Pathophysiology of SHPT in CKD-MBD

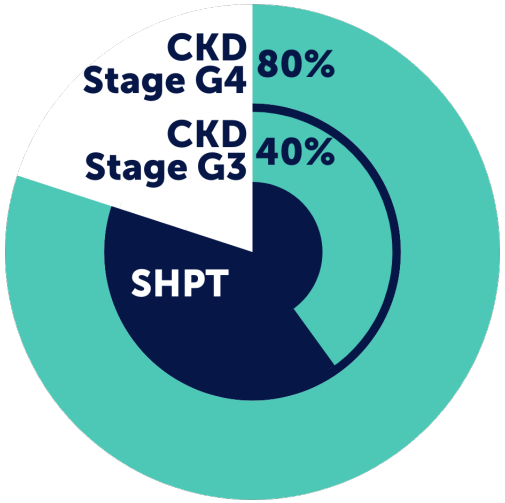
- Managing SHPT is key to **preventing CKD-MBD**
  - -SHPT progresses **slowly**
    - Silent process
- **Early** diagnosis and treatment are key to preventing side effects

Hypophosphatemia **Hypercalcemia**

Diagnosis of SHPT

Monitor Lab Values			
Serum calcium	Serum phosphate	PTH	Vitamin D

- Early diagnosis of SHPT in CKD is critical for **early treatment**
  - CKD stage **3A**, 3B
    - PTH level starts increasing
  - Patients with CKD can have **resistance** to current therapies
    - Nutritional (natural) vitamin D
    - Active vitamin D
      - Calcitriol or vitamin D receptor agonists

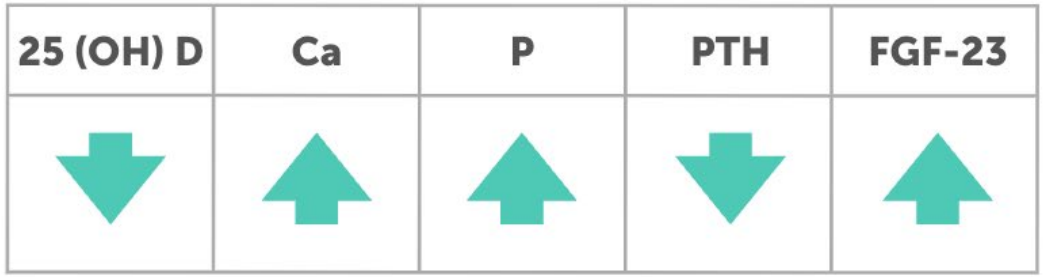


Cozzolino M, et al. *J Nephrol*. 2022;35(3):863-873.

Active Vitamin D

	% patients with hypercalcemia		*P*
	Paricalcitol	Placebo	
PRIMO	22.6%	0.9%	< 0.001
OPERA	43.3%	3.3%	< 0.001

ACTIVE VITAMIN D/ANALOGS:



Active vitamin D **should not be routinely used** for the treatment of patients with SHPT in CKD stages 3 and 4

