

A Phase 2 Clinical Trial of Oxylanthanum Carbonate in Patients Receiving Maintenance Hemodialysis with Hyperphosphatemia

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Key Points

- Oxylanthanum carbonate (OLC) was well tolerated with fewer than 10% of patients stopping treatment due to side effects.
- More than 90% of patients with hyperphosphatemia taking OLC achieved effective phosphate control.
- Two thirds of patients required three or fewer OLC tablets per day to control serum phosphate.

Abstract

Background In patients with kidney failure receiving maintenance dialysis, hyperphosphatemia is managed by dietary phosphate restriction and the provision of phosphate binders. Oxylanthanum carbonate (OLC) is a phosphate binder in development with high potency and formulated in a small pill swallowed whole.

Methods We conducted a phase 2, open-label, single-arm, multicenter trial in adult patients receiving maintenance hemodialysis with hyperphosphatemia. The primary objective was to evaluate the tolerability of OLC at clinically effective doses with a goal serum phosphate (sP) concentration ≤ 5.5 mg/dl. The trial included washout, titration, and maintenance periods. Eligible patients had sP ≥ 4.0 and ≤ 7.0 mg/dl for at least 8 weeks before screening while receiving thrice weekly hemodialysis and a stable phosphate binder regimen. Patients started titration when sP was > 5.5 mg/dl and entered maintenance once sP was ≤ 5.5 mg/dl. The starting dose of OLC during titration was 1500 mg/d (500 mg thrice daily). We assessed tolerability on the basis of the incidence of discontinuations due to treatment-related adverse events (TRAEs).

Results Eighty-six patients were treated with OLC during the study. At screening, sP was ≤ 5.5 mg/dl in 51 (59%) patients. Seventy-eight (91%) patients entered maintenance, and 71 (91%) patients achieved sP ≤ 5.5 mg/dl on a median OLC dose of 500 mg three times a day. The most common TRAEs were gastrointestinal and included diarrhea (9%) and vomiting (6%); all other TRAEs were reported in $< 5\%$ of patients. Three (4%) patients discontinued drug due to TRAEs. Minimal to no systemic absorption of lanthanum was observed after administration of OLC 1000 mg thrice daily.

Conclusions In this open-label phase 2 trial, OLC was well tolerated and enabled sP control in $> 90\%$ of patients with a low pill burden (two thirds of patients receiving three or fewer tablets/day).

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Introduction

More than half of patients who receive hemodialysis experience hyperphosphatemia, defined as serum phosphate (sP) concentration >4.5 mg/dl.¹ Hyperphosphatemia is associated with vascular, valvular, and myocardial calcification and increased risks of all-cause and cardiovascular mortality.^{2–9} sP concentrations within or near the population reference range are associated with enhanced survival⁸ and delayed progression of coronary artery calcification and bone disease.^{2,6} Although the Kidney Disease: Improving Global Outcomes 2017 guidelines recommend lowering phosphate levels “toward the normal range” of 2.5–4.5 mg/dl in patients with CKD stages G3a–G5D, achieving this target is often impractical in hemodialysis populations due to severe phosphate retention, dietary limitations, and the pill burden associated with binder therapy. Most clinicians recognize that a target of ≤ 5.5 mg/dl offers a realistic balance between efficacy, safety, and adherence, and it is incorporated as a goal into most dialysis clinic protocols.

An ideal phosphate binder would combine high phosphate-binding capacity with minimal systemic absorption, excellent safety and tolerability, low pill burden, and improved convenience (small tablet size, swallowed whole rather than chewed). Oxylanthanum carbonate (OLC) is a lanthanum-based phosphate binder in development for the treatment of hyperphosphatemia in patients with ESKD that uses proprietary nanoparticle technology and has a lower mol wt than lanthanum carbonate. The nanoparticle technology results in OLC tablets having higher surface area with greater porosity, allowing for improved dissolution in the gastrointestinal tract, rendering more lanthanum available for phosphate binding throughout the gastrointestinal tract compared with lanthanum carbonate. Moreover, 500 mg OLC is formulated as a round tablet, 12 mm in diameter, with a total volume of 0.35 cm³, and is swallowed whole. In contrast, 500 mg chewable lanthanum carbonate tablets are 20 mm in diameter, with a total volume of 1.33 cm³.¹⁰

In this study, we aimed to assess the tolerability of OLC at clinically effective doses, defined as those that achieve and maintain sP concentrations ≤ 5.5 mg/dl.

