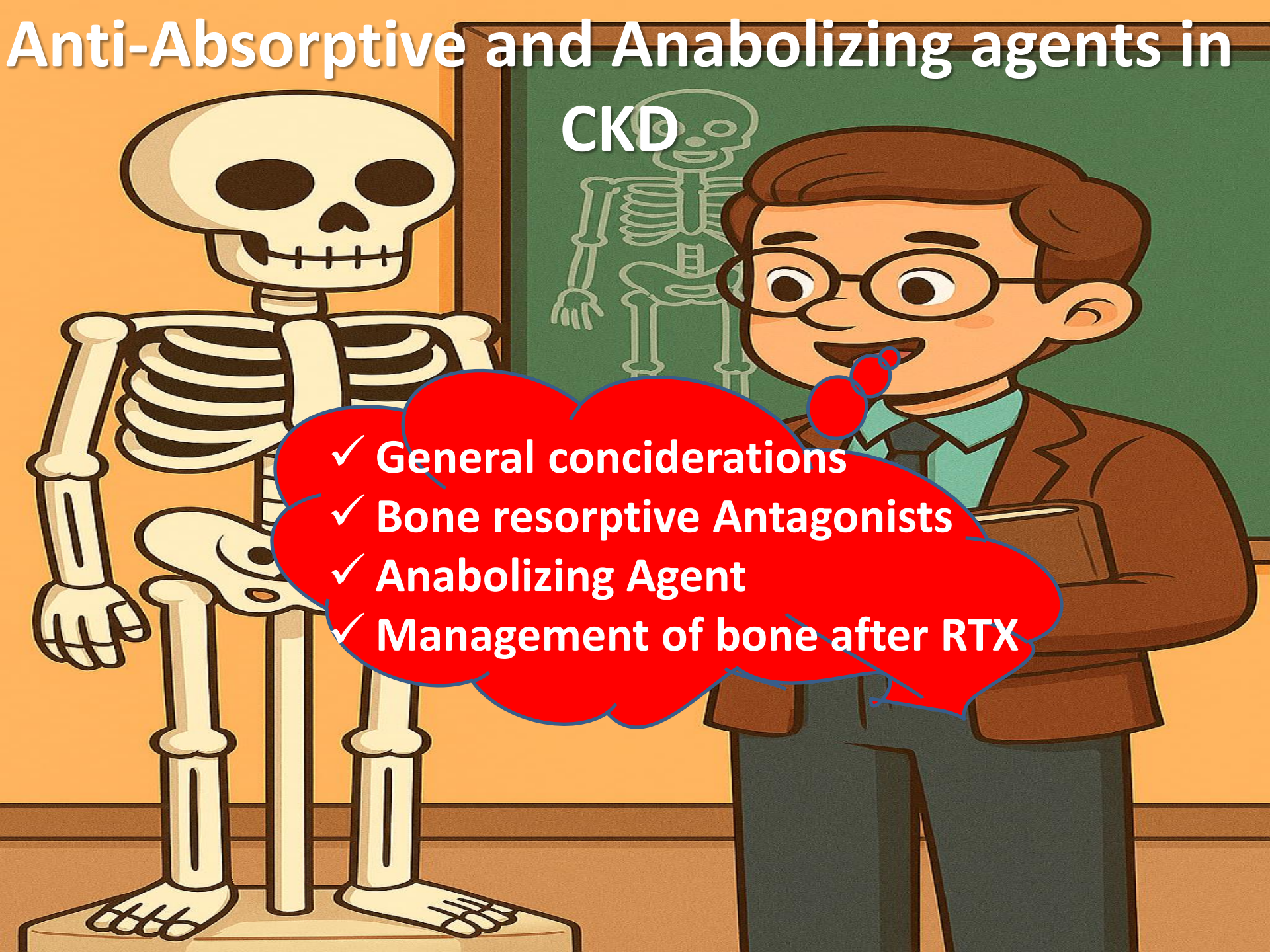
IN THE NAME OF GOD

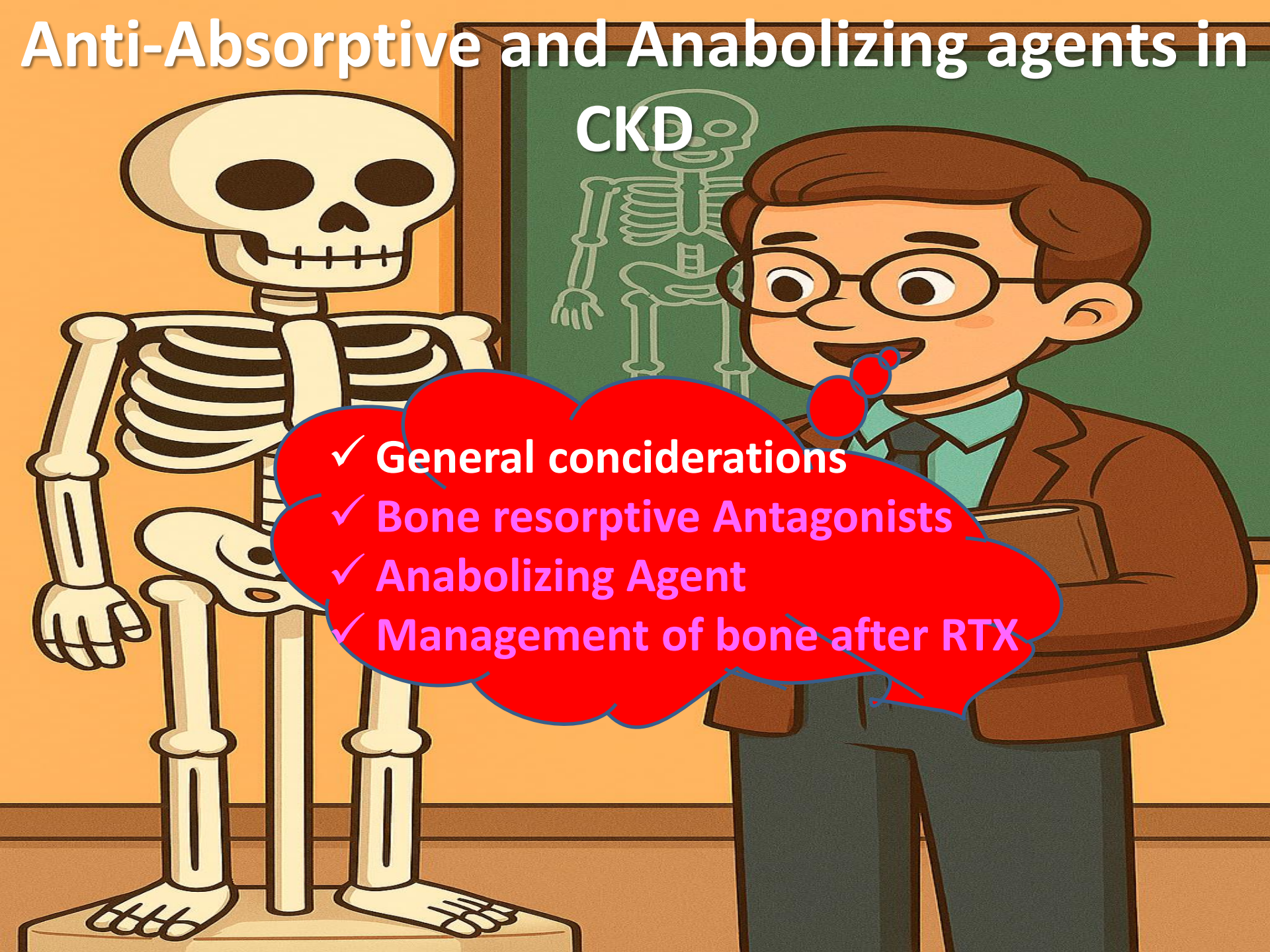
Anti-Absorptive and Anabolizing agents in Renal Osteodystrophy

gani, Professor of Nephro

Anti-Absorptive and Anabolizing agents in CKD



Anti-Absorptive and Anabolizing agents in CKD

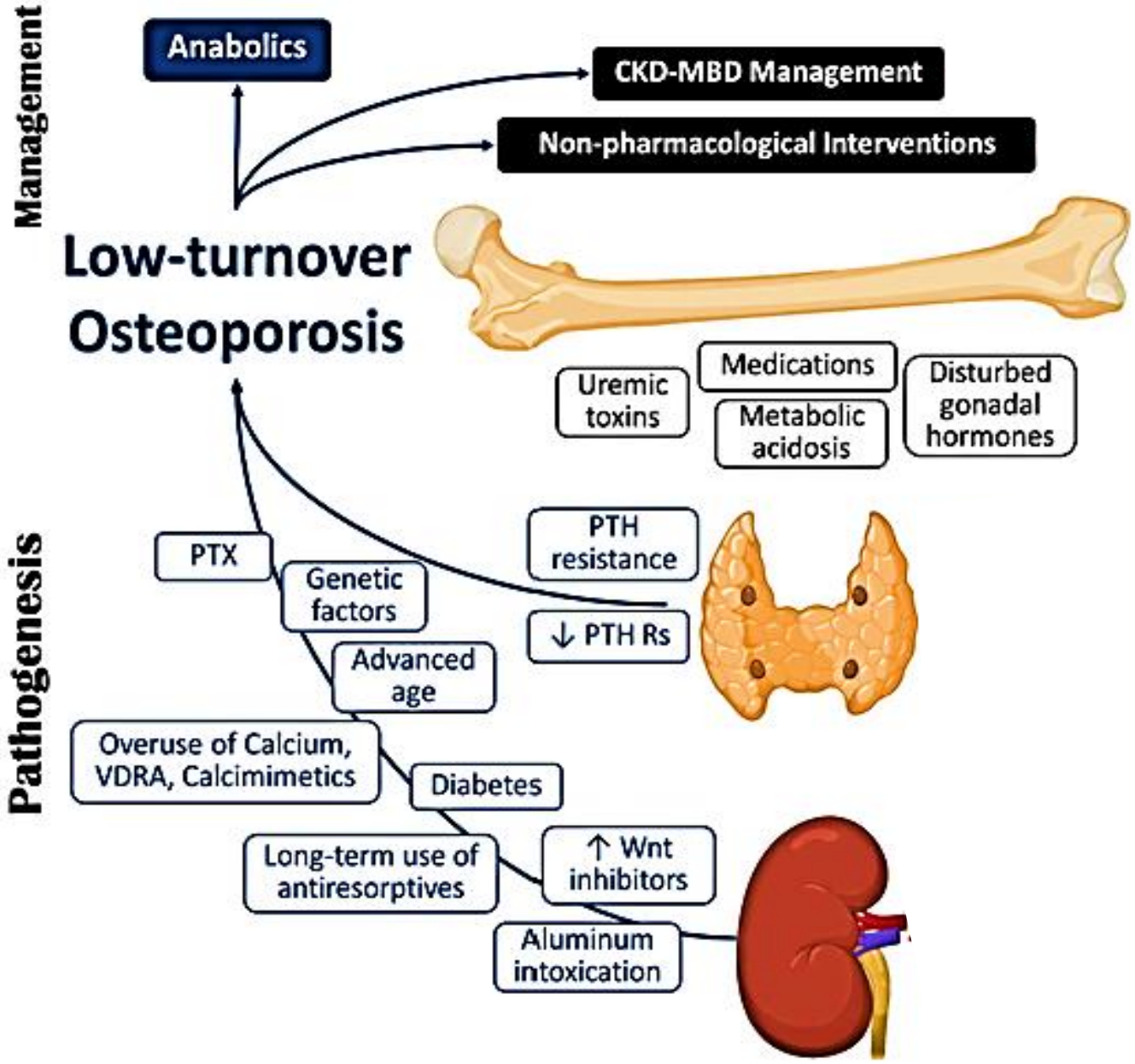


Associations of bone-related, CKD-modified blood parameters with bone formation, mineralization, and resorption

Parameter	Direction of change in bone		
	Formation	Mineralization	Resorption
Metabolic acidosis	↓	↓	↑
High PTH	↑	Normal	↑↑
High FGF23	?	?	?
High osteocalcin	↑	Normal	
High osteoprotegerin	↑		↓
High sclerostin	↓		

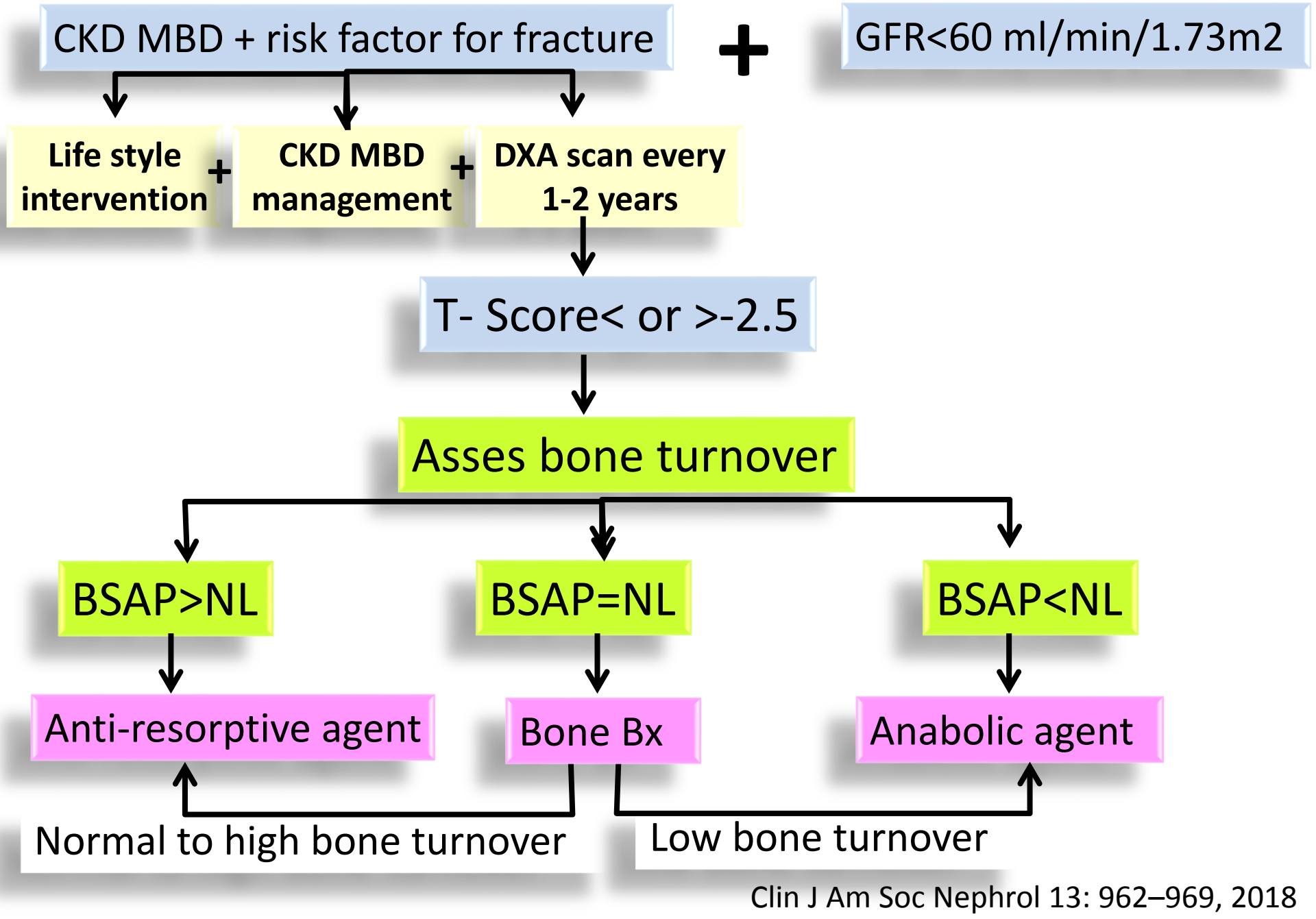
Kidney International (2016) 89, 289–302

The pathogenesis of osteoporosis in patients with CKD



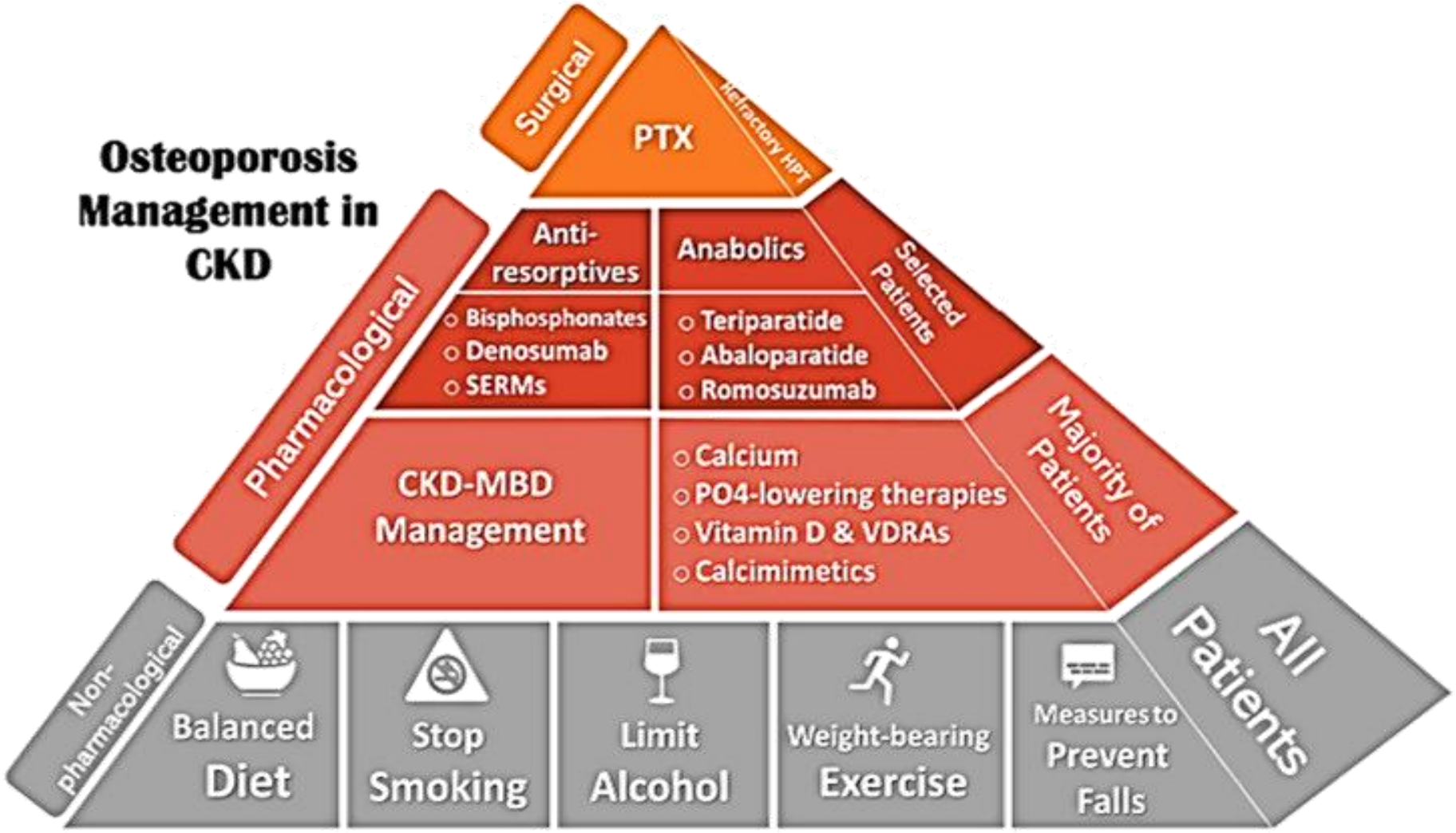
Osteoporosis International ·33; 2259–2274, (2022)

Treatment of BMD in CKD based on DEXA and BSAP



Clin J Am Soc Nephrol 13: 962–969, 2018

Osteoporosis management pyramid in patients with CKD



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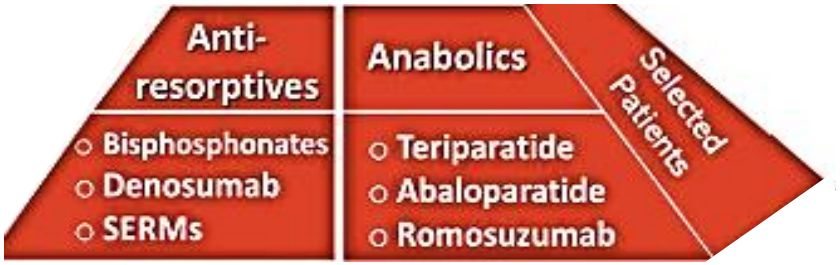
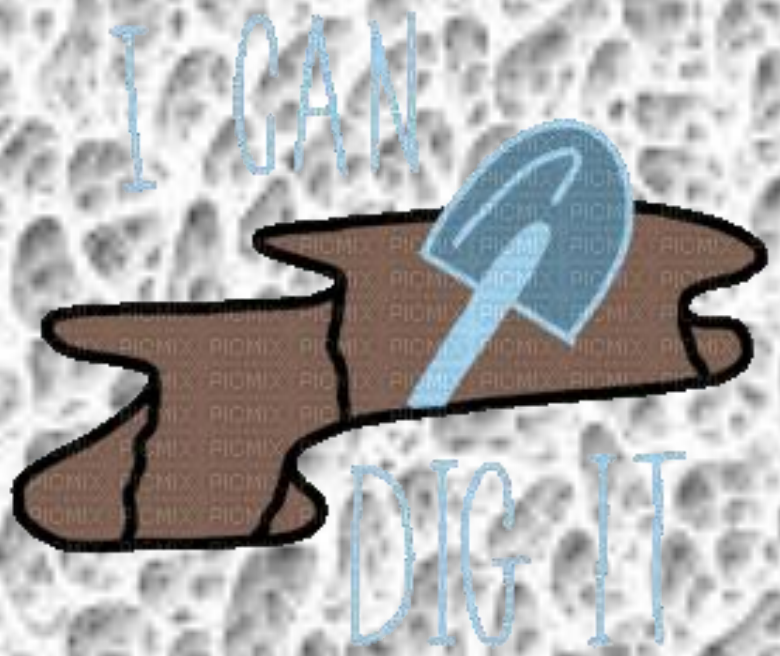


