



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	v2 (current)
This version publication date	21 April 2024
First version publication date	23 August 2023
Version creation reason	New data added to full data set Certain data fields need to be updated.

Trial information

Trial identification

Sponsor protocol code	ALN-GO1-002
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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	300 Third 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)	EMA-002079-PIP01-16
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
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Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at 9 study centers in France, Germany, Israel, Netherlands, and the United Kingdom from 04 April 2018 to 07 February 2023. A total of 20 subjects previously treated in Study 001B (2015-004407-23) were enrolled and treated within this study.

Pre-assignment

Screening details:

The cumulative dose of lumasiran administered over 6 months was the same for both 1 mg/kg QM & 3 mg/kg Q3M, these subjects were pooled into one arm as recommended by the Safety Review Committee (SRC). As pre-specified in the SAP, subjects who began treatment at 1 mg/kg QM, then transitioned to 3 mg/kg Q3M were to be summarised as a single group.

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.

All 3 subjects who began treatment at 1 mg/kg QM transitioned to 3 mg/kg Q3M regimen by Month 6. As the cumulative dose administered over 6 months was the same for both 1 mg/kg QM & 3 mg/kg Q3M, these subjects were pooled into one arm as recommended by the SRC.

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
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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
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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.

All 3 subjects who began treatment at 1 mg/kg QM transitioned to 3 mg/kg Q3M regimen by Month 6. As the cumulative dose administered over 6 months was the same for both 1 mg/kg QM & 3 mg/kg Q3M, these subjects were pooled into one arm as recommended by the SRC.

Reporting group title	Lumasiran (ALN-GO1): 3.0 mg/kg QM
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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 standard deviation	16.1 ± 12.31	12.6 ± 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
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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.

All 3 subjects who began treatment at 1 mg/kg QM transitioned to 3 mg/kg Q3M regimen by Month 6. As the cumulative dose administered over 6 months was the same for both 1 mg/kg QM & 3 mg/kg Q3M, these subjects were pooled into one arm as recommended by the SRC.

Reporting group title	Lumasiran (ALN-GO1): 3.0 mg/kg QM
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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]
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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. The cumulative dose of lumasiran administered over 6 months was the same for both 1 mg/kg QM & 3 mg/kg Q3M, these subjects were pooled into one arm as recommended by the SRC. As pre-specified in the SAP, subjects who began treatment at 1 mg/kg QM, then transitioned to 3 mg/kg Q3M were to be summarized as a single group. All 3 subjects who began treatment at 1 mg/kg QM transitioned to 3 mg/kg Q3M regimen by Month 6.

End point type	Primary
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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

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
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End point description:

Oxalate produced by liver is the key toxic metabolite driving disease pathology in subjects with PH1. Risk of disease complications increase 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. Baseline=derived baseline value from lumasiran treated period of Study ALN-GO1-001. Negative change from baseline indicated favorable outcome. Pharmacodynamic (PD) analysis set included all subjects who received any amount of study drug & had at least 1 post-dose urine sample for PD. Overall number analysed = number of subjects with data available for analysis. The cumulative dose of lumasiran administered over 6 months was the same for both 1 mg/kg QM & 3 mg/kg Q3M, these subjects were pooled into one arm as recommended by the SRC. As pre-specified in the SAP, subjects who began treatment at 1 mg/kg QM, then transitioned to 3 mg/kg Q3M were to be summarised as a single group.

End point type	Secondary
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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 ($\pm$ 0.2188)	-2.126 ($\pm$ 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
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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. The cumulative dose of lumasiran administered over 6 months was the same for both 1 mg/kg QM & 3 mg/kg Q3M, these subjects were pooled into one arm as recommended by the SRC. As pre-specified in the SAP, subjects who began treatment at 1 mg/kg QM, then transitioned to 3 mg/kg Q3M were to be summarized as a single group. All 3 subjects who began treatment at 1 mg/kg QM transitioned to 3 mg/kg Q3M regimen by Month 6.

End point type	Secondary
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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
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End point description:

Baseline was defined as last measurement prior to the first dose of lumasiran in the ALN-GO1-001 study. eGFR was calculated based on Modification of Diet in Renal Disease (MDRD) formula for subjects ≥ 18 years of age at enrollment & Schwartz Bedside formula for subjects < 18 years of age at enrollment. eGFR per MDRD formula was calculated as follows: $\text{eGFR (mL/min/1.73 m}^2\text{)} = 175 \times (\text{serum creatinine \{SCr\} } [\mu\text{mol/deciliter(dL)}]/88.4)^{-1.154} \times (\text{age})^{-0.203} \times (0.742, \text{ if female}), \text{ or } \times (1.212, \text{ if African American})$ or based on Schwartz formula: $\text{eGFR (mL/min/1.73m}^2\text{)} = (36.2 \times \text{height [cm]}) / \text{SCr } (\mu\text{mol /dL})$. Safety analysis set included all subjects who received any amount of study drug. Cumulative dose of lumasiran administered over 6 months was the same for both 1 mg/kg QM & 3 mg/kg Q3M, these subjects were pooled into one arm as recommended by the SRC. As pre-specified in the SAP, subjects who began treatment at 1 mg/kg QM, then transitioned to 3 mg/kg Q3M were to be summarised as a single group.

End point type	Secondary
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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. The cumulative dose of lumasiran administered over 6 months was the same for both 1 mg/kg QM & 3 mg/kg Q3M, these subjects were pooled into one arm as recommended by the SRC. As pre-specified in the SAP, subjects who began treatment at 1 mg/kg QM, then transitioned to 3 mg/kg Q3M were to be summarised as as a single group.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

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

All 3 subjects who began treatment at 1 mg/kg QM transitioned to 3 mg/kg Q3M regimen by Month 6. As the cumulative dose administered over 6 months was the same for both 1 mg/kg QM & 3 mg/kg Q3M, these subjects were pooled into one arm as recommended by the SRC.

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

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

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

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

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

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

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

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

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

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

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

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

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