Methods

Patients

Men and women 18 years or older at screening were eligible for participation if they were undergoing thrice weekly maintenance hemodialysis for at least 12 weeks, had mean sP 4.0–7.0 mg/dl inclusive while on phosphate binders over the prior 8 weeks, sP 4.0–7.5 mg/dl inclusive during screening, no change to their prescription for calcimimetic agents or vitamin D receptor activators over the prior 4 weeks, and single-pool $K_t/V_{\text{urea}} \geq 1.2$ at the most recent assessment before screening. Key exclusion criteria included treatment with a lanthanum-based phosphate binder over the prior 8 weeks, serum intact parathyroid hormone concentration >1500 pg/ml over the prior 3 months, or history of inflammatory bowel disease, irritable bowel syndrome with diarrhea, malabsorption syndrome, or a recent procedure affecting gastrointestinal function.

Study Design

We conducted the trial at seven centers in the United States between December 2023 and May 2024. OLC was supplied as immediate-release tablets containing 665.60 mg OLC equivalent to 500 mg elemental lanthanum as the active ingredient (hereafter referred to as 500 mg OLC tablets). We selected OLC doses on the basis of results from a first-in-human study of OLC¹¹ along with the development program of, and clinical experience with, lanthanum carbonate. All tablets were swallowed whole with or immediately after meals/snacks up to three times a day. Because the study's aim was to assess OLC tolerability at effective doses, dietary counseling was not provided beyond usual care, and no controlled diet was mandated.

This trial was conducted in accordance with the Declaration of Helsinki. All patients provided written informed consent before trial entry. All participating sites obtained independent ethics committee/institutional review board approval. The trial was registered with ClinicalTrials.gov (NCT06218290).

Procedures

Patients were assessed weekly for up to a total of 17 weeks (Supplemental Figure 1). After an up to 4-week screening period, the trial included three phases: a washout period (1–3 weeks), an open-label titration period (up to 6 weeks), and a 4-week open-label maintenance period.

Washout Period (1–3 Weeks)

Patients stopped taking their previously prescribed phosphate binders. Patients whose sP did not rise to >5.5 mg/dl within this period were discontinued from the trial. Patients with screening sP >5.5 to ≤ 7.0 mg/dl entered titration directly without washout ($N=35$).

Titration Period (up to 6 Weeks)

Once sP >5.5 mg/dl was reached, patients initiated the titration period ($N=86$). For the first 2 weeks of the titration period, all patients were treated with 1500 mg/d OLC (500 mg thrice daily with meals/snacks). OLC doses were adjusted every 2 weeks up to a maximum of 3000 mg/d until patients reached the target sP ≤ 5.5 mg/dl. Investigators could titrate OLC doses more often if it was deemed necessary for patient safety. Patients who achieved sP ≤ 5.5 mg/d earlier than 6 weeks advanced to the maintenance period. Patients whose sP remained >5.5 mg/dl at the end of 6 weeks of titration continued titration during the maintenance period if they had not reached the maximum dose or continued at the maximal dose based on the investigator's judgment. A subset of 14 patients was treated with 3000 mg/d for the first 2 days for pharmacokinetic (PK) assessment. After six doses, these patients resumed titration with 1500 mg/d.

Maintenance Period (4 Weeks)

The dose of OLC that lowered sP to ≤ 5.5 mg/dl was identified for each patient during the titration period and was continued during the maintenance period (“clinically effective dose”). Dose modifications were allowed during the maintenance period based on sP and safety. After

2 weeks, patients with sP >5.5–6.0, >6.0–6.5, or >6.5 mg/dl had their OLC dose increased by 500–1500 mg/d up to a maximum dose of 3000 mg/d (either 1000 mg thrice daily or 1500 mg twice daily). If patients had two consecutive sP \geq 10 mg/dl, they were to be withdrawn from the study and resume usual care. The OLC dose was reduced by 500 mg/d for patients with sP <4.0 mg/dl, and OLC was withheld for patients with sP <3.5 mg/dl until sP rose above 4.0 mg/dl. Treatment was then resumed at the lowest of either 1000 or 500 mg/d below the last dose taken before pausing OLC treatment.

Study Objectives and Assessments

We assessed tolerability weekly based on the incidence of discontinuations due to treatment-related adverse events (TRAEs). sP was assessed weekly. At the end of the study, patients reinitiated their prior phosphate binder therapy.

The primary objective was to evaluate the tolerability of clinically effective doses of OLC. The primary end point for tolerability was the incidence of discontinuations due to TRAEs. We defined “baseline” as the last laboratory measurement before the first dose of study drug.

