

Pharmacodynamic (PD) profiling of reloxaliase in patients with severe hyperoxaluria

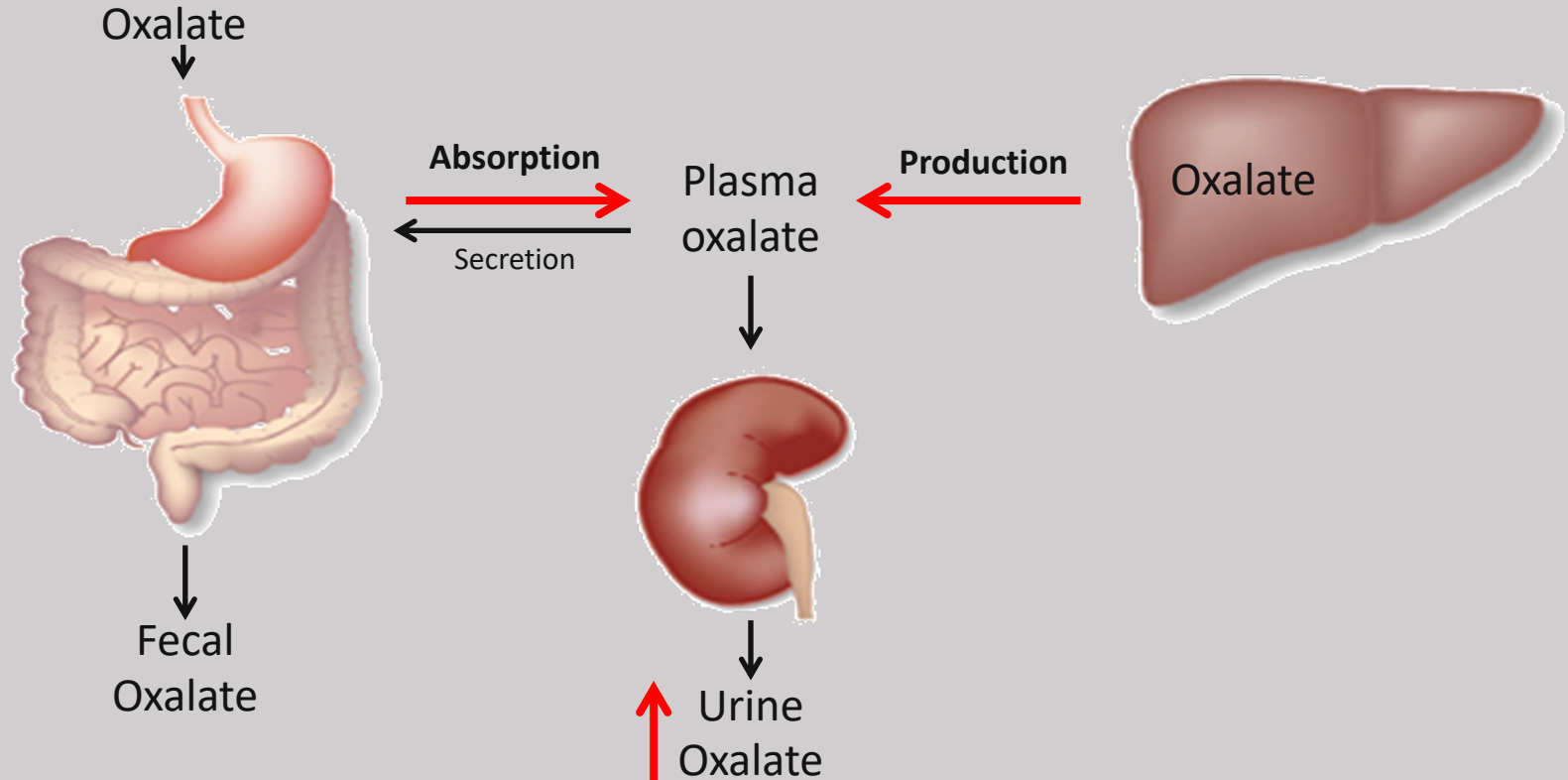
