Lumasiran: Dialysis

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SUMMARY

- ILLUMINATE-C was a phase 3, open-label, single-arm study designed to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of lumasiran in full term infants to adult patients with advanced PH1. Patients enrolled in the study included those not receiving hemodialysis in Cohort A (n=6) and those receiving hemodialysis in Cohort B (n=15).[1]
  - The primary estimate of the LS mean percent reduction in POx from baseline to Month 6 was 33.3% (95% CI: 15.2%, 81.8%) in Cohort A and 42.4% (95% CI: 34.2%, 50.7%) in Cohort B.[1]
  - POx reductions were sustained in both cohorts through Month 24 of the extension period.[2]
  - The majority of AEs were considered mild or moderate in severity. At Month 24, the most frequently reported AEs were pyrexia (38%), diarrhea (29%), and ISRs (24%).[2,3]
- Case reports from published medical literature discuss the use of lumasiran in patients on dialysis.[4–9]
- In a consensus statement developed by OxalEurope and the European Rare Kidney Disease Reference Network, graded recommendations on the management of patients with (or suspected to have) PH are provided. The indication and rationale for each management recommendation is contained within the guidance, including recommendations for treatment with dialysis and RNAi therapy.[10] Clinical discretion should be used in the assessment of the information provided.

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CLINICAL DATA

Drug Product Information

After subcutaneous administration, lumasiran is primarily distributed to the liver. Due to its large molecular weight of 16,341 Da and linear conformation of the double-stranded siRNA (compared to small organic molecules), lumasiran is not expected to pass through commonly used hemodialysis membranes (1-2 nm in pore sizes) and less than 10% of the amount in plasma is likely to be removed via peritoneal dialysis.[11–15]

ILLUMINATE-C Study

ILLUMINATE-C was a phase 3, open-label, single-arm study with a 6-month primary analysis period followed by an ongoing 54-month extension period to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of lumasiran in full term infants to adult patients with PH1 and advanced kidney disease with an eGFR ≤45 mL/min/1.73m^2 (or elevated serum creatinine if <12 months old) and POx ≥20 µmol/L. Patients enrolled in the study included those not receiving hemodialysis in Cohort A (N=6) and those receiving hemodialysis in Cohort B (N=15).[1]

In patients receiving hemodialysis, lumasiran was administered as soon as feasible following the end of dialysis, and no later than 120 minutes post-dialysis, under the supervision of the Investigator.[1]

All enrolled patients completed the 6-month primary analysis period and entered the 54-month extension period. Relevant baseline characteristics are detailed in **Table 1**.[1]

Table 1. Select ILLUMINATE-C Baseline Characteristics.[1]

Baseline Characteristic	Cohort A (n=6)	Cohort B (n=15)	All Treated (N=21)
Age at consent, median (range), years	9 (0-40)	6 (1-59)	8 (0-59)
Time from diagnosis to first dose, median (range), months	72.2 (4-350)	16.6 (6-440)	21.6 (4-440)
Pyridoxine use, n (%)	4 (67)	7 (47)	11 (52)
POx, median (range)[a], µmol/L	57.9 (22.7-134.0)	103.7 (56.3-167.0)	100.9 (22.7-167.0)
eGFR[b], median (range), mL/min/1.73 m^2	N=5[b] 16.5 (8.6-34.1)	NA	N=5 16.5 (8.6-34.1)
Number of dialysis therapy sessions per week, median (range)	NA	6 (3-7)	NA

Abbreviations: eGFR = estimated glomerular filtration rate; NA = not applicable; POx = plasma oxalate.

