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**Lumasiran for Primary Hyperoxaluria Type 1:  
Analysis of Urinary Oxalate and Estimated Glomerular Filtration Rate Over  
Time in Patients by Genotype**

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# Lumasiran for Primary Hyperoxaluria Type 1: Analysis of Urinary Oxalate and Estimated Glomerular Filtration Rate Over Time in Patients by Genotype

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# Disclosures

**David J. Sas:** Grants and other from Alnylam Pharmaceuticals, and personal fees from Advicenne

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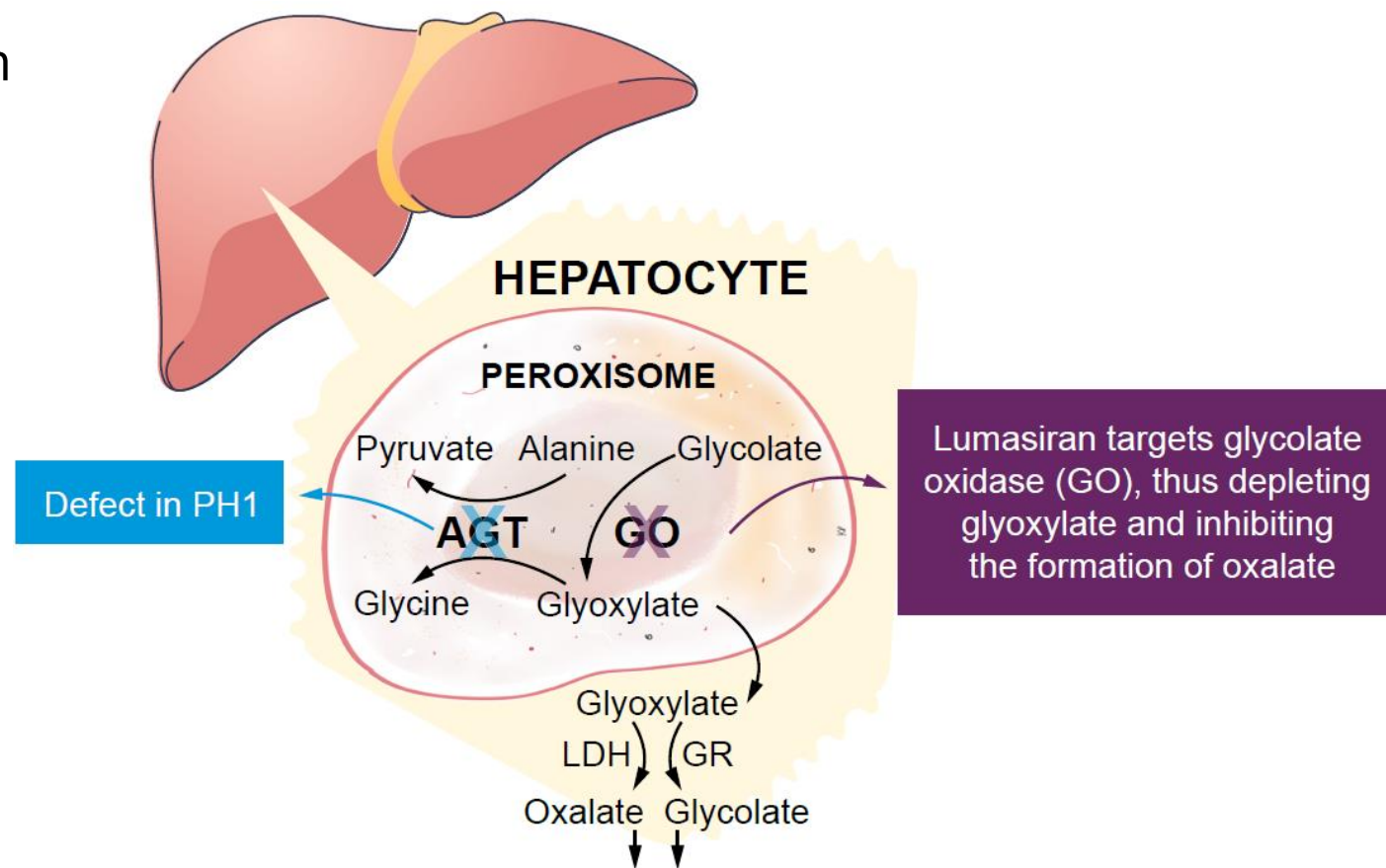
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# Introduction

- Primary hyperoxaluria type 1 (PH1) is a rare genetic disorder associated with overproduction of hepatic oxalate<sup>1,2</sup>
- Patient age at kidney failure in PH1 varies with *AGXT* genotype<sup>3,4</sup>
- Lumasiran is a liver-directed RNA interference (RNAi) therapeutic for PH1 that targets the *HAO1* mRNA, decreasing glycolate oxidase levels and, subsequently, oxalate levels<sup>5,6</sup>
- Lumasiran is the first approved RNAi treatment for PH1, with the longest duration of efficacy data<sup>7</sup>





## Objective

- Our aim was to evaluate UOx levels and eGFR over time in a *post hoc* analysis of 3 years of data for 3 lumasiran clinical trials

	Phase 2 <sup>1</sup>	ILLUMINATE-A <sup>2-4</sup>	ILLUMINATE-B <sup>5-7</sup>
<b>Design</b>	Open-label extension study including patients who completed the single-blind, placebo-controlled Phase 1/2 trial, Part B	Phase 3, randomized, double-blind, placebo-controlled study with extension period	Phase 3, single-arm, open-label study with extension period
<b>Participants, N</b>	20	39	18
<b>Age, y</b>	6-64	≥6	<6
<b>UOx</b>	24-hour UOx excretion >0.7 mmol/24h/1.73m <sup>2</sup>	24-hour UOx excretion >0.7 mmol/24h/1.73m <sup>2</sup>	UOx:Cr >ULN for age
<b>eGFR, mL/min/1.73m<sup>2</sup></b>	>45	≥30	>45 if age ≥12 months or normal serum creatinine if age <12 months
<b>Total duration</b>	Up to 54 months	Up to 60 months	Up to 60 months

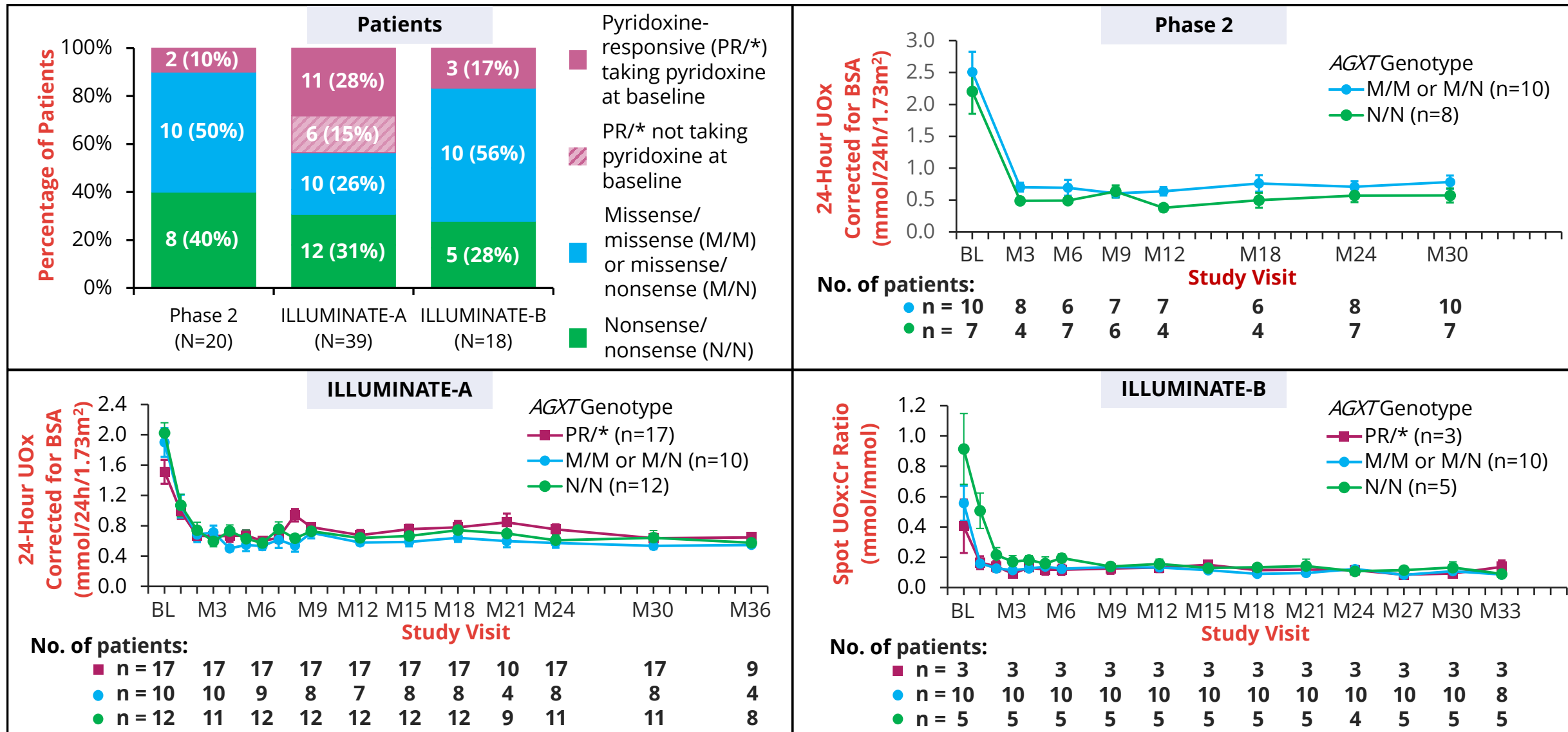
eGFR, estimated glomerular filtration rate; ULN, upper limit of normal; UOx, urinary oxalate; UOx:Cr, urinary oxalate:creatinine ratio.

ClinicalTrials.gov ID: Phase 2, NCT03350451; ILLUMINATE-A, NCT03681184; ILLUMINATE-B, NCT03905694.

1. Frishberg Y, et al. *Clin J Am Soc Nephrol*. 2021;16:1025-1036. 2. Garrelfs SF, et al. *N Engl J Med*. 2021;384:1216-1226. 3. Hulton SA, et al. *Kidney Int Rep*. 2022;7:494-506. 4. Saland JM, et al. *Kidney Int Rep*. 2024;9:2037-2046. 5. Sas DJ, et al. *Genet Med*. 2022;24:654-662. 6. Hayes W, et al. *Pediatr Nephrol*. 2023;38:1075-1086. 7. Michael M, et al. Efficacy and safety of lumasiran for infants and young children with primary hyperoxaluria type 1: 30-month analysis of the phase 3 ILLUMINATE-B trial. Presented at: Annual Meeting of the Pediatric Academic Societies; April 27-May 1, 2023; Washington, DC.

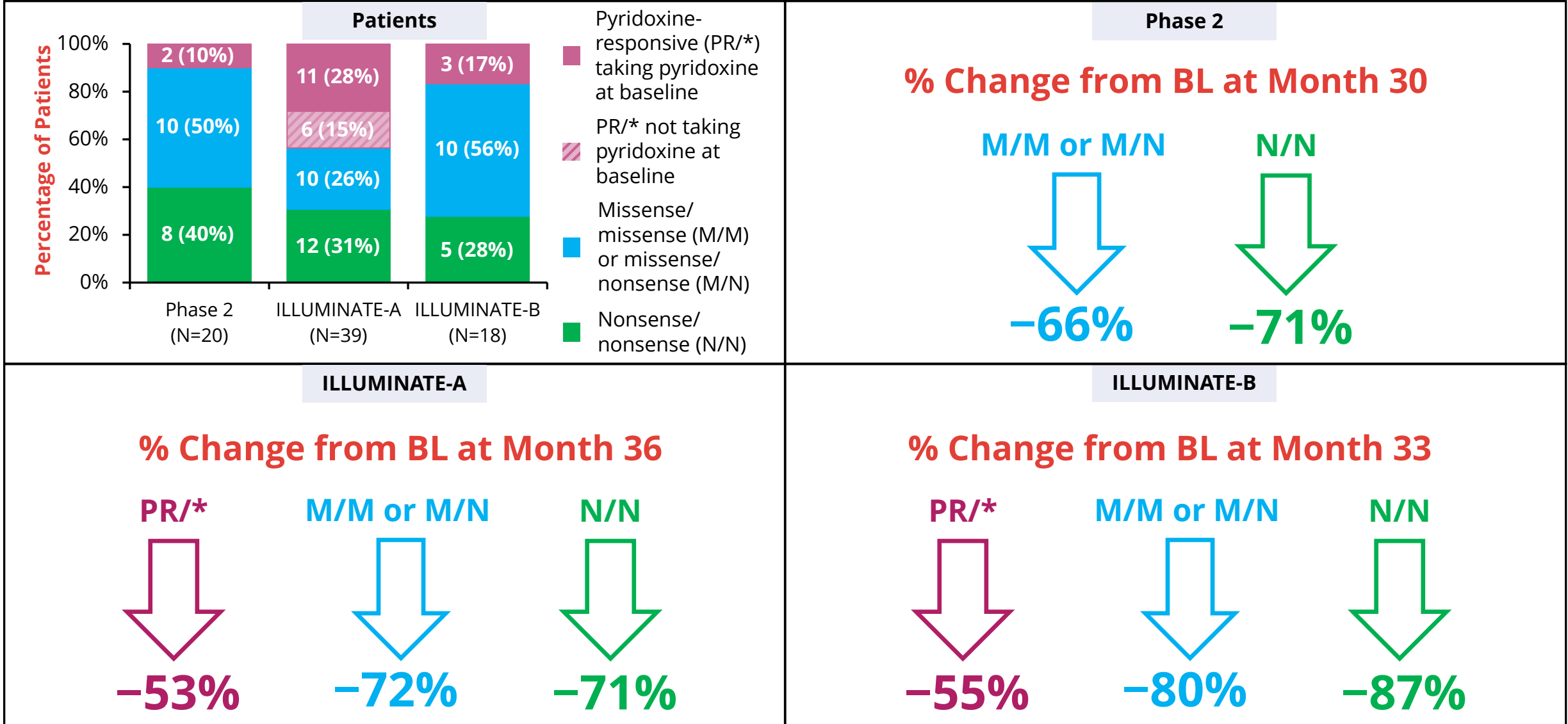


# Urinary Oxalate





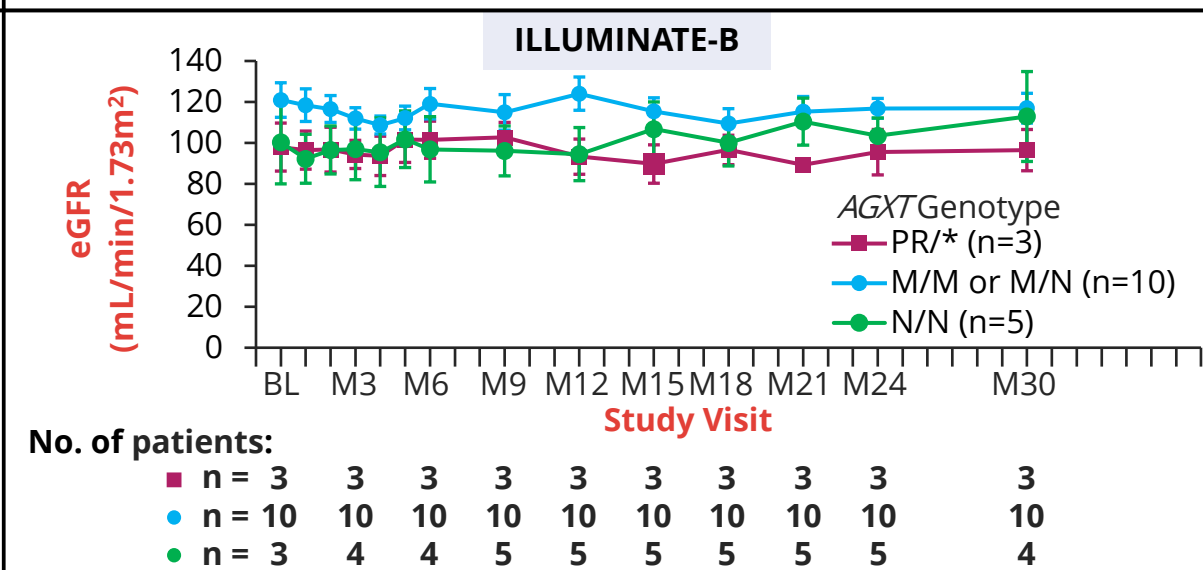
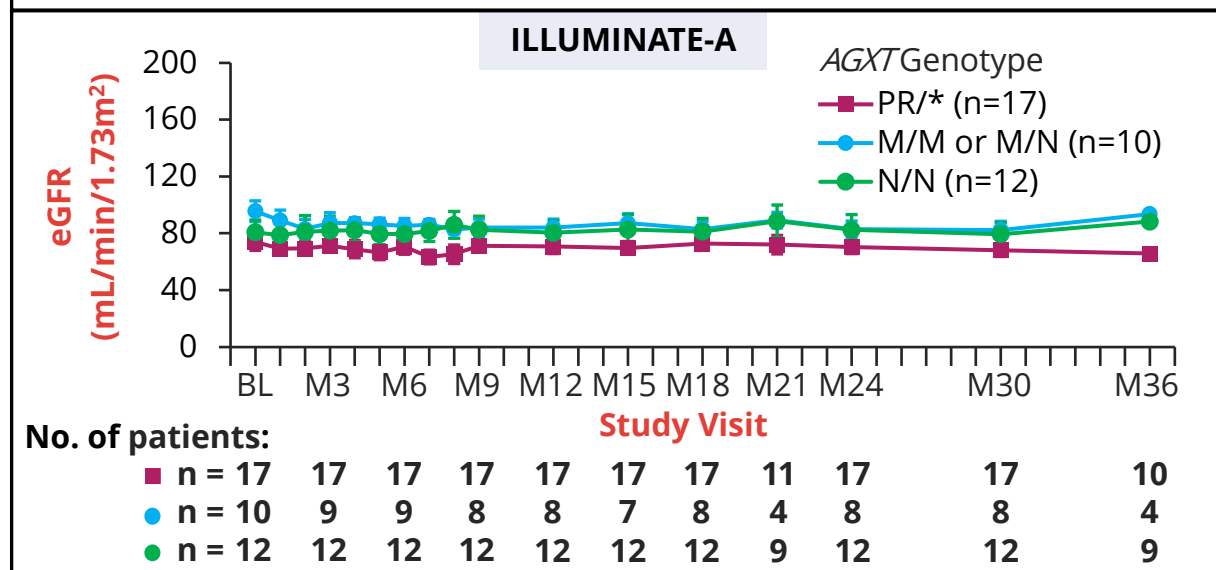
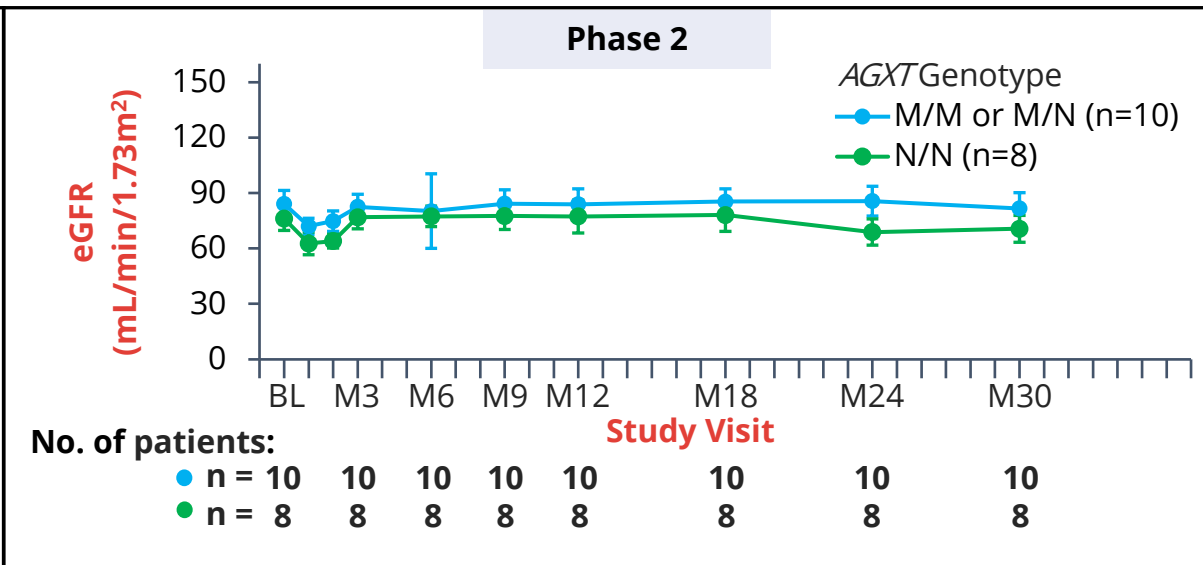
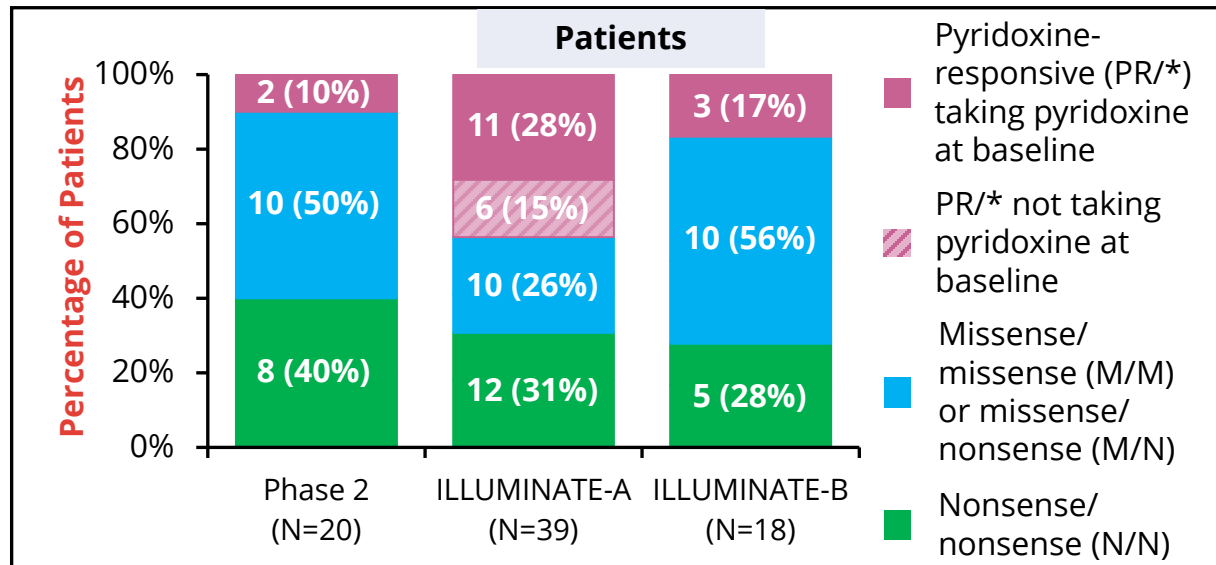
# Urinary Oxalate



BL, baseline; M/M, missense/missense; M/N, missense/nonsense; N/N, nonsense/nonsense; PR/\*, pyridoxine-responsive.



# eGFR





## Conclusions

- In an analysis of long-term data from 3 clinical trials, patients treated with lumasiran experienced rapid and sustained reductions in UOx levels and stable eGFR over time, regardless of PH1 genotype

Percentage changes from baseline in UOx in 3 clinical trials of lumasiran

<b>AGXT Genotype</b>	<b>Phase 2 (Month 30)</b>	<b>ILLUMINATE-A (Month 36)</b>	<b>ILLUMINATE-B (Month 33)</b>
PR/*	–	–53%	–55%
M/M or M/N	–66%	–72%	–80%
N/N	–71%	–71%	–87%

M/M, missense/missense; M/N, missense/nonsense; N/N, nonsense/nonsense;  
PR/\*, pyridoxine-responsive

- Interpretation may be limited by the *post hoc* nature of the analysis and small sample sizes

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