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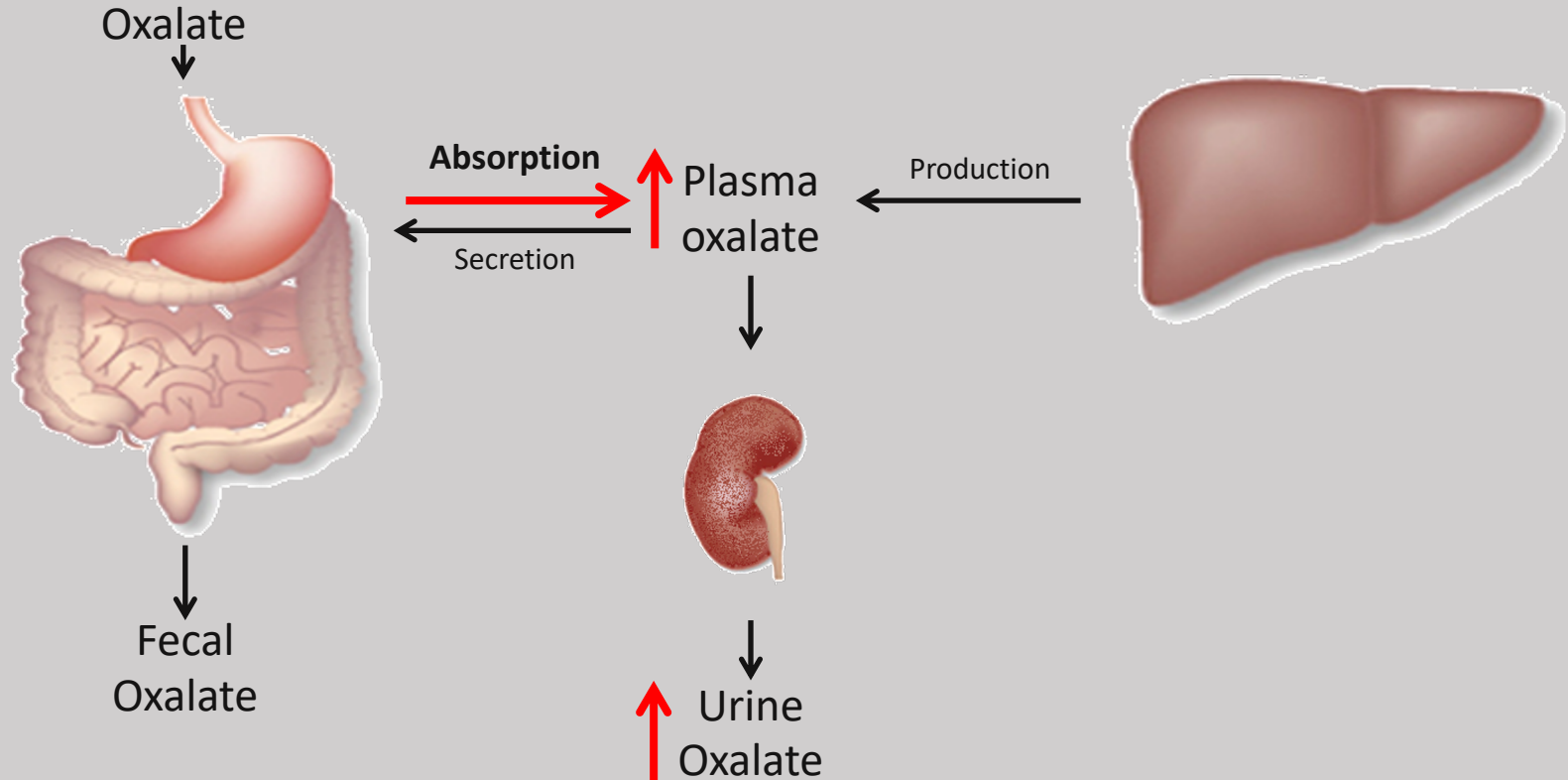