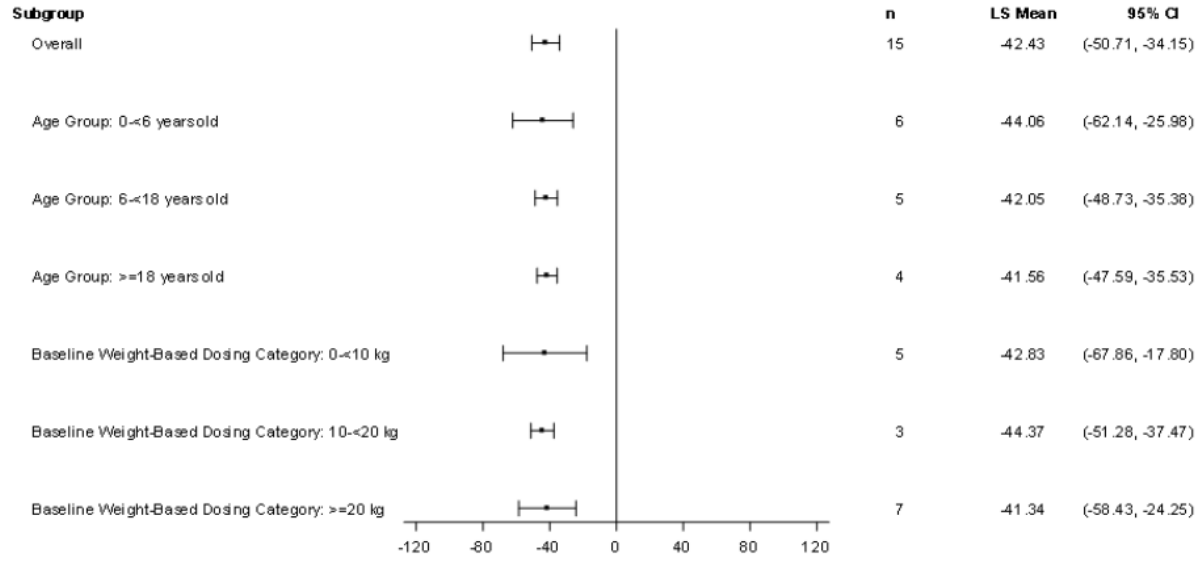
[a]Upper limit of normal = 12.11 µmol/L (1.09 mg/mL) for plasma oxalate, as determined based on data from 75 healthy adults.

[b]eGFR was calculated only in patients ≥12 months. eGFR (mL/min/1.73m^2) was calculated from serum creatinine based on the Modification of Diet in Renal Disease formula for patients age ≥ 18 years and the Schwartz Bedside Formula for patients aged 1 to <18 years. eGFR value available for 5 patients in Cohort A.

Efficacy Results: Plasma Oxalate

In ILLUMINATE-C, POx was evaluated as a primary endpoint: the percent change in POx from baseline to Month 6 was assessed in Cohort A and the percent change in predialysis POx from baseline to Month 6 was assessed in Cohort B. Data from the 6-month primary analysis period showed that patients in both cohorts had substantial reductions in POx, with POx reduction observed as early as Month 1. The primary estimate of the LS mean percent reduction in POx from baseline to Month 6 was 33.3% (95% CI -15.2, 81.8) in Cohort A and 42.4% (95% CI 34.2, 50.7) in Cohort B.[1] Subgroup analyses by age and weight-based dosing in Cohort B demonstrated a consistent treatment effect, as shown in **Figure 1**.[16]

Figure 1. Percent Change in POx in Prespecified Subgroups in Cohort B.[16]