Safety Outcomes and Assessments

We assessed safety based on reported/elicited treatment-emergent adverse events (TEAEs), vital signs, physical examinations, and clinical laboratory assessments, including kidney function panel, and sP. Serial immunoreactive parathyroid hormone values were not collected.

The assessment of TEAEs included serious adverse events (AEs), TEAEs leading to study drug discontinuation, and TRAEs, based on the investigators' assessment. We used the Medical Dictionary for Regulatory Activities version 26.0 for assigning System Organ Class and Preferred Term. Before discontinuing a patient for a TEAE, we attempted a reduction in the dose of OLC for symptom management.

PKs

A secondary objective was to assess OLC PKs. We drew PK blood samples on all subjects for sparse PK sampling on the first day of each period beginning with the washout period and at the end-of-study visit.

A subset of 14 patients had additional PK blood samples drawn for intensive PK analysis on day 1 of titration. These patients received OLC 1000 mg thrice daily for the first 2 days. We drew PK samples predose and at 1, 2, 4, 6, 12, 24, and 48 hours after the first dose of OLC. These 14 patients were required to take all three doses of study drug each day.

We measured serum lanthanum concentrations using a validated inductively coupled plasma tandem mass spectrometry assay with a lower limit of quantitation of 0.5 ng/ml. We imputed values below the lower limit of quantification (LLOQ) as 0. We performed noncompartmental PK analysis using Phoenix WinNonlin software (version 8.3) (Certara) to estimate area under the concentration versus time curve, maximum observed concentration (C_{max}), time of maximum observed sample concentration (T_{max}), and time of final quantifiable concentration (T_{last}).

Patient Satisfaction

As an exploratory objective, we evaluated patient satisfaction with their previously prescribed phosphate binder therapy compared with OLC. Patients completed sponsor-developed questionnaires to assess satisfaction, perceived pill burden, and adherence to treatment. We administered patient satisfaction surveys at the screening visit (reflecting their previously prescribed phosphate binder therapy) and at the end-of-study visit (reflecting their use of OLC; [Supplemental Material](#)).

Statistical Analysis

This trial was not powered to test a specific hypothesis, and the sample size was not based on statistical assumptions. Approximately 70% of patients were expected to achieve target sP \leq 5.5 mg/dl within the 6-week titration period with OLC. We planned to enroll approximately 90 patients to have at least 60 evaluable patients who entered the maintenance period. The evaluable population included all patients who achieved target sP and received at least one dose of OLC in the maintenance period. The safety population, which consisted of all patients who received at least one dose of OLC, was used for calculating all safety and tolerability results. We conducted all statistical analyses using SAS version 9.3 or later (SAS Institute, Cary, NC).

Results

Patient Disposition and Baseline Characteristics

As shown in [Figure 1](#), 128 patients were screened, and 106 patients were enrolled. Of these, 71 patients entered the washout period, and 35 patients had sP >5.5 to \leq 7.5 mg/dl and immediately entered the titration period. Fifty-one (72%) of 71 patients who entered the washout period continued to the titration period once their sP exceeded 5.5 mg/dl; 20 (28%) patients failed to reach a sP >5.5 mg/dl during washout and were discontinued from the study. The safety population comprised 86 patients who entered the titration period, and the evaluable population comprised 71 patients who achieved sP \leq 5.5 mg/dl by the end of the titration period and received at least one dose of OLC during the maintenance period. The mean (SD) age of patients in the safety population was 63 (\pm 11) years and ranged from 29 to 82; the study sample was 45% women and 34% of non-White race ([Table 1](#)). Seven patients did not achieve phosphate control during titration but continued treatment during the maintenance period. A total of 14 (16%) patients discontinued study participation: 8 patients during the titration period and 6 patients during the maintenance period. Five (6%) patients were discontinued due to TEAEs, 6 (7%) patients withdrew consent (no reason specified), and 3 (4%) patients were discontinued from the study by the investigators: one patient each due to poor adherence, kidney transplantation, and hospitalization. Four of six patients who withdrew consent had a TEAE temporally associated with their dates of withdrawal, but these were all mild in severity.

