ILLUMINATE-B CLINICAL STUDY RESULTS

A Study of Lumasiran in Infants and Young Children with Primary Hyperoxaluria Type 1

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Thank You

We thank the participants and caregivers for taking part in ILLUMINATE-B. Study participation allows Alnylam, and the doctors, nurses and study staff conducting the study, to evaluate how well lumasiran works and how safe it is in treating people with Primary Hyperoxaluria Type (PH1).

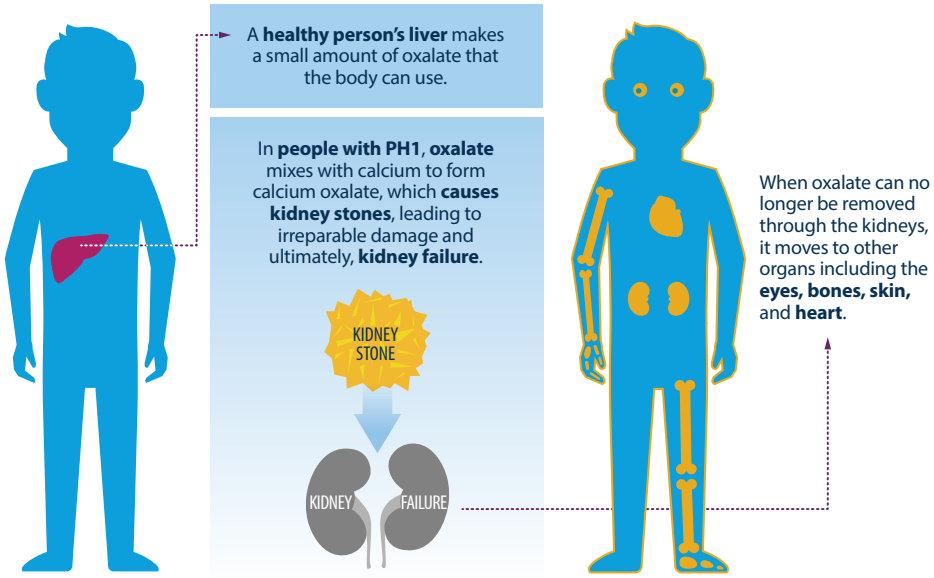
OVERVIEW

ILLUMINATE-B is an ongoing study of an investigational medication for children with Primary Hyperoxaluria Type 1 (PH1). This document is a brief summary of results from the first 6 months of the study. Scientific summaries of this research will also be available (links provided at the end of this summary). The following key results of the study are presented here.

- 18 pediatric patients with PH1 under the age of 6 years are participating in this study.
- The amount of oxalate in urine lowered an average of 71% for the 16 participants who received lumasiran for 6 months.
- Participants had minor medical problems, including irritation around the injection site and headache while receiving study medication.

What is Primary Hyperoxaluria Type 1 (PH1)?

PH1 is a rare inherited disorder of the liver that causes the over-production of a substance called oxalate. High levels of oxalate are toxic because oxalate cannot be broken down by the human body and builds up in the kidneys. The condition can lead to kidney stones and over time can cause kidney failure. In severe cases, it may damage other parts of the body.



About Lumasiran

Lumasiran (lu-MAH-si-ran) is a drug that reduces the ability of liver cells to make a protein called glycolate oxidase (GO). In patients with PH1, GO plays a role in the high levels of oxalate.

Researchers think that by lowering the amount of GO, lumasiran may reduce the production of oxalate and lessen the symptoms of PH1.

WHY WAS THIS RESEARCH NEEDED?