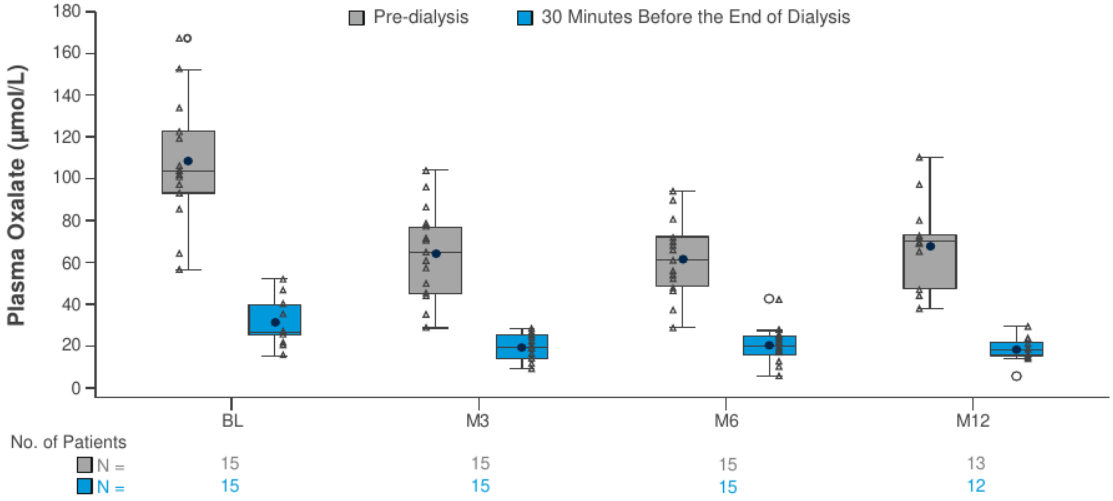


Abbreviations: CI = confidence interval; LS = least squares; POx = plasma oxalate.

At Months 12 and 24, data from the interim analyses of the extension period showed sustained POx reductions in both cohorts.[17,18] At Month 12, the mean (SEM) percent reduction from baseline for Cohorts A and B were 69.3% (6.9%) and 34.3% (6.9%), respectively.[17]

The distribution of pre-dialysis and post-dialysis POx levels in Cohort B through 12 months of lumasiran treatment is presented in **Figure 2**.[17]

Figure 2. Distribution of Pre- and Post-dialysis POx Levels in Cohort B.[17,a]

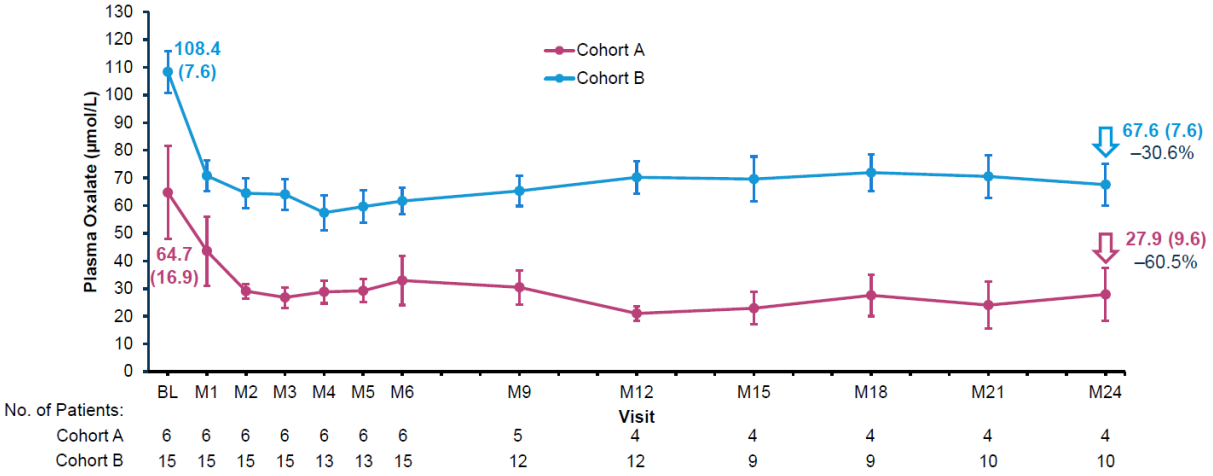


Abbreviation: BL = baseline; M = month; POx = plasma oxalate.
[a]Filled circles represent means; horizontal lines represent medians; triangles represent observed values for individual patients; open circles represent outliers.
From Frishberg et al.[17]

In Cohort A, 2 patients (33%) initiated dialysis by Month 24. In Cohort B, 2 patients (13%) underwent kidney-only transplantation by Month 24 and remained in the study. Three patients (20%) withdrew during the extension period, of which 2 patients withdrew due to liver-kidney transplantation.[2]

At Month 24, the mean (SEM) POx decreased from baseline values of 64.7 (16.9) µmol/L for Cohort A and 108.4 (7.6) µmol/L for Cohort B to 27.9 (9.6) µmol/L and 67.6 (7.6) µmol/L, respectively. The mean percent reduction in POx actual values from baseline were 60.5% for Cohort A and 30.6% for Cohort B (**Figure 3**).[2]

Figure 3. POx Mean Actual Values at Each Visit through Month 24.[2,a]



Abbreviations: BL = baseline; M = month; POx = plasma oxalate.