At study entry, 45 (52%) patients were taking sevelamer, 17 (20%) calcium acetate, and 25 (29%) iron-based binders; two patients were taking a combination of two phosphate binders and one patient was taking tenapanor

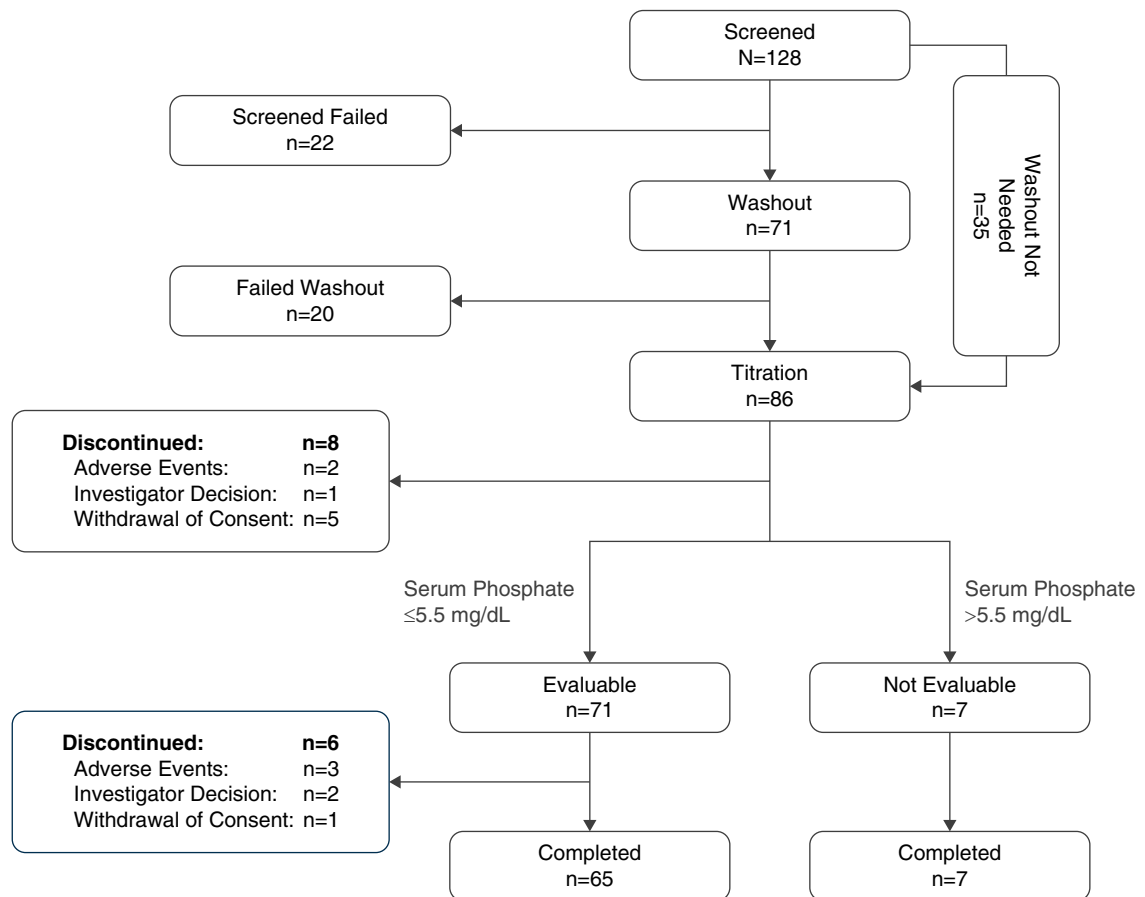


Figure 1. CONSORT diagram. CONSORT, Consolidated Standards of Reporting Trials.

Characteristic	Safety Population (N=86)	Evaluable Population (N=71)	PK Population (N=14)
Age, yr			
Mean (SD)	62.4 (10.71)	62.4 (10.22)	63.9 (10.71)
Median	63	63	63.0
Min, max	29, 82	29, 82	47, 82
Sex, n (%)			
Female	39 (45)	35 (49)	8 (57)
Male	47 (55)	36 (51)	6 (43)
Race, n (%)			
American Indian or Alaska Native	8 (9)	7 (10)	0
Asian	1 (1)	0	0
Black or African American	18 (21)	16 (23)	1 (7)
Other	2 (2)	0	0
White	57 (66)	48 (68)	13 (93)
Ethnicity, n (%)			
Hispanic or Latino	34 (40)	28 (39)	13 (93)
Not Hispanic or Latino	52 (61)	43 (61)	1 (7)
Phosphate binder, n (%)^a			
Sevelamer	45 (52)	36 (51)	7 (50)
Calcium acetate	17 (20)	11 (16)	0
Ferric citrate	13 (15)	11 (16)	3 (21)
Sucroferric oxyhydroxide	12 (14)	12 (17)	4 (29)
Tenapanor	1 (1)	1 (1)	0

Max, maximum; Min, minimum; PK, pharmacokinetic.
^aTwo patients had been taking two phosphate binding medications.

as monotherapy. Other baseline characteristics are presented in Table 1.

