Clinical trial results:
Open-Label, Phase 2 Study to Evaluate the Safety and Tolerability of Maralixibat in the Treatment of Infants with Cholestatic Liver Diseases Including Progressive Familial Intrahepatic Cholestasis and Alagille Syndrome.

Summary

EudraCT number	2020-004628-40
Trial protocol	BE FR PL
Global end of trial date	17 December 2024

Results information

Result version number	v1 (current)
This version publication date	17 July 2025
First version publication date	17 July 2025

Trial information

Trial identification

Sponsor protocol code	MRX-801

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04729751
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 119916, IND : 119917

Notes:

Sponsors

Sponsor organisation name	Mirum Pharmaceuticals Inc.
Sponsor organisation address	989 E Hillsdale Blvd. Suite 300, Foster City, United States, 94404
Public contact	Chief Medical Officer, Mirum Pharmaceuticals Inc., 1 6506674085, medinfo@mirumpharma.com
Scientific contact	Chief Medical Officer, Mirum Pharmaceuticals Inc., 1 6506674085, medinfo@mirumpharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001475-PIP02-13, EMEA-001475-PIP03-17
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 February 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 December 2024
Global end of trial reached?	Yes
Global end of trial date	17 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of maralixibat in infant participants with cholestatic liver disease, Alagille syndrome (ALGS) or progressive familial intrahepatic cholestatic (PFIC).

Protection of trial subjects:

All study participants (caregivers as applicable) were required to read and sign an Informed Consent Form (ICF). Participants were re-consented to the most current version of the ICF(s) during their participation in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 September 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	United States: 7
Country: Number of subjects enrolled	Poland: 7
Worldwide total number of subjects	27
EEA total number of subjects	11

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)	27
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 27 participants were enrolled in the study, across 10 sites in 6 countries (Belgium, Brazil, France, Poland, United Kingdom, and United States), 17 patients in the ALGS Cohort and 10 in the PFIC Cohort.

Pre-assignment

Screening details:

The screening period starts when informed consent (by the legally authorized representative) is signed. The duration of the screening period is up to 4 weeks, during which all procedures listed for the screening visit in the schedule of assessment must be completed.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Maralixibat

Arm description:

Open-label, multicenter, Phase 2 study to evaluate the safety and tolerability of maralixibat in the treatment of infants (<12 months of age) with cholestatic liver disease (ALGS or PFIC).
Participants with ALGS received maralixibat doses in the ranges of 200 to 400 µg/kg QD.
Participants with PFIC received maralixibat doses in the ranges of 300 QD to 600 µg/kg BID.

Arm type	Experimental
Investigational medicinal product name	Maralixibat Chloride
Investigational medicinal product code	
Other name	Maralixibat
Pharmaceutical forms	Oral solution in bottle
Routes of administration	Oral use

Dosage and administration details:

Four different strengths of the maralixibat oral solution (5, 10, 15, and 20 mg/mL) were used; dosing was based on participant weight.

Number of subjects in period 1	Maralixibat
Started	27
Completed	25
Not completed	2
Consent withdrawn by subject	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Maralixibat
Reporting group description:	
Open-label, multicenter, Phase 2 study to evaluate the safety and tolerability of maralixibat in the treatment of infants (<12 months of age) with cholestatic liver disease (ALGS or PFIC). Participants with ALGS received maralixibat doses in the ranges of 200 to 400 µg/kg QD. Participants with PFIC received maralixibat doses in the ranges of 300 QD to 600 µg/kg BID.	

Reporting group values	Maralixibat	Total	
Number of subjects	27	27	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	27	27	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: months			
least squares mean	7.1		
standard deviation	± 3.03	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	21	21	

Subject analysis sets	
Subject analysis set title	ALGS
Subject analysis set type	Full analysis
Subject analysis set description:	
Includes all participants with Alagille Syndrome (ALGS) who received at least one dose of maralixibat.	
Subject analysis set title	PFIC
Subject analysis set type	Full analysis
Subject analysis set description:	
Includes all participants with Progressive Familial Intrahepatic Cholestasis (PFIC) who received at least one dose of maralixibat.	

Reporting group values	ALGS	PFIC	
Number of subjects	17	10	

Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	17	10	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: months			
least squares mean	7.4	6.6	
standard deviation	± 2.48	± 3.89	
Gender categorical Units: Subjects			
Female	3	3	
Male	14	7	

End points

End points reporting groups

Reporting group title	Maralixibat

Reporting group description:

Open-label, multicenter, Phase 2 study to evaluate the safety and tolerability of maralixibat in the treatment of infants (<12 months of age) with cholestatic liver disease (ALGS or PFIC).
Participants with ALGS received maralixibat doses in the ranges of 200 to 400 µg/kg QD.
Participants with PFIC received maralixibat doses in the ranges of 300 QD to 600 µg/kg BID.