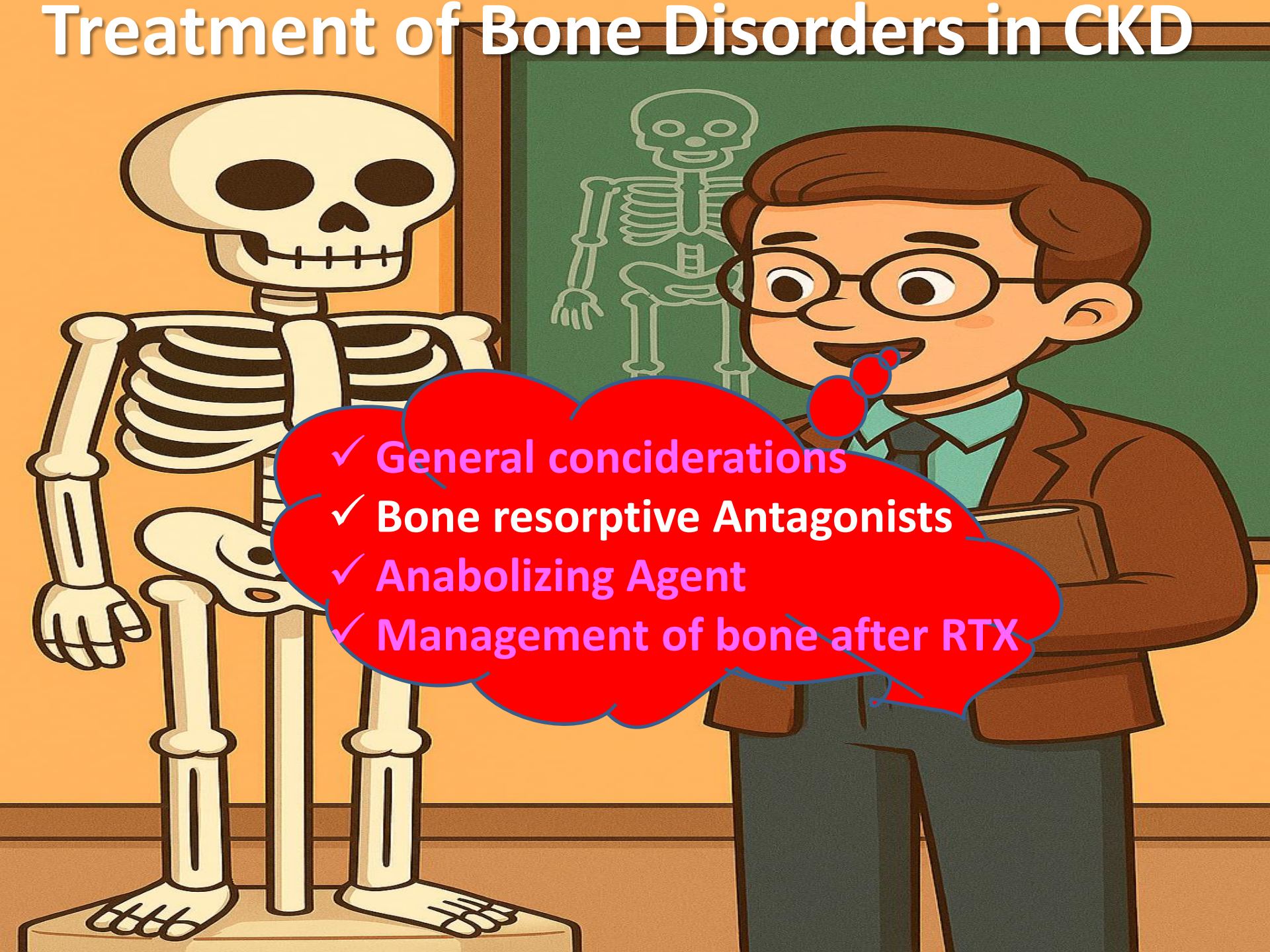
Osteoporosis International ·33; 2259–2274, (2022)

Anti-resorptive drugs



Anabolic agents

Treatment of Bone Disorders in CKD



In Practice Review

AJKD

Diagnosis and Management of Osteoporosis in Advanced Kidney Disease: A Review

Charles Ginsberg and Joachim H. Ix

Am J Kidney Dis. 79(3):427-436, 2022

Osteoporosis Drugs in Advanced CKD

Drug	Trials in eGFR < 45 (No. of Patients)	Trials in Dialysis Patients (No. of Patients)	Suggested Dosing Options	Side Effects	Efficacy
Antiresorptive					
Bisphosphonates	Yes (59-581)	Yes (ongoing)	(1) Oral alendronate 35 mg, weekly (2) IV pamidronate 60 mg, every other month	Hypocalcemia, AKI, eGFR decline, osteonecrosis	Benefits seen in CKD3; data lacking in CKD4 and dialysis
RANK ligand inhibitor	Yes (55)	Yes (8-12)	SC denosumab, 60 mg, ×1	Hypocalcemia (severe), rebound osteoclast activity	Efficacy seen in dialysis in observational studies
Hormonal	Yes (51-970)	Yes (50)	Oral raloxifene, 60 mg, daily	Minimal adverse events, thrombosis risk (theoretical)	Efficacy seen in RCTs in CKD and dialysis
Anabolic					
PTH analogues	Yes (168-736)	Yes (7)	(1) SC teriparatide, 20 µg, daily(2) SC abaloparatide, 80 µg, daily	Hypercalcemia, nausea, URI	Efficacy in CKD, unclear in dialysis
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Antisclerostin antibody	Yes (430)	Yes (12)	Romosozumab, 210 mg, monthly	CVD, hypocalcemia, arthralgias	Efficacy in CKD, unclear in dialysis

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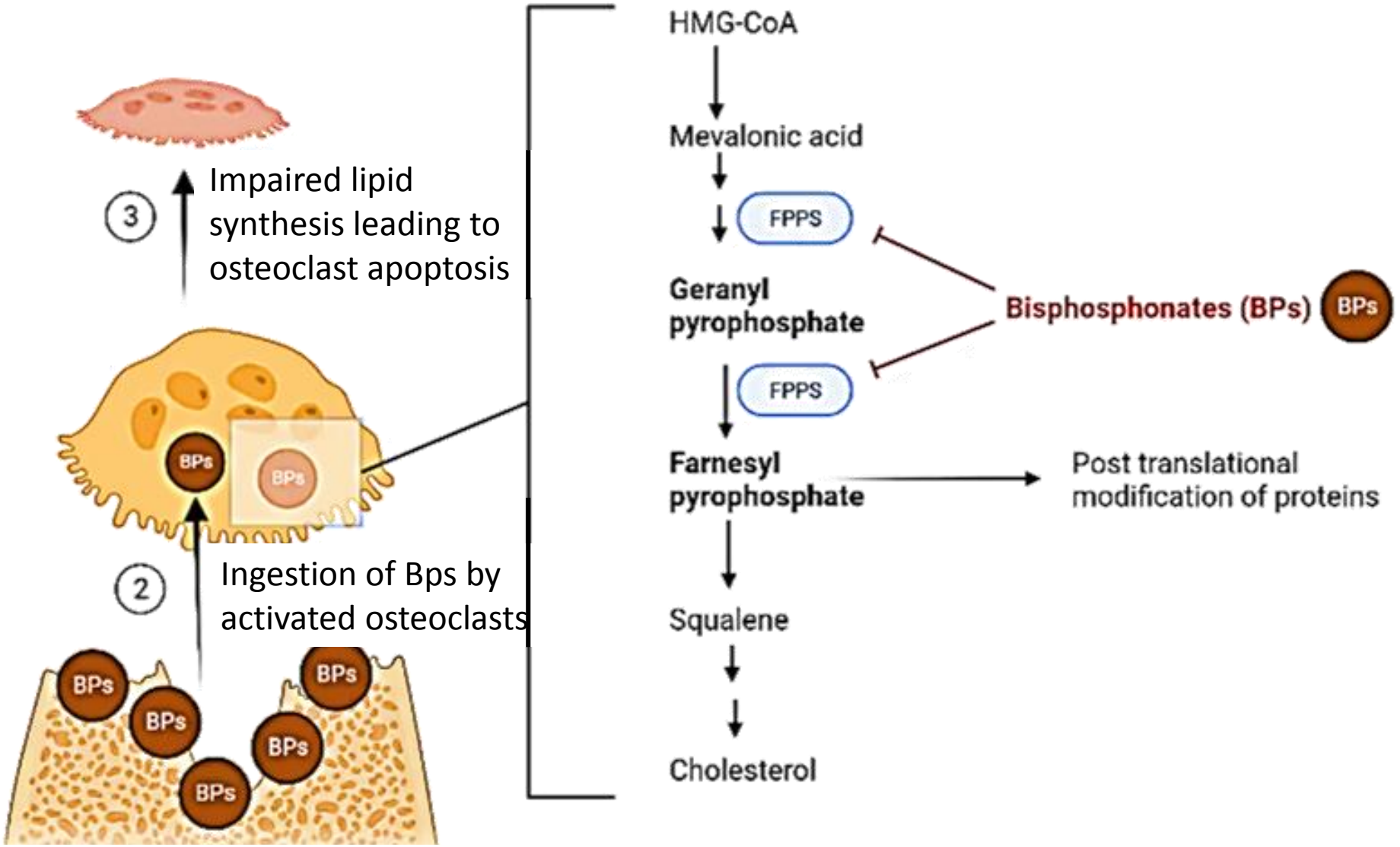
Am J Kidney Dis. 79(3):427-436, 2022

Mechanism of Bisphosphonates

- Bisphosphonates inhibit hydroxyapatite breakdown→ effectively suppressing bone resorption.

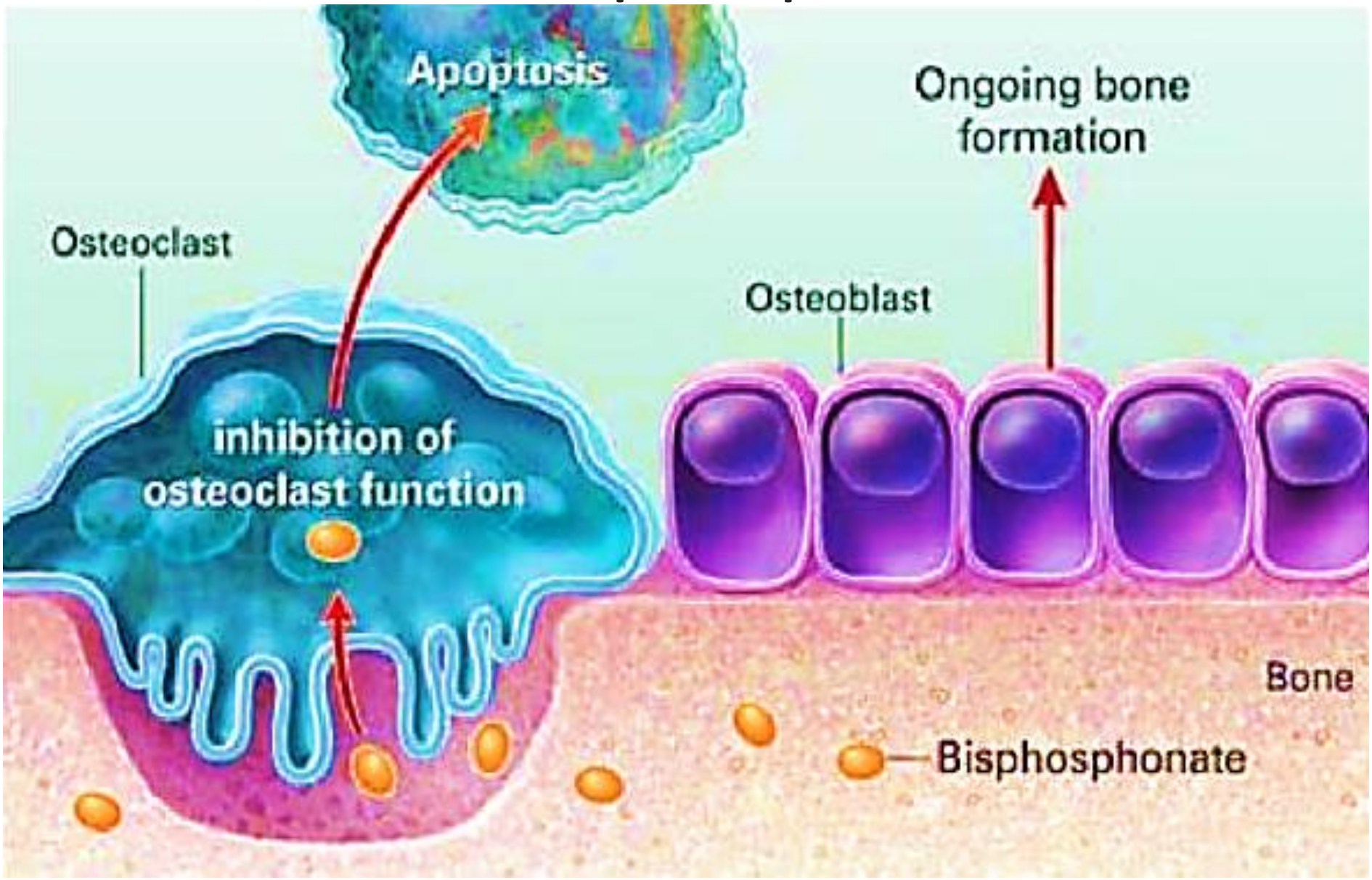
- Bisphosphonates limit both osteoblast and osteocyte apoptosis.

Mechanism of Action of Bisphosphonates



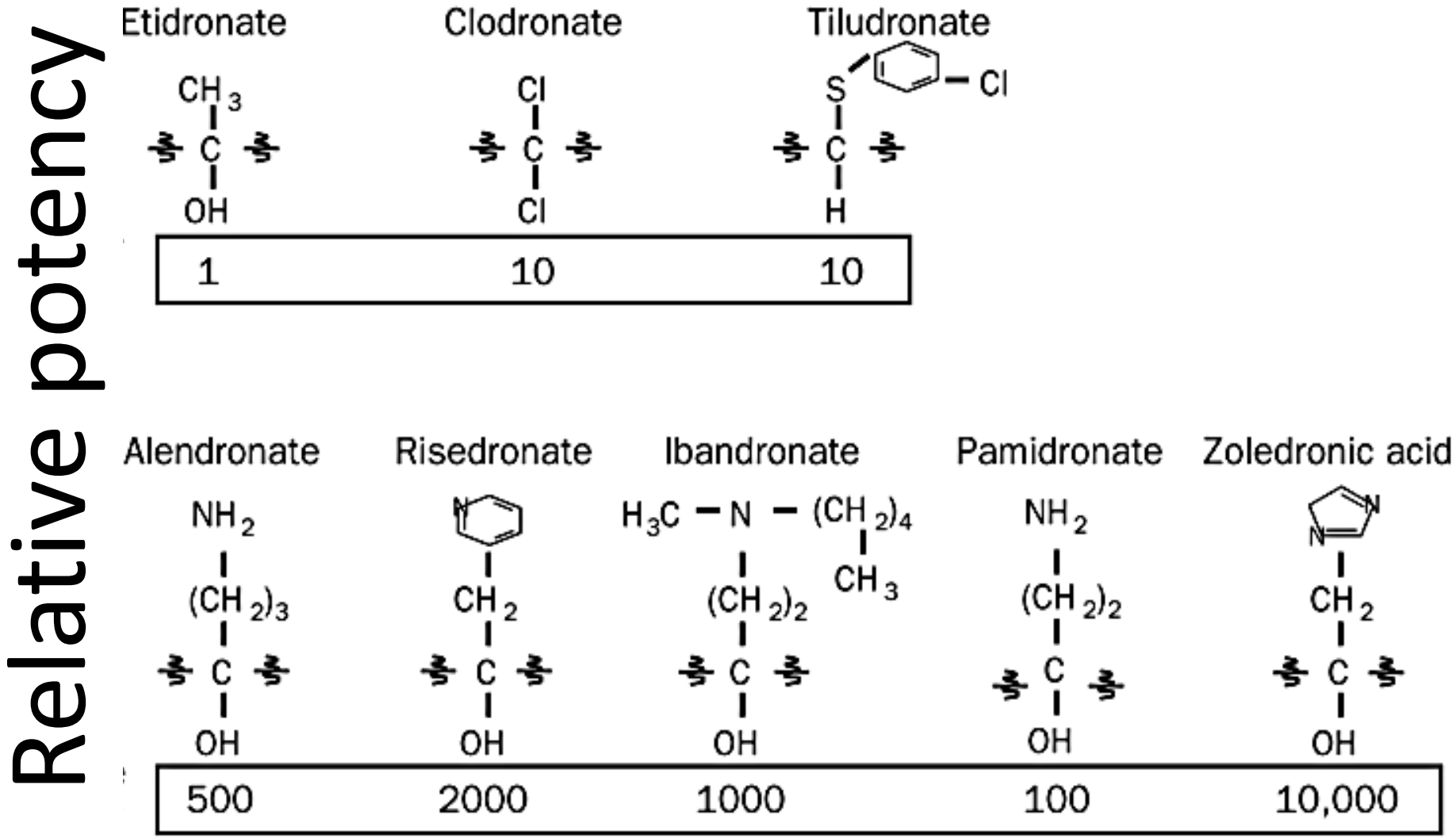
Bisphosphonates deposited in hydroxyapatite crystals of bone

Action of bisphosphonates



N Engl J Med. 2002; 346:642.

Bisphosphonate structures and approximate relative potencies for osteoclast inhibition



Mayo Clin Proc. 2008 September ; 83(9): 1032–1045

Relative Risk Reduction of Fractures after 3 Years of Oral Bisphosphonate Treatment

Type of fracture	Bisphosphonate		
	Risedronate	Alendronate	Ibandronate
Vertebral	**41**	**47**	**62**
Hip	**40**	**51**	**NS**
Nonvertebral	**39**	**20**	**NS**

Maximum suppression of bone resorption: within 3 months

ORIGINAL ARTICLE

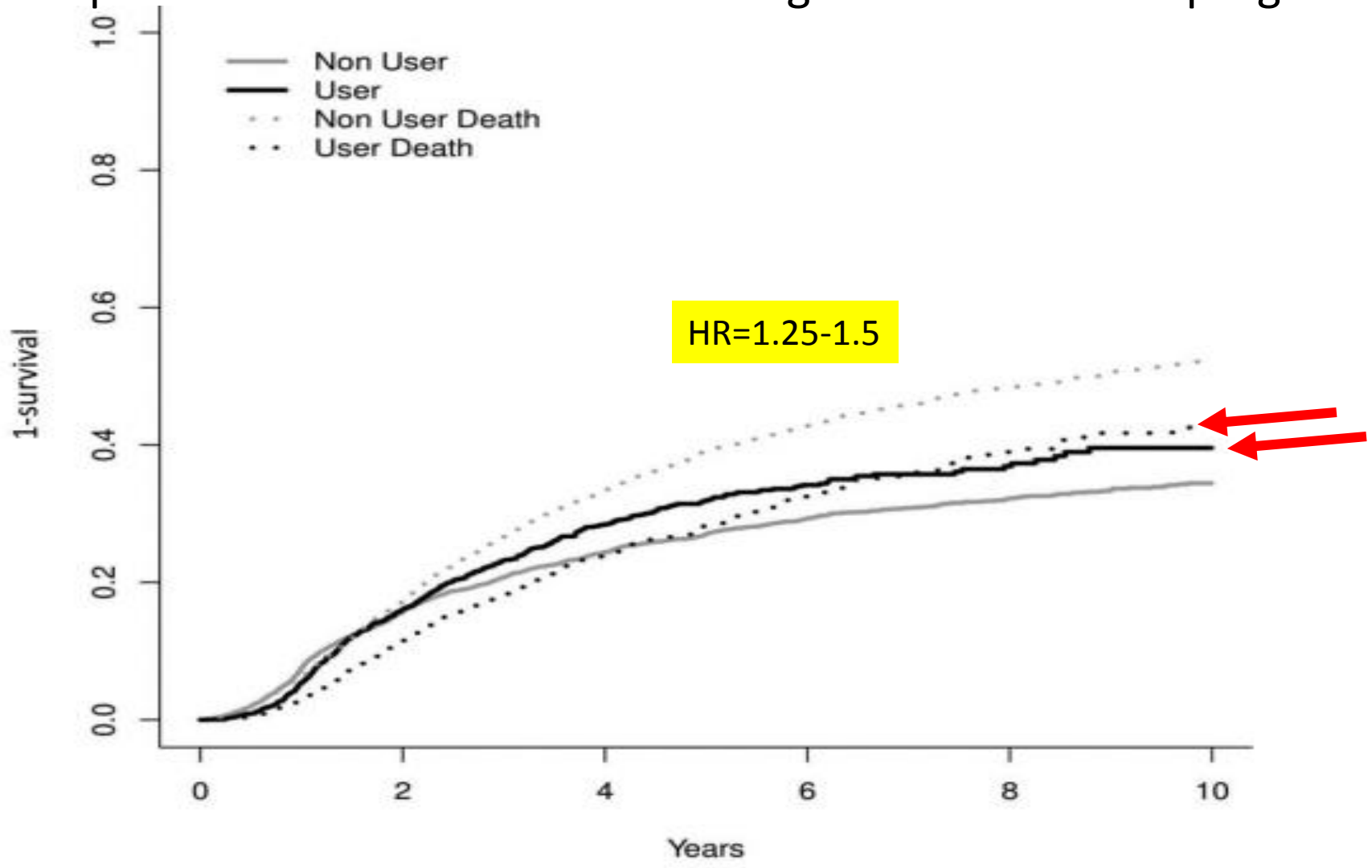
JBMR®

Safety of Oral Bisphosphonates in Moderate-to-Severe Chronic Kidney Disease: A Binational Cohort Analysis

Danielle E Robinson,[1†] M Sanni Ali,[1,2,3†] Natalia Pallares,[4] Cristian Tebé,[4,5] Leena Elhussein,[1] Bo Abrahamsen,[6,7,8] Nigel K Arden,[9] Yoav Ben-Shlomo,[10] Fergus J Caskey,[10,11] Cyrus Cooper,[6,12] Daniel Dedman,[13] Antonella Delmestri,[1] Andrew Judge,[1,12,14] María José Pérez-Sáez,[15] Julio Pascual,[15] Xavier Nogues,[16,17] Adolfo Diez-Perez,[16] Victoria Y Strauss,[1] M Kassim Javaid,[6‡] and Daniel Prieto-Alhambra[1,18‡]

ROBINSON ET AL.,Journal of Bone and Mineral Research, 2021

Bisphosphonate use was associated with greater risk of CKD progression



Years	0	2	4	6	8	10
Non users	8931	4634	1784	664	249	90
Users	2447	1247	459	175	56	19