The median duration of treatment with OLC was 49 days and ranged from 1 to 71 days in the safety population and 28–71 days in the evaluable population. The median dose of OLC during the maintenance period was 1500 mg/d. Final doses for patients in both populations during the titration period and maintenance period ranged from 500 to 3000 mg/d (Figure 2A).

Study Assessments

SP

The clinical efficacy of OLC to control sP was not the primary objective; rather, we evaluated the tolerability of OLC at a clinically effective doses (*i.e.*, doses that achieved sP ≤ 5.5 mg/dl). As shown in Figure 2B, at the screening visit, sP was adequately controlled (≤ 5.5 mg/dl) for 51 (59%) patients, and the mean sP for all patients was 5.5 mg/dl (range: 4.0–7.5 mg/dl). Thirty-five patients had baseline sP >5.5 to ≤ 7.5 mg/dl (mean sP 6.2 [± 0.5] mg/dl) and immediately started the titration period without washout. The mean screening sP of the remaining 51 patients in the safety population was 4.9 (± 0.4) mg/dl and rose to 6.4 (± 0.8) mg/dl during the washout period.

Of the 78 patients who completed the titration period and started the maintenance period, 71 (91%) patients achieved sP control (≤ 5.5 mg/dl; mean sP 4.7 [± 0.5] mg/dl) during titration with a median dose of 1500 mg/d. Forty-nine (69%) patients achieved sP ≤ 5.5 mg/dl with ≤ 1500 mg/d (≤ 3 tablets/d; Figure 2A). At the end of study, 44 (51%) patients reported taking ≤ 3 OLC tablets/day compared with 23 (27%) patients taking ≤ 3 pretrial phosphate binder tablets/day (Figure 2C).

Safety Assessments

Adverse Events

A summary of TEAEs by treatment population is presented in Table 2. In the safety population, 30 (35%) patients experienced TEAEs. Most TEAEs (19%) were mild in severity, 9% were of moderate severity, and 7% were severe, with each severe TEAE reported in one patient each. Most TEAEs were in the gastrointestinal disorders category (20%), and the only TEAEs reported in more than 5% of patients were diarrhea (12%) and vomiting (6%; Table 3). Most reports of diarrhea and all reports of vomiting were assessed as TRAEs. Patients in the PK subsample were treated with a higher initial dose (3000 mg/d) than other patients for the first 2 days, and 5/14 (36%) of these patients experienced TRAEs. Three events of diarrhea, two events of vomiting, and two events of nausea were reported during the first 2 days of treatment with 1000 mg thrice daily. Five (6%) patients had treatment-emergent serious AEs; none of these were assessed by investigators as treatment related. No deaths occurred during this study (Table 2).

Physical Examination and Laboratory Assessments

There were no consistent changes in observed vital signs or relevant treatment-related changes in hematology or chemistry values over the course of the trial.