[a]In Cohort A, baseline was defined as the mean of all POx samples (µmol/L) collected prior to the first dose of lumasiran. In Cohort B, baseline was defined as the mean of the last 4 predialysis POx samples (µmol/L) collected prior to the first dose of lumasiran. Oxalate data collected after liver transplant, hemodialysis initiation (cohort A), or hemodialysis discontinuation (cohort B) were censored.

From Sellier-Leclerc et al.[2]

Safety Results

The majority of AEs were considered mild or moderate in severity. Serious AEs reported during the 6-month primary analysis period were primarily associated with dialysis procedural complications and may be attributed to the underlying advanced kidney disease in the ILLUMINATE-C patient population.[1]

An overview of AEs reported through Month 24 is summarized in **Table 2**. The most frequently reported AEs were pyrexia (38%), diarrhea (29%), and ISRs (24%). There were no lumasiran-related deaths or lumasiran-related serious or severe AEs, discontinuations, or withdrawals.[2,3]

Table 2. Lumasiran Safety Overview through Month 24.[2,3,a]

Event, n (%)	Original Assignment[b]		After Dialysis Change[c]		All Treated[d] N=21, PY 39.9
	Cohort A n=6, PY 9.0	Cohort B n=15, PY 26.2	Cohort A (on dialysis) n=2, PY 1.4	Cohort B (not on dialysis) n=5, PY 3.3	
Patients with ≥1 AE	6 (100)	15 (100)	1 (50)	5 (100)	21 (100)
AEs leading to treatment discontinuation and study withdrawal[e]	0 (0)	2 (13)	0 (0)	0 (0)	2 (10)
Severe AEs[f]	3 (50)	8 (53)	0 (0)	0 (0)	11 (52)
Serious AEs[g]	3 (50)	11 (73)	0(0)	4 (80)	15 (71)
Death	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Abbreviations: AE = adverse event; PY = patient-years.

[a]Safety analyses during extension period includes all available data through cutoff date of October 17, 2022 (beyond Month 24).

[b]"Original Assignment" columns display AEs prior to any change in dialysis, ie, while not on dialysis for Cohort A/while on dialysis for Cohort B.

[c]"After Dialysis Change" columns display AEs reported after patients in Cohort A initiated dialysis (n=2), and after patients in Cohort B went off dialysis (n=5; due to kidney-only transplant in 4 patients and liver-kidney transplant in 1 patient).

[d]"All Treated" column displays total patients reporting AEs regardless of cohort/dialysis status.

[e]AEs led to both treatment discontinuation and study withdrawal in 2 patients; both were due to liver-kidney transplant.

[f]Severe AEs that occurred in 2 patients included liver/kidney transplant and kidney transplant; other severe AEs affected no more than 1 patient.

[g]Serious AEs of pyrexia occurred in 6 patients; serious AEs of renal transplant occurred in 4 patients; and serious AEs of liver/kidney transplant occurred in 2 patients. Other serious AEs affected no more than 1 patient.

CASE REPORTS

The following information provides an overview of published case reports regarding patients with PH1 who received dialysis while being treated with lumasiran. It is not intended to be an all-inclusive list or summary of relevant publications, abstracts, and manuscripts.

Sellier-Leclerc AL, et al. Real-life data of 2-year lumasiran use in the DAILY-LUMA cohort. *Kidney Int Rep*. 2025;10(4):1020-1036. doi:10.1016/j.ekir.2024.12.033[4]

- The DAILY-LUMA was a quasi-exhaustive retrospective and prospective study designed to provide real-life data on 5-year follow-up of lumasiran treatment in patients with PH1 in France as requested by French authorities. An analysis was conducted on all patients not previously included in the ILLUMINATE trials that had received lumasiran for at least 2 years. Cohorts were divided into 3 groups: DAILY-A (patients aged ≥6 years with eGFR > 45 ml/min/1.73 m^2), DAILY-B (patients aged < 6 years, with eGFR > 45 ml/min/1.73 m^2), and DAILY-C (patients of all ages, eGFR < 45 ml/min/1.73 m^2).
- In the DAILY-C subcohort (n=10), 6 patients were on dialysis (4 on hemodialysis and 2 on peritoneal dialysis). In the 2 patients (aged 5 and 13 months) receiving peritoneal dialysis only, POx levels plateaued around 110 µmol/L; POx levels were lower in the 4 patients receiving hemodialysis.
- For patients on hemodialysis, the median number of dialysis hours per week was 22 hours at lumasiran initiation and 18 hours at 2 years. One patient switched from peritoneal dialysis to hemodialysis after 9 months of lumasiran. Two patients died while on dialysis (1 from Ear Nose Throat cancer and 1 from skin cancer).

- There were no reports of metabolic acidosis. In the overall population, lumasiran was well-tolerated, and no severe AEs were reported. Injection site reactions, abdominal pain, and headaches were the most commonly reported AEs.

Bahbah H, et al. Hidden in CAKUT: post-transplant diagnosis of primary hyperoxaluria type 1 and rescue management using lumasiran. *Pediatr Transplant*. 2025;29(3). doi:10.1111/petr.70079[5]

- A case report detailed a 9-year-old pediatric patient who was diagnosed with PH1 following kidney transplantation. Genetic testing confirmed PH1, and the variant c.33dup (p.Lys12Glnfs*156) was detected in probable homozygosity of AGXT.
- At 7.5 months post-kidney transplant, lumasiran treatment was initiated at a dose of 3 mg/kg for 4 months, followed by an every-3-month regimen. Concurrently, the patient received intensive hemodialysis with six 5-hour sessions per week. The regimen was reduced to four sessions after the 4th dose of lumasiran. One month after the 4th dose of lumasiran, the POx level was 5 µmol/L and hemodialysis was decreased to twice weekly.
- Hemodialysis was discontinued, and the patient had a creatinine level of 104 µmol/L (eGFR, 48 mL/min/1.73 m^2) 1 month after discontinuation. Prior to the 5th dose of lumasiran, 24-hour UOx was performed and was 45.6 mg/24 h.
- At 16 months post-kidney transplant, kidney ultrasound revealed persistent medullary nephrocalcinosis and new lower pole tiny renal calculi. The patient's estimated eGFR was 48 mL/min/1.73 m^2.

Taroni F, et al. Lumasiran treatment in pediatric patients with PH1: real-world data within a compassionate use program in Italy. *Clin Kidney J*. 2024;17(5). doi:10.1093/ckj/sfae090[6]

- A case report detailed the treatment outcomes of 9 pediatric patients with PH1 who received lumasiran therapy in a compassionate use setting across various centers in Italy.
- One patient was diagnosed with PH1 at half a year old and received peritoneal dialysis due to the severity of kidney impairment. Lumasiran treatment was initiated at 1.7-years-old.
- Before treatment with lumasiran, the patient's POx was 116 mmol/L. At months 3, 6, and 12 of follow up, POx was 86, 79, and 90 mmol/L, respectively.
- Patients enrolled in the study did not report any major clinical or laboratory AEs. The most frequently reported AE was erythema at the injection site.

Martin-Higueras C, et al. Multicenter long-term real world data on treatment with lumasiran in patients with primary hyperoxaluria type 1. *Kidney Int Rep*. 2024;9(1):114-133. doi:10.1016/j.ekir.2023.10.004[7]

- A case report detailed the treatment outcomes of 33 patients with PH1 who received lumasiran therapy outside of clinical trials from 12 European centers. Of the 13 patients who received dialysis, 6 adults and 5 pediatric patients received hemodialysis, 1 adult received peritoneal dialysis, and 1 child received hemodialysis and peritoneal dialysis.
- Data were analyzed for patients grouped either in preserved kidney function or hemodialysis, with consideration of those with the same dose regimen and according to vitamin B6 medication.
- Median follow up of the 13 patients on dialysis was 15 months. Among the 9 patients who were treated with 3 mg/kg monthly (or 6 mg/kg monthly according to age) of lumasiran for the first 4 months and then quarterly, mean POx (SD) decreased from 78 µmol/L (40.2) to 37.2 µmol/L (16.9) at month 3, then increased to 43.1 µmol/L (16.3) at month 12, and to 59.3 µmol/L (23.8) at month 18.

- Additional details regarding the treatment outcomes of individual patients are provided in the publication.

