FRI-141

Lanthanum Dioxycarbonate Effectively Reduces Urinary Phosphate Excretion in Healthy Volunteers

Pramod Gupta[1], PhD; Atul Khare[1], PhD; Guru Reddy[1], PhD; Shalabh Gupta[1], MD
[1]Unicycive Therapeutics, Inc

BACKGROUND

- About 600K kidney failure patients in the US undergo dialysis[1]
- Over 43% of these patients have phosphate (P) >5.5 mg/dL, leading to an increased risk of death[2]
- Patients usually rely on dietary restriction and phosphate binders to avoid hyperphosphatemia
- Current P binders often do not achieve normal levels of P and have a high pill burden due to large and high quantity of pills[4,5]
- A treatment that reduces pill burden while maintaining efficacy would improve patient adherence and quality of life and may be more likely to achieve P goals
- Currently available 3,000 mg/day lanthanum carbonate effectively reduces urinary P excretion by 236-468 mg/day[6]
- Lanthanum dioxycarbonate (LDC), RENAZORB™, is a novel nanotechnology product that combines lanthanum, which has the highest binding capacity vs. other P binders,[7] with a potentially smaller pill size that is swallowed with water rather than chewed

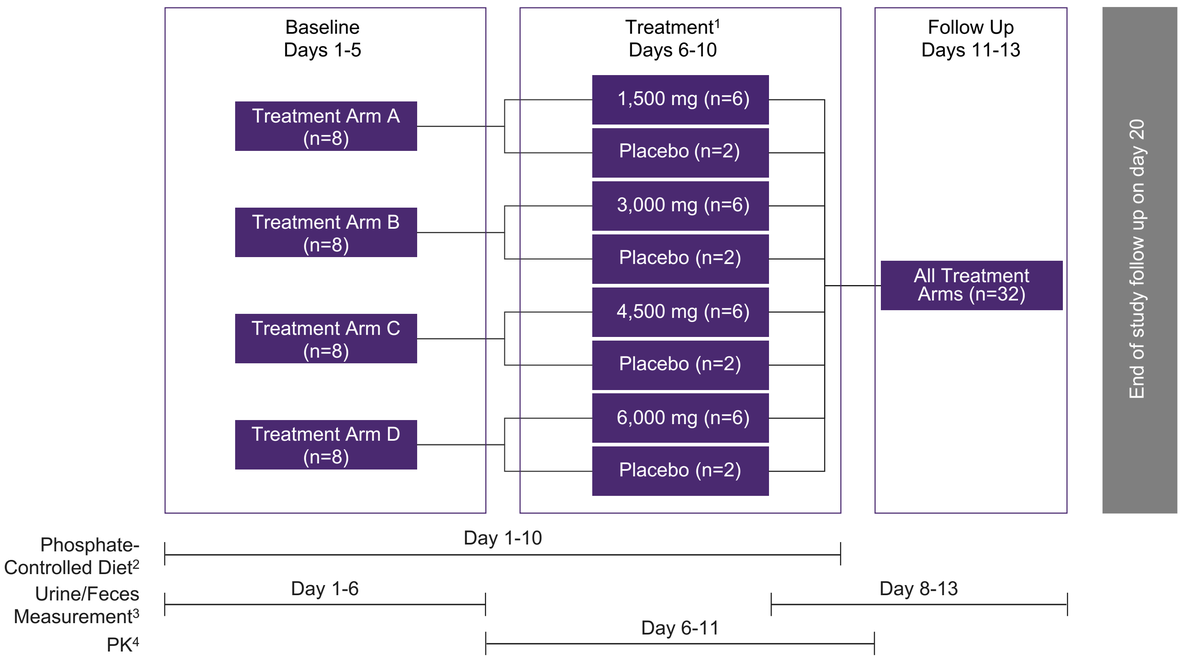
OBJECTIVE

We present results of a phase 1 study evaluating LDC's P binding capacity and tolerability

METHODS

- A phase 1, double-blind, placebo-controlled study evaluated LDC's P binding capacity and tolerability in 4 treatment arms of 8 healthy adults
- Four separate LDC doses of 500 mg tablets were administered after meals for 5 days: 1,500, 3,000, 4,500, and 6,000 mg/day **(Figure 1)**

Figure 1. Unicycive Phase 1 Study Design

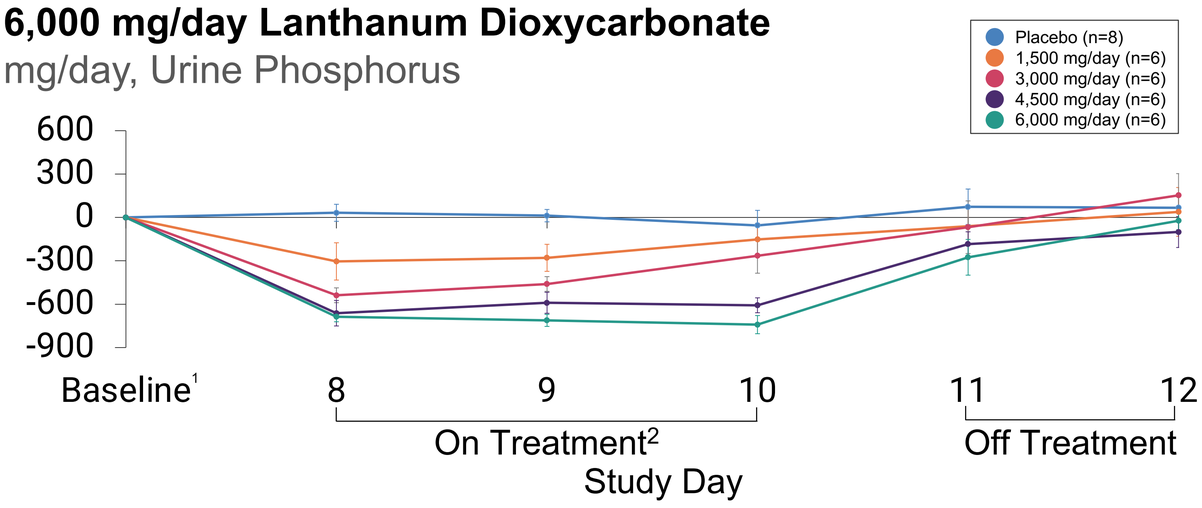


1 The subjects received lanthanum dioxycarbonate or placebo within 15 minutes after each of the 3 main meals
2 Designed to provide 37.5 mmol (1,200 mg) of elemental phosphorus per day (3 meals and 1 snack)
3 24-hour urine and feces was collected at each voiding and pooled in separate containers for baseline phosphorus content
4 Venous blood samples for determination of serum concentrations of lanthanum were drawn starting on day 6 at the following time points: 0 (within 1 hour pre-dose), 1, 2, 4, 7, 11, 24, 48, 72, 96, and 120 hours after first dose and ending on day 11

RESULTS

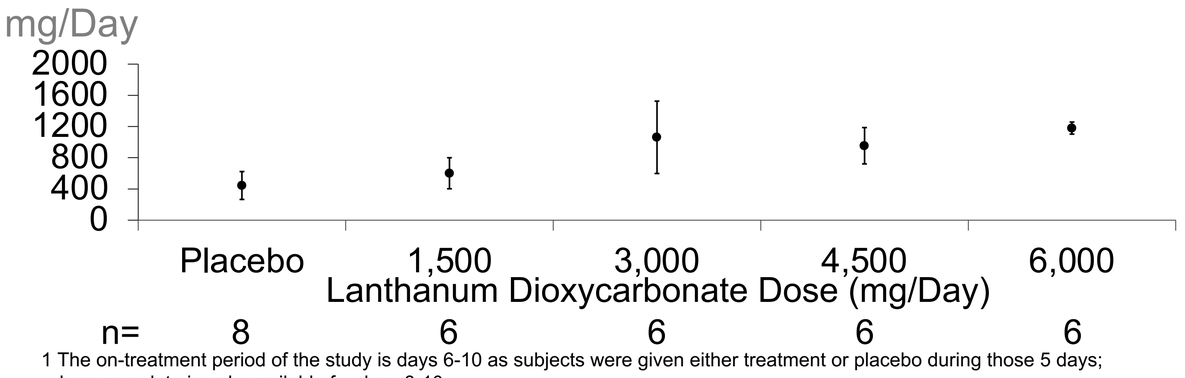
- All doses reduced the amount of P excreted in urine **(Figure 2)** and increased the amount excreted in feces **(Figure 3)**
- LDC showed statistically significant mean reduction in urine P excretion with 3,000 mg/day (p=0.0004), 4,500 mg/day (p<0.0001), and 6,000 mg/day (p=0.0001)
- Mean overall change in urine P excretion showed a statistically significant dose-response trend (p<0.01) **(Figure 4)**
- All treatment-related adverse events (AEs) were mild
- There were no severe/life-threatening AEs, serious AEs, deaths, or AEs leading to discontinuation **(Table 1)**
- Systemic absorption of lanthanum was minimal and dose-proportional
- Of 384 serum samples, only 53 (13.8%) had measurable lanthanum concentrations (above the assay lower limit of quantification: 0.5 ng/mL)

Figure 2. Mean (±SE) Urine Phosphorus Change from Baseline[1]: Placebo vs. 1,500, 3,000, 4,500, and 6,000 mg/day Lanthanum Dioxycarbonate



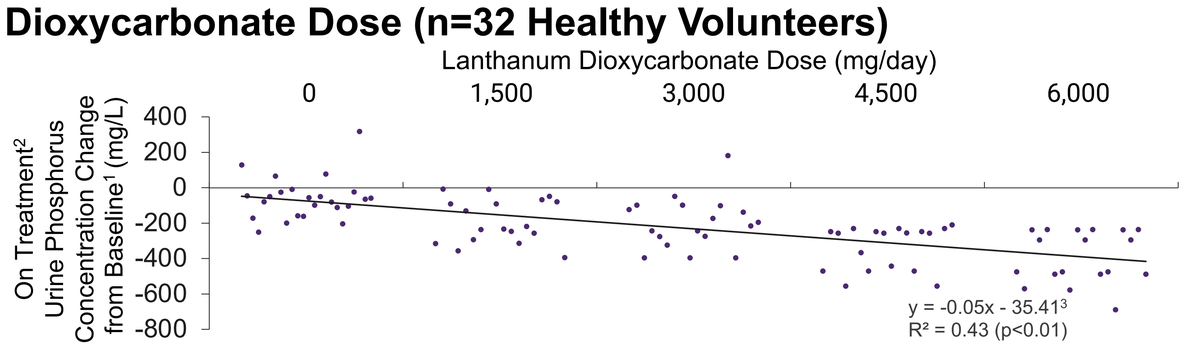
1 Baseline is the mean of phosphorus concentrations from study day 1 to day 5
2 The on-treatment period of the study is days 6-10 as subjects were given either treatment or placebo during those 5 days; however, data is only available for days 8-10
Note: Urine phosphorus concentrations for each day is recorded on the morning of the following day at a 24-hour interval; Phosphorus values <LLOQ are imputed as 0

Figure 3. Mean (±SE) On-Treatment[1] Fecal Phosphorus Excretion by Lanthanum Dioxycarbonate Dose



1 The on-treatment period of the study is days 6-10 as subjects were given either treatment or placebo during those 5 days; however, data is only available for days 8-10

Figure 4. Correlation Between On Treatment[2] Urine Phosphorus Concentration (Change from Baseline[1]) and Lanthanum Dioxycarbonate Dose (n=32 Healthy Volunteers)



1 Baseline is the mean of phosphorus concentrations from study day 1 to day 5
2 The on-treatment period of the study is days 6-10 as subjects were given either treatment or placebo during those 5 days; however, data is only available for days 8-10
3 Linear regression was used to plot the fitted line
Note: Urine phosphorus concentrations for each day are recorded on the morning of the following day at a 24-hour interval

Table 1. Overall Summary of Adverse Events by Treatment Group

Number (Percent) of Patients

		RENAZORB™ (mg/Day)				
		1,500 (n=6)	3,000 (n=6)	4,500 (n=6)	6,000 (n=6)	Placebo (n=8)
Adverse Events (AE)		2	10	8	14	4
Subjects with at Least One AE		2(33.3)	6(100.0)	3(50.0)	5(83.3)	3(37.5)
Subjects with AE by Severity Grade	Mild	1(16.7)	6(100.0)	3(50.0)	5(83.3)	3(37.5)
	Moderate	1(16.7)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Subjects with AE by Relationship to Study Drug	Related	1(16.7)	4(66.7)	2(33.3)	4(66.7)	2(25.0)
	Not Related	1(16.7)	2(33.3)	2(33.3)	2(33.3)	2(25.0)
Outcome	Not Recovered /Not Resolved	1(16.7)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
	Recovered /Resolved	1(16.7)	6(100.0)	3(50.0)	5(83.3)	3(37.5)

CONCLUSIONS

- LDC was effective in binding to dietary P and the efficacy was dose proportional
- It was well tolerated, with minimal systemic absorption of lanthanum

IMPLICATIONS

LDC may be a welcome choice for patients as it is effective and is a small swallowable pill

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