Clinical trial results:
A Phase 2, Multicenter, Open-Label, Extension Study to Evaluate the Long-Term Administration of ALN-GO1 in Patients with Primary Hyperoxaluria Type 1

Summary

EudraCT number	2016-003134-24
Trial protocol	DE GB NL FR
Global end of trial date	07 February 2023

Results information

Result version number	v1
This version publication date	23 August 2023
First version publication date	23 August 2023

Trial information

Trial identification

Sponsor protocol code	ALN-GO1-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03350451
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alnylam Pharmaceuticals, Inc.
Sponsor organisation address	675 West Kendall Street, Cambridge, United States, 02142
Public contact	Clinical Trial Information Line, Alnylam Pharmaceuticals, Inc., +1 8772569526, clinicaltrials@alnylam.com
Scientific contact	Clinical Trial Information Line, Alnylam Pharmaceuticals, Inc., +1 8772569526, clinicaltrials@alnylam.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001855-PIP02-16
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 February 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the long-term safety of multiple doses of ALN-GO1 in subjects with primary hyperoxaluria type 1 (PH1).

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form (ICF).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 April 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Israel: 7
Worldwide total number of subjects	20
EEA total number of subjects	10

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	10
Adolescents (12-17 years)	6
Adults (18-64 years)	4
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at 9 study centres in France, Germany, Israel, Netherlands and the United Kingdom from 04 April 2018 to 07 February 2023.

Pre-assignment

Screening details:

A total of 20 subjects previously treated in Study 001B (2015-004407-23) were enrolled and treated within this study.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Lumasiran (ALN-GO1): 1.0 mg/kg QM or 3.0 mg/kg Q3M

Arm description:

Subjects enrolling from study 001B, received lumasiran, subcutaneous (SC) injection, at a starting dose of 1.0 milligrams per kilograms (mg/kg) once monthly (QM) or 3.0 mg/kg once every 3 months [Q3M]) from Day 1 up to a maximum of Month 6. By Month 6, all subjects were approved to change dose and/or dosing regimen to receive lumasiran, SC injection at a dose of 3.0 mg/kg, Q3M, up to Month 51 of the treatment period.

Arm type	Experimental
Investigational medicinal product name	Lumasiran
Investigational medicinal product code	ALN-GO1
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Lumasiran, SC injection, administered at a starting dose of 1.0 mg/kg, QM or 3.0 mg/kg Q3M from Day 1 up to a maximum of Month 6. By Month 6, lumasiran, SC injection was administered at a dose of 3.0 mg/kg, Q3M, up to Month 51 of the treatment period.

Arm title	Lumasiran (ALN-GO1): 3.0 mg/kg QM

Arm description:

Subjects enrolling from study 001B, received lumasiran, SC injection, at a starting dose of 3.0 mg/kg, QM, from Day 1 up to a maximum of Month 21. By Month 21, all subjects were approved to change dosing regimen to receive lumasiran, SC injection, at a dose of 3.0 mg/kg, Q3M, up to Month 51 of the treatment period.

Arm type	Experimental
Investigational medicinal product name	Lumasiran
Investigational medicinal product code	ALN-GO1
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Lumasiran, SC injection, administered at a starting dose of 3.0 mg/kg, QM, from Day 1 up to a maximum of Month 21. By Month 21, lumasiran, SC injection, was administered at a dose of 3.0 mg/kg, Q3M, up to Month 51 of the treatment period.

Number of subjects in period 1	Lumasiran (ALN-GO1): 1.0 mg/kg QM or 3.0 mg/kg Q3M	Lumasiran (ALN-GO1): 3.0 mg/kg QM
Started	13	7
Safety Analysis Set	13	7
Pharmacodynamic Analysis Set	13	7
Completed	13	7

Baseline characteristics

Reporting groups	
Reporting group title	Lumasiran (ALN-GO1): 1.0 mg/kg QM or 3.0 mg/kg Q3M
Reporting group description:	
Subjects enrolling from study 001B, received lumasiran, subcutaneous (SC) injection, at a starting dose of 1.0 milligrams per kilograms (mg/kg) once monthly (QM) or 3.0 mg/kg once every 3 months [Q3M]) from Day 1 up to a maximum of Month 6. By Month 6, all subjects were approved to change dose and/or dosing regimen to receive lumasiran, SC injection at a dose of 3.0 mg/kg, Q3M, up to Month 51 of the treatment period.	
Reporting group title	Lumasiran (ALN-GO1): 3.0 mg/kg QM
Reporting group description:	
Subjects enrolling from study 001B, received lumasiran, SC injection, at a starting dose of 3.0 mg/kg, QM, from Day 1 up to a maximum of Month 21. By Month 21, all subjects were approved to change dosing regimen to receive lumasiran, SC injection, at a dose of 3.0 mg/kg, Q3M, up to Month 51 of the treatment period.	