Poyah P, et al. Primary hyperoxaluria type 1 (PH1) presenting with end-stage kidney disease and cutaneous manifestations in adulthood: A case report. *Can J Kidney Health Dis*. 2021;8. doi:10.1177/20543581211058931[8]

- A case report detailed a 40-year-old female patient with a history of nephrolithiasis at age 19 and 33 who presented with ESRD and cutaneous symptoms. The patient was diagnosed with PH1, and genetic testing confirmed a homozygous splice donor mutation (AGXT c.680+IG>A).
- The patient was maintained on oral pyridoxine and high-intensity hemodialysis. She developed bilaterial swan-neck deformities of the fingers and limited grasp, and lumasiran 1 mg/kg monthly for 3 months, then every 3 months was initiated 11 months after presentation on a compassionate use basis.
- After 3 months of lumasiran treatment, there were no AEs reported and the patient remained dialysis dependent. Predialysis POx decreased by 36%, from 98.2 µmol/L prior to lumasiran treatment to 62.8 µmol/L after lumasiran treatment.
- After 14 months of high-intensity hemodialysis and 3 months of lumasiran treatment, extrarenal involvement increased, with progressive swan-neck deformities, reduced cardiac systolic function, and pulmonary hypertension. The patient was waitlisted for kidney-liver transplantation.

Stone HK, et al. Primary hyperoxaluria diagnosed after kidney transplant: A review of the literature and case report of aggressive renal replacement therapy and lumasiran to prevent allograft loss. *Am J Transplant*. 2021;21(12):4061-4067. doi:10.1111/ajt.16762[9]

- A case report detailed a 7-year-old pediatric patient who was diagnosed with PH1 following kidney transplantation. Due to early post-transplant complications, PH1 was clinically suspected and confirmed with genetic testing, which resulted with two AGXT variants: c.33dup (p.Lys12Glnfs*156) and c.454T>A (p.Phe152Ile).
- Following the diagnosis of PH1, the patient received aggressive renal replacement therapy and lumasiran was initiated on day 34 post-transplant. The hemodialysis regimen was slowly weaned while following oxalate levels and discontinued at approximately 4 months post-transplant. In the first 5 months of lumasiran treatment, UOx decreased by 65.9%. UOx continued to decline since discontinuing hemodialysis, although levels remained above the upper limit of normal. The patient was also prescribed high fluid intake, pyridoxine, and potassium citrate.
- The patient was closely monitored for any AEs associated with treatment; overall, lumasiran was well tolerated.

OXLUMO PRESCRIBING INFORMATION – RELEVANT CONTENT

For relevant labeling information, please refer to the following sections of the OXLUMO Prescribing Information[11]:

- DOSAGE AND ADMINISTRATION Section 2.1 Recommended Dosage
- USE IN SPECIFIC POPULATIONS Section 8.7 Renal Impairment
- CLINICAL PHARMACOLOGY Section 12.3 Pharmacokinetics

ABBREVIATIONS

AE = adverse event; AGXT = alanine-glyoxylate aminotransferase; BL = baseline; CI = confidence interval; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; ISR = injection site reaction; LS = least squares; NA = not applicable; PH = primary hyperoxaluria; PH1 = primary hyperoxaluria type 1; POx = plasma oxalate; PY = patient-years; RNAi = ribonucleic acid interference; SD = standard deviation; SEM = standard error of the mean; siRNA = small interfering ribonucleic acid; UOx = urinary oxalate.