ROBINSON ET AL.,Journal of Bone and Mineral Research, 2021

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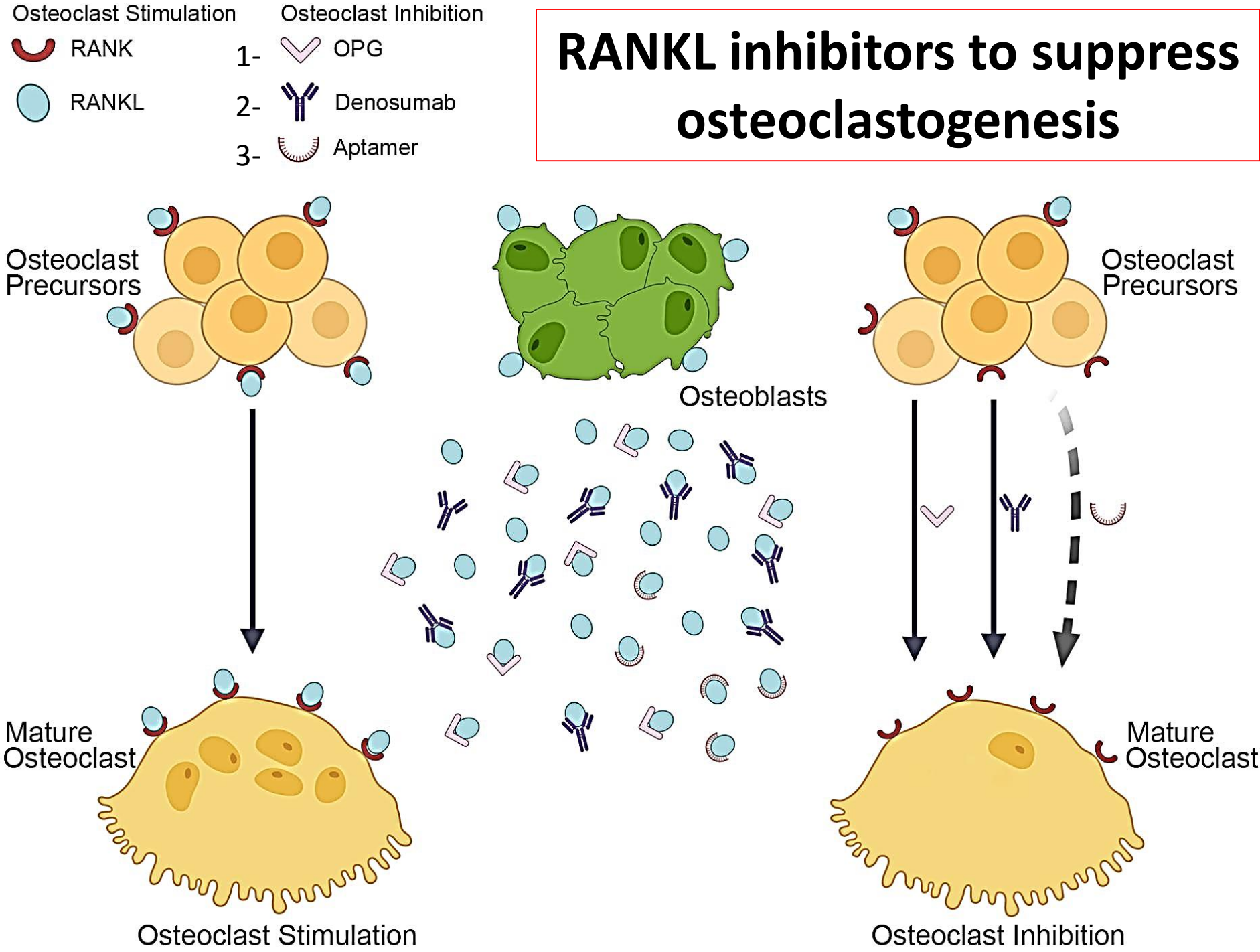
RANKL inhibitors to suppress osteoclastogenesis



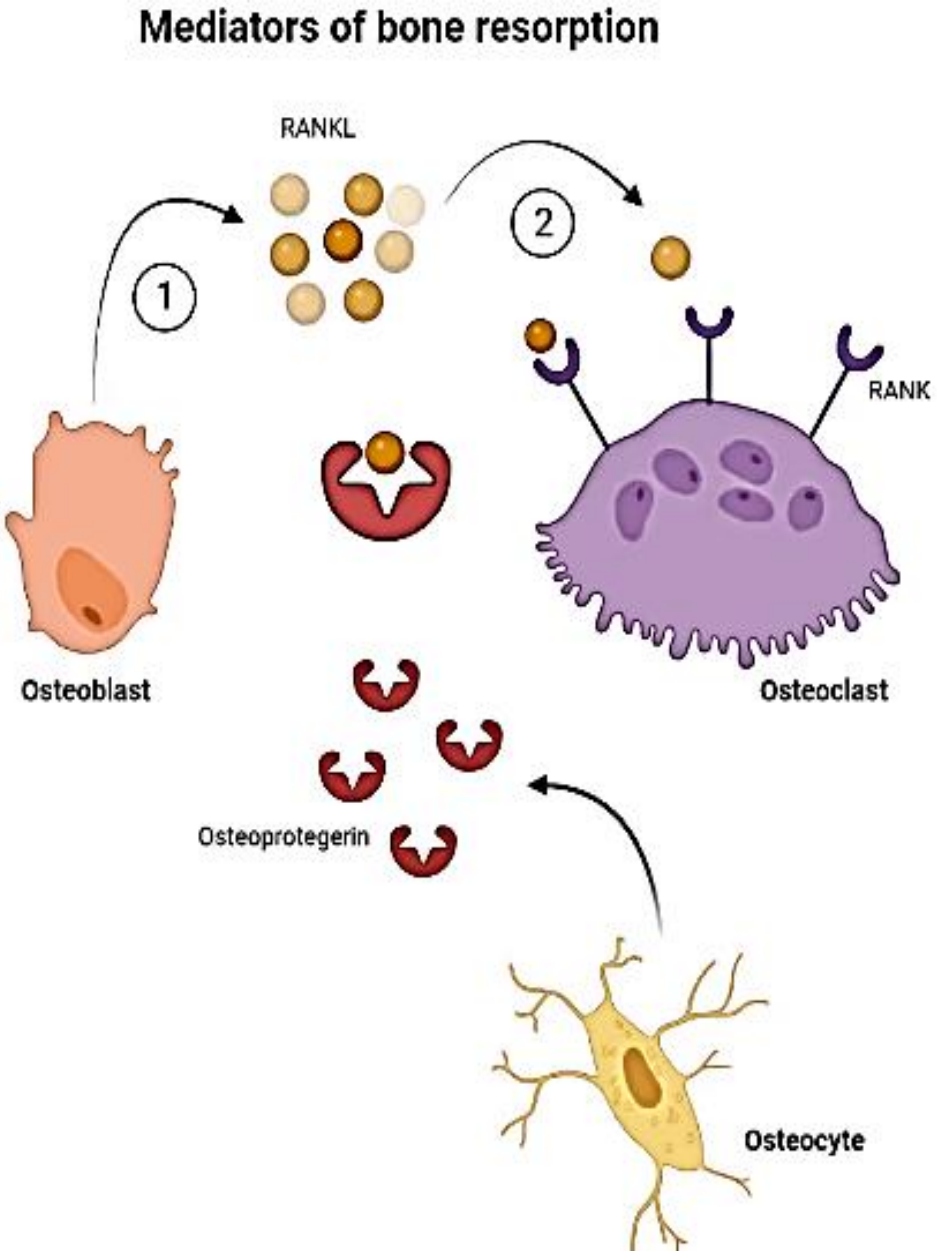
CURRENT THERAPEUTIC STRATEGIES TARGETING RANKL

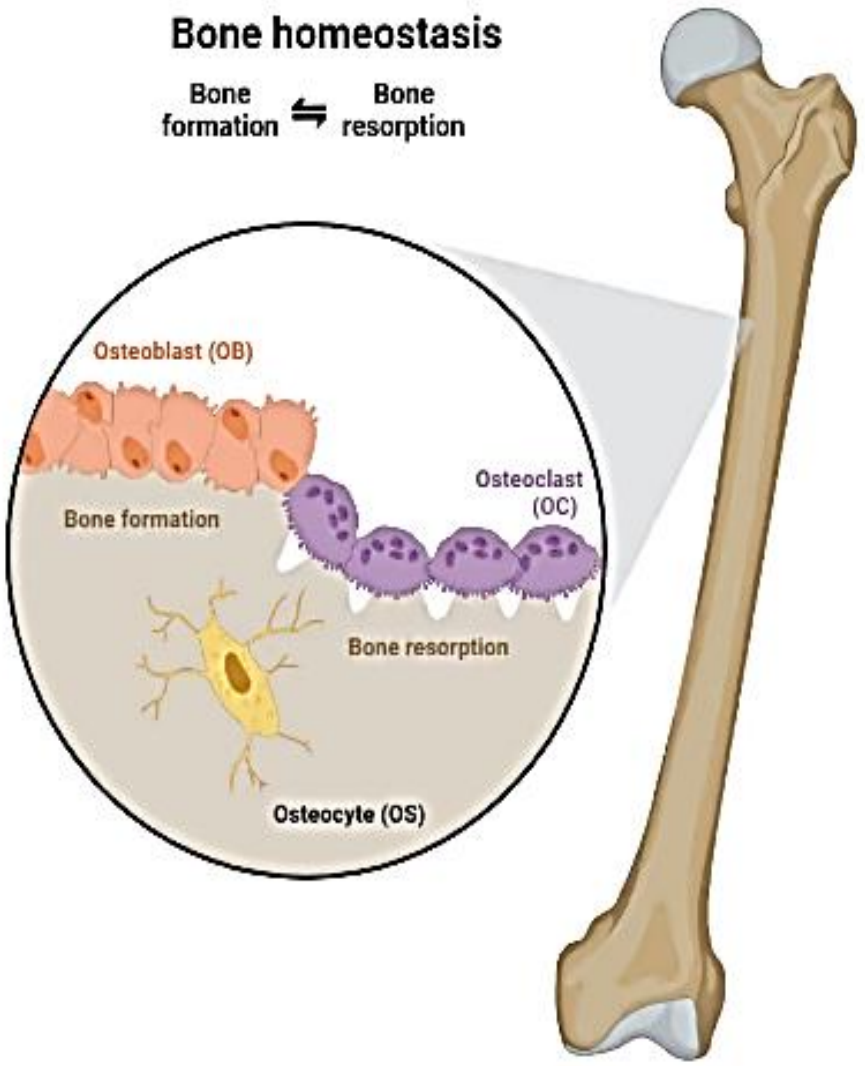
- Recombinant human osteoprotegerin.
- Strontium compounds.
- human RANKL monoclonal antibodies.

THE POTENTIAL PROBLEMS RELATED TO THE ANTI-RANKL MONOCLONAL ANTIBODY, DENOSUMAB

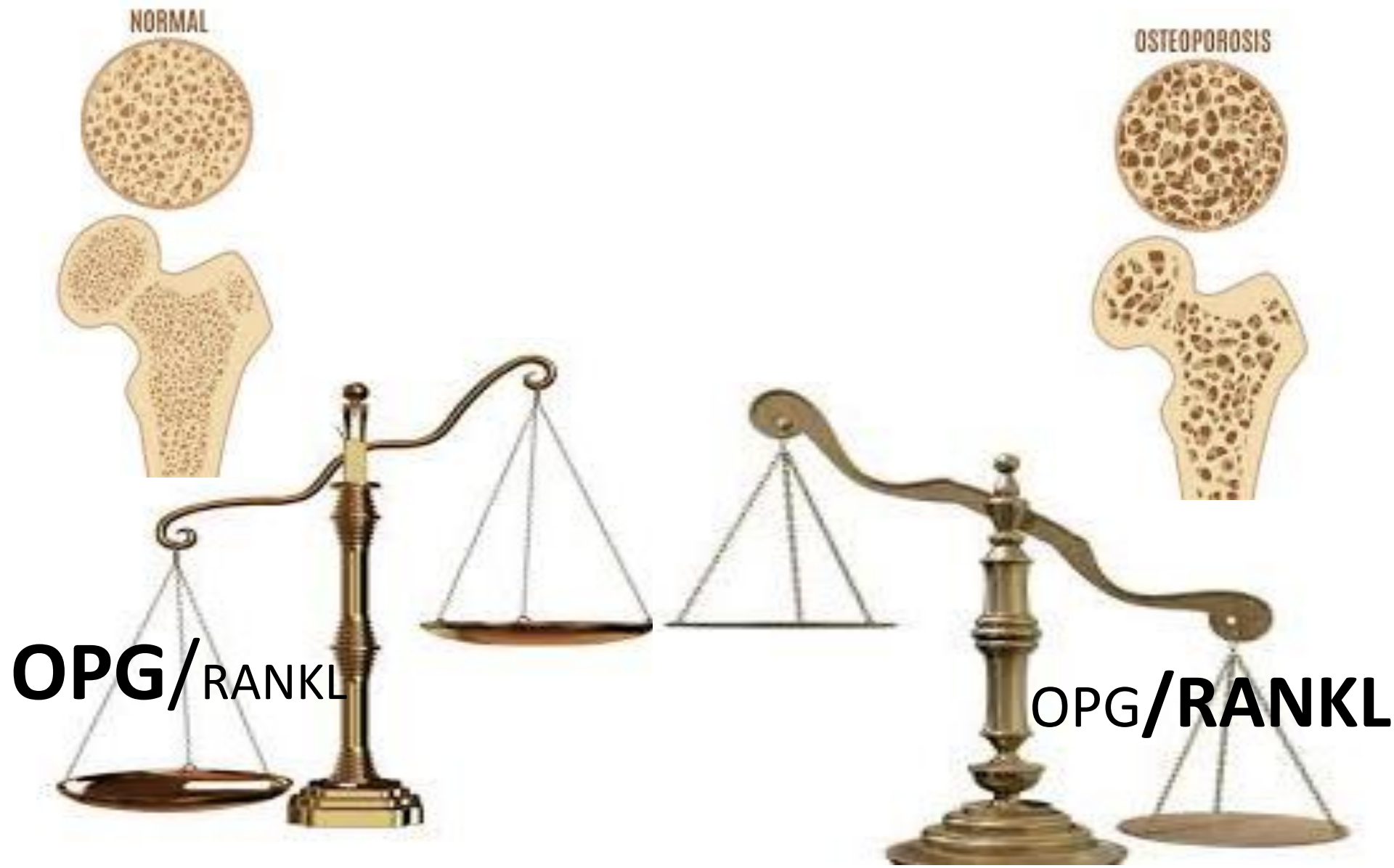
- **Infection:** Since RANKL is also abundantly expressed by dendritic cells and activated T lymphocytes, the antagonistic effect caused by denosumab could affect the immune system and result in individual risk of adverse events.
- **skin eczema** (3%),
- **flatulence** (2.2%),
- **cellulitis (0.3%)**
- **osteonecrosis of the jaw** 1.7%
- **Hypocalcemia** up to 14% especially in CKD (specially in the Older GFR, Lowe basal serum ca level)

mechanism of action of Osteoprotegrin





OPG/RANKL ratio is closely related to osteoclast formation



The Egyptian Rheumatologist (2014) 36, 111–116

Egyptian Society for Joint Diseases and Arthritis

The Egyptian Rheumatologist

www.rheumatology.eg.net
www.sciencedirect.com

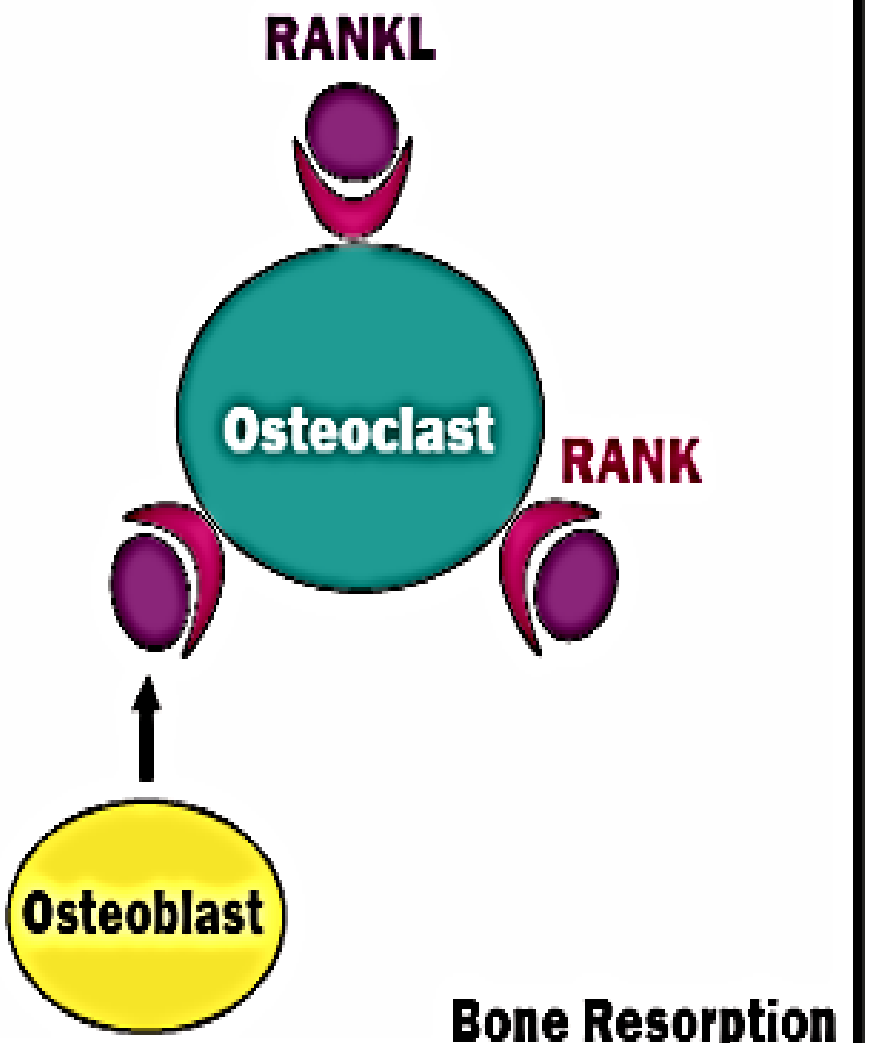
ORIGINAL ARTICLE

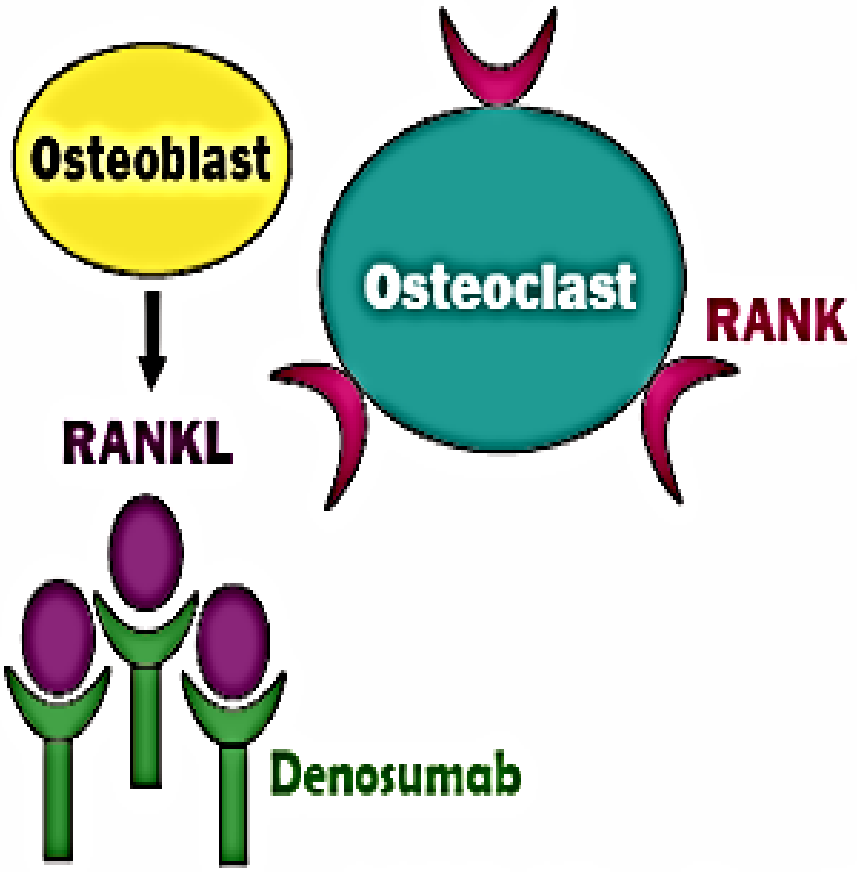
Osteoprotegerin (OPG) and Matrix Gla protein (MGP) in rheumatoid arthritis patients: Relation to disease activity

Amir Ghorbanihaghjo [a], Mehrzad Hajialilo [b], Maryam Shahidi [b], Alireza khabazi [c], Susan Kolahi [c], Mohammad Reza Jafari Nakhjavani [a], Sina Raeisi [a], Hassan Argani [a], Nadereh Rashtchizadeh [a,*]

Conclusion: The significant elevation of the OPG level in RA patients

The mechanism of action of denosumab in the treatment of osteoporosis.





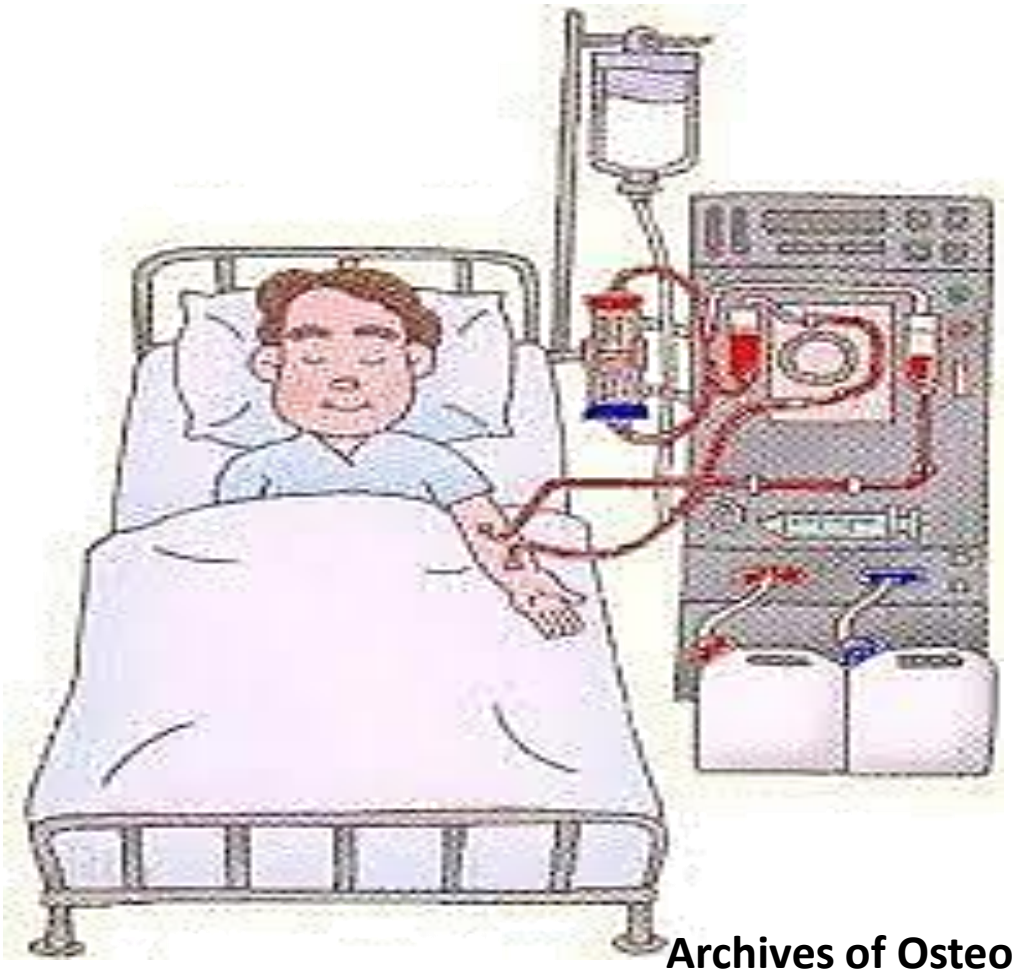
human RANKL monoclonal antibodies characteristics (Denosumab)

- It is a human monoclonal IgG2 antibody
- Binds with RANKL selectively and displays high affinity➔ neutralizes the activity of human RANKL to inhibit bone resorption
- Decreases Bone resorption markers
- It is recommended that secondary hyperparathyroidism be corrected before administrating of anti-resorptive medication

Archives of Osteoporosis (2021) 16:116
https://doi.org/10.1007/s11657-021-00971-0

REVIEW ARTICLE

Denosumab in chronic kidney disease: a narrative review of treatment efficacy and safety



Check Ca and Po4 at each HD session for 2 weeks.