Reporting group values	Lumasiran (ALN-GO1): 1.0 mg/kg QM or 3.0 mg/kg Q3M	Lumasiran (ALN-GO1): 3.0 mg/kg QM	Total
Number of subjects	13	7	20
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	16.1	12.6	
standard deviation	± 12.31	± 3.95	-
Gender categorical Units: Subjects			
Female	9	4	13
Male	4	3	7
Ethnicity Units: Subjects			
Not Hispanic or Latino	13	7	20
Race Units: Subjects			
Asian	2	2	4
White	10	5	15
Other	1	0	1

End points

End points reporting groups

Reporting group title	Lumasiran (ALN-GO1): 1.0 mg/kg QM or 3.0 mg/kg Q3M

Reporting group description:

Subjects enrolling from study 001B, received lumasiran, subcutaneous (SC) injection, at a starting dose of 1.0 milligrams per kilograms (mg/kg) once monthly (QM) or 3.0 mg/kg once every 3 months [Q3M]) from Day 1 up to a maximum of Month 6. By Month 6, all subjects were approved to change dose and/or dosing regimen to receive lumasiran, SC injection at a dose of 3.0 mg/kg, Q3M, up to Month 51 of the treatment period.

Reporting group title	Lumasiran (ALN-GO1): 3.0 mg/kg QM

Reporting group description:

Subjects enrolling from study 001B, received lumasiran, SC injection, at a starting dose of 3.0 mg/kg, QM, from Day 1 up to a maximum of Month 21. By Month 21, all subjects were approved to change dosing regimen to receive lumasiran, SC injection, at a dose of 3.0 mg/kg, Q3M, up to Month 51 of the treatment period.

Primary: Number of Subjects With at Least One Adverse Event (AE)

End point title	Number of Subjects With at Least One Adverse Event (AE)[1]

End point description:

AE is any untoward medical occurrence in a subject or clinical investigational participant administered a medicinal product and which does not necessarily have a causal relationship with this treatment. Safety analysis set included all subjects who received any amount of study drug.

End point type	Primary

End point timeframe:

Baseline (Day -1) up to 54 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned for this outcome measure.

End point values	Lumasiran (ALN-GO1): 1.0 mg/kg QM or 3.0 mg/kg Q3M	Lumasiran (ALN-GO1): 3.0 mg/kg QM		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	7		
Units: subjects	13	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 24-hour Urinary Oxalate Corrected for Body Surface Area (BSA) at 54 Months

End point title	Change From Baseline in 24-hour Urinary Oxalate Corrected for Body Surface Area (BSA) at 54 Months

End point description:

Oxalate produced by the liver is the key toxic metabolite that drives disease pathology in subjects with primary hyperoxaluria type 1 (PH1). The risk of disease complications increase continuously as oxalate

levels increase. 24-hour urinary oxalate (millimole [mmol]/ 24 hour [h]/1.73 meters squared [m^2]) corrected for BSA at each visit per subject was calculated as follows: [Urine oxalate concentration (micromole per liter [umol/L])/1000 (umol/mmol)]*[24hour urine volume (mL)/1000 (mL/L)]* [24 hours/actual collection hours]*1.73/(BSA). Baseline was the derived baseline value from the lumasiran treated period of Study ALN-GO1-001. A negative change from baseline indicated a favorable outcome. Pharmacodynamic (PD) analysis set included all subjects who received any amount of study drug and who had at least 1 post-dose urine sample for PD. Overall number of subjects analysed are the number of subjects with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline (Day -1) up to 54 months

End point values	Lumasiran (ALN-GO1): 1.0 mg/kg QM or 3.0 mg/kg Q3M	Lumasiran (ALN-GO1): 3.0 mg/kg QM		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	6		
Units: mmol/24hr/1.73m^2				
arithmetic mean (standard error)	-1.425 (± 0.2188)	-2.126 (± 0.5528)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 24-hour Urinary Oxalate:Creatinine Ratio at 54 Months

End point title	Change From Baseline in 24-hour Urinary Oxalate:Creatinine Ratio at 54 Months

End point description:

Baseline is the derived baseline value from the lumasiran treated period of Study ALN-GO1-001. A negative change from baseline indicates a favorable outcome. PD analysis set included all subjects who received any amount of study drug and who had at least 1 post-dose urine sample for PD.

