Effects of Oxylanthanum Carbonate in Patients Receiving Maintenance Hemodialysis with Hyperphosphatemia

Geoff A. Block[1], MD; Glenn M. Chertow, MD, MPH[2]; Guru Reddy, PhD[3]; Sanjay Mourya[3]; Martha Block[1]; Steven J. Hasal, PhD[3], Shalabh Gupta, MD[3], Pablo E. Pergola, MD, PhD[4]

[1]US Renal Care, San Antonio, TX, 78211; [2]Stanford University School of Medicine, Stanford, CA, 94305; [3]Unicycive Therapeutics, Inc, Los Altos, CA, 94022; [4]Renal Associates, PA, San Antonio, TX, 78212

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BACKGROUND

- In healthy individuals, serum phosphate (sP) concentrations are maintained within a relatively narrow range
- Renal tubular reabsorption of phosphate is reduced in patients with impaired kidney function
- Three primary phosphate control strategies are available—restricting dietary phosphate intake, enhancing phosphate elimination through more frequent or longer duration hemodialysis sessions, and using oral phosphate lowering therapy
- Oxylanthanum carbonate (OLC) is a novel compound being developed for the treatment of hyperphosphatemia in patients with ESRD that utilizes proprietary nanoparticle technology

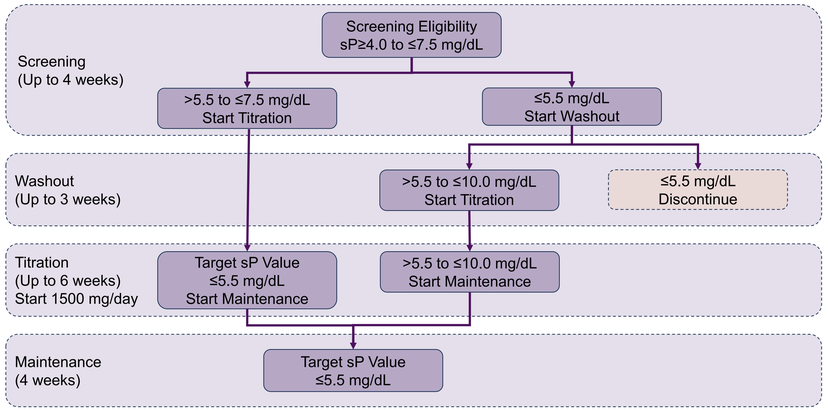
STUDY PURPOSE

- We conducted this study to assess the tolerability of and safety of OLC at doses that achieve satisfactory control of sP (≤5.5 mg/dL) in patients with CKD on hemodialysis receiving maintenance therapy for hyperphosphatemia

STUDY DESIGN

- This was a Phase 2, open-label, single-arm, multicenter, multidose study in adult patients with CKD with hyperphosphatemia receiving maintenance hemodialysis
- After an up to 4-week Screening Period, the trial was divided into three parts: a washout period (1 to 3 weeks), a 6-week, open-label, dose-titration period, and a 4-week, open-label, maintenance period (**Figure 1**).
- The study was designed to enroll approximately 90 patients to have 60 evaluable patients who entered the maintenance period; the number of patients was not based on statistical assumptions.
- Once weekly, we assessed tolerability based on the incidence of discontinuations due to treatment-related adverse events/adverse drug reactions (ADRs) and laboratory panel, including sP, was performed. At the end of the study, patients reinitiated their prior phosphate binder therapy.
- We defined baseline as the last measurement prior to the first dose of study drug.
- We assessed safety based on reported/elicited AEs, clinical laboratory assessments, vital signs, 12-lead electrocardiograms, and physical examinations.
- Patients were considered evaluable if their sP was ≤5.5 mg/dL at the end of titration and received at least one dose of OLC in maintenance.

Figure 1. Serum Phosphate/OLC Dose Flow Chart



RESULTS

- Baseline demographics were typical of the target population (**Table 1**).
- 128 patients were screened, and 86 patients received at least one dose of OLC in titration. 78 patients entered maintenance of whom 71 were evaluable and 7 were not evaluable but followed for safety.
- Most TEAEs were mild to moderate in severity (**Table 2**)
- There were no deaths. Five patients with SAEs, but none were assessed as related to OLC and 5 patients discontinued due to AEs, but only 3 were due to ADRs.

Table 1. Baseline Demographics (N=86)

Adverse Event Term	(N=86)
Age (years)	
Mean (SD)	62.4 (10.71)
Sex (male, n, %)	47 (54.7)
Race, n (%)	
White	57 (66.3)
Black or African American	18 (20.9)
American Indian or Alaska Native	8 (9.3)
Other	3 (3.5)
Ethnicity	
Hispanic or Latino	34 (39.5)
Previous Phosphate Lowering Therapy [a], n (%)	
Sevelamer	45 (52.3)
Calcium Acetate	17 (19.8)
Ferric Citrate	13 (15.1)
Sucroferric Oxyhydroxide	12 (14.0)
Tenapanor	1 (1.2)

a) Two patients had been taking two phosphate lowering therapies.

Table 2. Summary of Adverse Events

	Treatment-Emergent Adverse Event	Adverse Drug Reactions
Patients with Any Adverse Event	30 (34.9)	15 (17.4)
Mild	16 (18.6)	8 (9.3)
Moderate	8 (9.3)	5 (5.8)
Severe	6 (7.0)	2 (2.3)
Patients with Treatment-Emergent SAEs	5 (5.8)	0
Patients with TEAEs Leading to Discontinuation	5 (5.8)	3 (3.5)
Patients with TEAE Leading to Death	0	0
Common Adverse Events (≥5% patients)		
Diarrhea	10 (12)	8 (9)
Vomiting	5 (6)	5 (6)

RESULTS Cont.

- Most patients (69%) who achieved the target sP did so with ≤1500 mg/day (**Figure 2**).
- The percent of patients with sP≤5.5 mg/dL increased from 59% at Screening to 91% at the end of titration (**Figure 3**).

Figure 2. Dose to Achieve sP≤5.5 mg/dL (N=71)

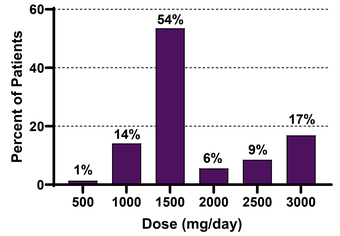
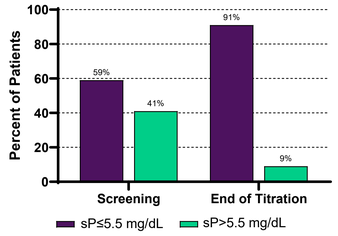


Figure 3. sP ≤5.5 mg/dL at Screening vs End of Titration (N=78)



CONCLUSIONS

- OLC was safe and well-tolerated with ADRs commonly seen in this patient population and with other P binders.
- Use of OLC enabled adequate control of serum phosphate in >90% of patients who entered maintenance.

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