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REFERENCES

1. Michael M, Groothoff JW, Shasha-Lavsky H, et al. Lumasiran for advanced primary hyperoxaluria type 1: phase 3 ILLUMINATE-C trial. *Am J Kidney Dis*. 2023;81(2):145-155. doi:10.1053/j.ajkd.2022.05.012
2. Sellier-Leclerc A-L, Magen D, Shasha-Lavsky H, et al. Lumasiran for advanced primary hyperoxaluria type 1: phase 3 ILLUMINATE-C trial. *Am J Kidney Dis*. 2025. doi:10.1053/j.ajkd.2025.01.016
3. Supplement to: Sellier-Leclerc A-L, Magen D, Shasha-Lavsky H, et al. Efficacy and safety of lumasiran for advanced primary hyperoxaluria type 1: 24-month follow-up of the phase 3 Illuminate-C trial. *Am J Kidney Dis*. 2025;86(2):285-288. doi:10.1053/j.ajkd.2025.01.016
4. Sellier-Leclerc A-L, Cloarec M, Knebelmann B, et al. Real-life data of 2-year lumasiran use in the DAILY-LUMA cohort. *Kidney Int Rep*. 2025;10(4):1020-1036. doi:10.1016/j.ekir.2024.12.033
5. Bahbah H, Azzam A, Hamed A, Aldaoud N, Alshami A. Hidden in CAKUT: post-transplant diagnosis of primary hyperoxaluria type 1 and rescue management using lumasiran. *Pediatr Transplant*. 2025;29(3). doi:10.1111/petr.70079
6. Taroni F, Peruzzi L, Longo G, et al. Lumasiran treatment in pediatric patients with PH1: real-world data within a compassionate use program in Italy. *Clin Kidney J*. 2024;17(5). doi:10.1093/ckj/sfae090
7. Martin-Higueras C, Borghese L, Torres A, et al. Multicenter long-term real world data on treatment with lumasiran in patients with primary hyperoxaluria type 1. *Kidney Int Rep*. 2024;9(1):114-133. doi:10.1016/j.ekir.2023.10.004
8. Poyah P, Bergman J, Geldenhuys L, et al. Primary hyperoxaluria type 1 (PH1) presenting with end-stage kidney disease and cutaneous manifestations in adulthood: a case report. *Can J Kidney Health Dis*. 2021;8. doi:10.1177/20543581211058931
9. Stone HK, VandenHeuvel K, Bondoc A, Flores FX, Hooper DK, Varnell CD. Primary hyperoxaluria diagnosed after kidney transplant: A review of the literature and case report of aggressive renal replacement therapy and lumasiran to prevent allograft loss. *Am J Transplant*. 2021;21(12):4061-4067. doi:10.1111/ajt.16762
10. Groothoff JW, Metry E, Deesker L, et al. Clinical practice recommendations for primary hyperoxaluria: an expert consensus statement from ERKNet and OxalEurope. *Nat Rev Nephrol*. 2023;19(3):194-211. doi:10.1038/s41581-022-00661-1
11. OXLUMO (lumasiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals.
12. Alnylam Pharmaceuticals. Data on File. MED-ALL-GO1-2100019.
13. Kabanda A, Goffin E, Bernard A, Lauwerys R, van Ypersele de Strihou C. Factors influencing serum levels and peritoneal clearances of low molecular weight proteins in continuous ambulatory peritoneal dialysis. *Kidney Int*. 1995;48(6):1946-1952. doi:10.1038/ki.1995.495
14. Azar AT, Canaud B. Hemodialysis System. In: *Modelling and Control of Dialysis Systems*. Springer Berlin Heidelberg; 2013:99-166. doi:10.1007/978-3-642-27458-9_3
15. Gillham M. Acute renal failure and renal support. In: Sidebotham D, Mckee A, Gillham M, Levy JH, eds. *Cardiothoracic Critical Care*. Butterworth-Heinemann; 2007:481-494. doi:10.1016/B978-075067572-7.50036-9
16. Supplement to: Michael M, Groothoff JW, Shasha-Lavsky H, et al. Lumasiran for advanced primary hyperoxaluria type 1: phase 3 ILLUMINATE-C trial. *Am J Kidney Dis*. 2023;81(2):145-155. doi:10.1053/j.ajkd.2022.05.012
17. Frishberg Y, Michael M, Groothoff JW, et al. Lumasiran for patients with primary hyperoxaluria type 1 and impaired kidney function: 12-month analysis of the phase 3 ILLUMINATE-C trial. Presented at: American Society of Nephrology (ASN) Kidney Week; November 3-6, 2022; Orlando, FL, USA.
18. Lieske J, Sellier-Leclerc AL, Shasha-Lavsky H, et al. Lumasiran for primary hyperoxaluria type 1 with impaired kidney function: 24-month analysis of the phase 3 ILLUMINATE-C trial. Presented at: American Society of Nephrology (ASN) Kidney Week; November 2-5, 2023; Philadelphia, PA, USA.