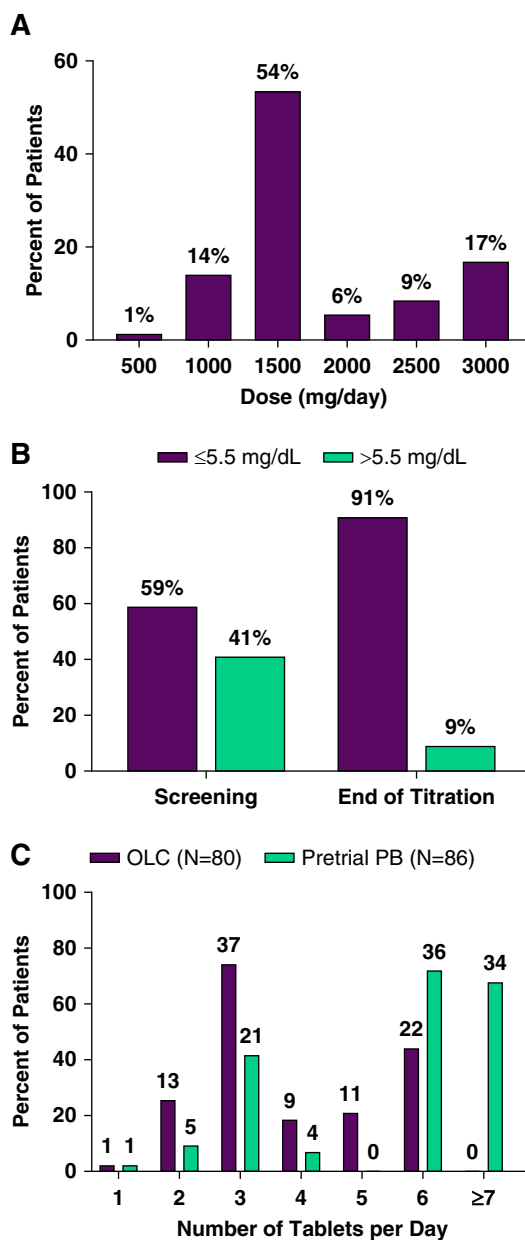


Figure 2. sP control. (A) Doses required for phosphate control (sP ≤ 5.5 mg/dl) with OLC at end of titration (N=71); includes patients whose sP was ≤ 5.5 mg/dl at their last visit during titration. (B) Phosphate control at baseline and at end of titration; the baseline value was the last sP value before washout or before titration if their sP was >5.5 mg/dl during screening. (C) Patient-reported daily PB pill count; pill counts are from patient responses to satisfaction questionnaires (Supplemental Material). OLC, oxylanthanum carbonate; PB, phosphate binder; sP, serum phosphate.

Patient-Reported Outcomes

All 86 patients in the safety population completed the screening questionnaire and 80 patients completed the end-of-study visit questionnaire. At study entry, the median daily pretrial phosphate binder tablet intake was 6 tablets/day with 34% of patients taking ≥ 7 tablets/day (Figure 2C) and 58% of patients reporting consistent adherence to

Table 2. Overall summary of treatment-emergent adverse events

Adverse Event Category	Safety Population (N=86), n (%)	Evaluable Population (N=71), n (%)
Patients with TEAEs		
Patients with any TEAE	30 (35)	22 (31)
Mild	16 (19)	11 (16)
Moderate	8 (9)	7 (10)
Severe	6 (7)	4 (6)
Patients with treatment-emergent SAEs	5 (6)	4 (6)
Patients with TEAEs leading to discontinuation	5 (6)	3 (4)
Patients with TEAEs leading to death	0	0
TRAEs^a		
Patients with any treatment-related AEs	15 (17)	9 (13)
Mild	8 (9)	5 (7)
Moderate	5 (6)	3 (4)
Severe	2 (2)	1 (1)
Patients with treatment-related SAEs	0	0
Patients with treatment-related AEs leading to discontinuation	3 (4)	1 (1)

AE, adverse event; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.
^aRelated=related + possibly related as assessed by the Investigator

treatment (Figure 3C). At study end, the median daily tablet intake for OLC was three tablets/day with 70% of patients reporting that they were consistently adherent to treatment (Figure 3C). More than three quarters (79%) of respondents indicated that they preferred OLC over their pretrial phosphate binders (Figure 3D). More patients expressed satisfaction with OLC treatment (Figure 3A) and reported that OLC was easier to take than their previous phosphate binder (Figure 3B). More details from patient surveys are presented in Supplemental Figures 2 and 3.

PKs

For patients in the safety population, the mean plasma concentration of lanthanum before treatment was 0.079 ng/ml. Systemic absorption of lanthanum was minimal with a mean lanthanum concentration of 0.295 ng/ml at the end of titration and 0.277 ng/ml at the end of study visit. In the subset of 14 patients in the PK subsample, there was minimal to no systemic absorption of lanthanum and serum concentrations were below the LLOQ in 72% of 112 samples. PK summary parameters are presented in Table 4.

Discussion

The primary objective of this study was to assess the tolerability of clinically effective doses of OLC in patients

on hemodialysis with hyperphosphatemia requiring phosphate lowering therapy. Tolerability was measured based on the rate of discontinuations due to TRAEs in the evaluable population during the maintenance period. Demographic and clinical characteristics of trial participants were typical of real-world patient populations in the United States. At screening, the proportion of patients with sP \leq 5.5 mg/dl was 59% and the distribution of sP was consistent with what has been previously reported.¹

A total of five patients discontinued OLC treatment due to AEs. The low discontinuation rate (6%) in this study compares favorably to what has been reported in the package insert for the reference drug, lanthanum carbonate (Fosrenol; 14%),¹² although the sample size in this trial was smaller.

Overall, OLC was generally well tolerated. As has been observed with other phosphate binders,^{5,13} the most common TEAEs were gastrointestinal, including vomiting or diarrhea, which was typically transient and resolved despite continued OLC administration. It should be noted that three of eight patients who experienced treatment-related diarrhea, two of five patients who experienced vomiting, and two of the three patients who experienced nausea were patients in the PK subsample. Unlike those not participating in the PK substudy, who had the dose of OLC titrated up as needed from a starting dose of 500 mg

Table 3. Summary of adverse events in at least two patients (safety population)

Adverse Event Preferred Term	TEAEs (N=86), n (%)	TRAEs ^a (N=86), n (%)
Patients having at least one AE	30 (35)	15 (17)
Diarrhea	10 (12)	8 (9)
Vomiting	5 (6)	5 (6)
Constipation	3 (4)	3 (4)
Nausea	3 (4)	3 (4)
Abdominal distension	2 (2)	2 (2)
Hyperkalemia	2 (2)	0

AE, adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.
^aRelated=related+possibly related adverse events as assessed by the investigator.

