Effects of Oxylanthanum Carbonate in Patients Receiving Maintenance Hemodialysis with Hyperphosphatemia

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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

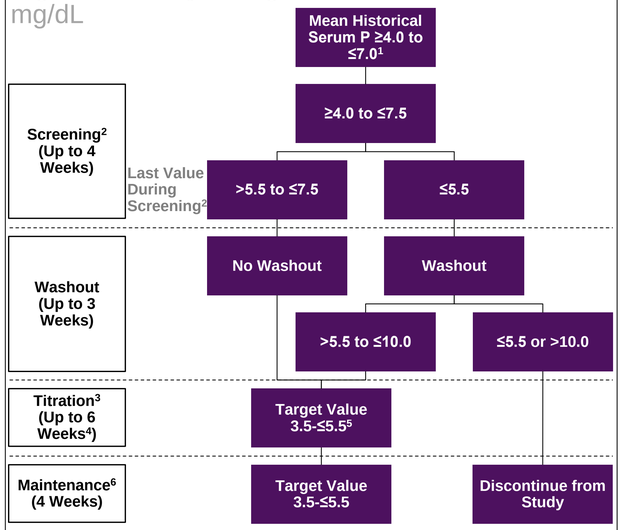
- This was a Phase 2, open-label, single-arm, multicenter, multidose study in adult patients with CKD with hyperphosphatemia receiving maintenance hemodialysis
- After an up to 4-week Screening Period, the trial was divided into three parts: a Washout Period (1 to 3 weeks), a 6-week, open-label, Dose-Titration 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

STUDY DESIGN CONT.

- Once weekly, we assessed tolerability based on the incidence of discontinuations due to treatment-related adverse events (AEs)/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. Study Design

mg/dL



1 Eligible patients had mean historical serum phosphate ≥4.0 to ≤7.5mg/dL while on their current phosphate binder for at least 8 weeks prior to Screening
2 Screening assessments were performed within 4 weeks prior to the Washout Period
3 Starting dose 500 mg TID to maximum dose 1,000 mg TID or 1,500 mg BID
4 Doses were titrated every 2 weeks until patients reached the target serum phosphate range (≤5.5mg/dL), up to 6 weeks
5 Patients whose serum phosphate was still >5.5mg/dL at the end of 6 weeks of titration continued titration during Maintenance Period based on Investigator's judgment
6 Safety analysis and renal panel, including phosphate concentrations, were evaluated every week; Patients reinitiated their prior standard therapy on the day after the last dose of OLC

RESULTS

- Baseline demographics were typical of the target population (**Table 1**)
- 128 patients were screened, and 86 patients received ≥1 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 2)**

Table 1. Baseline Demographics (n=86)

Characteristics		Safety Population
Age (Years)	Mean (SD)	62 (10.7)
Gender, n (%)	Male	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, n (%)	Hispanic or Latino	34 (39.5)
Phosphate Binder[1], n (%)	Sevelamer	45 (52.3)
	Calcium Acetate	17 (19.8)
	Ferric Citrate	13 (15.1)
	Sucroferric Oxyhydroxide	12 (14.0)
	Tenapanor	1 (1.2)

1 Two patients had been taking two phosphate lowering therapies

Table 2. Summary of Adverse Events

Number of Patients (%)

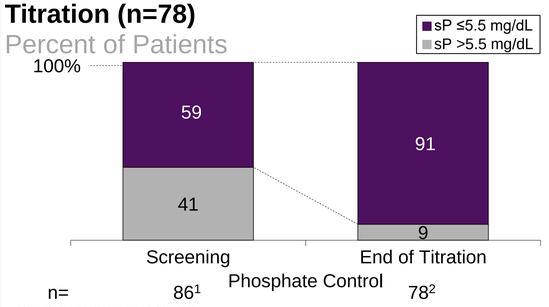
		Treatment-Emergent AEs	Treatment-Related AEs
Any AEs		30 (34.9)	15 (17.4)
Severity	**Mild**	16 (18.6)	8 (9.3)
	Moderate	8 (9.3)	5 (5.8)
	Severe	6 (7.0)	2 (2.3)
Serious AEs		5 (5.8)	0 (0.0)
Led to Discontinuation		5 (5.8)	3 (3.5)
Led to Death		0 (0.0)	0 (0.0)
Common AEs (≥5%)	**Diarrhea**	10 (11.6)	8 (9.3)
	Vomiting	5 (5.8)	5 (5.8)

RESULTS CONT.

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

Figure 2. sP ≤5.5 mg/dL at Screening vs End of Titration (n=78)

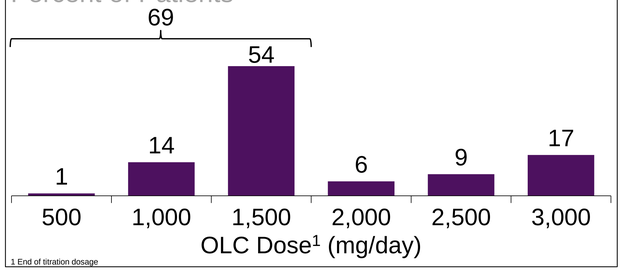
Percent of Patients



1 Patients with serum phosphate levels before washout
2 Patients who are in the study by the end titration (excludes patients who discontinued during titration)

Figure 3. Dose to Achieve sP ≤5.5 mg/dL (n=71)

Percent of Patients



1 End of titration dosage

CONCLUSIONS

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

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