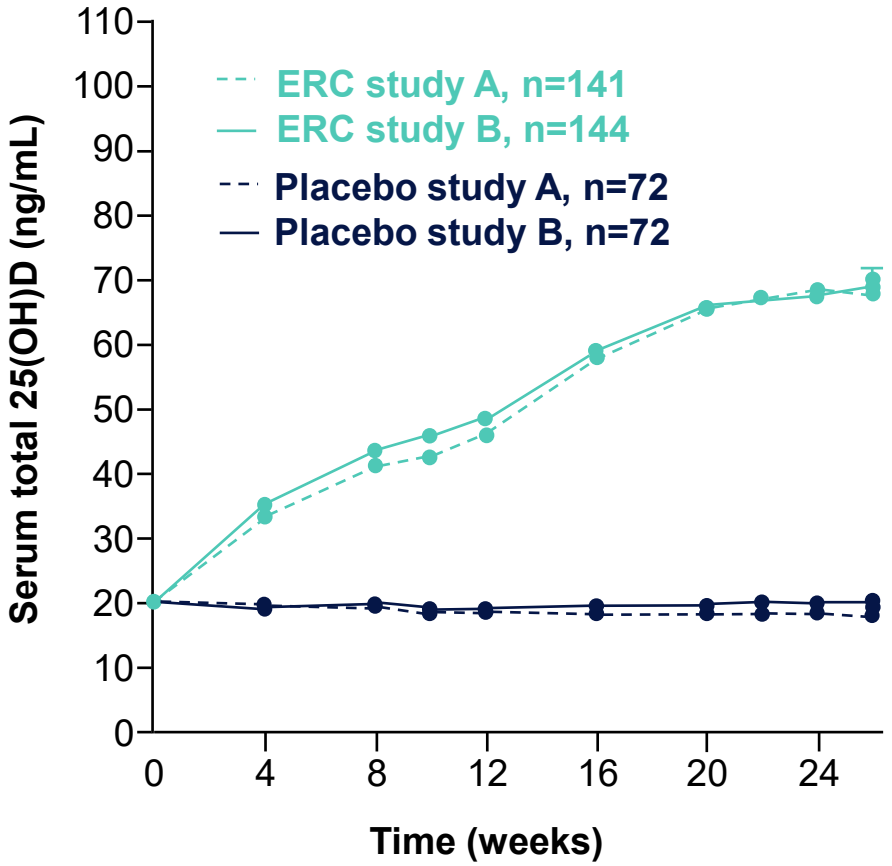
Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. *Kidney Int Suppl (2011)*. 2017;7(1):1-59.
Thadhani R, et al. *JAMA.* 2012;307(7):674-684.
Wang AYM, et al. *J Am Soc Nephrol.* 2014;25(1):175-186.

Extended-Release Calcifediol (Gradual Release Over 12 Hours): Randomized Clinical Trials with Patients with CKD Stage 3 and 4

	25 (OH) D	Ca	P	PTH	FGF-23
NUTRITIONAL VITAMIN D:	↑	—	—	— ↓	—
ACTIVE VITAMIN D/ANALOGS:	↓	↑	↑	↓	↑
ERC:	↑	—	—	↓	—

Average steady-state 25(OH)D levels **≥50** ng/mL

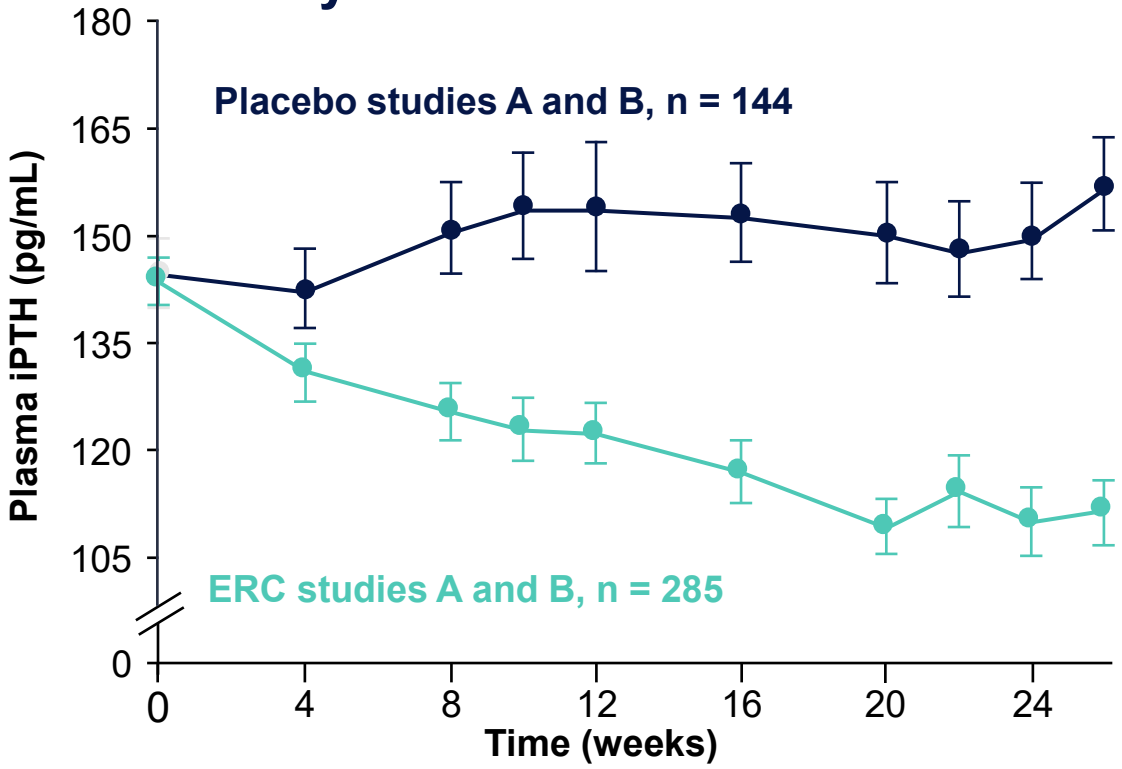
ERC dose	25(OH)D Week 26 (ng/mL)
30 µg	50
60 µg	70



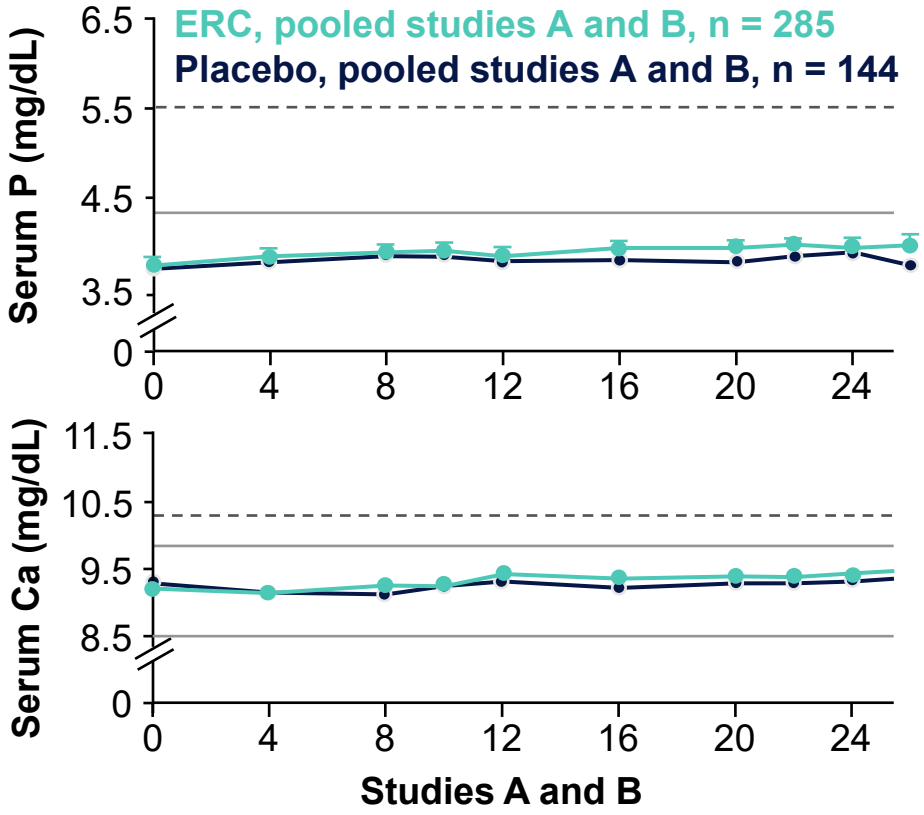
Sprague SM, et al. *Am J Nephrol*. 2016;44(4):316-325.