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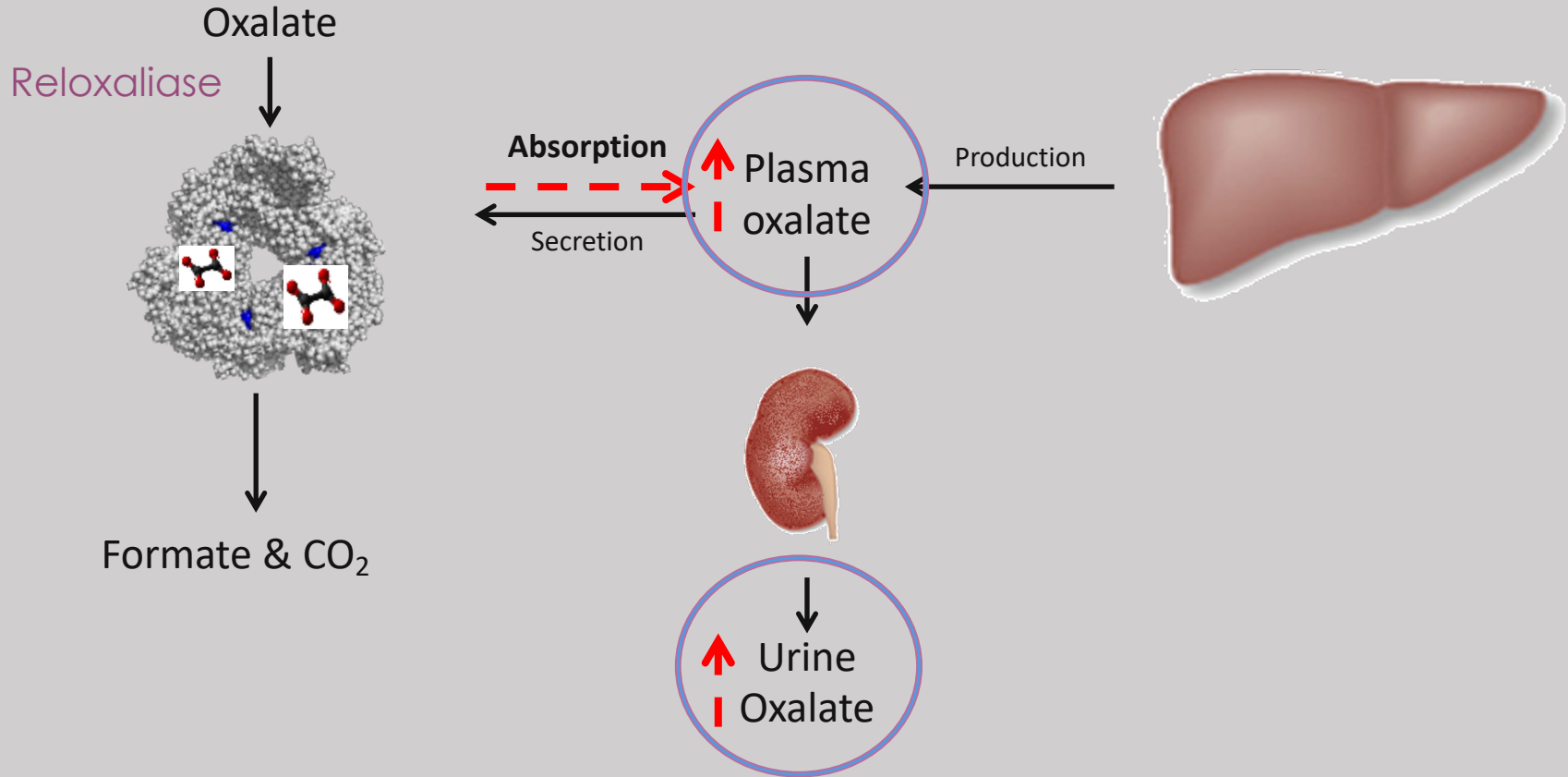
Pathophysiology of hyperoxaluria