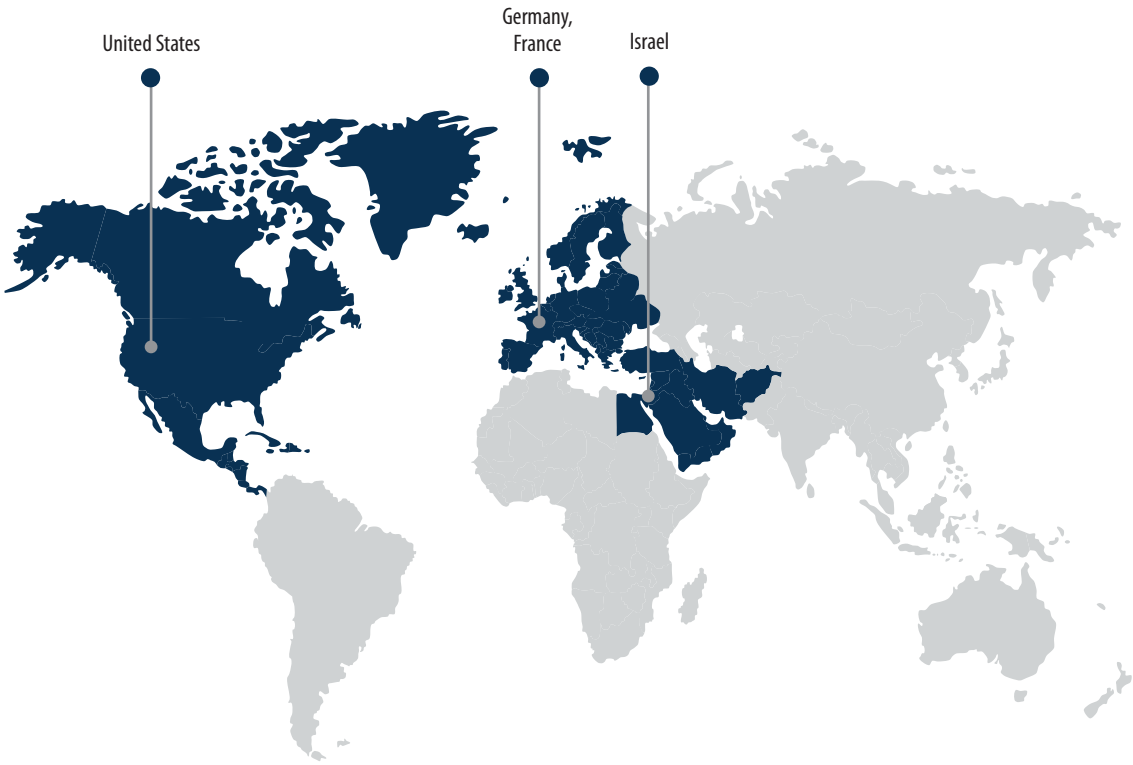
There are no approved medications for PH1. Current therapies include high fluid intake, vitamin B6 treatment, and medicine to reduce the formation of kidney stones from the mixture of oxalate and calcium. For some patients with severe symptoms of PH1, a liver or a dual liver and kidney transplant may become necessary.

A goal of the ILLUMINATE-B study is to answer the following main questions:

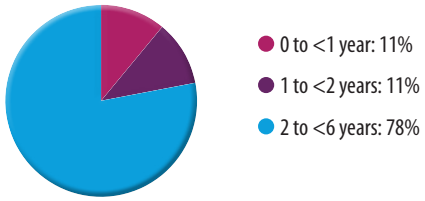
- Is the study medication able to reduce the amount of oxalate in urine?
- Does the study medication cause medical problems?

WHO TOOK PART IN THE STUDY?

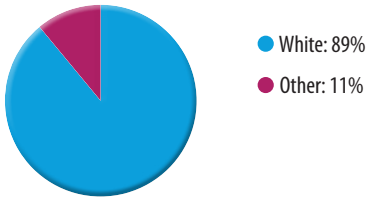
The study includes 18 participants (8 male and 10 female) between the ages of 3 months to 6 years who have been diagnosed with PH1. There are 9 locations across Europe, Israel, and the United States. The study started in April 2019 and is ongoing.