End point type	Secondary

End point timeframe:

Baseline (Day -1) up to 54 months

End point values	Lumasiran (ALN-GO1): 1.0 mg/kg QM or 3.0 mg/kg Q3M	Lumasiran (ALN-GO1): 3.0 mg/kg QM		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	7		
Units: mmol/mmol				
arithmetic mean (standard error)	-0.2175 (± 0.03880)	-0.2480 (± 0.04047)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Estimated Glomerular Filtration Rate (eGFR) at 54 Months

End point title	Change From Baseline in Estimated Glomerular Filtration Rate (eGFR) at 54 Months

End point description:

Baseline was defined as the last measurement prior to the first dose of lumasiran in the ALN-GO1-001 study. eGFR was calculated based on the Modification of Diet in Renal Disease (MDRD) formula for subjects >=18 years of age at enrollment and the Schwartz Bedside formula for subjects <18 years of age at enrollment. eGFR based on MDRD formula was calculated as follows: eGFR (mL/min/1.73 m^2) = 175 × (serum creatinine {SCr} [µmol/deciliter(dL)]/88.4)-1.154 × (age)-0.203 × (0.742, if female), or × (1.212, if African American) and based on Schwartz formula: eGFR (mL/min/1.73m2) = (36.2 × height [cm])/ SCr (µmol /dL). Safety analysis set included all subjects who received any amount of study drug.

End point type	Secondary

End point timeframe:

Baseline (Day -1) up to 54 months

End point values	Lumasiran (ALN-GO1): 1.0 mg/kg QM or 3.0 mg/kg Q3M	Lumasiran (ALN-GO1): 3.0 mg/kg QM		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	7		
Units: mL/min/1.73m^2				
arithmetic mean (standard error)	0.674 (± 3.7970)	-12.026 (± 3.6369)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline (Day -1) up to 54 months

Adverse event reporting additional description:

Safety analysis set included all subjects who received any amount of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Lumasiran (ALN-GO1): 1.0 mg/kg QM or 3.0 mg/kg Q3M

Reporting group description:

Subjects enrolling from study 001B, received lumasiran, SC injection, at a starting dose of 1.0 mg/kg QM or 3.0 mg/kg Q3M from Day 1 up to a maximum of Month 6. By Month 6, all subjects were approved to change dose and/or dosing regimen to receive lumasiran, SC injection at a dose of 3.0 mg/kg, Q3M, up to Month 51 of the treatment period.

Reporting group title	Lumasiran (ALN-GO1): 3.0 mg/kg QM

Reporting group description:

Subjects enrolling from study 001B, received lumasiran, SC injection, at a starting dose of 3.0 mg/kg, QM, from Day 1 up to a maximum of Month 21. By Month 21, all subjects were approved to change dosing regimen to receive lumasiran, SC injection, at a dose of 3.0 mg/kg, Q3M, up to Month 51 of the treatment period.

Serious adverse events	Lumasiran (ALN-GO1): 1.0 mg/kg QM or 3.0 mg/kg Q3M	Lumasiran (ALN-GO1): 3.0 mg/kg QM	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 13 (30.77%)	3 / 7 (42.86%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Glomerular Filtration Rate Decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Bone Contusion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral Injury			

subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Renal Stone Removal			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid Operation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Colic			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	2 / 13 (15.38%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Thyroid Mass			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pyelonephritis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Lumasiran (ALN-GO1): 1.0 mg/kg QM or 3.0 mg/kg Q3M	Lumasiran (ALN-GO1): 3.0 mg/kg QM	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)	7 / 7 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Orthostatic Hypotension			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Surgical and medical procedures			
Gastrostomy Closure			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Tooth Extraction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Wisdom Teeth Removal			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Feeling Cold			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Influenza Like Illness			

subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Injection Site Reaction			
subjects affected / exposed	4 / 13 (30.77%)	4 / 7 (57.14%)	
occurrences (all)	7	6	
Non-cardiac Chest Pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	4	
Pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	1	5	
Vaccination Site Pain			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	2	2	
Vessel Puncture Site Haematoma			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Immunisation Reaction			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	1	4	
Seasonal Allergy			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Genital Pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Heavy Menstrual Bleeding			

subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	3	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 13 (7.69%)	2 / 7 (28.57%)	
occurrences (all)	3	3	
Epistaxis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Nasal Congestion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Oropharyngeal Pain			
subjects affected / exposed	1 / 13 (7.69%)	2 / 7 (28.57%)	
occurrences (all)	1	2	
Upper-airway Cough Syndrome			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Psychiatric disorders			
Affective Disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Nightmare			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Sleep Disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Product issues			
Device Breakage			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Investigations			
Bilirubin Conjugated Increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	