Extended-Release Calcifediol

Steady Release of PTH



Minimal changes in serum calcium and phosphate



Hyperphosphatemia: serum *P* > 5.5 mg/dL

Physiological range: 2.5 – 4.5 mg/dL

Hypercalcemia: serum Ca > 10.3 mg/dL

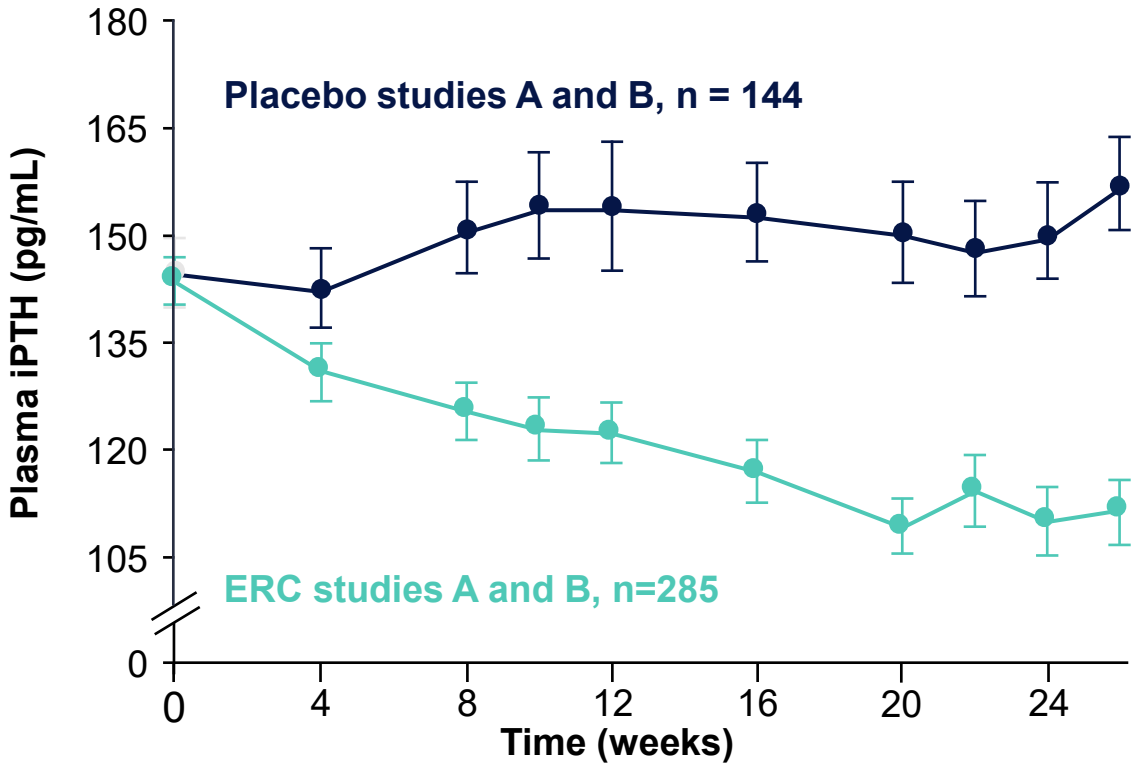
Physiological range: 8.5 –10.0 mg/dL (depending on assay)

Primary endpoint met: 33% and 34% of patients in study A and B, respectively, achieved **≥ 30% reduction** in iPTH from baseline at Week 26 (vs 8% and 7%, respectively, with placebo)

Sprague SM, et al. *Am J Nephrol.* 2016;44(4):316-325.