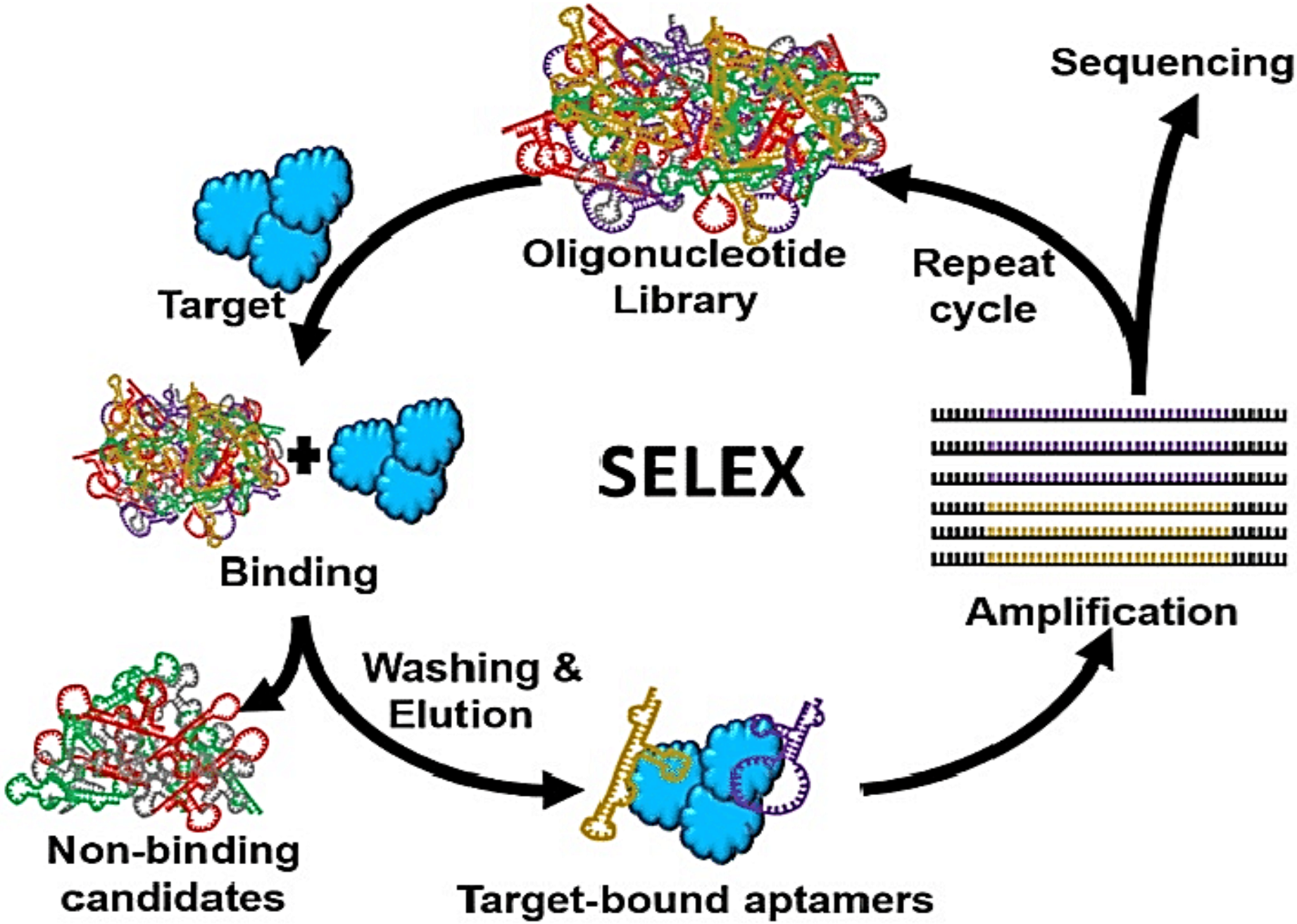
Followed by weekly monitoring for 2 weeks thereafter

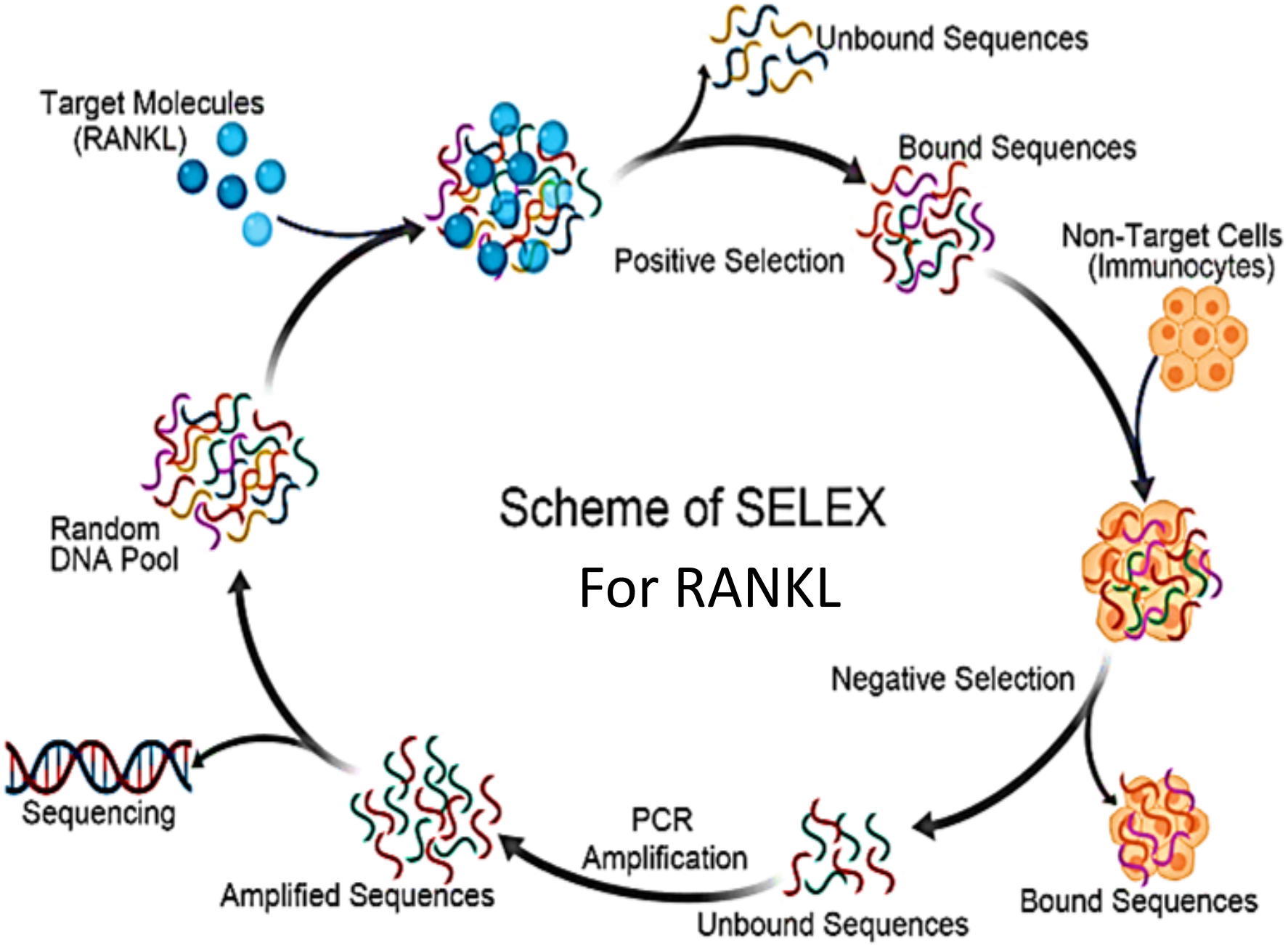
Archives of Osteoporosis 2021 16:116

APTAMER: A PROMISING THERAPEUTIC STRATEGY FOR OSTEOPOROSIS (Artificial Ab.)

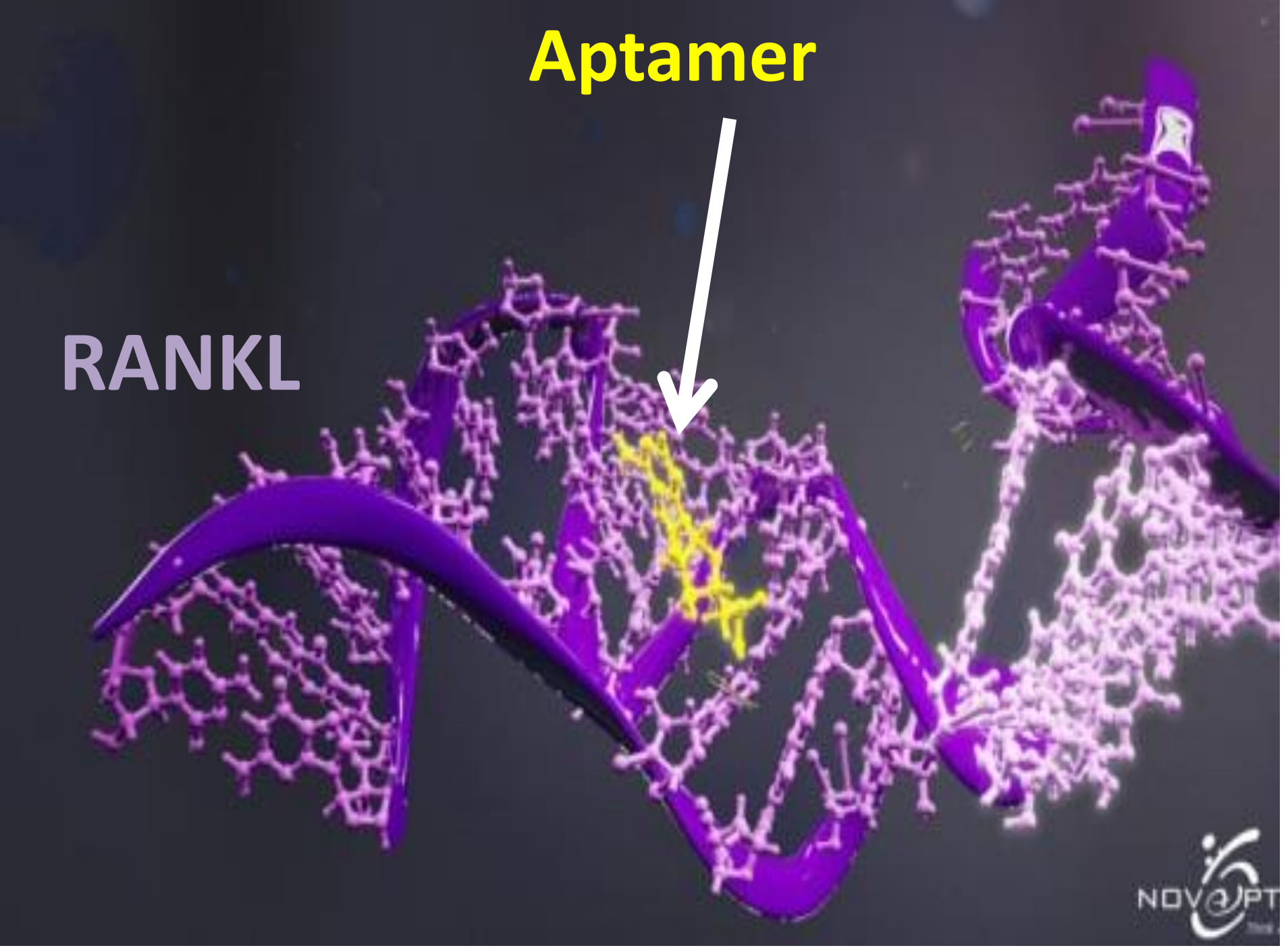
- Aptamers are small single-stranded oligonucleotides➔ Specifically bind with target molecules.
- Aptamers are screened from oligonucleotide libraries, which generally consists of a fixed sequence at both ends of the oligonucleotide chain and a random sequence with a length of 20–60 bp in the middle, using a gold-standard methodology named SELEX (Systematic Evolution of Ligands by Exponential Enrichment)

Systematic Evolution of Ligands by Exponential Enrichment





Therapy. Front. Cell Dev. Biol. 8:325, May; 2020


Aptamer
RANKL
NOVAPT

Advantages of Aptamers over antibodies

- **Greater stability :** Aptamers are more resistant to temperature and pH variations.
- **Cost-effective synthesis :** Aptamers are less expensive to produce.
- **Reproducibility** : Aptamers abolish batch-to-batch variations, ensuring consistent quality.
- **Flexibility of modification** : Aptamers can be easily modified to improve binding or stability.
- **Non-immunogenicity :** They are less likely to trigger undesirable immune responses.
- **Miniature characteristic:** they are smaller than antibodies and can be used for intracellular diagnosis and treatment

Sociedad Española de Nefrología

nefrología
Revista de la Sociedad Española de Nefrología
www.revistanefrologia.com

Original article

Osteoporosis management in patients with chronic kidney disease (ERCOS Study): A challenge in nephrological care

nefrologia. 2024;44(2):241–250

Treatment for osteoporosis and prescribing physician according to specialty

Variable	Descriptive statistics
Treatment for osteoporosis, n (%)	
Yes	98 (60.1%)
No	65 (39.9%)
Years since initiation of first osteoporosis treatment, median (P25,P75)	4.02 (1.66–6.54)
Specialist who initiated treatment for osteoporosis, n (%)	
Rheumatology	46 (46.9%)
Family doctor	10 (10.2%)
Internal medicine	23 (23.5%)
Gynecology	1 (1.02%)
Nephrology	13 (13.3%)
Other[a]	5 (5.10%)

nefrologia. 2024;44(2):241–250

First antiosteoporotic treatment according to stage of CKD

Stages of CKD	Stage: 3 N = 56	Stage: 4-5 N = 23	Stage: 5D N = 19
Treatment with bisphosphonates, n (%)	29 (51.8%)	12 (52.2%)	4 (21.1%)
Oral	22 (75.9%)	11 (91.7%)	4 (100%)
Intravenous (zoledronic acid)	7 (24.1%)	1 (8.33%)	0 (0.00%)
Oral bisphosphonates, n (%)			
Alendronate	10 (45.5%)	5 (45.5%)	2 (50.0%)
Risedronate	10 (45.5%)	5 (45.5%)	2 (50.0%)
Ibandronate	2 (9.09%)	1 (9.09%)	0 (0.00%)
Treatment with denosumab, n (%):	24 (42.9%)	8 (34.8%)	13 (68.4%)
Treatment with teriparatide, n (%):	2 (3.57%)	1 (4.35%)	2 (10.5%)
Treatment with SERM, n (%):	1 (1.79%)	2 (8.70%)	0 (0.00%)

CKD, chronic kidney disease; SERM, selective estrogen receptor modulator.

nefrologia. 2024;44(2):241–250

NEFROLOGIA. 2025;45(4):344–350

Sociedad Española de Nefrología

nefrología

Revista de la Sociedad Española de Nefrología

www.revistanefrologia.com

Letter to the Editor

Optimizing osteoporosis management in CKD patients

Comparison of Anti-resorptive agents in different stages CKD

Stage of GFR	Denosumab treatment (Duration of 6months to 4 years)	Bisphosphonate (Duration of treatment for 6 months to 2 years)
GFR<60	Increased Lumbar BMD (upto12%), and increased Hip BMD (upto 6%)	Increased Spinal and Hip BMD upto 5 %
GFR<30	Increased Lumbar BMD (upto9%), and increased Hip BMD (upto 3.8%) over 4 years	Increased Spinal and Hip BMD upto 5 %
GFR<15	Increased Lumbar BMD (upto6%), and no increase in Hip BMD	Contraindicated (at least in high doses)

n e f r o l o g i a. 2 0 2 5;4 5(4):344–350

Anti resorptive drugs

	Bisphosphonate	Denosumab
Secondary mineralization	+	++
Increased BMD	+	++
Bone structure	Preserved with Bisphosphonate	Increased more cortical bone

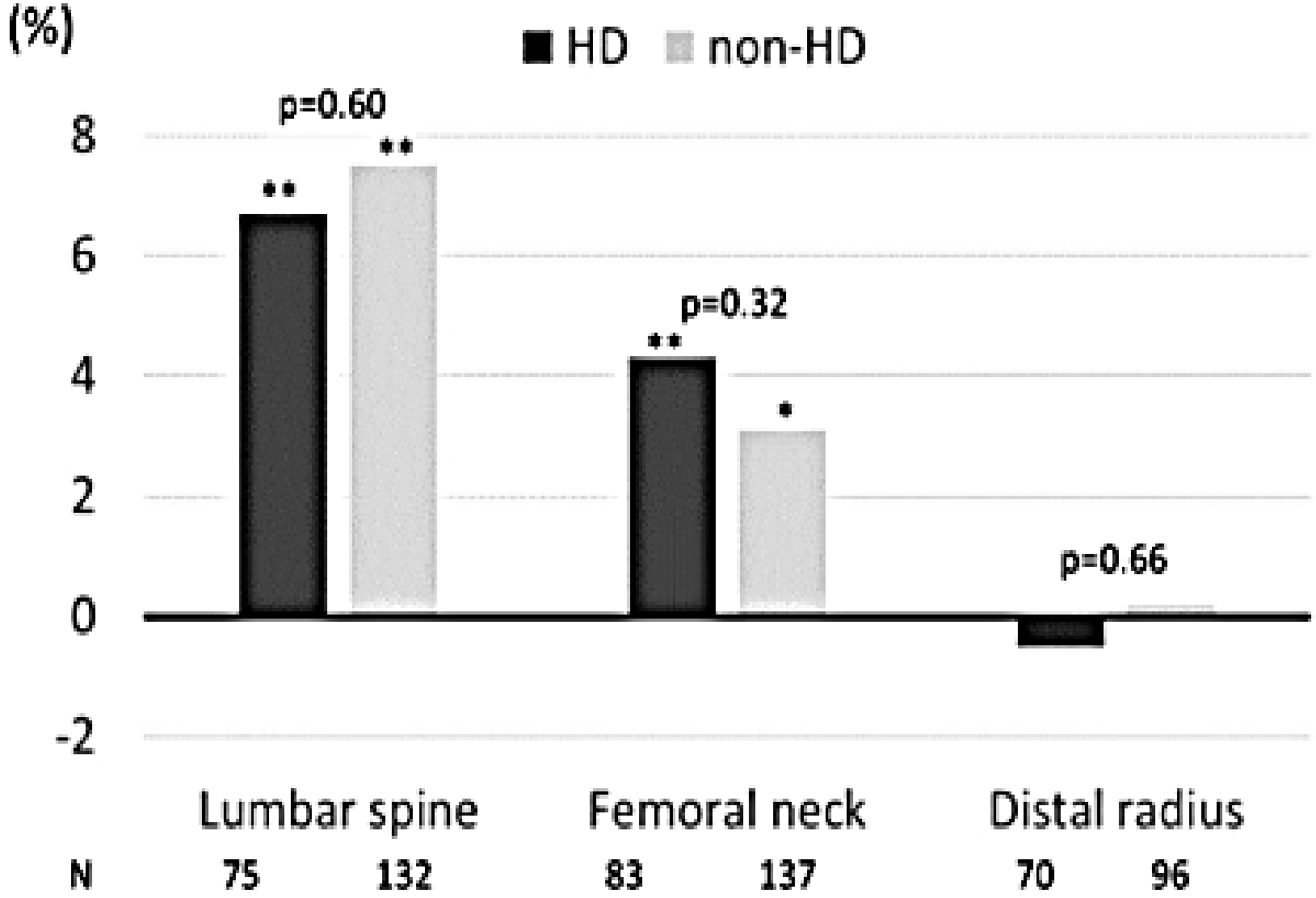
SCIENTIFIC REPORTS
nature research

Denosumab for dialysis patients with osteoporosis: A cohort study

Kyohei Kunizawa[1,2], Rikako Hiramatsu[1], Junichi Hoshino[1,3,4*], Hiroki Mizuno[3], Yuko Ozawa[3], Akinari Sekine[3], Masahiro Kawada[3], Keiichi Sumida[1], Eiko Hasegawa[3], Masayuki Yamanouchi[1], Noriko Hayami[1], Tatsuya Suwabe[1], Naoki Sawa[1], Yoshifumi Ubara[1,4] & Kenmei Takaichi[1,3,4]

Scientific Reports (2020) 10:2496

Annual change in bone mineral density in HD and non-HD patients after Denosumab.



Scientific Reports (2020) 10:2496

Conclusion

- Denosumab is effective for the treatment of osteoporosis in HD patients.
- Increasing BMD to a degree similar to that seen in patients not on dialysis.
- Careful monitoring of serum calcium is necessary in HD patients due to the high risk of hypocalcemia.
- Baseline serum TRACP5b could be a potential predictor of hypocalcemia in these patients after denosumab injection.
- Denosumab may be the first- or second-line of choice for management of osteoporosis in the HD patients.