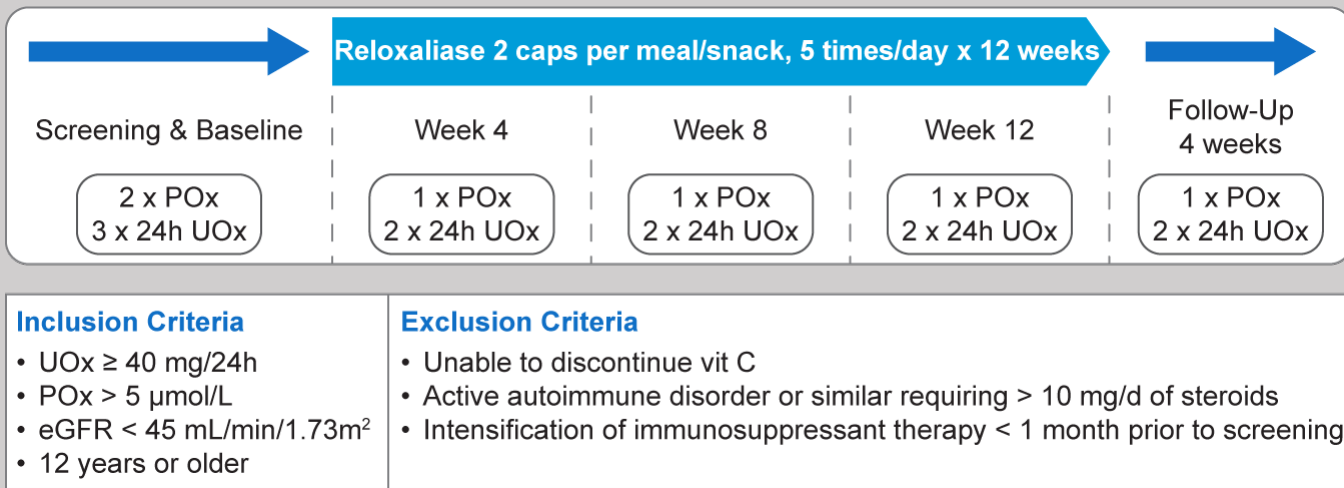
Enteric Hyperoxaluria and CKD



Oral reloxaliase degrades oxalate in the GI tract



Phase 2 Study in patients with EH and CKD



Objective: Examine potential to reduce plasma oxalate (POx) and urine oxalate (UOx)

Efficacy analyses :

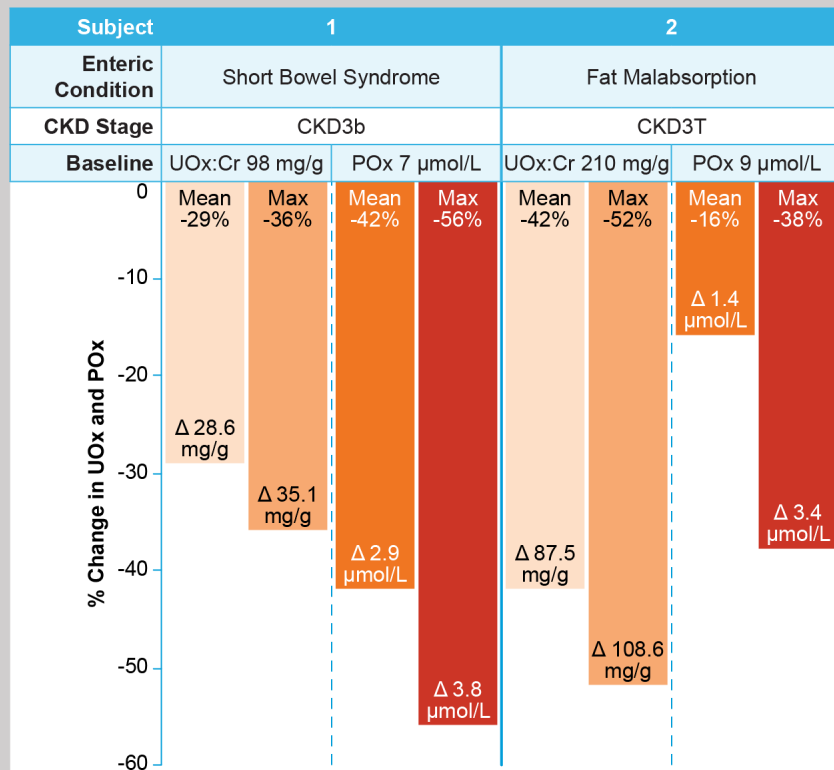
- Change from baseline to the average of Weeks 4-12
- Maximal reduction (based on lowest achieved on-treatment value)
- *UOx = results from 2 collections averaged for each timepoint, and shown as mg/g creatinine*