Subject analysis set title	ALGS
Subject analysis set type	Full analysis

Subject analysis set description:

Includes all participants with Alagille Syndrome (ALGS) who received at least one dose of maralixibat.

Subject analysis set title	PFIC
Subject analysis set type	Full analysis

Subject analysis set description:

Includes all participants with Progressive Familial Intrahepatic Cholestasis (PFIC) who received at least one dose of maralixibat.

Primary: Incidence of Treatment-Emergent Adverse Events (TEAEs)

End point title	Incidence of Treatment-Emergent Adverse Events (TEAEs)[1]

End point description:

TEAE = Treatment -emergent Adverse Event

End point type	Primary

End point timeframe:

From Baseline through End of Treatment (up to approximately 13 weeks).

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: High-level summary of treatment-emergent adverse events have been provided by the number and percentage of participants who experienced them. The summary includes the total number and percent of participants by cohort and overall maralixibat treated population.

End point values	Maralixibat	ALGS	PFIC	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	27	17	10	
Units: number of participants				
At least one TEAE	26	16	10	
TEAE related to study drug	7	4	3	
Grade ≥3 TEAE	7	6	1	
Grade ≥3 TEAE related to study drug	0	0	0	
Serious TEAE	8	6	2	
Serious TEAE related to study drug	0	0	0	
TEAE that led to study discontinuation	1	0	1	
TEAE that led to death	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting serum bile acid (sBA) levels

End point title	Change in fasting serum bile acid (sBA) levels

End point description:

End point type	Secondary

End point timeframe:

From Baseline through to Week 13, including the change from Baseline value.

End point values	Maralixibat	ALGS	PFIC	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	27	17	10	
Units: Serum bile acid levels (µmol/L)				
arithmetic mean (standard deviation)				
Baseline	270.49 (± 187.898)	292.81 (± 218.756)	228.32 (± 107.525)	
Week 13	157.83 (± 102.890)	172.49 (± 109.924)	130.33 (± 88.204)	
Change from Baseline	-86.91 (± 124.960)	-75.68 (± 115.669)	-107.96 (± 146.766)	

Statistical analyses

Statistical analysis title	Descriptive Analysis of Serum Bile Acid Change

Statistical analysis description:

Descriptive statistics were used to summarize the serum bile acid levels at Baseline and Week 13. Change from Baseline values were reported to assess long-term trends. No inferential statistical tests were applied.

Comparison groups	ALGS v PFIC
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.05 [3]
Method	not applicable
Parameter estimate	not applicable

Notes:

[2] - Descriptive statistics were used to summarize the serum bile acid levels at Baseline and Week 13. Change from Baseline values were reported to assess long-term trends. No inferential statistical tests were applied.

[3] - Descriptive statistics were used to summarize the serum bile acid levels at Baseline and Week 13. Change from Baseline values were reported to assess long-term trends. No inferential statistical tests were applied.

Secondary: To evaluate the effect on liver enzymes (ALT, AST) and bilirubin

End point title	To evaluate the effect on liver enzymes (ALT, AST) and bilirubin

End point description:

AST= aspartate aminotransferase, and ALT= alanine aminotransferase.

End point type	Secondary

End point timeframe:

From Baseline through to Week 13

End point values	Maralixibat	ALGS	PFIC	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	27	17	10	
Units: ALT, AST and bilirubin levels (U/L)				
arithmetic mean (standard deviation)				
ALT, U/L Baseline	160.56 (± 105.807)	167.35 (± 106.018)	149.00 (± 110.108)	
ALT, U/L Week 13	208.00 (± 182.954)	256.87 (± 190.732)	126.56 (± 143.630)	
ALT, U/L Change from Baseline	56.17 (± 161.298)	99.00 (± 190.981)	-15.22 (± 42.387)	
AST, U/L Baseline	174.85 (± 100.999)	184.12 (± 105.042)	159.10 (± 97.034)	
AST, U/L Week 13	196.87 (± 140.529)	236.87 (± 142.540)	121.88 (± 107.591)	
AST, U/L Change from Baseline	35.57 (± 102.183)	69.27 (± 136.827)	-27.63 (± 30.905)	
Total bilirubin, µmol/L Baseline	104.94 (± 95.564)	142.54 (± 102.323)	41.02 (± 23.651)	
Total bilirubin, µmol/L Week 13	79.51 (± 93.302)	114.89 (± 102.789)	20.53 (± 16.668)	
Total bilirubin, µmol/L Change from Baseline	-21.79 (± 37.737)	-22.85 (± 46.252)	-20.02 (± 18.575)	

Statistical analyses

Statistical analysis title	Descriptive Analysis of Liver enzymes

Statistical analysis description:

Descriptive statistics were used to summarize the liver enzymes (ALT, AST and bilirubin) levels at Baseline and Week 13. Change from Baseline values were reported to assess long-term trends. No inferential statistical tests were applied.