Scientific Reports (2020) 10:2496

International Journal of Nanomedicine 2020:15 7967–7977

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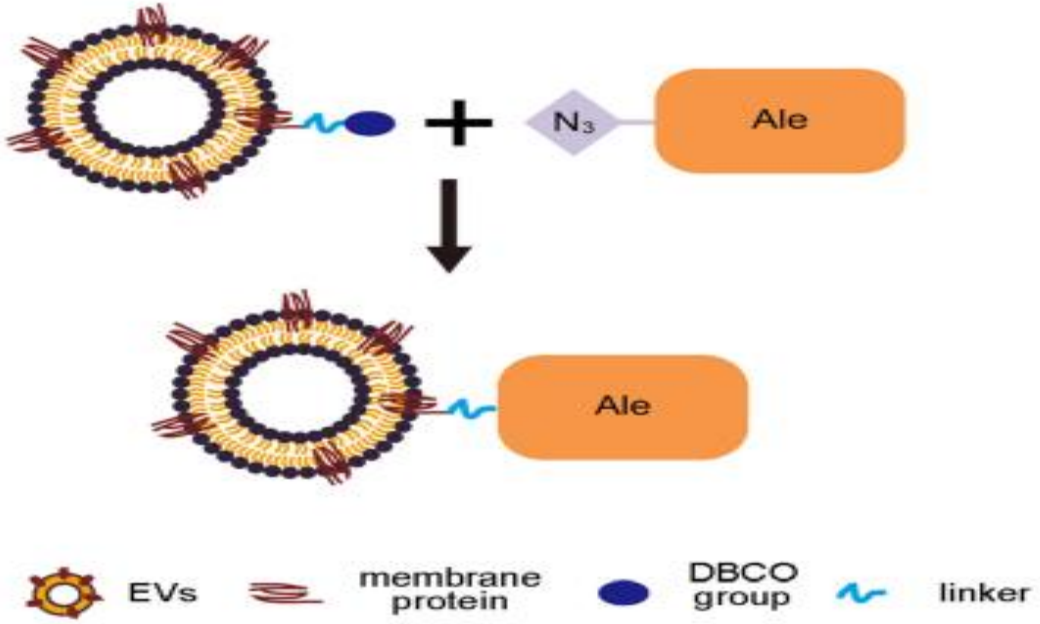
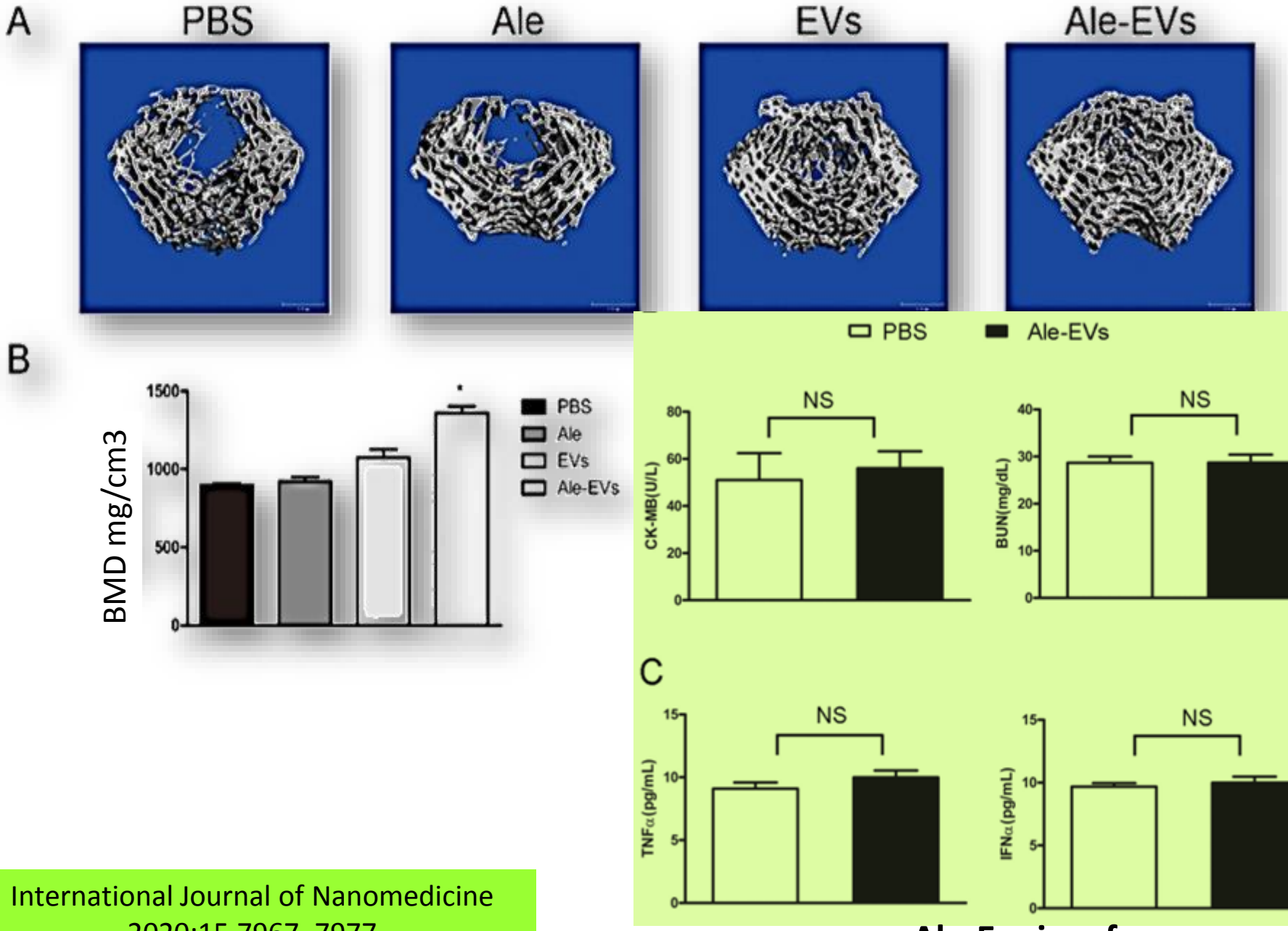
ORIGINAL RESEARCH

Bone-Targeted Extracellular Vesicles from Mesenchymal Stem Cells for Osteoporosis Therapy



Anti-osteoporosis efficacy of Ale-EVs in vivo.



International Journal of Nanomedicine
2020:15 7967–7977

Ale-Evs is safe

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Bisphosphonates	Yes (59-581)	Yes (ongoing)	(1) Oral alendronate 35 mg, weekly (2) IV pamidronate 60 mg, every other month	Hypocalcemia, AKI, eGFR decline, osteonecrosis	Benefits seen in CKD3; data lacking in CKD4 and dialysis
RANK ligand inhibitor	Yes (55)	Yes (8-12)	SC denosumab, 60 mg, ×1	Hypocalcemia (severe), rebound osteoclast activity	Efficacy seen in dialysis in observational studies
Hormonal	Yes (51-970)	Yes (50)	Oral raloxifene, 60 mg, daily	Minimal adverse events, thrombosis risk (theoretical)	Efficacy seen in RCTs in CKD and dialysis
Anabolic					
PTH analogues	Yes (168-736)	Yes (7)	(1) SC teriparatide, 20 µg, daily(2) SC abaloparatide, 80 µg, daily	Hypercalcemia, nausea, URI	Efficacy in CKD, unclear in dialysis
Mixed					
Antisclerostin antibody	Yes (430)	Yes (12)	Romosozumab, 210 mg, monthly	CVD, hypocalcemia, arthralgias	Efficacy in CKD, unclear in dialysis

Estrogen deficiency

RANKL activation

↓OPG production

↓Wnt/β-catenin signaling

T-cells activation

Inflammatory cytokines secretion

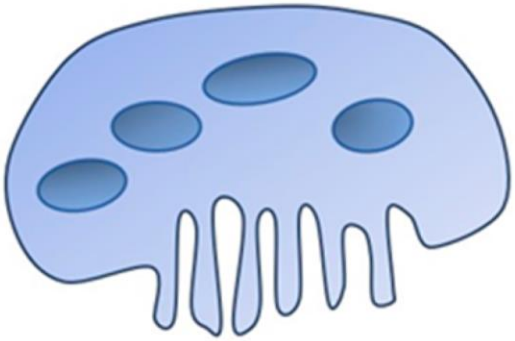
Diffentitiation of BMSCs to adypocytes

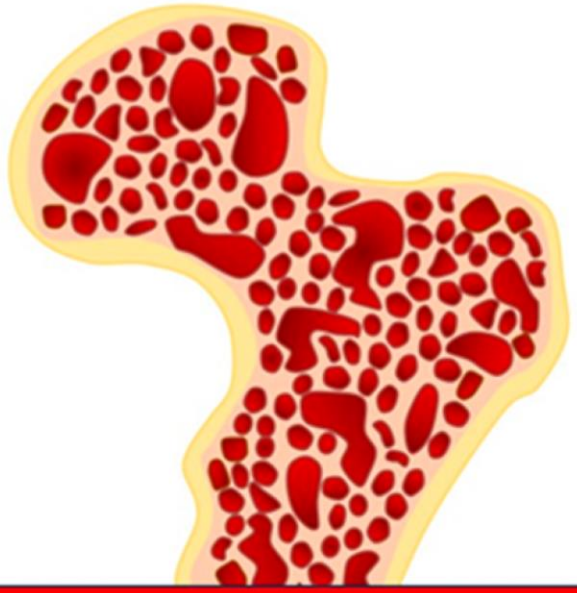
Differentiation of dendritic cells to OC

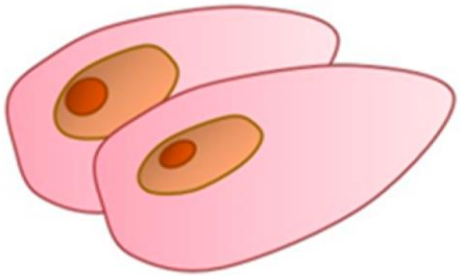
Osteoclastogenesis

↓Bone matrix proteins

Apoptosis of osteoblasts





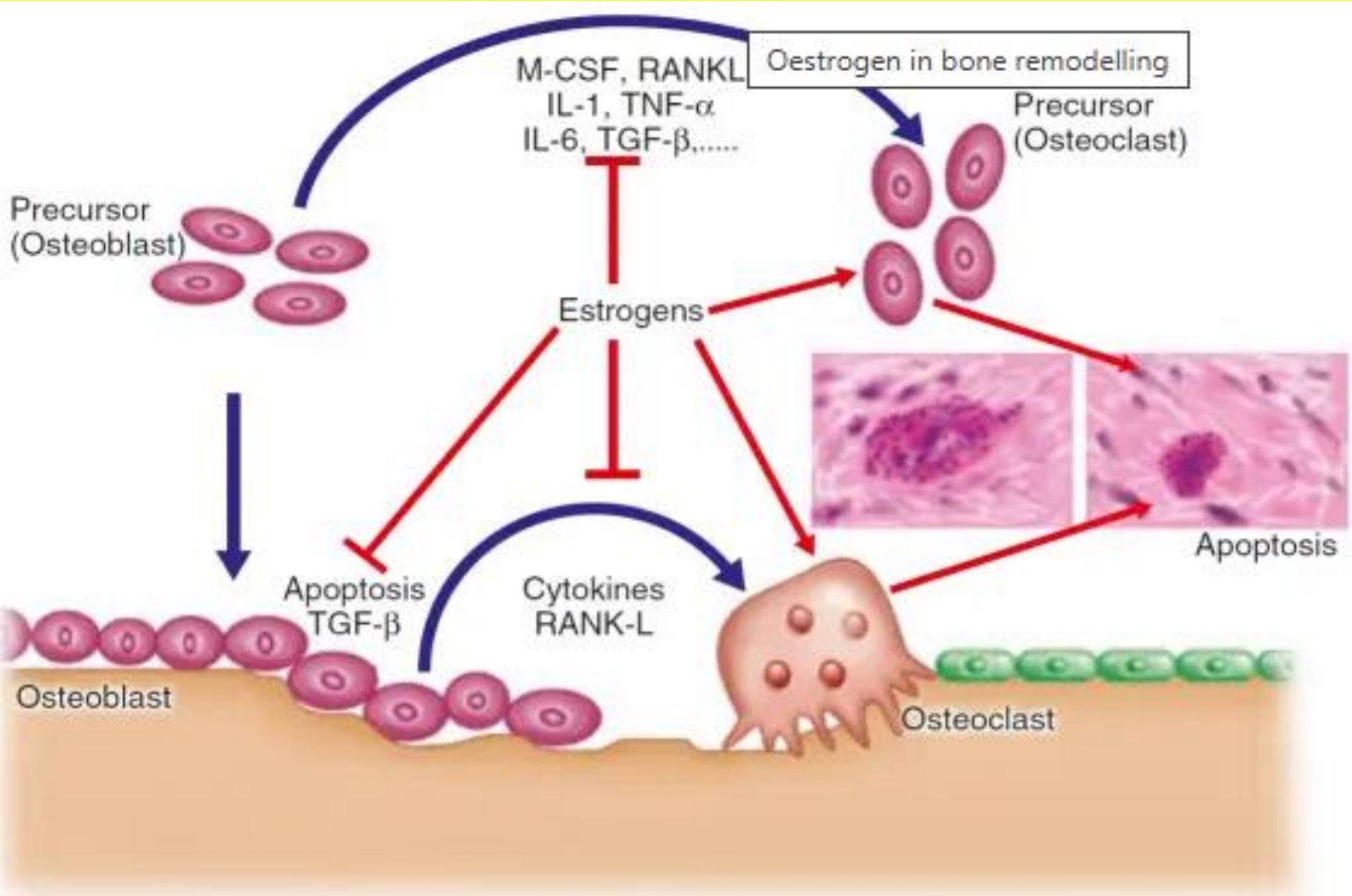


Bone resorption

↓Mineralization of bone matrix

Osteoporosis

Cytokine production under the control of estrogen in bone and bone remodeling



SERMS: Chemical groups

Triphenylethylenes

- Tamoxifen
- Droloxifene
- Idoxifene
- Clomiphene
- Toremifene

Benzotiophenes

- Raloxifene
- Arzoxifene

Tetrahydronafthylenes

- Lasofoxifene
- Nafoxidine

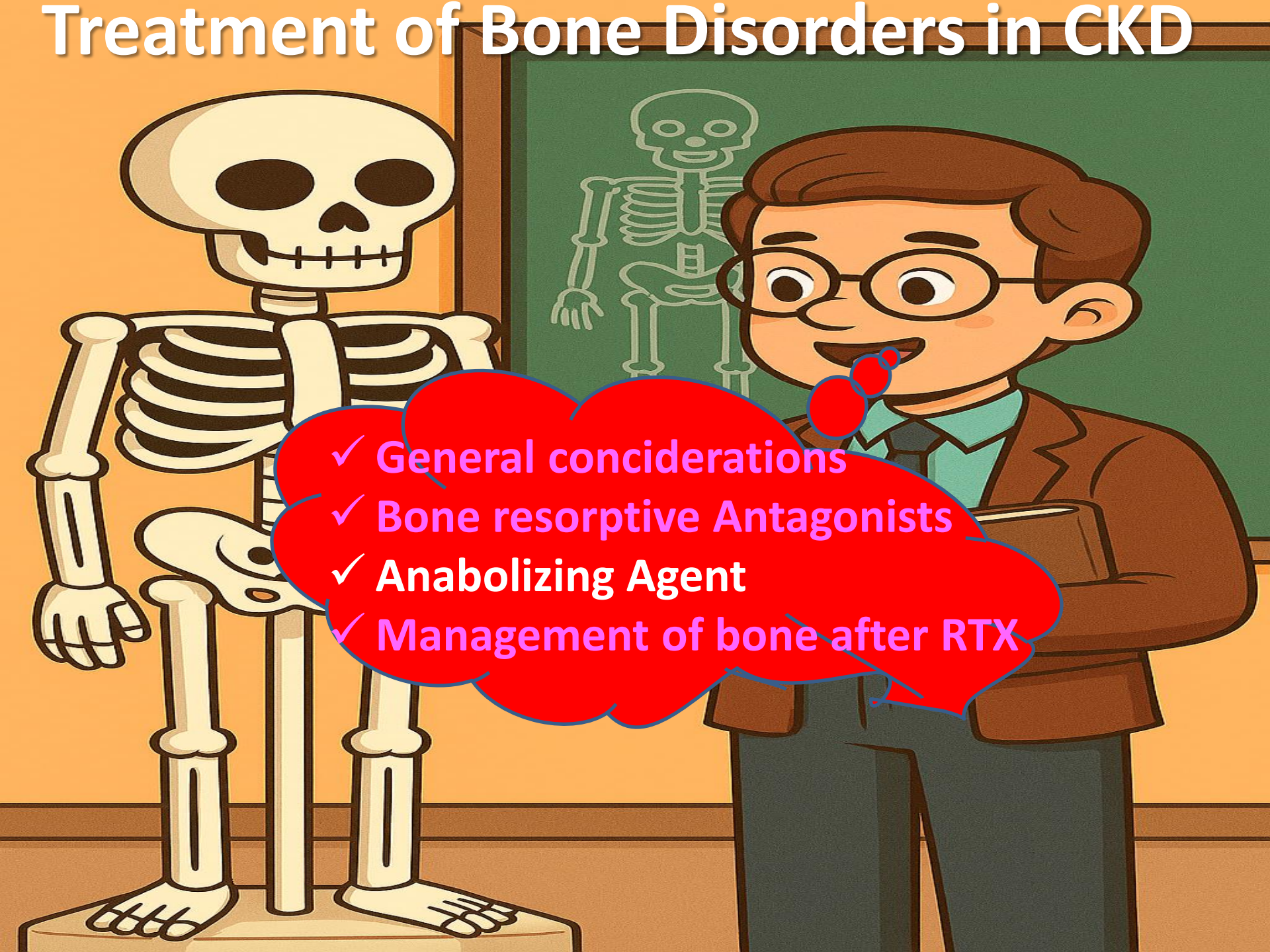
Indoles

- Bazedoxifene

Benzopyrans

- EM-800
- Levormeloxifene

Treatment of Bone Disorders in CKD



Osteoporosis Drugs in Advanced CKD

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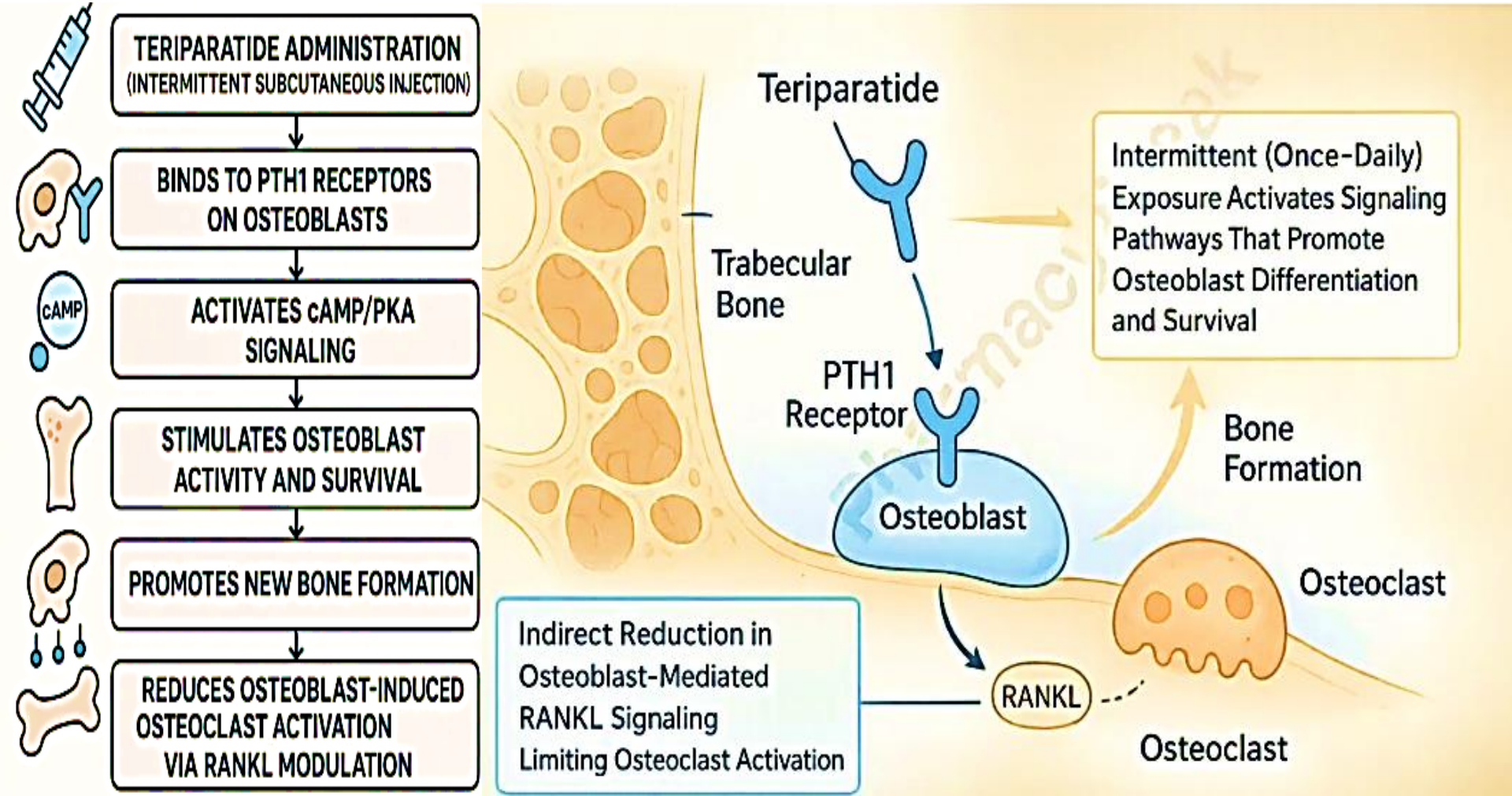
Comparison of Anti-Resorptive and Anabolic Agents for Renal Osteodystrophy Treatment

Agent	Type	Efficacy	Indications	Price Range	Side Effects
Denosumab	Anti-Resorptive	Increases BMD, reduces fracture risk	CKD patients with high fracture risk	$1,500 - $2,000/year	Hypocalcemia, osteonecrosis of jaw
Zoledronic Acid	Anti-Resorptive	Increases BMD, reduces fracture risk	CKD patients, especially with osteoporosis	$800 - $1,200/year	Renal impairment, gastrointestinal issues
Teriparatide	Anabolic	Increases BMD significantly, reduces fractures	Osteoporosis in CKD patients	$4,000 - $6,000/year	Hypercalcemia, injection site reactions
Abaloparatide	Anabolic	Increases BMD, favorable safety profile	Osteoporosis in CKD patients	$4,000 - $6,000/year	Hypercalcemia, injection site reactions

Teriparatide mechanism of action



Concerns to Teriparatide injection

❖ Indications: 1-_Osteoprotic CKD patients with iPTH concentrations < 2 times + Low BSAP.

2-Patient with worsening osteoporosis after PTX.

❖ Contraindications: 1-Patients with hypercalcemia,

2-patients with previous skeletal radiotherapy,

3-patients with Bone malignancies, or metastases

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2-patients with previous skeletal radiotherapy,

3-patients with Bone malignancies, or metastases

❖Administration should not exceed 24 months due to theoretical osteosarcoma risk➔BMD thereafter

❖ After discontinuation of teriparatide, denosumab or bisphosphonate is necessary.

❖ Transient hypotension has been reported in 36% of hemodialysis patients.

Anabolic compounds approved for treatment of *osteoporosis in CKD*

Property	Teriparatide	Abaloparatide	Romosozumab
Regulatory approval	2002	2017	2019
Molecule	PTH(1-34)	PTHrP(1-34)	Humanized Monoc. Ab
Mechanism	PTH relat. Agonist	PTH rec. agonist	Anti-sclerostin
Bone formation	Increases	increases	Increases
Bone resorption	Increases	increases	**Decreases**
Dose	20 mcg SC /day	80 mcg SC daily	210 mg SC monthly
Administration	Self-injection	Self-injection	By professionals
Duration limit	24 months	24 months lifetime	12 months (may repeat)
Rat osteosarcoma	**Yes**	**Yes**	No
Avoid in patients at high risk for osteosarcoma	Yes	Yes	No
Avoid in patients with MI/stroke in the past year	No	No	**Yes**

Limitations of anabolic therapy

- Inconvenience of dosing (daily self-injections with teriparatide and abaloparatide; monthly injections by a healthcare professional with romosozumab)
- Lack of availability in some regions.
- High cost.

