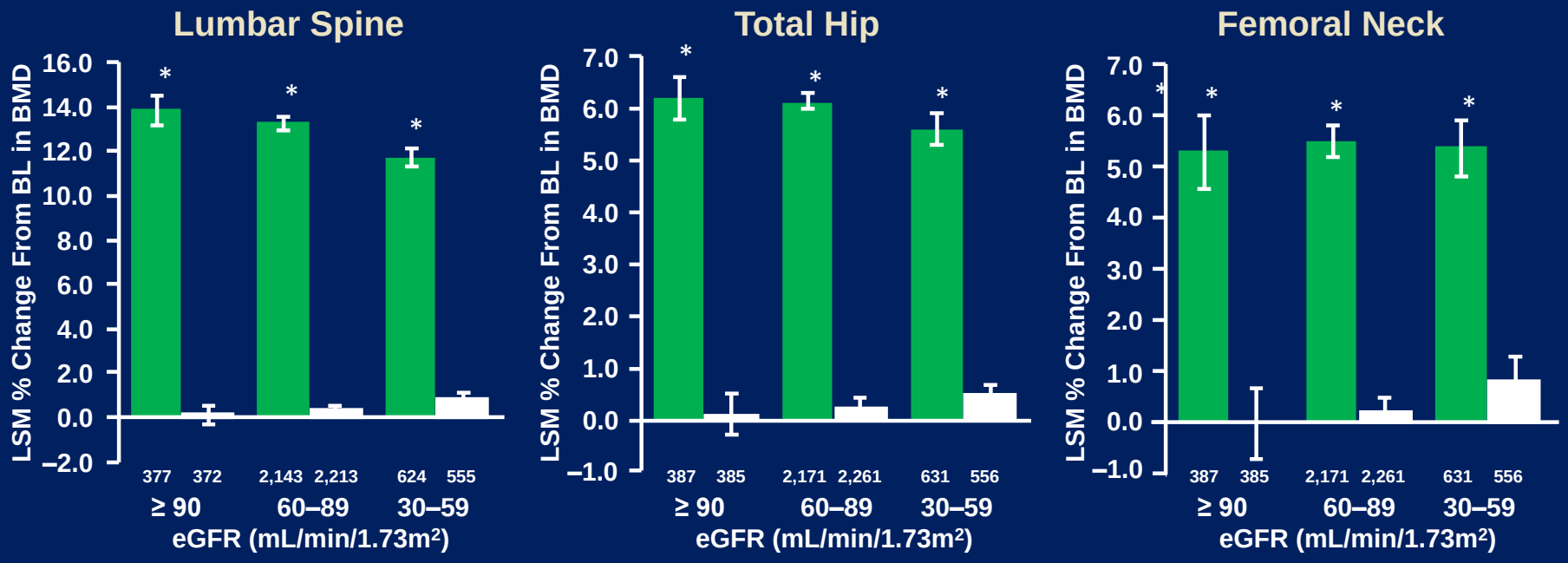
Exclusion criteria

- BMD T-score ≤ –3.5 at the total hip or femoral neck
- History of hip fracture or any severe or > 2 moderate vertebral fractures
- Recent osteoporosis therapy



[a]Loading dose of 50,000–60,000 IU vitamin D

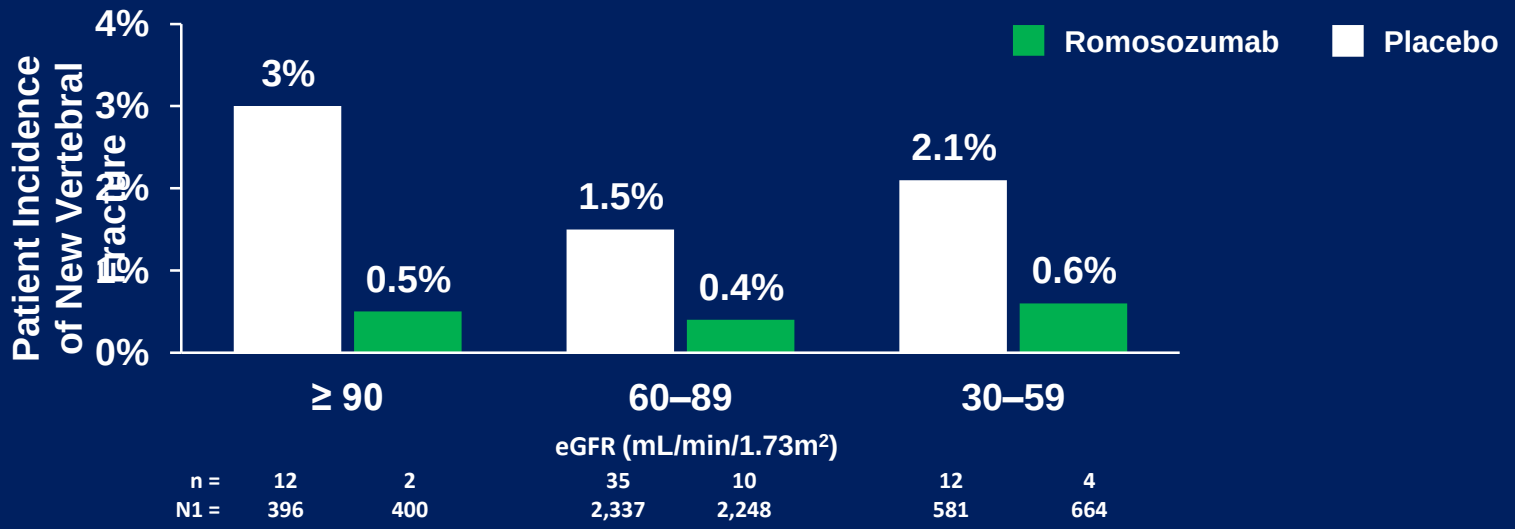
Percentage Change in BMD From Baseline at Month 12



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

*$p < 0.001$ (romosozumab – placebo). Abbreviations: BL, baseline; LSM, least squares mean.