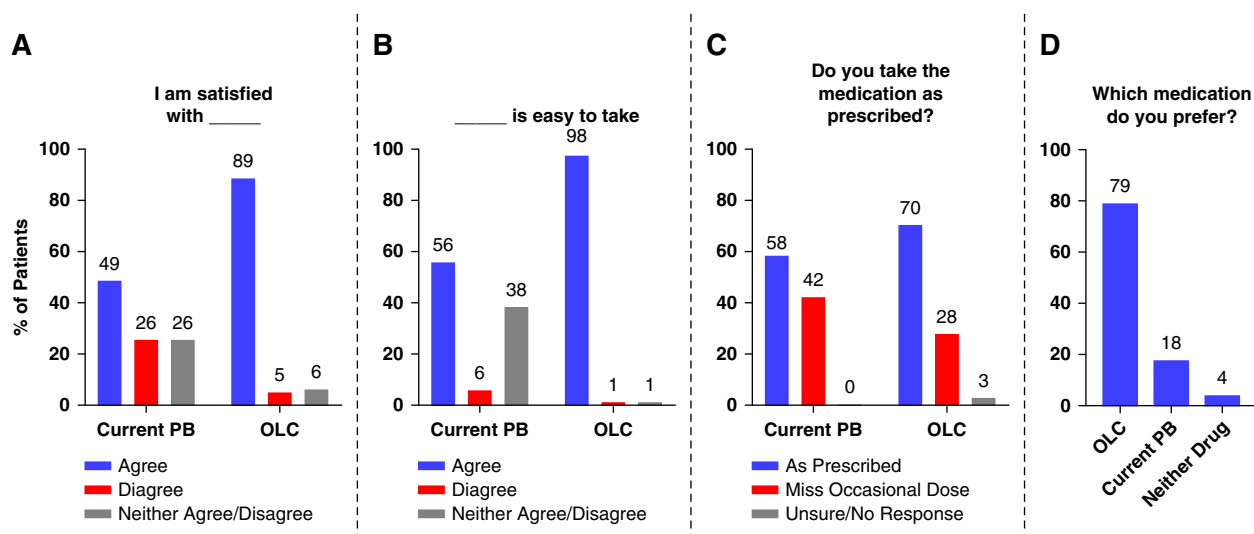


Figure 3. Patient reported outcomes. (A) I am satisfied with my current phosphate binder medication/OLC (B) my current phosphate binder medication/OLC is easy to take. (C) do you take your current phosphate binder medication/OLC as prescribed or do/did you miss doses (for any reason)? (D) based on your experience in this clinical study, do you prefer you current phosphate binder medication or OLC? Current PB (N=86); OLC (N=80). OLC, oxylanthanum carbonate; PB, phosphate binder. Sample patient satisfaction questionnaires are included in the Supplemental Material.

three times a day or 1500 mg/d, patients in the PK study received an initial dose of OLC of 3000 mg/d for the first 2 days of treatment. These findings support the starting dose of OLC used in the non-PK participants of 500 mg three times daily.

Although efficacy was not formally evaluated, the ability of OLC to achieve the goal sP target was integral to determining whether patients were exposed to effective, clinically meaningful drug doses during the study, validating the tolerability findings. According to Kidney Disease: Improving Global Outcomes recommendations,³ the goal of phosphate lowering treatment is to reduce sP toward the population reference range (2.5–4.5 mg/dl); however, many clinicians adopt a less stringent target of 3.5–5.5 mg/dl.² Previous studies evaluating lanthanum carbonate used target sP concentrations <6.0 mg/dl.^{14,15} Thus, the goal sP ≤5.5 mg/dl selected for this study both encompassed prior threshold levels for lanthanum carbonate studies and aligned with clinical practice.