Differences between Abaloparatide and Teriparatide

	Abaloparatide	Teriparatide
Anabolic efficacy	+++	+
Risk of hypercalcemia	+	+++

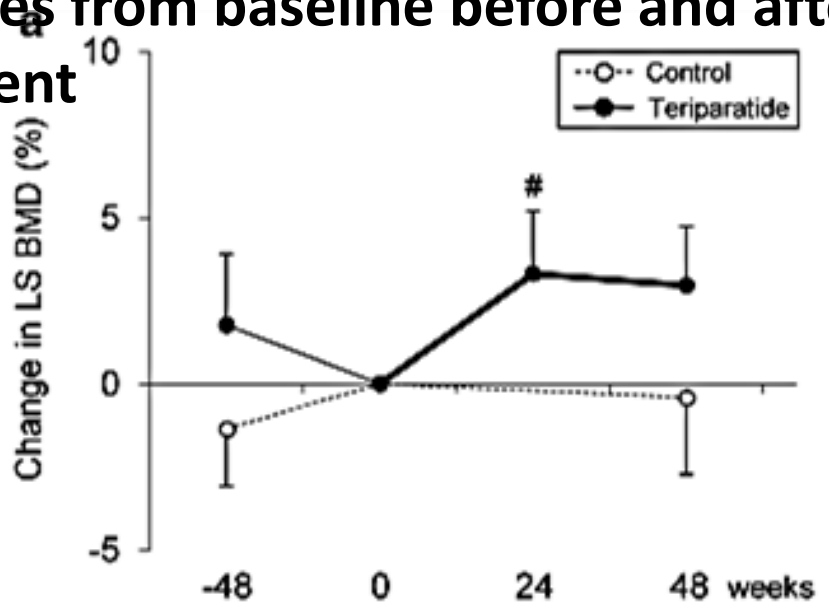
Osteoporos Int (2016) 27:1441–1450
DOI 10.1007/s00198-015-3377-6

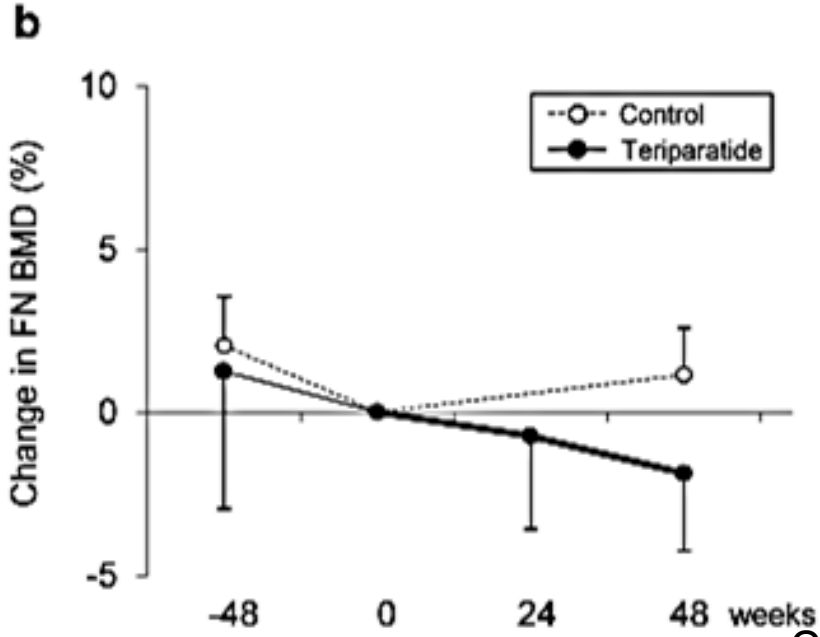
ORIGINAL ARTICLE

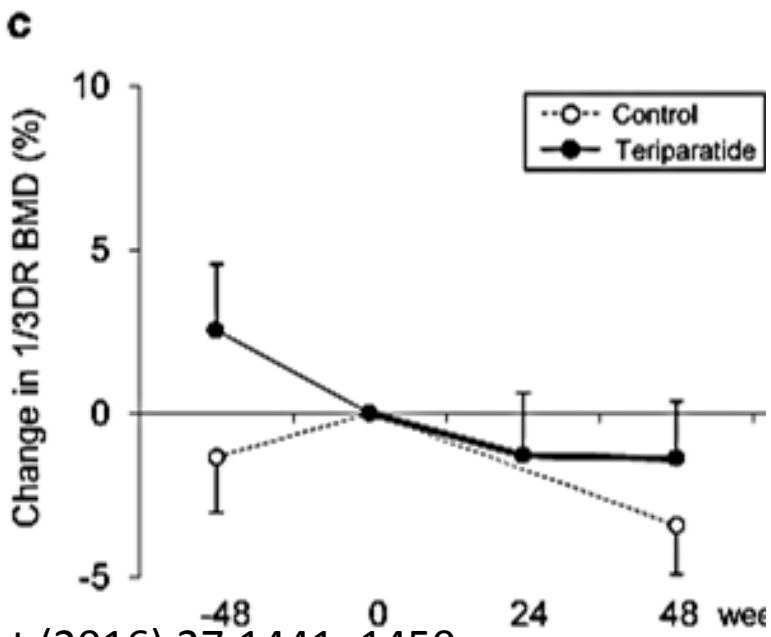
Once-weekly teriparatide in hemodialysis patients with hypoparathyroidism and low bone mass: a prospective study

K. Sumida[1,2,3] · Y. Ubara[1,2,3] · J. Hoshino[1,2] · K. Mise[1] · N. Hayami[1,2] · T. Suwabe[1,2] · M. Kawada[2] · A. Imafuku[2] · R. Hiramatsu[2] · E. Hasegawa[2] · M. Yamanouchi[2] · N. Sawa[2] · K. Takaichi[1,2,3]

Percent BMD changes from baseline before and after once weekly teriparatide treatment







Osteoporos Int (2016) 27:1441–1450

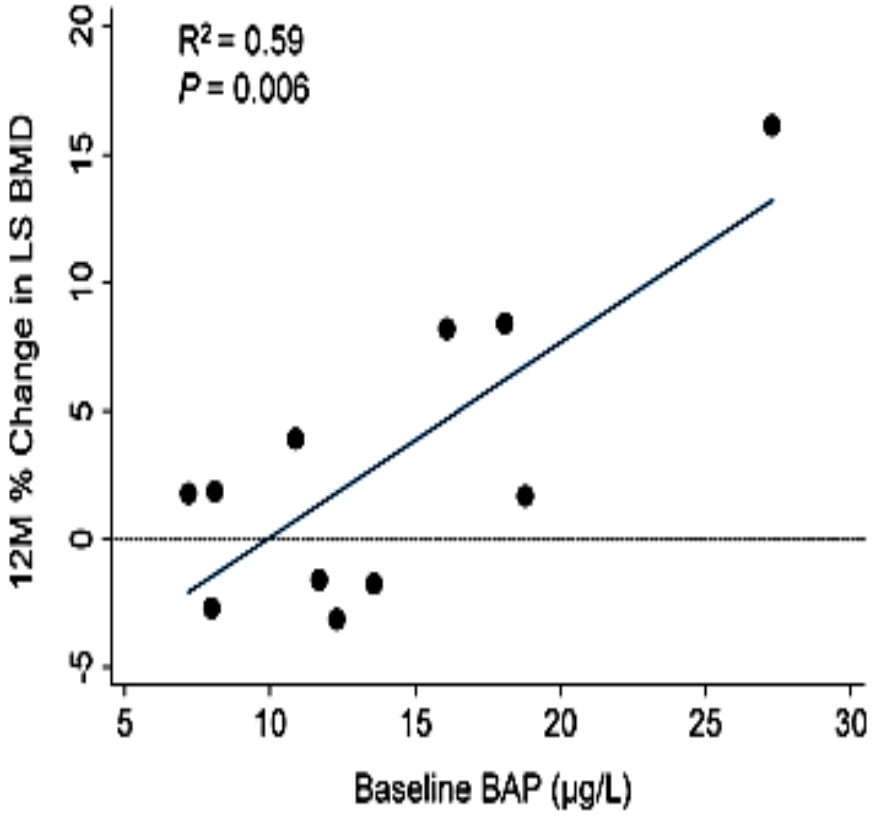


Table 3 Summary of treatment-emergent adverse events

Adverse event	*n* (%)
N	22
AE	
Transient hypotension	8 (36.4)
Fever	6 (27.2)
Palpitation	5 (22.7)
Skin rash	4 (18.2)
Nausea	1 (4.5)
Hypersensitivity syndrome	1 (4.5)
Hyperthyroidism	1 (4.5)
SAE	
Femoral neck fracture	1 (4.5)
Obstructive ileus	1 (4.5)
Renal cyst infection	1 (4.5)
Discontinuation of treatment due to AE	10 (45.5)

Osteoporos Int (2016) 27:1441–1450

CURRENT MEDICAL RESEARCH AND OPINION
2019, VOL. 35, NO. 12, 2097–2102
https://doi.org/10.1080/03007995.2019.1656955
Article ST-0269/1656955

Taylor & Francis
Taylor & Francis Group

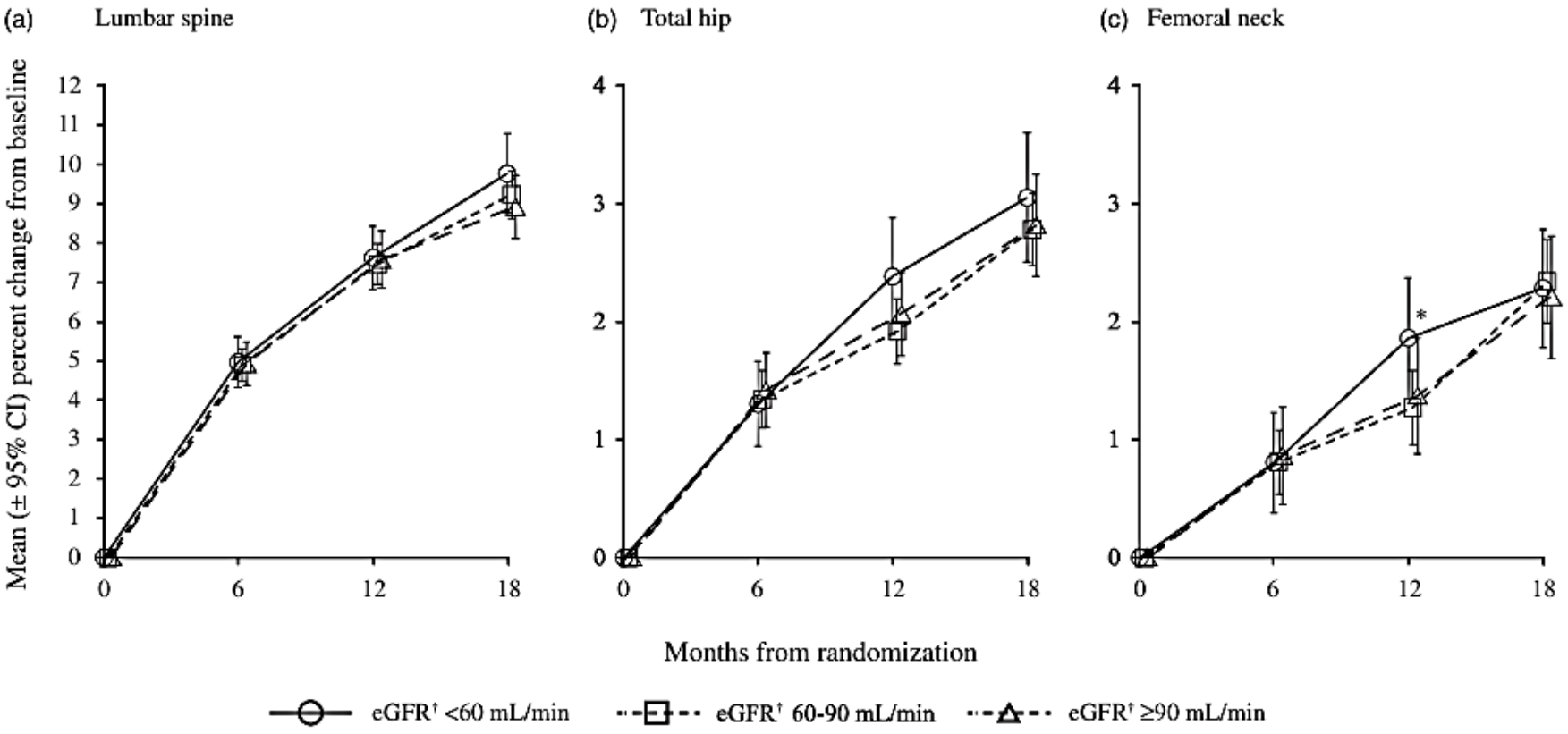
ORIGINAL ARTICLE

Abaloparatide in patients with mild or moderate renal impairment: results from the ACTIVE phase 3 trial

John P. Bilezikian[a], Gary Hattersley[b], Bruce H. Mitlak[b], Ming-Yi Hu[b], Lorraine A. Fitzpatrick[b], Christine Dabrowski[b], Paul D. Miller[c] and Socrates E. Papapoulos[d]

[a]College of Physicians and Surgeons, Columbia University, New York, NY, USA; [b]Research & Development, Radius Health, Inc, Waltham, MA, USA; [c]Colorado Center for Bone Research at Panorama Orthopedics and Spine Center, Golden, CO, USA; [d]Center for Bone Quality, Leiden University Medical Center, Leiden, The Netherlands

BMD changes in patients treated with Teriparatide based on renal function



CURRENT MEDICAL RESEARCH AND OPINION 2019, 12, 2097–2102

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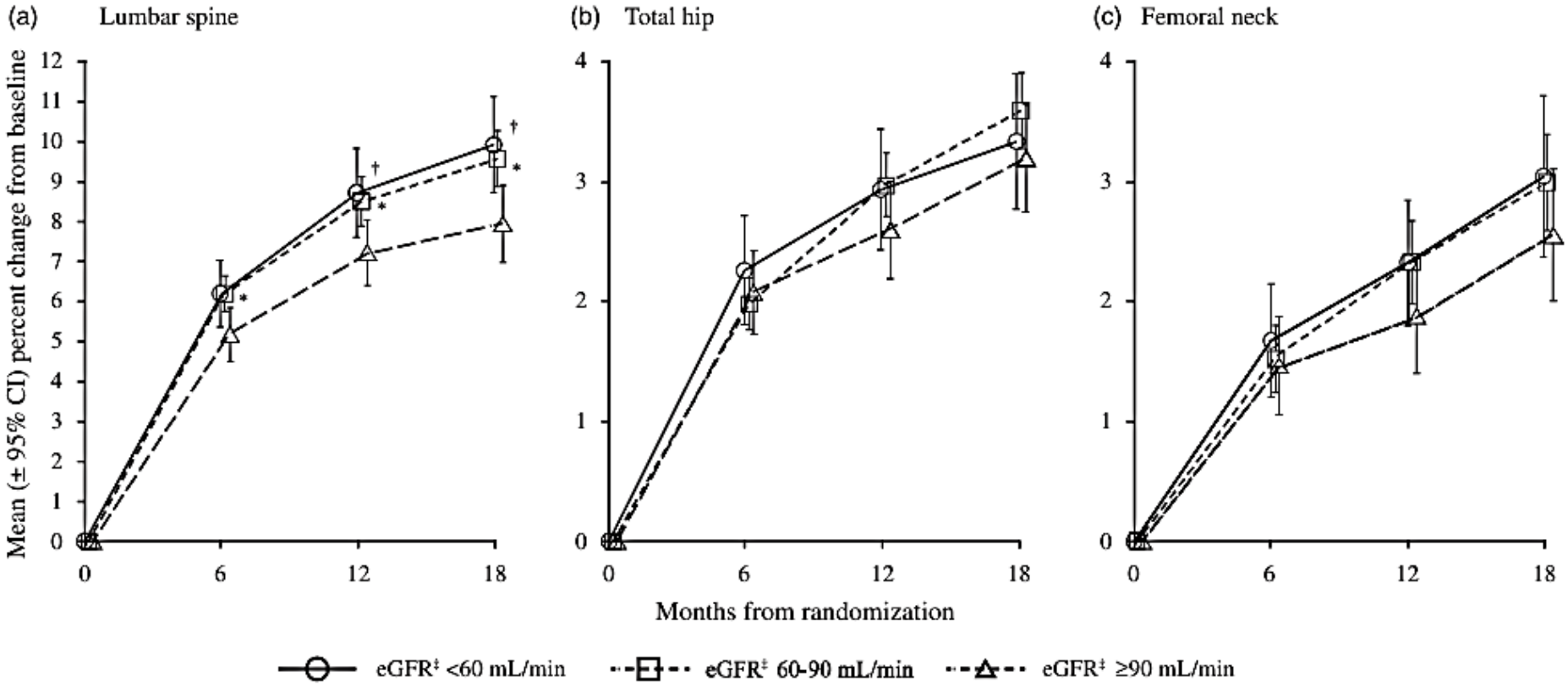

CURRENT MEDICAL RESEARCH AND OPINION 2019, 12, 2097–2102

Conclusions

- No differences in efficacy or safety of abaloparatide among patients with different degrees of baseline renal function.
- The findings support the use of abaloparatide in patients with mild or moderate renal impairment without dose adjustments.
- Abaloparatide is particularly suitable as an osteoanabolic agent to treat patients at high risk for fracture with impaired renal function.

CURRENT MEDICAL RESEARCH AND OPINION 2019, 12, 2097–2102

Bone 97 (2017) 314–319

Contents lists available at ScienceDirect

Bone

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

Full Length Article

Effects of abaloparatide-SC (BA058) on bone histology and histomorphometry: The ACTIVE phase 3 trial☆

Table 3
Bone mineral density at lumbar spine, femoral neck, and total hip at 18 months in the bone biopsy cohort.

	Placebo (n=35)		Abaloparatide-SC (n=36)		Teriparatide (n=34)	
	Value (g/cm^2)	% change from BL	Value (g/cm^2)	% change from BL	Value(g/cm^2)	% change from BL
LS-BMD	0.855	0.49	0.960	12.45	0.943	9.70
	(0.136)	(4.72)	(0.139)	(7.95)[a,b]	(0.126)	(5.05)[a]
FN-BMD	0.747	-0.49	0.760	4.75	0.788	3.02
	(0.101)	(3.63)	(0.108)	(4.44)[a]	(0.086)	(3.64)[a]
TH-BMD	0.785	-0.42	0.802	4.40	0.826	3.10
	(0.096)	(2.41)	(0.093)	(3.98)[a]	(0.087)	(3.95)[a]

BL=baseline; BMD=bone mineral density; LS=lumbar spine; FN=femoral neck; TH=total hip. Values are expressed as the mean (SD); [a] $p<0.0001$ vs placebo. [b] $p=0.0054$ vs teriparatide.

Osteoporosis Drugs in Advanced CKD

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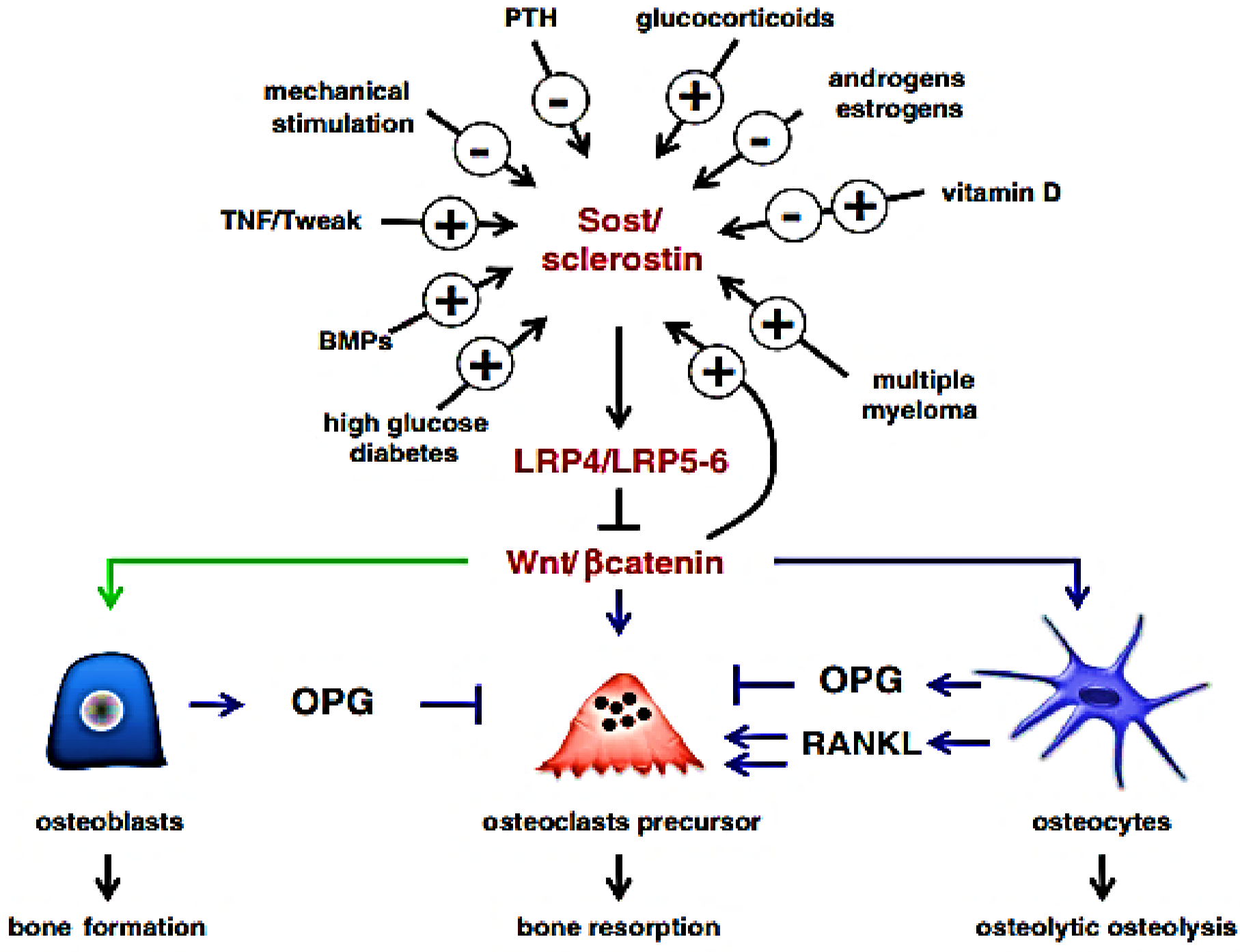

PTH
glucocorticoids
mechanical stimulation
androgens estrogens
vitamin D
TNF/Tweak
Sost/ sclerostin
BMPs
high glucose diabetes
multiple myeloma
LRP4/LRP5-6
Wnt/ βcatenin
OPG
OPG
RANKL
osteoblasts
osteoclasts precursor
osteocytes
bone formation
bone resorption
osteolytic osteolysis