Comparison groups	ALGS v PFIC
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.05 [5]
Method	not applicable
Parameter estimate	not applicable

Notes:

[4] - Descriptive statistics were used to summarize the liver enzymes (ALT, AST and bilirubin) levels at Baseline and Week 13. Change from Baseline values were reported to assess long-term trends. No inferential statistical tests were applied.

[5] - Descriptive statistics were used to summarize the liver enzymes (ALT, AST and bilirubin) levels at Baseline and Week 13. Change from Baseline values were reported to assess long-term trends. No inferential statistical tests were applied.

Secondary: To evaluate the effect on Lipid-Soluble Vitamins (LSVs)

End point title	To evaluate the effect on Lipid-Soluble Vitamins (LSVs)

End point description:

The values marked with 0 reported for Vitamin K values for PFIC Week 13 and Change from Baseline indicates that the values were not calculated.

End point type	Secondary

End point timeframe:

Change from baseline to Week 13 in vitamins A, D, E, and K

End point values	Maralixibat	ALGS	PFIC	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	27	17	10	
Units: serum levels				
arithmetic mean (standard deviation)				
Vitamin A umol/L Baseline	1.68 (± 1.108)	1.78 (± 1.189)	1.50 (± 0.991)	
Vitamin A umol/L Week 13	2.16 (± 0.969)	2.08 (± 1.031)	2.32 (± 0.884)	
Vitamin A umol/L Change from Baseline	0.51 (± 0.732)	0.45 (± 0.678)	0.61 (± 0.878)	
Vitamin D nmol/L Baseline	62.73 (± 58.027)	62.64 (± 58.563)	62.87 (± 60.308)	
Vitamin D nmol/L Week 13	84.47 (± 57.160)	78.42 (± 58.952)	94.84 (± 56.849)	
Vitamin D nmol/L Change from Baseline	12.42 (± 67.451)	7.63 (± 79.383)	20.65 (± 44.394)	
Vitamin E mg/L Baseline	5.28 (± 4.833)	6.54 (± 5.351)	2.78 (± 2.149)	
Vitamin E mg/L Week 13	5.39 (± 4.701)	5.99 (± 5.084)	3.98 (± 3.658)	
Vitamin E mg/L Change from Baseline	-0.04 (± 2.074)	-0.46 (± 2.214)	0.92 (± 1.422)	
Vitamin K nmol/L Baseline	21.68 (± 70.436)	31.22 (± 84.315)	0.21 (± 0.133)	
Vitamin K nmol/L Week 13	14.64 (± 0)	14.64 (± 0)	0 (± 0)	
Vitamin K nmol/L Change from Baseline	-241.14 (± 0)	-241.14 (± 0)	0 (± 0)	

Statistical analyses

Statistical analysis title	Descriptive Analysis of Lipid-Soluble Vitamins

Statistical analysis description:

Descriptive statistics were used to summarize the Lipid-Soluble Vitamins levels at Baseline and Week 13. Change from Baseline values were reported to assess long-term trends. No inferential statistical tests were applied.

Comparison groups	ALGS v PFIC
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.05 [7]
Method	not applicable
Parameter estimate	not applicable

Notes:

[6] - Descriptive statistics were used to summarize the Lipid-Soluble Vitamins levels at Baseline and Week 13. Change from Baseline values were reported to assess long-term trends. No inferential statistical tests were applied.

[7] - Descriptive statistics were used to summarize the Lipid-Soluble Vitamins levels at Baseline and Week 13. Change from Baseline values were reported to assess long-term trends. No inferential statistical tests were applied.

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline to end of treatment.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1
Reporting groups	
Reporting group title	ALGS
Reporting group description: All participants in the ALGS arm who received maralixibat and were included in the AE analysis.	
Reporting group title	PFIC
Reporting group description: All participants in the PFIC arm who received maralixibat and were included in the AE analysis.	