Additional parameters: change in blood formate and oxalate decarboxylase

Study Demographics

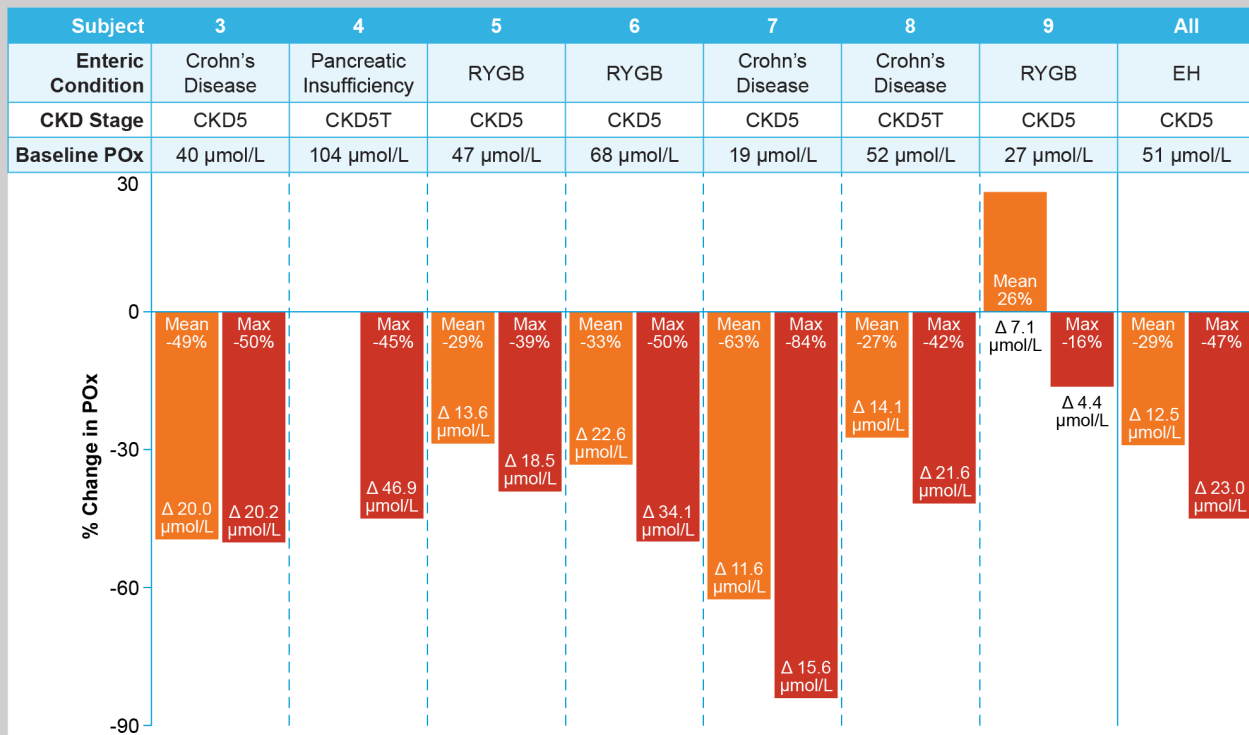
Parameters	EH-CKD Stage 3-5 (n = 10)	EH-CKD Stage 3-4 (n = 3)	EH-CKD Stage 5 (n = 7)
Age (years) Mean (SD)	63.7 (9.1)	71.3 (5.0)	60.4 (8.6)
Gender Female/Male	3/7	2/1	1/6
Race White/Caucasian American Indian/Asian	9 1	3 0	6 1
BMI Mean (SD)	25.0 (6.6)	23.5 (4.0)	25.6 (7.6)
Type of EH Bariatric surgery Short Bowel Syndrome Fat Malabsorption Crohn's Disease Pancreatic Insufficiency	4 1 1 3 1	1 1 1 - -	3 - - 3 1
History of Kidney Stones	5	2	3
Kidney stone episodes in last 5 years Mean (SD)	32.3 (94.2)	3.7 (5.5)	44.6 (112.7)
Transplant status Post-transplant	3	1	2
Urinary Oxalate (mg/gCr) Mean (SD) Median	-	137.3 (62.9) 104.0	-
Plasma Oxalate (μmol/L) Mean (SD) Median	37.8 (31.6) 33.9	6.9 (2.1) 6.8	51.1 (28.5) 47.0

Reloxaliase reduces UOx and POx in patients with CKD stage 3



Δ = Difference between baseline and mean/max on a treatment

Reloxaliase reduces POx in patients with CKD stage 5



Δ = Difference between baseline and mean/max on a treatment

Subject 6 was not on dialysis, subject 2 had only one blood sample collected on the treatment

Reloxaliase is well tolerated

Adverse Events (AEs)	Subjects (n = 10)	Events (n)
Any treatment-emergent adverse events (TEAEs)	10	38
Any related TEAEs	2	5
Any treatment-emergent serious AE	3	3
Any related emergent serious AE	0	0
Any TEAE resulting in study drug discontinuation	1	1

- Although all subjects reported at least 1 AE, most were mild to moderate and not related to study drug
- The most commonly reported AEs were gastrointestinal complaints: diarrhea and nausea in 2 subjects each
- The remainder of GI AEs were reported by only 1 subject
- There was no formate accumulation, and lack of OxDc absorption was demonstrated

Conclusion

- Oral reloxaliase therapy results in a substantial reduction in both POx and UOx in enteric hyperoxaluria subjects with CKD 3-5
- Adverse events were mild and mostly GI related
- The study represents an important first step in characterizing a new therapeutic approach for patients with enteric hyperoxaluria and CKD