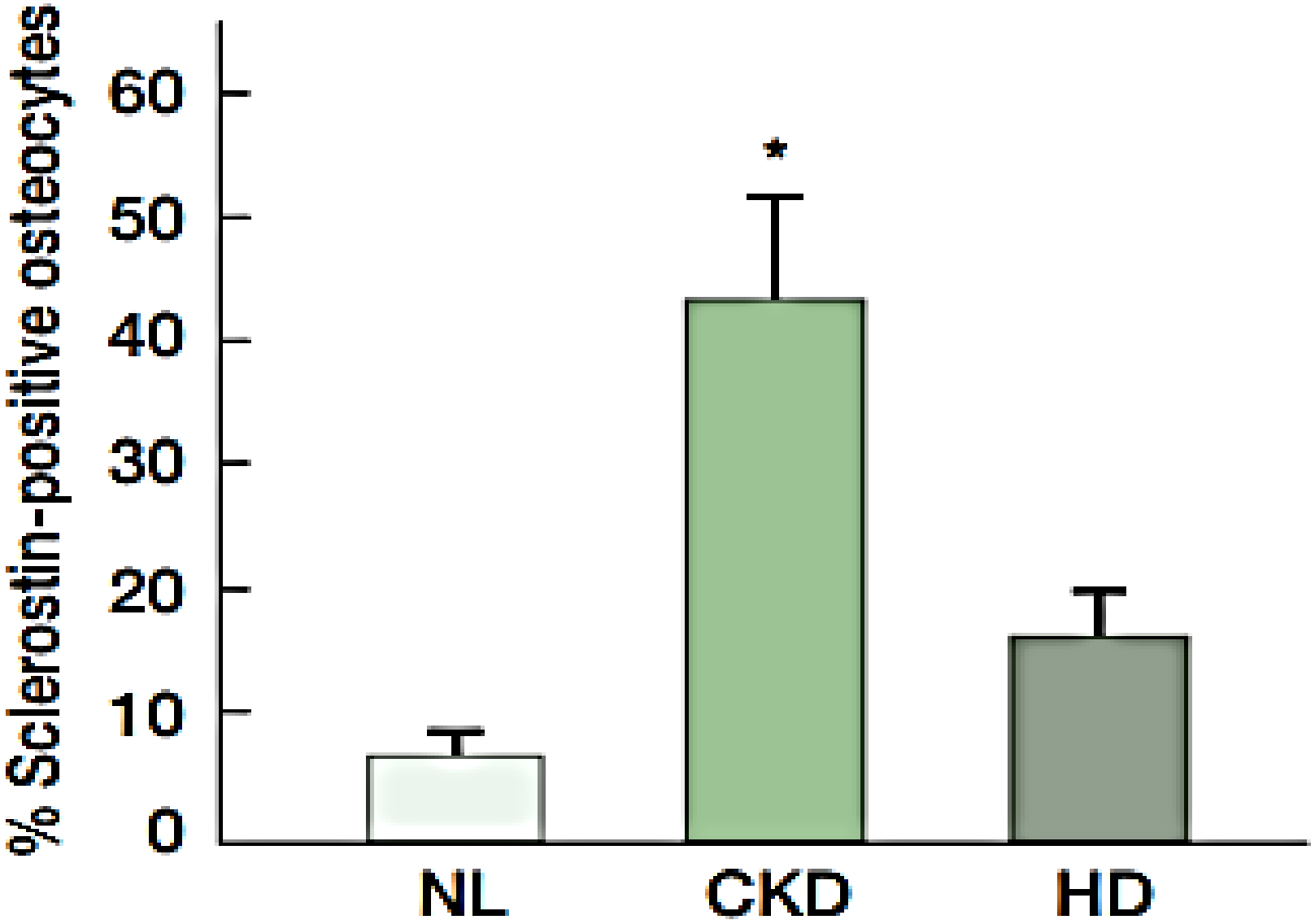
Table 1. Factors Involved in the Bone-Vascular Axis in CKD (Nonexhaustive)

Factor	Role in Bone Metabolism	Role in Vascular Calcification
Inflammation	Promotes bone resorption	Promotes VC
Klotho	Acts as a Wnt-inhibitor; in addition may modify mineral metabolism	Inhibits VC
Sclerostin (Wnt-inhibitor)	Inhibits bone turnover	Marker of VC burden; attenuates progression of VC
Osteoprotegerin	Inhibits osteoclastic bone resorption	Marker of VC burden; inhibits VC
Vitamin K deficiency	Reduces bone mineral density	Promotes vascular calcification
PTH	Key mediator of bone turnover; effect is dependent on duration and periodicity of PTH exposure and skeletal responsiveness	Complex, composite of incongruent paracrine and systemic effects
BMPs	Induce osteoblastic differentiation and bone formation	Proinflammatory and pro-oxidant effects
Osteopontin	Activates osteoclasts	Inhibits vascular calcification
Vitamin D	Maintains bone mass, pending sufficient calcium supply	Complex, U-shaped relationship

Adv Chronic Kidney Dis. 2019;26(6):472-483

Sclerostin deficiency➔Van Buchem disease

Increase in osteocyte sclerostin expression in early CKD (stages 2–4).



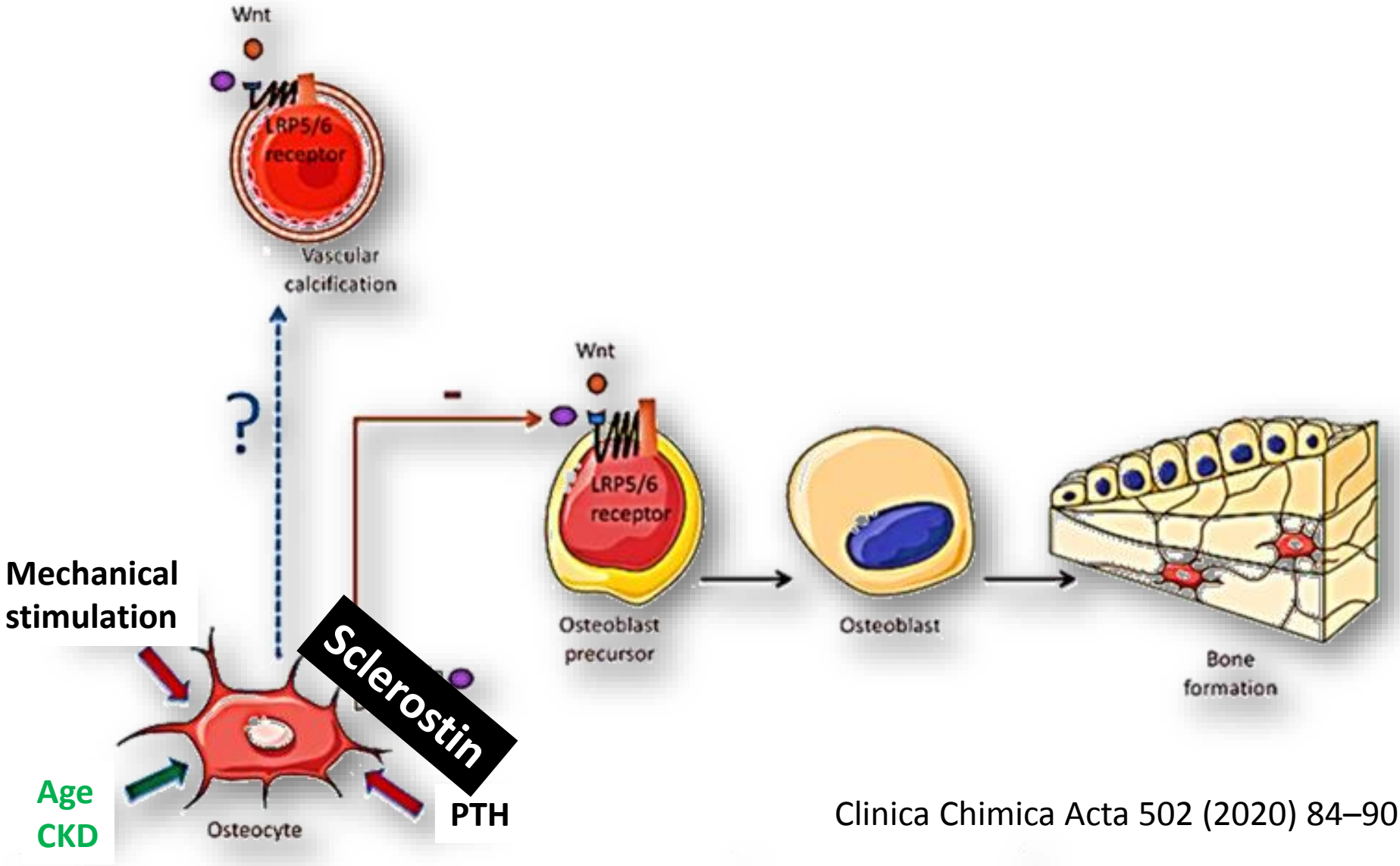
Kidney International (2016) 89, 289–302

Determinants of Sclerostin expression

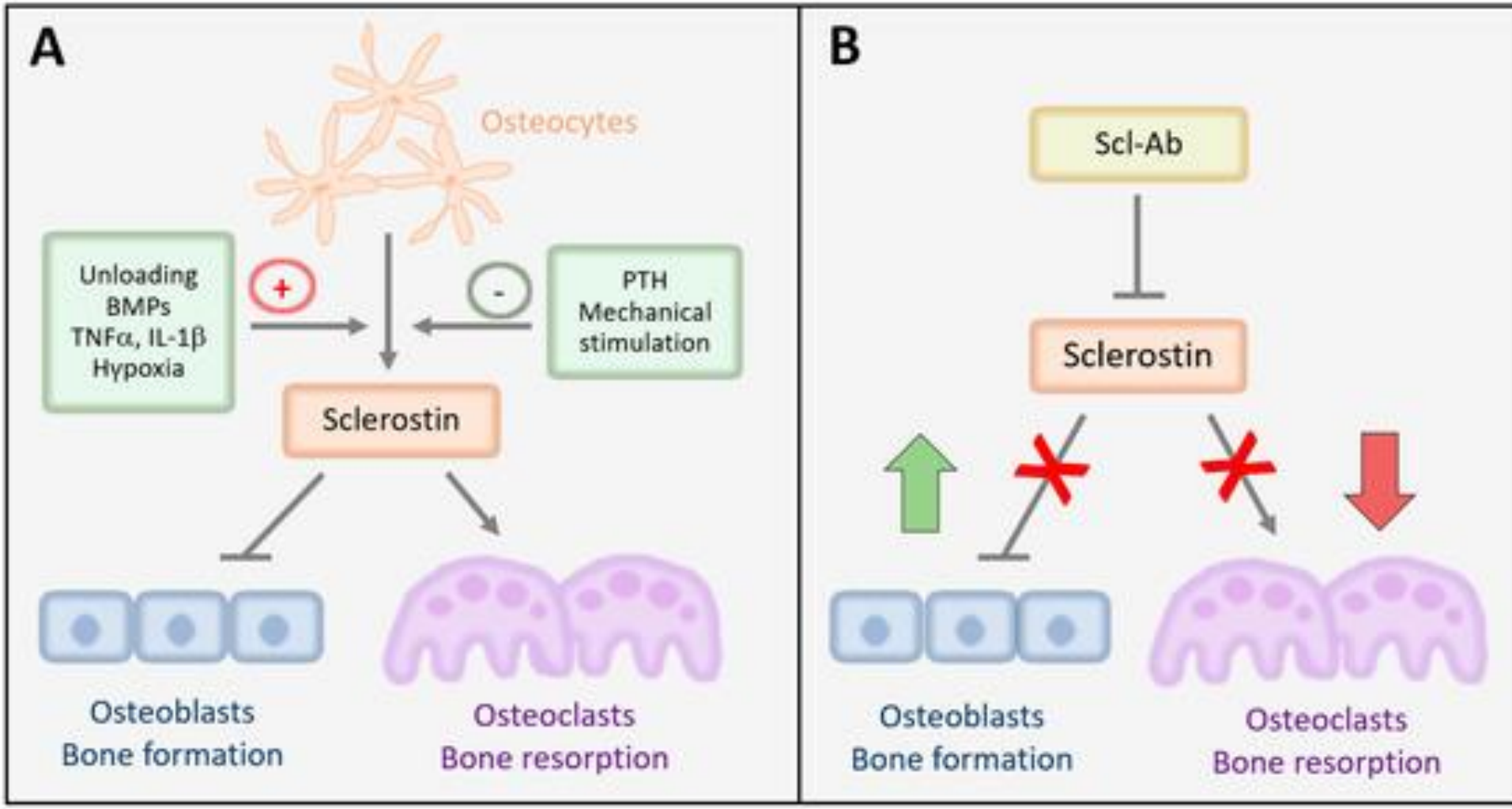
Determinant	Impact	Mechanism
Age	+	❖ Reduction of daily activity. ❖ Decreased osteocyte number
PTH	-	Direct action of PTH promoting Wnt-B catenin pathway Direct impact on osteoblast differentiation
Phosphorus	+	Through increased FGF 23 Changes on the sclerostin expression gen
Calcitriol	-	Decreased activation of 1-alpha Hydroxylase
Estrogens	-	Increased TNF-a ➔ increased sclerostin
Diabetes	+	Wnt–β-catenin pathway implicated in pancreatic islet development and the production of incretin hormone • Role in Wnt signaling in hepatic glucose metabolism

Clinica Chimica Acta 502 (2020) 84–90

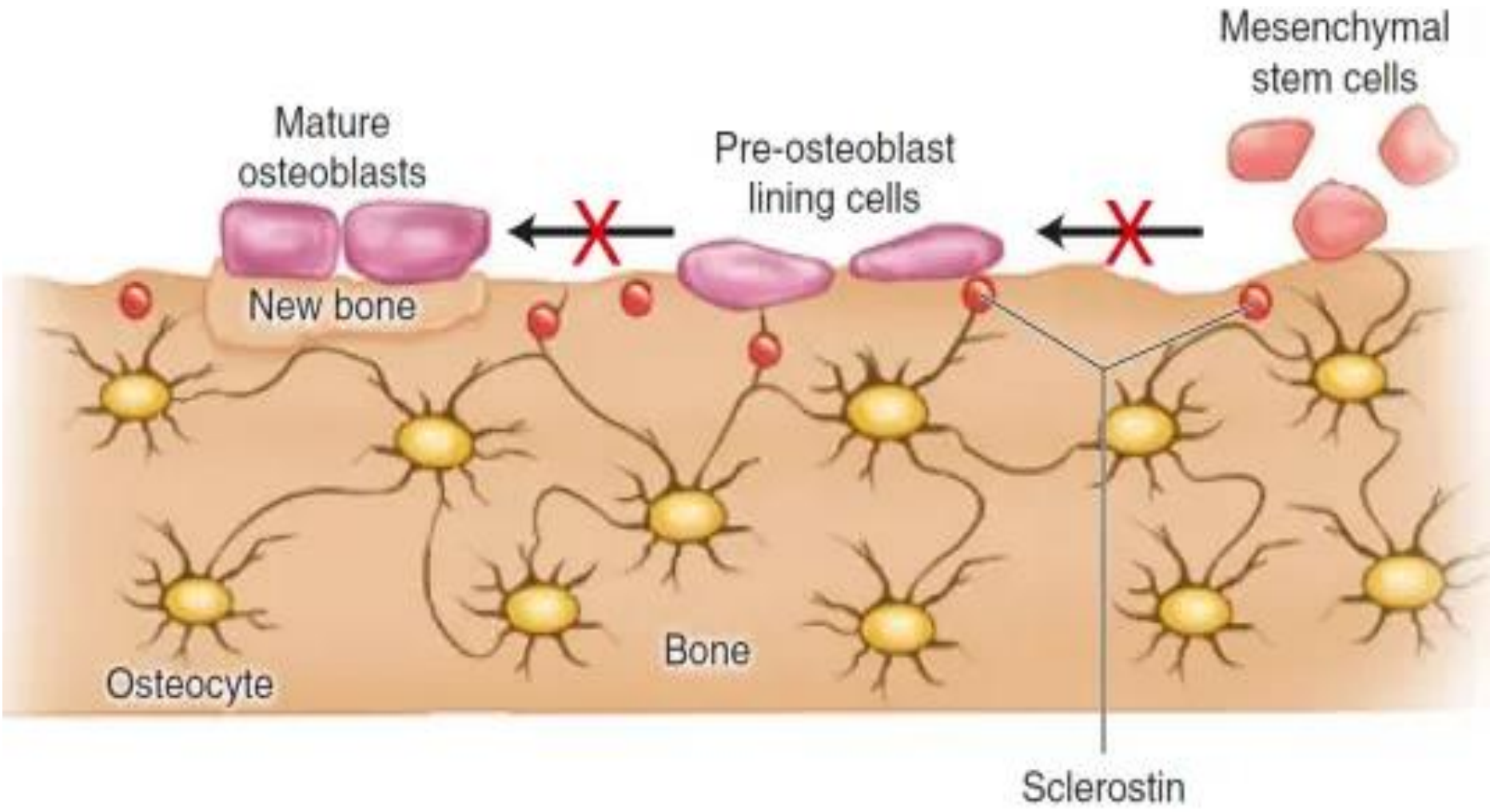
Sclerostin: regulation, bone effect, and link with vascular calcifications



Clinica Chimica Acta 502 (2020) 84–90


A
Osteocytes
Unloading
BMPs
TNFα, IL-1β
Hypoxia
+
-
PTH
Mechanical
stimulation
Sclerostin
Osteoblasts
Bone formation
Osteoclasts
Bone resorption
B
Scl-Ab
Sclerostin
Osteoblasts
Bone formation
Osteoclasts
Bone resorption

Osteocytes producing sclerostin inhibits bone formation.



Concerns about Romosozumab

- It is a fully human monoclonal anti sclerostin antibody with concurrent anabolic and antiresorptive action, activates bone formation.
- Anti-sclerostin antibodies may be a beneficial therapeutic option in patients with G4–G5D CKD and low bone turn over
- this therapy can have synergistic action with PTH analogs
- the BMD increase was higher with romosozumab compared with alendronate or teriparatide.
- switching from a bisphosphonate to romosozumab led to a higher increase of cortical rather than trabecular BMD in patients with CKD. Whereas patients switched from a bisphosphonate to teriparatide, the cortical BMD decreased.
- The bone turnover rebound phenomenon and bone loss have been observed after romosozumab cessation necessitating the rapid transition to an antiresorptive treatment.
- Romosozumab is associated with cardiovascular adverse events

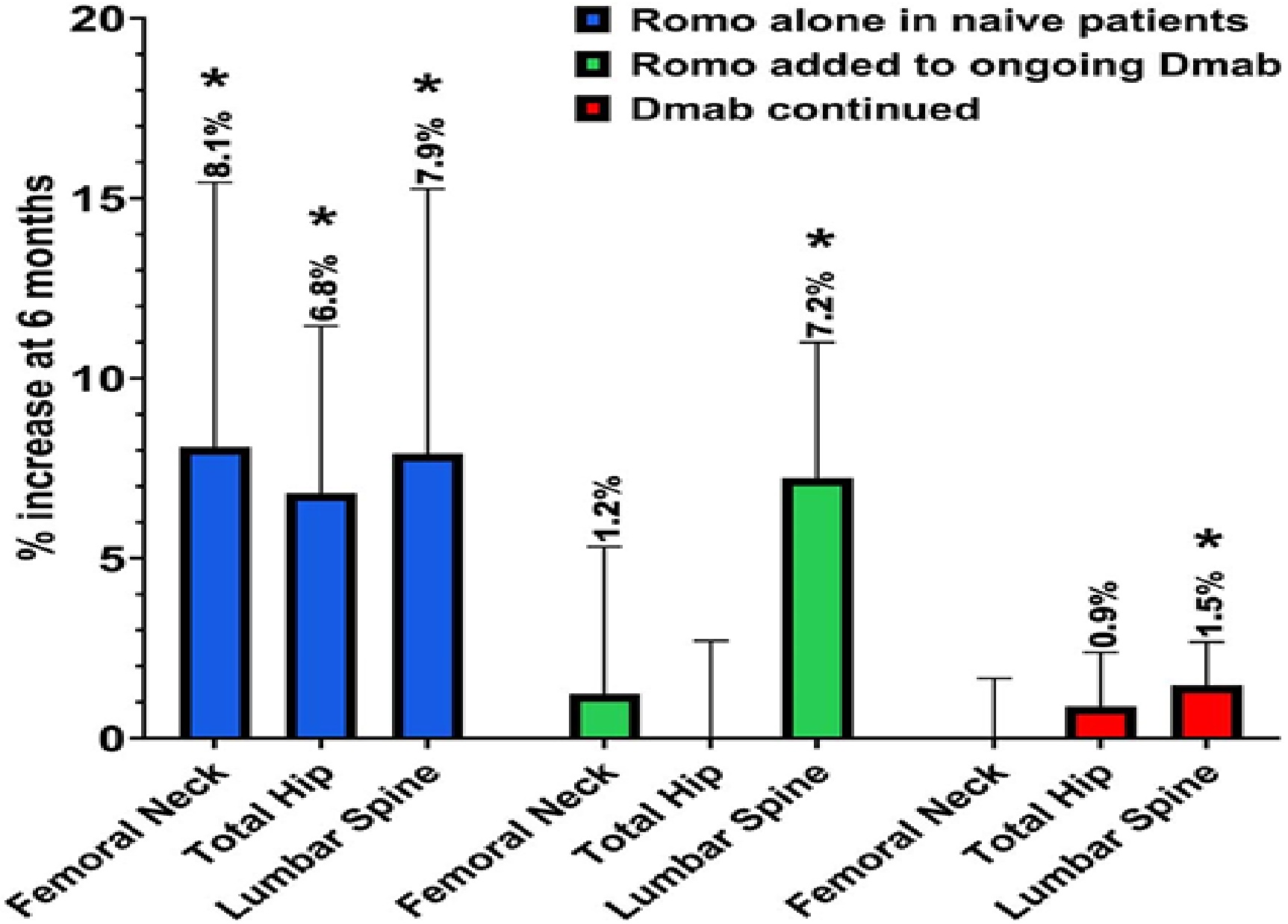
JBMR Plus, 2024, **8**, ziae016
https://doi.org/10.1093/jbmrpl/ziae016
Advance access publication: February 7, 2024
Research Article

ASBMR
The American Society for Bone and Mineral Research
OXFORD

Romosozumab added to ongoing denosumab in postmenopausal osteoporosis, a prospective observational study

Giovanni Adami*, Elisa Pedrollo, Maurizio Rossini, Angelo Fassio, Vania Braga, Emma Pasetto, Francesco Pollastri, Camilla Benini, Ombretta Viapiana, Davide Gatti

Rheumatology Unit, Department of Medicine, University of Verona, Verona, 37134, Italy
*Corresponding author: Giovanni Adami, Rheumatology Unit, Department of Medicine, University of Verona, P.le Scuro 10, Verona, 37134, Italy (giovanni.adami@univr.it).