Incidence of New Vertebral Fractures at Month 12

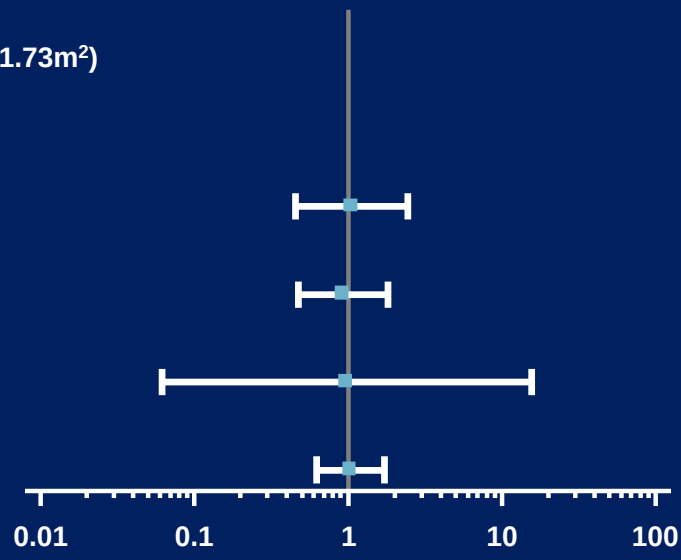


	% (SE) [95% CI]		
	eGFR ≥ 90	eGFR 60–89	eGFR 30–59
Risk ratio[a]	0.2 (0.7) [0.04, 0.7]	0.3 (0.4) [0.2, 0.6]	0.3 (0.6) [0.1, 0.9]
OR[b]	0.2 (0.8) [0.03, 0.7] *P* = 0.005	0.3 (0.4) [0.1, 0.6] *P* < 0.001	0.3 (0.6) [0.1, 0.8] *P* = 0.017

N1=number of patients in analysis set; n=number of patients with new vertebral fracture.

[a]Based on the Mantel-Haenszel method. [b]Based on logistic regression model. [ab]Adjusted for prevalent vertebral fracture stratification variable. *P*-value based on score test.

Patient Incidence of Positively Adjudicated Major Adverse Cardiovascular Events



eGFR (mL/min/1.73m^2)	Placebo N = 3576 n/N1 (%)	Romosozumab N = 3581 n/N1 (%)	Hazard Ratio (95% CI)	p-value of Treatment-by-Subgroup Interaction
				0.85
15–29	0/8 (0.0)	1/10 (10.0)	NE	
30–59	10/625 (1.6)	12/734 (1.6)	1.05 (0.45, 2.43)	
60–89	18/2526 (0.7)	16/2406 (0.7)	0.92 (0.47, 1.81)	
≥ 90	1/416 (0.2)	1/431 (0.2)	0.98 (0.06, 15.63)	
Overall	29/3576 (0.8)	30/3581 (0.8)	1.03 (0.62, 1.72)	

Cardiovascular events defined as cardiovascular deaths, myocardial infarction, and stroke.

Treatment of Bone: Osteoporosis Medications

- **4.3.1. In patients with CKD stages 1–2 with osteoporosis and/or high risk of fracture, as identified by World Health Organization criteria, we recommend management as for the general population *(1A)*.**
- **4.3.2. In patients with CKD stage 3 with PTH in the normal range and osteoporosis and/or high risk of fracture, as identified by World Health Organization criteria, we suggest treatment as for the general population *(2B)*.**

Treatment of Bone: Osteoporosis Medications

- **4.3.3. In patients with CKD stage 3 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 *(2D)*.**
- **4.3.4. In patients with CKD stages 4–5D having biochemical abnormalities of CKD–MBD, and low BMD and/or fragility fractures, we suggest additional investigation with bone biopsy prior to therapy with antiresorptive agents *(2C)*.**

Management Decisions in Stage 5 CKD in Fracturing Patients

No Data

Only Opinion

Benefits and Harms of Osteoporosis Medications in Patients with CKD: A Systematic Review and Meta-analysis

- Limitations: Unclear rigor of evidence, possible reporting biases, and scant evidence among patients with stage 3 to 5
- Effects of osteoporosis medications on BMD, fracture risk and safety among patients with CKD are not clearly established

Wilson et al., Ann Intern Med, 2017

Conclusions

- Stage 1-3 CKD: manage as you would for PMO or idiopathic male osteoporosis. (FGF-23 not elev)
- Stage 4-5 CKD: screen DDX with BTM-especially PTH and BSAP and serum phosphorus. (FGF-23 elev)
- Fractured 4-5 CKD without biochemical evidence suggesting OM or adynamic bone disease: treat on label with denosumab or off-label with bisphosphonates, or teriparatide, if not OFC.
- Fractured 4-5 CKD that you don't know the turnover, or with a lower PTH/BSAP- treat with teriparatide first.