Extended-Release Calcifediol

- Steady levels of 25(OH)D are achieved after approximately 3 months of treatment
- Current practice guidelines need **revision** based on recent clinical trial data



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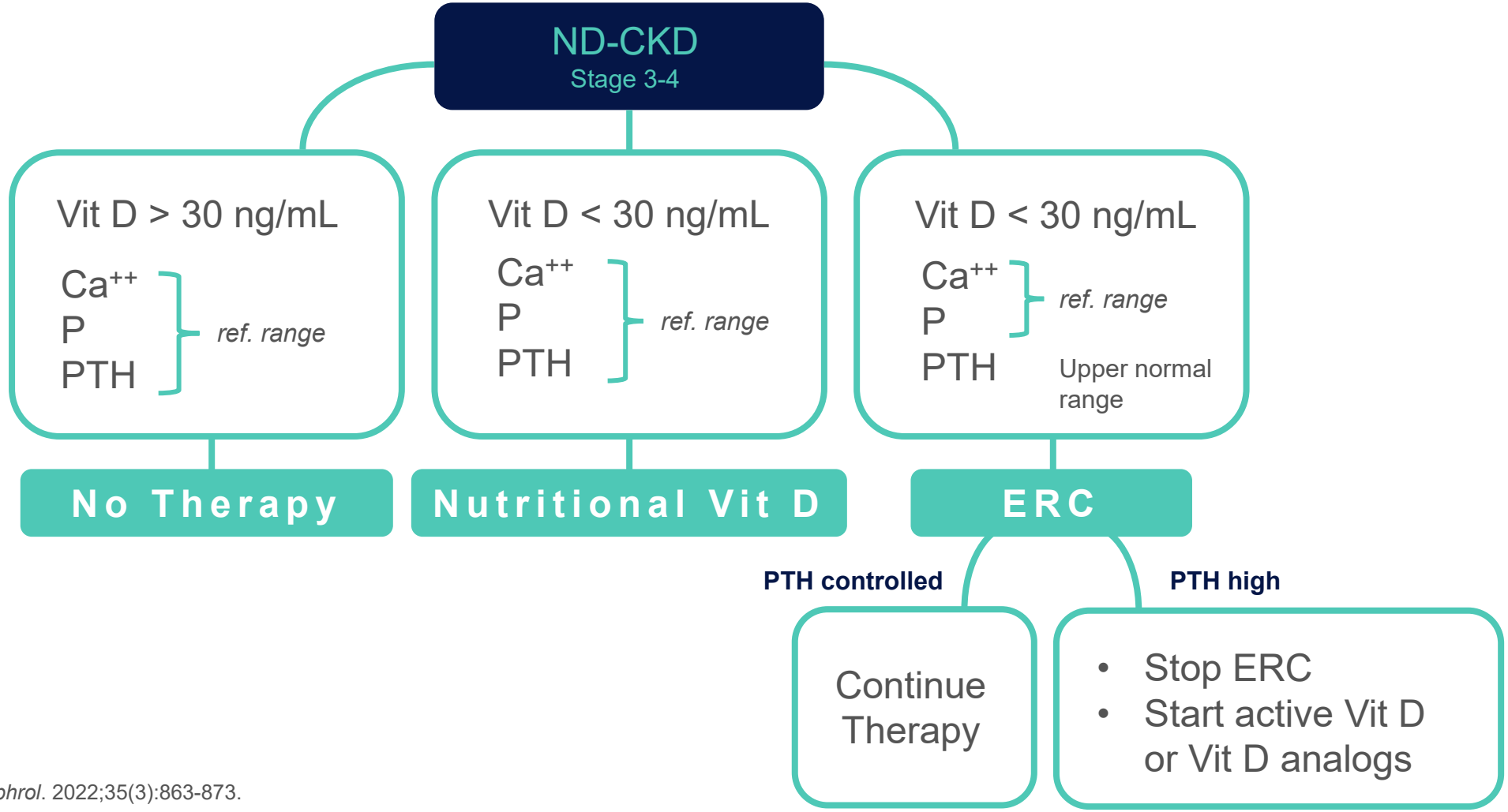
Management of Patients with CKD Stage 3 and 4



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