JBMR Plus, 2024, Volume 8 Issue 4

Discontinuation of osteoporosis therapy is followed by a decline of BMD

Discontinuation of long-term treatment with denosumab

→ rapid decreased in BMD

Discontinuation of long-term treatment with Biphosphonate

→ BMD declines slowly

Discontinuation of long-term treatment with Teriparatide

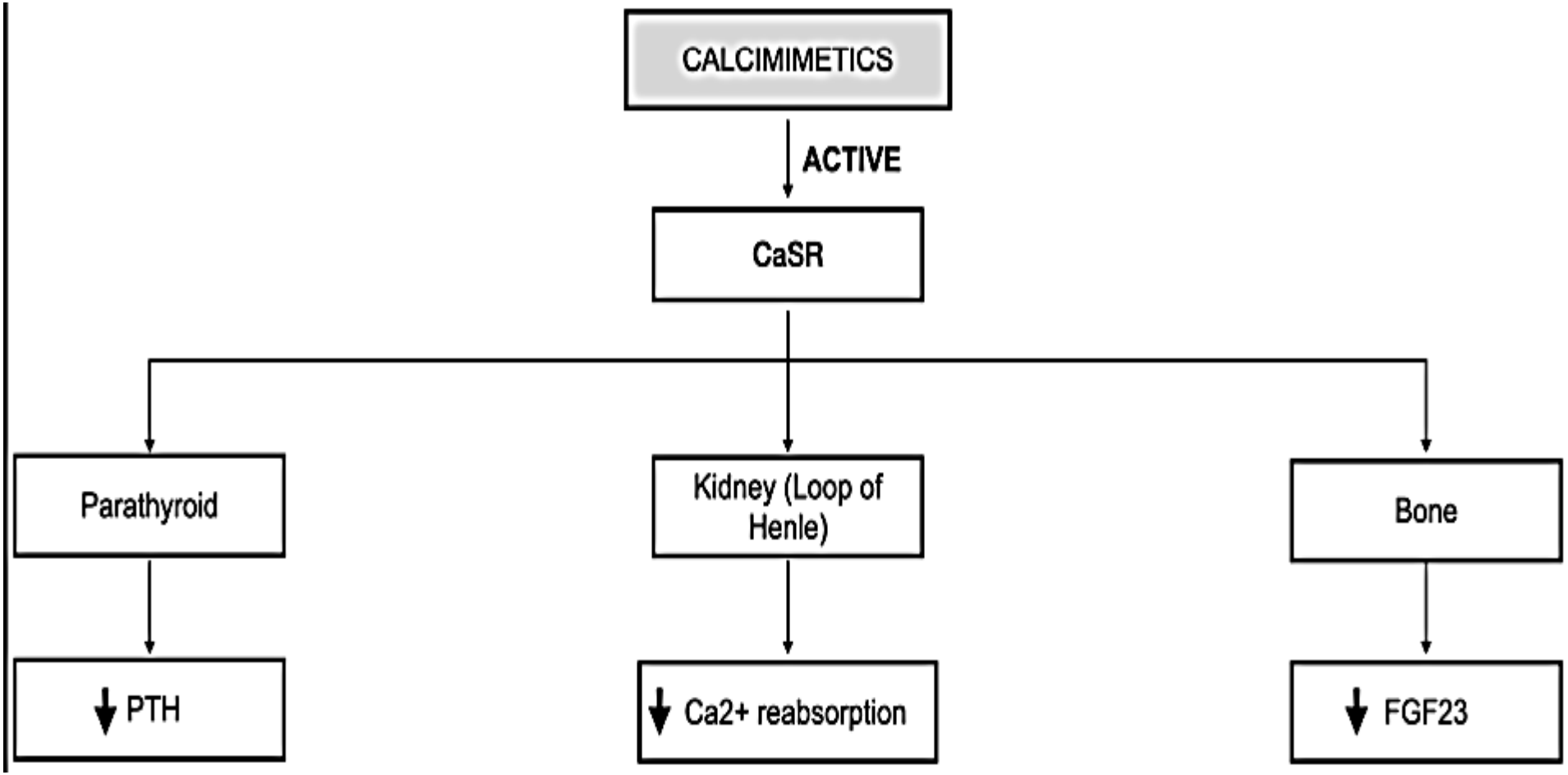
→ BMD rapidly decreases

Discontinuation of long-term treatment with Romosozumab

→ large decrease of BMD

What about of Combo treatment of Calcimimetics+ Teriparatide?

Action of calcimimetics on the main target organs of the body



nefrologia 2025;45(2):116–134

Osteoporosis and Sarcopenia 9 (2023) 121–130

Contents lists available at ScienceDirect

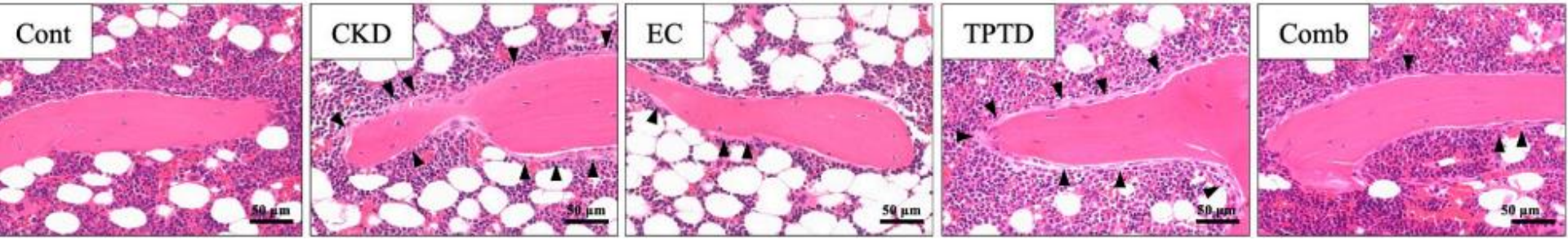
Osteoporosis and Sarcopenia

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

Original article

Teriparatide and etelcalcetide improve bone, fibrosis, and fat parameters in chronic kidney disease model rats

Shun Igarashi [a], Yuji Kasukawa [b,*], Koji Nozaka [a], Hiroyuki Tsuchie [a], Kazunobu Abe [a], Hikaru Saito [a], Ryo Shoji [a], Fumihito Kasama [a], Shuntaro Harata [a], Kento Okamoto [a], Keita Oya [a],



Combination therapy provides a beneficial effect in improving bone deterioration in CKD that cannot be achieved with monotherapy

Chronic kidney disease–mineral and bone disorder: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

OPEN

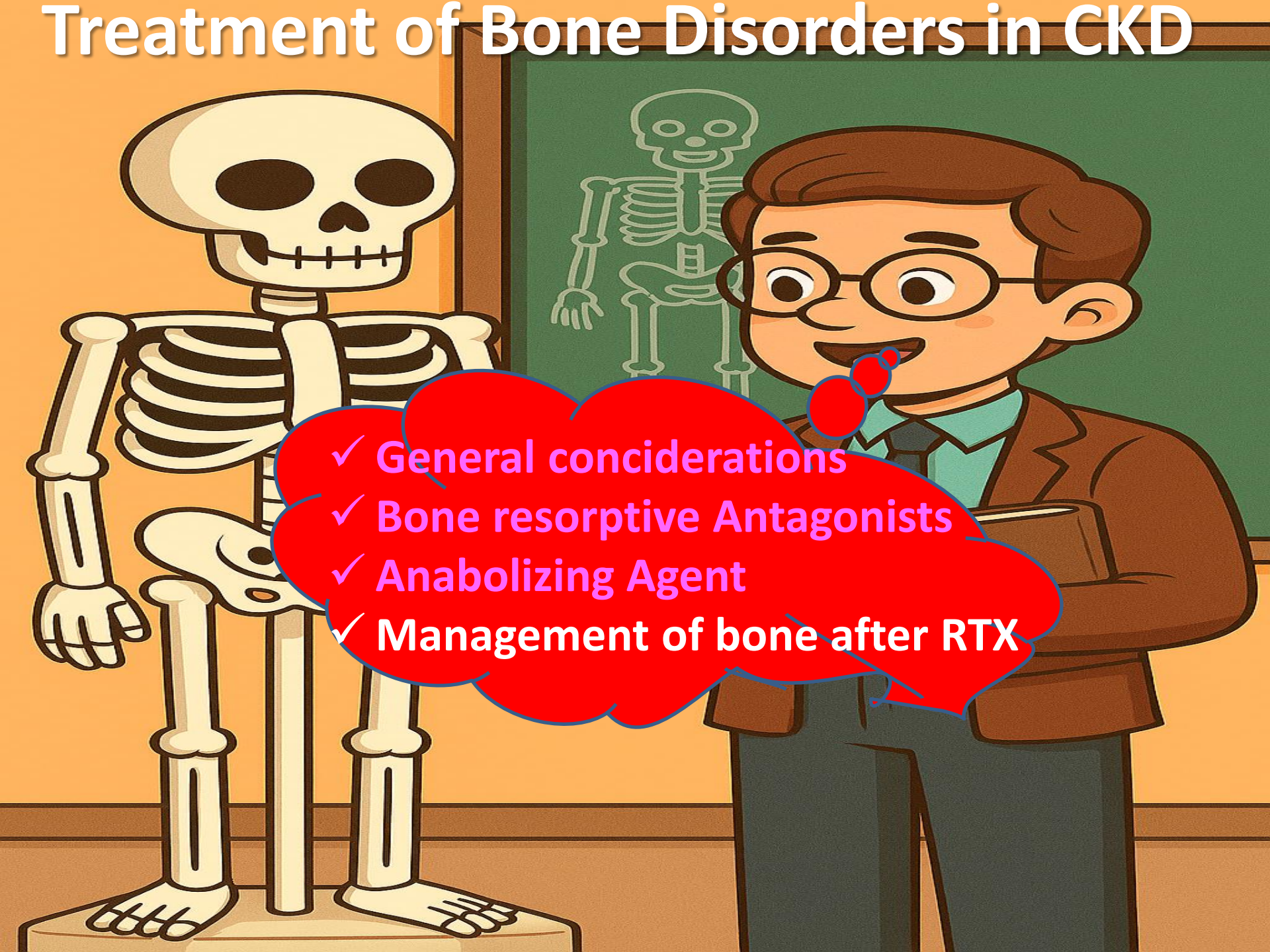
Markus Ketteler[1], Pieter Evenepoel[2,3], Rachel M. Holden[4], Tamara Isakova[5], Hanne Skou Jørgensen[6,7], Hirotaka Komaba[8], Thomas L. Nickolas[9], Smeeta Sinha[10,11], Marc G. Vervloet[12], Michael Cheung[13], Jennifer M. King[13], Morgan E. Grams[14], Michel Jadoul[15] and Rosa M.A. Moysés[16]; for Conference Participants[17]

Conclusion

The use of artificial intelligence systems could aid in predicting risks and informing management strategies in CKD-MBD.

Kidney International (2025) 107, 405–423

Treatment of Bone Disorders in CKD



Endocrinol Metab 2024;39:267-282

EnM
ENDOCRINOLOGY AND METABOLISM

Review Article

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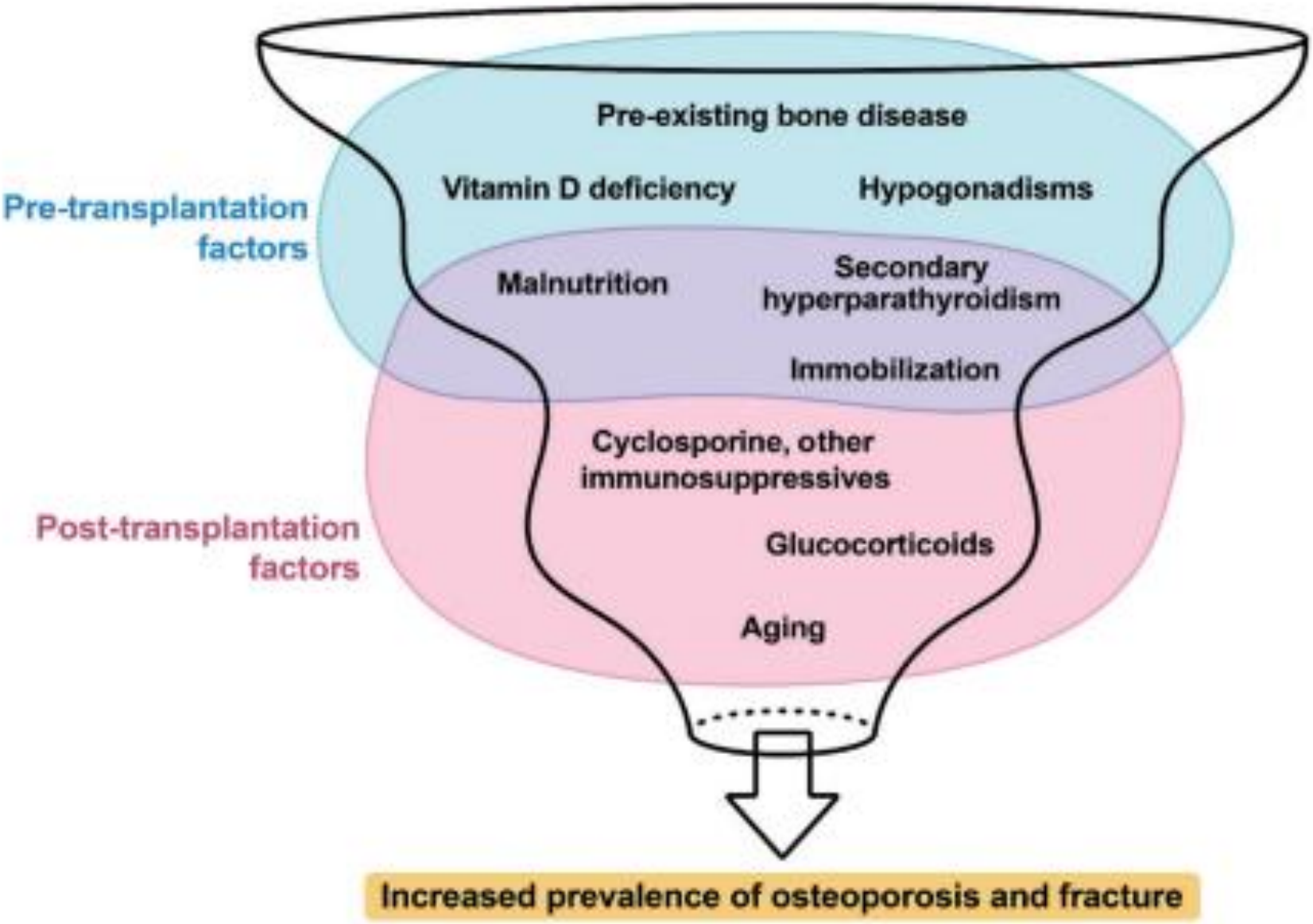
Bone Loss after Solid Organ Transplantation: A Review of Organ-Specific Considerations

Organ transplant type	After transplantation		
	Prevalence of osteoporosis	Prevalence of fracture	Bone loss in the first year
Kidney	Lumbar spine: 17%–49% Femur neck: 11%–56% Radius: 22%–52%	Overall: 7%–44%	Lumbar spine: 4%–10% Femur neck: 5%–8%
Liver	Overall: 46%	Fracture rate: 24%–65%	Lumbar spine: 2%–24%
Heart	Overall: 50%	Vertebral fracture: 33%–36%	Lumbar spine: 6%–10% Femur neck: 6%–11%
Lung	Overall: 73%	Fracture rate: 18%–37%	Lumbar spine & Femur neck: 2%–5%

Pathophysiology of transplantation-induced osteoporosis



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Effects of Immunosuppressive Drug on Bone in Transplant Patients

Drug type	Key mechanisms	Net effect on bone
Glucocorticoids	Inhibit osteoblasts Stimulate osteoclasts Disrupt intestinal and renal calcium transport Decreased gonadal function	Early: increased bone resorption Late: decreased bone formation and remodeling
Calcineurin inhibitors (cyclosporine, tacrolimus)	Inhibit cytokine transcription in T lymphocytes	Less bone loss compared to glucocorticoids, variable effects on bone turnover
mTOR inhibitors (sirolimus, everolimus)	Inhibit mTOR, affecting lymphocyte response	Potential reduction in bone resorption, bone-protective effects observed in some studies
Others (MPA, azathioprine)	Inhibit lymphocyte proliferation and antibody production (MPA); antagonize purine metabolism (Azathioprine)	Indirect protective effect on bone health by reducing the need for glucocorticoids, but specific effects on bone less clear

Article

TRANSPARENT PROCESS

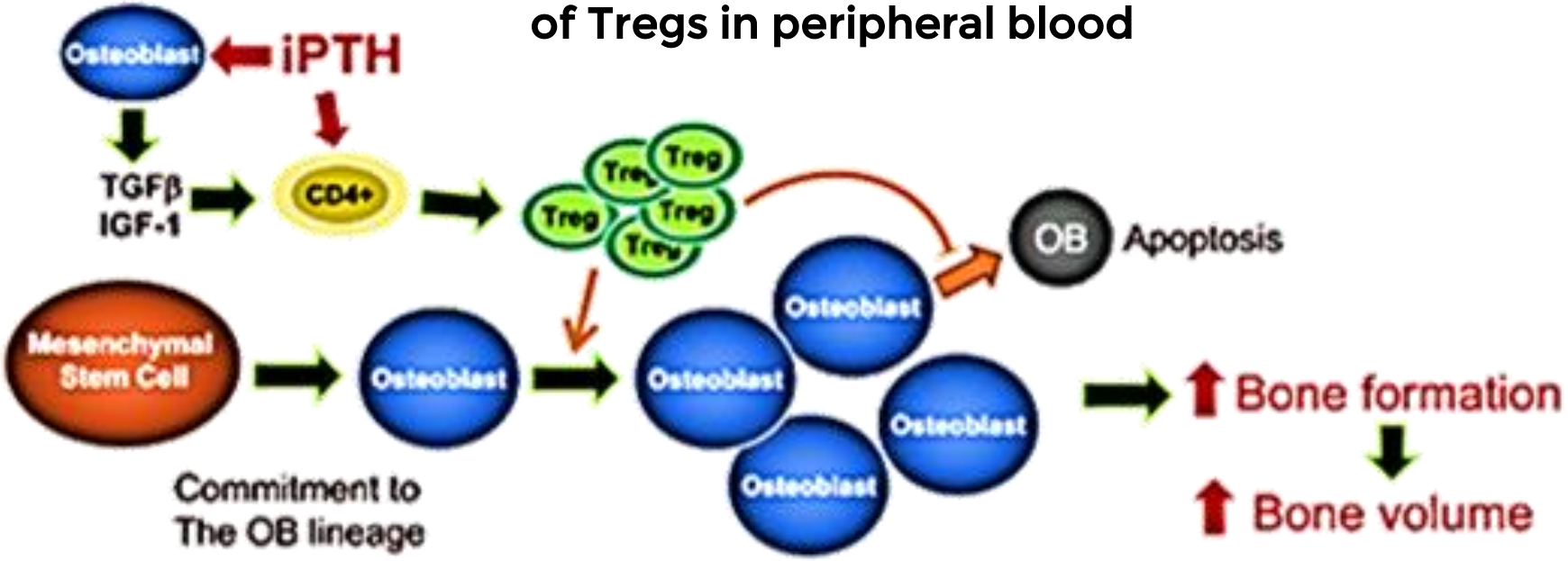
EMBO reports

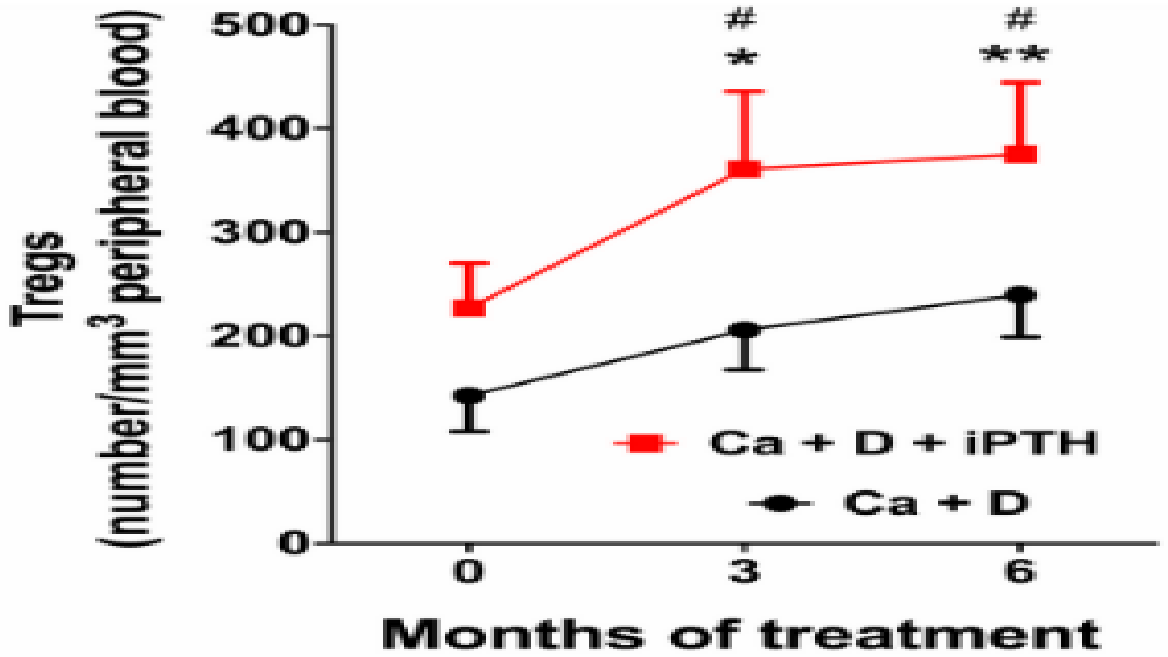
Regulatory T cells are expanded by Teriparatide treatment in humans and mediate intermittent PTH-induced bone anabolism in mice

Mingcan Yu[1], Patrizia D'Amelio[2], Abdul Malik Tyagi[1], Chiara Vaccaro[1], Jau-Yi Li[1], Emory Hsu[1], Ilaria Buondonno[2], Francesca Sassi[2], Jonathan Adams[1], M Neale Weitzmann[1,3], Richard DiPaolo[4] & Roberto Pacifici[1,5,*]

EMBO Reports (2018) 19: 156–171

Teriparatide treatment in humans increases the absolute and relative number of Tregs in peripheral blood





Management of bone health in post-transplant patient

Solid Organ Transplant Recipient

- Adequate daily Ca: 800-1000mg
- Maintain serum vit D3>20-30 ng/ml by calcitriol
- Encourage in physical activity

- Bone evaluation pre-transplantation
- Measure BMD 6 mo. after transplantation
- Monitoring biochemical tests frequently:Ca,P, ALP, VitD3, PTH

Initiate drugs in the case of osteoporosis with:

- Oral bisphosphonate or IV bisphosphonate (Especially Zolendronic acid)
- Denozumab
- Calcitriol

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Conclusion

- Teriparatide is safe and effective in increasing BMD and bone formation in patients with severe CKD, with no new safety concerns observed.
- The use of antiresorptive medications should be carefully evaluated, with close monitoring for potential nephrotoxicity and hypocalcemia.
- Emerging therapies such as romosozumab show promise but come with cardiovascular risks, necessitating careful consideration.
- Anabolic agents must be followed with anti-resorptive agents


Thanks