Serious adverse events	ALGS	PFIC	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 17 (35.29%)	2 / 10 (20.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Crying			
subjects affected / exposed	1 / 17 (5.88%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infantile colic			

subjects affected / exposed	1 / 17 (5.88%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 17 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal sepsis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	0 / 17 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corona virus infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis adenovirus			
subjects affected / exposed	0 / 17 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 17 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			

subjects affected / exposed	1 / 17 (5.88%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	1 / 17 (5.88%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	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	ALGS	PFIC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 17 (94.12%)	10 / 10 (100.00%)	
Investigations			
Investigations			
subjects affected / exposed	3 / 17 (17.65%)	3 / 10 (30.00%)	
occurrences (all)	5	6	
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications			
subjects affected / exposed	1 / 17 (5.88%)	2 / 10 (20.00%)	
occurrences (all)	1	4	
Nervous system disorders			

Nervous system disorders subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2	2 / 10 (20.00%) 2	
Blood and lymphatic system disorders Coagulopathy subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	3 / 10 (30.00%) 6	
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	3 / 17 (17.65%) 8	2 / 10 (20.00%) 2	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Teething subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all)	7 / 17 (41.18%) 15 2 / 17 (11.76%) 5 3 / 17 (17.65%) 7 3 / 17 (17.65%) 4	4 / 10 (40.00%) 8 5 / 10 (50.00%) 8 2 / 10 (20.00%) 3 1 / 10 (10.00%) 1	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all)	4 / 17 (23.53%) 5 2 / 17 (11.76%) 3 2 / 17 (11.76%) 2	2 / 10 (20.00%) 2 3 / 10 (30.00%) 4 0 / 10 (0.00%) 0	
Skin and subcutaneous tissue disorders			

Skin and subcutaneous tissue disorders			
subjects affected / exposed	4 / 17 (23.53%)	2 / 10 (20.00%)	
occurrences (all)	5	2	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 17 (35.29%)	4 / 10 (40.00%)	
occurrences (all)	9	6	
Upper respiratory tract infection			
subjects affected / exposed	4 / 17 (23.53%)	4 / 10 (40.00%)	
occurrences (all)	12	5	
Viral infection			
subjects affected / exposed	4 / 17 (23.53%)	4 / 10 (40.00%)	
occurrences (all)	4	7	
Corona virus infection			
subjects affected / exposed	3 / 17 (17.65%)	2 / 10 (20.00%)	
occurrences (all)	3	2	
Rhinitis			
subjects affected / exposed	3 / 17 (17.65%)	2 / 10 (20.00%)	
occurrences (all)	3	2	
Ear infection			
subjects affected / exposed	4 / 17 (23.53%)	0 / 10 (0.00%)	
occurrences (all)	8	0	
Gastroenteritis			
subjects affected / exposed	2 / 17 (11.76%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Influenza			
subjects affected / exposed	1 / 17 (5.88%)	2 / 10 (20.00%)	
occurrences (all)	1	1	
Conjunctivitis			
subjects affected / exposed	2 / 17 (11.76%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Otitis media			
subjects affected / exposed	2 / 17 (11.76%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Respiratory tract infection viral			

subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2	0 / 10 (0.00%) 0	
Metabolism and nutrition disorders Hypervitaminosis D subjects affected / exposed occurrences (all)	 2 / 17 (11.76%) 2	 0 / 10 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 April 2021	Protocol version 2 (Global) released on 26 April 2021. Key Changes made: - Change in inclusion criteria (lower age limit removed) - Inclusion of 75mcg/kg dose for patients <1month - Clarifications/corrections from the previous version in SOA, participant compliance, neurodevelopmental assessments, laboratory evaluations - Addition of Adverse Event of Special Interest (AESI) - Change in the dose continuation/stopping rules - Removed the requirement for dose escalation in the presence of an investigator or trained study staff
01 June 2021	Protocol version 3 (Global) released on 01 June 2021. Key Changes made: - The Schedule of Assessments, Table 1, has been revised to reduce the number of site visits to decrease participant and caregiver burden - Inclusion of participants with gestational age <36 weeks, with approval by the medical monitor - Update of blood volumes to be drawn from participants during the study - Clarification of timepoints for PK assessments
14 January 2022	Protocol version 5 (Global) released on 14 January 2022. Key changes made: - Added LTE 16 week repeating cycle period, LTE final study visit, and safety follow-up contact. - Revised to remove the option for participants to roll over into Study 800 and to instead add the Study 801 LTE. Participants will no longer roll over into Study 800; they will remain within Study 801 LTE or transition to commercially available drug or an expanded access program, as applicable - Endpoints of assessments using the Itch Reported Outcome Observer (ItchRO[Obs]) instrument - Clarification regarding the inclusion of preterm-born infants. - Details for procedures related to study medication interruption or participant withdrawal due to AEs or disease progression. - Disease-related questionnaire to the long-term follow up period - Updated blood volume requirements and priority of sample collection

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None reported.

Notes: