Lumasiran: Dosing Regimen

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SUMMARY

- The recommended dosing regimen of lumasiran consists of monthly loading doses for 3 doses, followed by maintenance doses beginning one month after the last loading dose. The dosing is based on actual body weight.[1]

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OXLUMO PRESCRIBING INFORMATION – RELEVANT CONTENT

The DOSAGE AND ADMINISTRATION section provides the following information[1]:

Recommended Dosage

The recommended dosing regimen of OXLUMO consists of loading doses (monthly for 3 doses) followed by maintenance doses (beginning 1 month after the last loading dose) administered subcutaneously as shown in Table 1.

Dosing is based on actual body weight.

Table 1. OXLUMO Weight-Based Dosing Regimen

Body Weight	*Loading Dose*	*Maintenance Dose*
Less than 10 kg	*6 mg/kg once monthly for 3 doses*	*3 mg/kg once monthly, beginning 1 month after the last loading dose*
10 kg to less than 20 kg	*6 mg/kg once monthly for 3 doses*	*6 mg/kg once every 3 months (quarterly), beginning 1 month after the last loading dose*
20 kg and above	*3 mg/kg once monthly for 3 doses*	*3 mg/kg once every 3 months (quarterly), beginning 1 month after the last loading dose*

For Patients on Hemodialysis

Administer OXLUMO after hemodialysis if administered on dialysis days.

Missed Dose

If a dose is delayed or missed, administer OXLUMO as soon as possible. Resume prescribed monthly or quarterly dosing, from the most recently administered dose.

CLINICAL DATA

Phase 1/2 Study

The Phase 1/2 study was a single-blind, placebo-controlled, single and multiple ascending dose study to evaluate the safety, tolerability, pharmacokinetic and pharmacodynamics of subcutaneously administered lumasiran in healthy adult subjects (Part A) and patients with PH1 (Part B).[2]

- In Part A of the study, 32 healthy volunteers were randomized to receive a single SC dose of lumasiran 0.3 mg/kg (n=6), 1.0 mg/kg (n=6), 3.0 mg/kg (n=6), 6.0 mg/kg (n=6), or placebo (n=8).[2]
- In Part B of the study, patients with PH1 were randomized (3:1) to receive multiple doses of placebo (n=3), 1.0 mg/kg of lumasiran every 28 days for 3 doses (n=3), 3.0 mg/kg every 28 days for 3 doses (n=3), or 3.0 mg/kg every 84 days for 2 doses (n=3).[2]
- The OLE cohorts received doses of lumasiran at a dosage of 1.0 mg/kg every 28 days for 3 doses (n=4) or 3.0 mg/kg every 28 days for 3 doses (n=4).[2]

Doses of lumasiran demonstrated rapid and sustained reduction of UOx levels in patients with PH1 at doses of 1.0 mg/kg monthly, 3.0 mg/kg monthly, and 3.0 mg/kg once every 3 months. Results from the Phase 1/2 study demonstrated a more rapid and higher magnitude of UOx reduction relative to baseline in the 3 mg/kg monthly cohort compared to other cohorts. This allowed for an earlier steady state pharmacodynamic effect and led to the dose selection of the lumasiran Phase 3 clinical studies. All 20 patients enrolled in the Phase 1/2 Part B arm of the study completed the study and enrolled in the OLE.[2]

Phase 2 OLE Study

The Phase 2 OLE study was a multicenter, open-label, extension study to evaluate the long-term safety and tolerability of lumasiran in patients with PH1. Patients with PH1 previously dosed in the Phase 1/2 parent study were eligible to enroll in the Phase 2 OLE study.[2,3]

At the start of the study, patients received their original dose of lumasiran from the Phase 1/2 study. All patients were transitioned to the maintenance dose regimen of 3.0 mg/kg every 3 months following the completion of the patient's respective starting doses.[3]

ILLUMINATE-A Study

ILLUMINATE-A was a phase 3, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of lumasiran in adults and children ≥6 years old with PH1 and an eGFR ≥30 mL/min/1.73m^2. After the 6-month double-blind treatment period, all patients received lumasiran in an optional 54-month OLE.[4]

During the 6-month double-blind treatment period, 39 patients were randomized (2:1) to receive loading doses of 3.0 mg/kg of lumasiran (n=26) or placebo (n=13) as a subcutaneous injection once monthly for 3 doses, followed by a maintenance dose of 3.0 mg/kg of lumasiran 1 month after the last loading dose. Patients that were originally randomized to the placebo arm received loading doses of 3.0 mg/kg of lumasiran at Months 6, 7, and 8 study visits during the extension period.[4,5]

ILLUMINATE-B Study

ILLUMINATE-B was a phase 3, open-label, single-arm study with a 6-month primary analysis period followed by a 54-month extended dosing period to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of lumasiran in full term infants and young children <6 years old with PH1 and an eGFR >45 mL/min/1.73m^2 (or normal serum creatinine for infants <12 months old).[6]

During the 6-month treatment period, 18 patients received loading doses (weight dependent) of lumasiran once monthly for 3 doses, followed by a maintenance dose once monthly or once every 3 months as

recommended by weight-based dosing (**Table 1**).[6] Continued weight-based dosing utilized the patient's weight that was obtained 7 days prior to dosing during the extension period.[7]

ILLUMINATE-C Study

The ILLUMINATE-C study 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 advanced PH1 with an eGFR ≤45 mL/min/1.73m^2 (or elevated serum creatinine if <12 months old) and POx ≥20 µmol/L. Patients (N=21) enrolled in the study included those not receiving hemodialysis in Cohort A (N=6) and those receiving hemodialysis in Cohort B (N=15).[8]

Patients received loading doses (weight dependent) of lumasiran once monthly for 3 doses, followed by a maintenance dose once monthly or once every 3 months as recommended by weight-based dosing (**Table 1**). In patients on dialysis, lumasiran was administered no later than 120 minutes after receiving dialysis.[8]

ABBREVIATIONS

eGFR = estimated glomerular filtration rate; OLE = open-label extension; PH1 = primary hyperoxaluria type 1; POx = plasma oxalate; SC = subcutaneous; UOx = urinary oxalate.

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