

Lumasiran Offers a New, Effective Treatment for Primary Hyperoxaluria Type 1 (PH1)

By Stephanie Perez Kerkvliet and Michelle N. Rheault

Primary hyperoxaluria type 1 (PH1) is a rare metabolic disease that leads to oxalate overproduction and results in kidney stones, nephrocalcinosis, kidney failure, and eventually systemic oxalosis. Garrelfs et al. (1) recently published results of the multinational, randomized, double-blind, placebo-controlled ILLUMINATE-A clinical trial evaluating the effectiveness of treating PH1 with lumasiran, an RNA interference (RNAi) agent directed against the mRNA encoding glycolate oxidase in the liver. The trial included 39 participants with PH1, ages 6–60 years (median age 14 years, including 22 pediatric participants), with an estimated glomerular filtration rate (eGFR) greater than or equal to 30 mL/min/1.73 m², 26 of whom were randomized to lumasiran treatment. After 6 months of treatment, the least-squares mean percent change in 24-hour urinary oxalate excretion decreased 65.4% in the lumasiran group compared to 11.8% in the placebo group. Moreover, 84% of patients in the lumasiran group had 24-hour urinary oxalate levels no higher than 1.5 times the upper limit of normal compared to 0% of patients in the placebo group ($p < 0.001$). The most common side effect of lumasiran was injection-site reactions (38%), and no severe or serious adverse events occurred. Lumasiran is the first US Food and Drug Administration (FDA)-approved specific treatment for patients with PH1. Lumasiran has not been tested in other genetic forms of PH1 and would not be expected to be efficacious in secondary hyperoxaluria.

Prior to lumasiran, treatment strategies for PH1 focused on preventing oxalate stone formation and slowing disease progression and included hyperhydration, high-dose pyridoxine, and citrate. Despite these burdensome treatments,

patients with PH1 often experienced progressive kidney failure. Liver transplant is curative, and patients often receive combined liver and kidney transplants after kidney failure. However, organ transplantation carries many peri- and post-operative risks, and many patients and their families experience transplantation as trading one disease for another. The findings of the ILLUMINATE-A clinical trial offer an apparently safe and effective subcutaneous treatment with the opportunity to improve both disease control and quality of life in patients with PH1. ■

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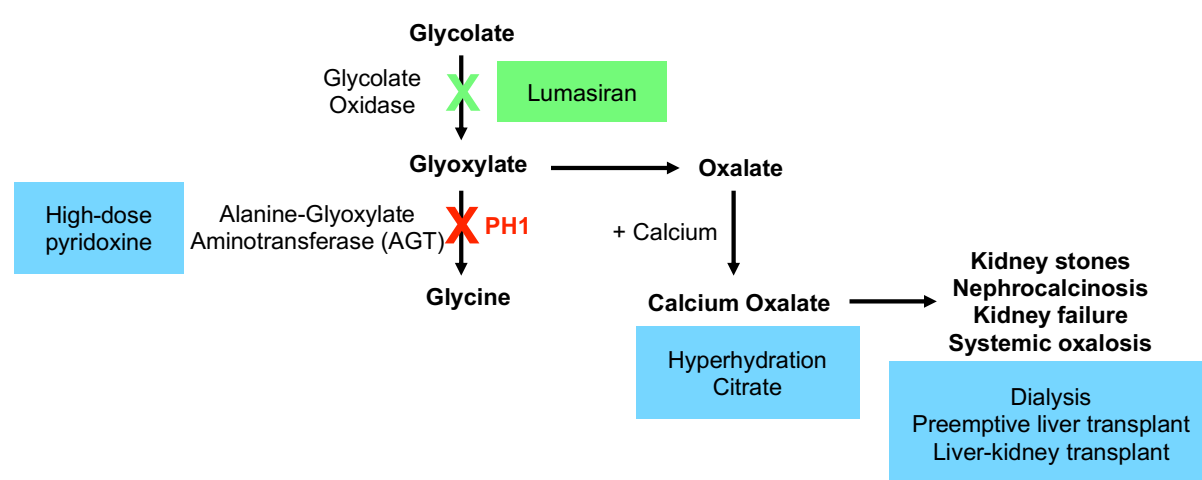
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Dr. Rheault is the site principal investigator with Advicenne, Travere, Reata, Sanofi, and Genentech. Dr. Perez Kerkvliet has no disclosures.

Reference

- Garrelfs SF, et al. Lumasiran, an RNAi therapeutic for primary hyperoxaluria type 1. *N Engl J Med* 2021; 384:1216–1226. doi: 10.1056/NEJMoa2021712

Figure 1. Treatments for primary hyperoxaluria type 1 (PH1)



Adding Life to Their Years

By Holly M. Koncicki

Adding life to their years: The current state of pediatric palliative care in CKD,” by House and Wightman, calls pediatric nephrologists to action for the integration of palliative care into their practice. In an effort to distinguish palliative care from being inappropriately conflated with “end-of-life care,” the rebranding of the nephrology-palliative care integration has already occurred in adult nephrology, highlighting the ability of palliative care to be delivered alongside CKD care (1).

By highlighting the effects of pediatric CKD on the child and family unit, the authors describe some challenges similar to adult CKD care, including adverse effects on health-related quality of life and increased symptom burden, as well as the unique needs of children, including subsequent transplants, detrimental effects on well-being, financial stress, and anxiety experienced by siblings and parents. Integration of palliative care into other pediatric chronic illnesses has proven valuable, with improved psychosocial outcomes in oncology; physical and psychological symptoms in patients with cystic fibrosis; and maternal anxiety in children with hypoplastic left heart syndrome. It is time for pediatric nephrologists to spearhead this integration for their patients as well. Continued exposure in fellowship and continuing education can increase pediatric nephrologists’ familiarity with primary palliative care skills, including basic symptom management, communication, and incorporation of the patient’s perspective in shared decision-making. More

complex care needs of patients and families should prompt consultation with specialist palliative care providers, social workers, psychologists, and child life specialists. Similar to the adult integration of nephrology and palliative care (Table 1), the most effective way to deliver this integrated care remains as yet undefined, but through conscious efforts and research, this model can be better delineated to best “add life to the child’s years, not simply years to the child’s life.” ■

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Reference

- House TR, Wightman A. Adding life to their years: The current state of pediatric palliative care in CKD. *Kidney360* April 2021. doi: 10.34067/KID.0000282021; <https://doi.org/10.34067/KID.0000282021>

Table 1. Comparison of adult vs. pediatric palliative care

Similarities	Differences
Palliative care can be delivered at any stage of illness, including alongside curative treatments.	Childhood illness can occur in a broad spectrum of ages varying from perinatal to young adult and may persist through varying stages of development. The palliative care team will need to adapt to the child’s evolving emotional maturity and cognitive understanding of the illness.
The palliative care team can help with decision-making and establishing goals of care with the patient and/or surrogate/proxy.	Medical decisions for young children are made by their parents or guardians.
The care model involves an interdisciplinary team including a doctor, nurse, and social worker.	The interdisciplinary team for pediatric palliative care has unique members including a child life specialist.
A focus of care is to improve quality of life by early identification and treatment of symptoms.	Having a serious illness in childhood can present unique features in caring for the child, siblings, and parents. This includes addressing emotional and psychological needs and the potential need for respite care.

Adapted from Center to Advance Palliative Care. Pediatric versus adult palliative care. <https://getpalliativecare.org/whatis/pediatric/adult-vs-pediatric-palliative-care/#:~:text=Medical%20decisions%20for%20young%20children,and%20For%20child%20behavioral%20specialist>