Age of Participants



Race of Participants

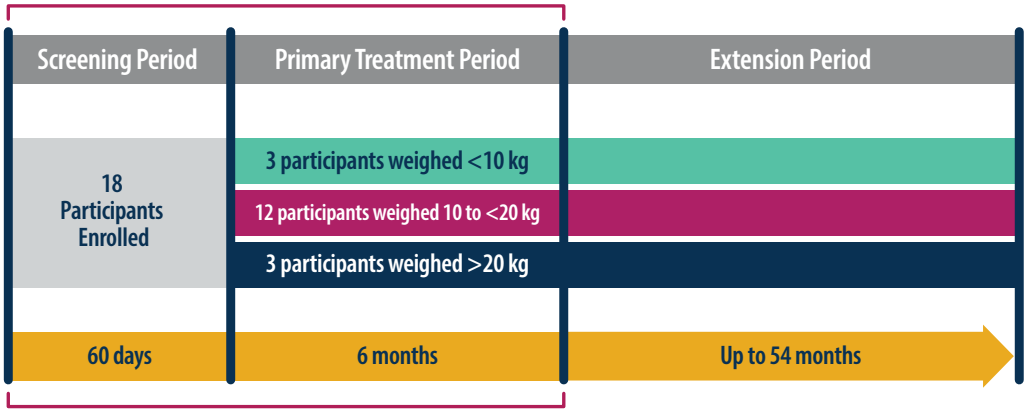


WHAT HAPPENED DURING THE STUDY?

Before the study started, patients whose guardians agreed to participation were checked to be sure they could join the study. The doctors collected urine samples from each patient to measure the amount of oxalate that was in the urine. Patients with oxalate above a certain level were able to participate.

During the first 6 months, the "Primary" Treatment Period, lumasiran was given to all participants. The amount of lumasiran given to each patient was based on their weight. After completing the 6-month Primary Treatment Period, participants continue to receive study medication in the "Extension" Period for up to 4 and a half years. This period is ongoing and the results are not yet available.

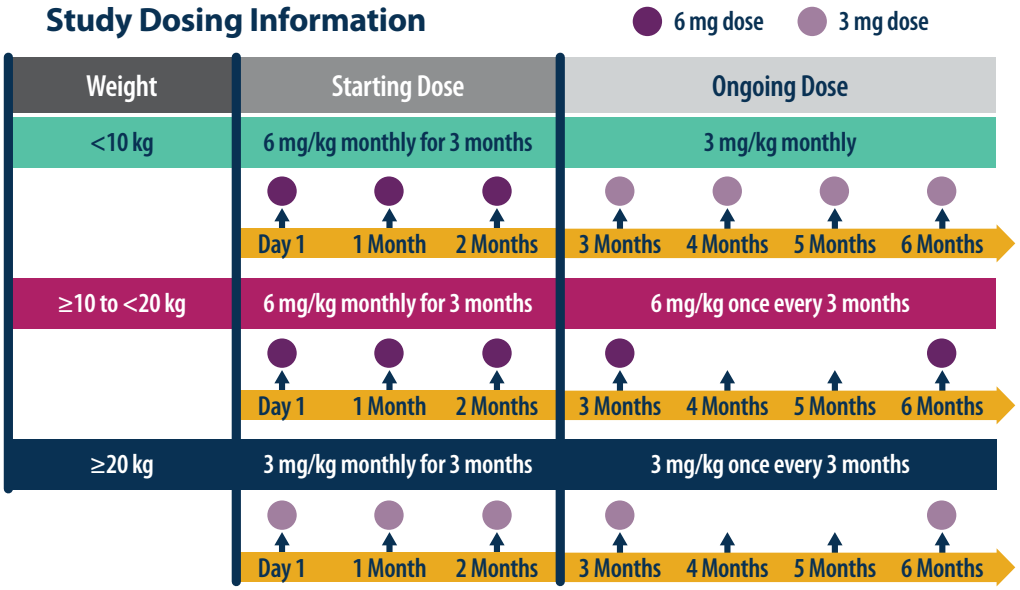
The figure below shows the study design:



When this summary was written, 16 participants had received lumasiran for 6 months of the Primary Treatment Period and 2 participants had received lumasiran for 2 months of the Extension Period.

How were study medications given?

Study medications are given by a shot just under the skin (an injection). The preferred injection site is the stomach area, but the doctor may also use the upper arms or thighs. Participants received "loading" or starting doses and then "maintenance" or ongoing doses as shown below.