Blood Bilirubin Increased			
subjects affected / exposed	3 / 13 (23.08%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Blood Creatinine Increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	3	
Electrocardiogram QRS Complex Prolonged			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Glycolic Acid Increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
SARS-CoV-2 Test Positive			
subjects affected / exposed	3 / 13 (23.08%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Ultrasound Breast Abnormal			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Ultrasound Kidney Abnormal			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Weight Increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Head Injury			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Ligament Sprain			
subjects affected / exposed	2 / 13 (15.38%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Limb Injury			

subjects affected / exposed	2 / 13 (15.38%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Skin Abrasion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Skin Wound			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Stoma Site Pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Thermal Burn			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Tibia Fracture			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Atrioventricular Block			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 13 (23.08%)	1 / 7 (14.29%)	
occurrences (all)	4	2	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	1	2	
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hyperacusis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Hypoacusis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Eye disorders			
Eye Allergy			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Periorbital Swelling			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Abdominal Pain			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Abdominal Pain Upper			
subjects affected / exposed	0 / 13 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	
Dental Caries			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Diverticulum Intestinal			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Food Poisoning			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Large Intestine Polyp			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Nausea			

subjects affected / exposed	0 / 13 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	
Toothache			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	2 / 13 (15.38%)	4 / 7 (57.14%)	
occurrences (all)	3	6	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Alopecia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Blister			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Nephrolithiasis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	4	3	
Renal Cyst			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Renal Pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			

Thyroid Mass			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Back Pain			
subjects affected / exposed	1 / 13 (7.69%)	2 / 7 (28.57%)	
occurrences (all)	2	4	
Flank Pain			
subjects affected / exposed	2 / 13 (15.38%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Infections and infestations			
Asymptomatic COVID-19			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
COVID-19			
subjects affected / exposed	6 / 13 (46.15%)	3 / 7 (42.86%)	
occurrences (all)	6	3	
Conjunctivitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Cystitis Escherichia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Ear Infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Gastroenteritis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Gastroenteritis Viral			

subjects affected / exposed	2 / 13 (15.38%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Influenza			
subjects affected / exposed	2 / 13 (15.38%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Nasopharyngitis			
subjects affected / exposed	2 / 13 (15.38%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Pharyngitis			
subjects affected / exposed	2 / 13 (15.38%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Pyelonephritis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	2 / 13 (15.38%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Tinea Versicolour			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	3	
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 13 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	3	
Urinary Tract Infection			
subjects affected / exposed	2 / 13 (15.38%)	0 / 7 (0.00%)	
occurrences (all)	4	0	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Increased Appetite			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Iron Deficiency			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	

Vitamin D Deficiency subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	3 / 7 (42.86%) 7	
Weight Gain Poor subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 2	0 / 7 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 August 2019	The primary purpose for this protocol amendment was to extend the study duration from up to 2 years to up to 54 months. In addition, the amendment: • Updated adverse event of clinical interest (AECI) • Added liver function test (LFT) criteria for withholding, monitoring, and stopping study drug dosing to align with other studies of lumasiran • Provided dosing information for subjects who progress to end-stage renal disease (ESRD) and require dialysis, a potential occurrence in PH1 subjects.
04 May 2020	The primary purpose for this protocol amendment was to incorporate urgent safety measures (USMs) that were communicated to investigators in a Dear Investigator Letter to assure the safety of study subjects while minimizing risks to study integrity amid the Coronavirus disease 2019 (COVID-19) pandemic. Changes not related to USMs were also incorporated. • Permitted lumasiran administration at locations other than study center that had undergone appropriate training • Allowed assessment of AEs and concomitant medication to be conducted offsite • Expanded study assessment window to ±28 days at Month 12 and ±14 days thereafter • Allowed, after 12 months, renal ultrasound and ECG assessments to be completed up to 9 months after intended time point. • Removed quality of life (QOL) questionnaire and assessment as part of the exploratory objective and endpoint.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported