Lumasiran: Pediatric Weight-Based Dosing Increase Regimen

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SUMMARY

- In the phase 3 ILLUMINATE-B and ILLUMINATE-C studies:
  - Patients that experienced weight increases crossing the threshold for the next weight-based dosing category (<10 kg to ≥10 kg or <20 kg to ≥20 kg) followed the new lumasiran dosing regimen for the remainder of the study or until the next dosing category threshold was reached.[1,2]
  - Patients transitioning from <10 kg to ≥10 kg on monthly maintenance doses continued to receive 3.0 mg/kg once monthly doses until the next study visit according to the study protocol, which was then followed by every-3-months maintenance dosing through the end of the study.[1,2]

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CLINICAL DATA

ILLUMINATE-B Study

ILLUMINATE-B (N=18) was a phase 3, open-label, single-arm study with a 6-month primary analysis period followed by a 54-month extension period to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of lumasiran in infants and young children <6 years old with PH1 and an eGFR >45 mL/min/1.73m^2 (normal serum creatinine for infants less than 12 months old). Patients received subcutaneous injections of lumasiran as determined by a body weight-based dosing regimen. The primary endpoint was the percent change from baseline in spot UOx:Cr at 6 months.[3]

During the 6-month treatment period, patients received 3 loading doses, once monthly (at Day 1, Month 1, and Month 2) at a dose based on body weight category. At Month 3 and beyond, patients received lumasiran either monthly (patients weighing <10 kg) or every 3 months (patients weighing ≥10 kg) at the maintenance dose. Study drug administration was at least 21 days apart.[1]

For patients who weighed <20 kg, the lumasiran dose was based on a weight obtained within 7 days prior to dosing. For patients who weighed ≥20 kg, the dose was based on a weight obtained up to 4 months prior to the planned quarterly dose.[1]

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). Patients received subcutaneous injections of lumasiran as determined by a body weight-based dosing regimen. The primary endpoints were the percent change from baseline in POx at 6 months (Cohort A) and percent change from baseline in predialysis POx at 6 months (Cohort B).[4]

During the 6-month treatment period, patients received 3 loading doses, once monthly (at Day 1, Month 1, and Month 2) at a dose based on body weight category. At Month 3 and beyond, patients received lumasiran either monthly (patients weighing <10 kg) or every 3 months (patients weighing ≥10 kg) at the maintenance dose. Study drug administration was at least 21 days apart. In patients on dialysis therapy, study drug was administered as soon as feasible following the end of dialysis, and no later than 120 minutes post-dialysis.[2]

For patients <6 years of age, the dose was based on a weight obtained within 7 days prior to dosing. In patients ≥6 years of age, body weight collected within 3 months prior to the study drug dose or the pre-dose weight collected on the study visit day or dosing day was used for dose calculations.[2]

ILLUMINATE-B and ILLUMINATE-C Protocol Specifications for Weight-Based Dosing Regimen
In patients that experienced weight increases crossing the threshold for the next weight-based dosing category (<10 kg to ≥10 kg or <20 kg to ≥20 kg), the lumasiran dose followed the new dosing regimen for the remainder of the study or until the next dosing category threshold was reached.[1,2]

Patients transitioning from <10 kg to ≥10 kg on monthly maintenance doses continued to receive 3.0 mg/kg once monthly doses until the next study visit according to the study protocol, which was then followed by every-3-months maintenance dosing through the end of the study.[1,2]

OXLUMO PRESCRIBING INFORMATION – RELEVANT CONTENT

For relevant labeling information, please refer to the following sections of the OXLUMO Prescribing Information[5]:

- DOSAGE AND ADMINISTRATION Section 2.1 Recommended Dosage
- CLINICAL PHARMACOLOGY Section 12.2 Pharmacodynamics

ABBREVIATIONS

Cr = creatinine; eGFR = estimated glomerular filtration rate; PH1= primary hyperoxaluria type 1; POx = plasma oxalate; UOx = urinary oxalate; UOx:Cr = urinary oxalate:creatinine ratio.

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