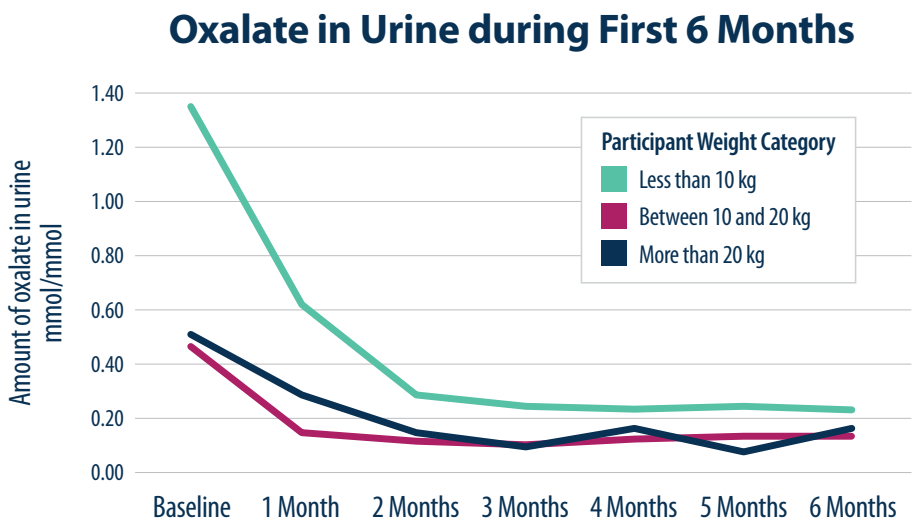
WHAT ARE THE STUDY RESULTS SO FAR?

Did lumasiran lower the amount of oxalate in urine?

At the beginning of the study (called the baseline), participants that weighed less than 10 kg had the highest amount of oxalate in their urine compared to the participants that weighed more than 10 kg. The amount of oxalate in the urine lowered an average of 71% for the 16 participants that received lumasiran for 6 months. Participants in each weight category had an oxalate reduction of 67% or more as shown below.

	3 participants weighing <10kg	11 participants weighing 10 to <20kg	2 participants weighing ≥20kg
After 6 months of lumasiran treatment	84% ▼	67% ▼	71% ▼

The figure below shows the actual amount of oxalate in urine at each month.



What medical problems did participants have during the study?

Doctors record any medical problems (called "adverse events") that a participant has during a study. Participants can have adverse events that are either related or not related to the study medication; this is decided by the study doctor.

- Adverse events can be caused by another disease, by another medication, or by chance. Sometimes the cause is unknown.
- An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or requires hospital care.

How many participants reported an adverse event?

The study found that all 18 patients had an adverse event.

- One participant had a serious adverse event of hospitalization for viral infection that the doctor considered not related to lumasiran.

PARTICIPANT WEIGHT CATEGORY		
<10kg	**10 to <20kg**	**≥20kg**
3 out of **3** patients reported a total of **18** events	**12** out of **12** patients reported a total of **44** events	**3** out of **3** patients reported a total of **17** events
Of these, **none** were thought to be related to lumasiran	Of these, **3 events** were thought to be related to lumasiran	Of these, **3 events** were thought to be related to lumasiran

Most adverse events that were related to study medication included symptoms at or near the site of injection.

Most Common Adverse Events Reported by at Least 10% of Participants in any Group

Category	Number of Patients (%)
At least 1 adverse event	18 (100%)
Injection site reaction	3 (17%)
Fever	6 (33%)
Symptoms of a common cold	4 (22%)
Upper respiratory tract infection	3 (17%)

WHAT WILL HAPPEN NEXT?

The study will continue for up to 4 more years as the Extension Period. All participants will continue to receive lumasiran and will provide additional urine samples for researchers to test the level of oxalate in urine over time. The full results will be available after the study completes, which is currently planned for September 2024. Additional clinical studies with lumasiran are ongoing.

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WHERE CAN I LEARN MORE ABOUT THE ILLUMINATE-B STUDY?

For more details on this study please speak with a doctor, or visit:

www.clinicaltrials.gov	Use the study identifier **NCT03905694**
www.clinicaltrialsregister.eu	Use the study identifier **2018-004014-17**

Full Title: ILLUMINATE-B: An Open-Label Study to Evaluate the Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of Lumasiran in Infants and Young Children with Hyperoxaluria Type 1

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We appreciate our patients' continued participation in ILLUMINATE-B!

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