More than 90% of OLC-treated patients achieved sP ≤5.5 mg/dl with a median dose of 1500 mg/d (three pills/day), which is substantially lower than the median number of pills required for the patients' previous phosphate binders (six pills/day). Observational data indicate that patients receiving in-center hemodialysis or peritoneal dialysis who achieve sustained control of sP experience more favorable clinical outcomes than those who do not. Despite the use of one or multiple phosphate binders, typically obligating ingestion of 9–12 or more tablets or capsules per day, most patients on dialysis have sP consistently >4.5 mg/dl.^{1,8,16} Some variability in sP control may be due to patient issues, including differences in enteral phosphate absorption, severity of secondary hyperparathyroidism, interindividual differences in phosphate binder efficacy, and the ability to comply with dietary restrictions or phosphate binder use.¹⁷ Nearly 80% of

patients on dialysis are unable to adhere to their prescribed dosing schedule of phosphate binder treatment.¹⁸ This low adherence stems, at least in part, from the pill burden required for adequate phosphate binding.¹⁹ In addition to the high number of pills needed per day, the need to take pills with meals, issues such as texture and taste with some oral phosphate binders, including lanthanum carbonate, which needs to be chewed completely before swallowing, and gastrointestinal adverse effects contribute to low or incomplete adherence to phosphate binder treatment.^{18,20–24}

In an *in vitro* study comparing OLC with five commercially available phosphate binders, OLC was able to bind 1 g of phosphate with the lowest daily dose volume and the smallest total volume.¹⁰ These results support the

Table 4. Mean±SD pharmacokinetic parameters of lanthanum in human serum after oral administration of oxylanthanum carbonate 1000 mg thrice daily

Parameter	Mean±SD
C_{max} (ng/ml)	0.837±1.02
T_{max} (h), median (min–max)	8.68 (0.00–25.9)
T_{last} (h), median (min–max)	16.9 (1.95–25.9)
AUC_{last} (h·ng/ml)	15.0±NC ^a
AUC_{0-24} (h·ng/ml)	21.1±NC ^a

AUC_{0-24} , area under the concentration versus time curve from the start of dose administration to 24 hours postdose; AUC_{last} , area under the concentration-time curve from time 0 to the time of the final quantifiable sample; C_{max} , maximum observed concentration; h, hours; max, maximum; min, minimum; NA, not calculated; OLC, oxylanthanum carbonate; T_{last} , time of final quantifiable concentration; T_{max} , time of maximum observed sample concentration.

^aSD is not calculated when $n < 3$.

contention that a more potent phosphate binder could lower sP with a lower pill burden, improving adherence to treatment and thus potentially leading to a more sustainable and effective therapy.

Regarding the PKs of OLC, systemic exposure to lanthanum was low as has also been observed with lanthanum carbonate.²⁵ Most plasma samples were below the LLOQ for lanthanum, with no suggestion of accumulation over the course of the trial.

There were several strengths to this study. This was a multicenter trial using real-world clinical approaches to treatment, and, therefore, less likely to be influenced by practices or preferences of a single research location. In addition, the population was broadly representative for age, sex, self-reported race and ethnicity, and diabetes status and had been receiving commonly prescribed phosphate binders.

The limitations of this study must be clearly acknowledged. Most notably, the open-label, single-arm design without an active comparator weakens any formal conclusions regarding efficacy. While the regulatory pathway for OLC leverages existing data on lanthanum carbonate—thus not requiring further toxicity or efficacy studies relative to other phosphate binders—this regulatory context does not mitigate the need for rigorous comparative clinical evaluation in the setting of this study. Second, although the trial duration was short, clinicians and clinical investigators have expressed concern regarding risks of untreated hyperphosphatemia for periods longer than 4–6 weeks. Finally, questionnaires used to assess patient satisfaction in exploratory analyses were not formally validated.

In conclusion, in this single-arm, open-label trial conducted in patients receiving maintenance hemodialysis, we demonstrate that the phosphate binder OLC was safe and well-tolerated, had low systemic absorption, and enabled control of sP in >90% of patients, with most requiring no more than one tablet with each meal.

Disclosures

Disclosure forms, as provided by each author, are available with the online version of the article at <http://links.lww.com/CJN/C338>.

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Data Availability Statements

Partial restrictions to the data and/or materials apply. The data underlying this article will not be made publicly available to protect the privacy of the study participants. Individual de-identified participant data and additional study-related documents will not be available before the trial results have been reviewed by regulatory agencies. Select data can be shared on reasonable request to corresponding authors, after approval by Unicyclic Therapeutics.

Supplemental Material

This article contains the following supplemental material online at <http://links.lww.com/CJN/C339>.

[Screening Patient Satisfaction Questionnaire](#)

[End-of-Study Patient Satisfaction Questionnaire](#)

[Supplemental Figure 1](#). Study design diagram.

[Supplemental Figure 2](#). Satisfaction with phosphate binder treatment.

[Supplemental Figure 3](#). Phosphate binder is easy to take.

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