Clinical trial results:
A Long-Term Safety Study of Maralixibat, an Apical Sodium Dependent Bile Acid Transporter Inhibitor (ASBTi), in the Treatment of Cholestatic Liver Disease in Subjects Who Previously Participated in a Maralixibat Study.

Summary

EudraCT number	2019-002755-42
Trial protocol	BE GB PL FR ES
Global end of trial date	04 September 2024

Results information

Result version number	v1
This version publication date	18 May 2025
First version publication date	18 May 2025

Trial information

Trial identification

Sponsor protocol code	MRX-800

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04168385
WHO universal trial number (UTN)	-
Other trial identifiers	INDs: 119916; 119917; 147617

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 Development Officer, Mirum Pharmaceuticals Inc., +1 6506674085, medinfo@mirumpharma.com
Scientific contact	Chief Development Officer, Mirum Pharmaceuticals Inc., +1 6506674085, medinfo@mirumpharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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	16 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 September 2024
Global end of trial reached?	Yes
Global end of trial date	04 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the long-term safety of maralixibat in subjects with cholestatic liver disease including, but not limited to, ALGS and 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	16 January 2020
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	Poland: 2
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	United States: 26
Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	Canada: 2
Worldwide total number of subjects	52
EEA total number of subjects	9

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)	34
Adolescents (12-17 years)	12
Adults (18-64 years)	6
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 52 participants were enrolled at 17 sites across 8 countries (Australia, Belgium, Canada, France, Poland, Spain, United Kingdom and United States). Participants were previously on maralixibat for an average of 4 years before entering this study.

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. A total of 43 subjects completed the study and a total of 9 discontinued early.

Period 1

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

Arms

Arm title	Maralixibat

Arm description:

Maralixibat chloride oral solution orally twice daily Up to 1.2* mg/kg/day), and according to indication. *equivalent to 1.14 mg/kg/day maralixibat. Doses reported here are in maralixibat chloride.

Participants with ALGS received maralixibat doses in the range of 0.15 mg/kg QD to 0.45 mg/kg BID. Participants with PFIC received maralixibat doses in the range of 0.3 mg/kg QD to 0.6 mg/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	52
Completed	43
Not completed	9
Consent withdrawn by subject	1
Adverse event	3
Liver transplant	4
Listed for liver transplant	1

Baseline characteristics

Reporting groups	
Reporting group title	Maralixibat
Reporting group description:	
Maralixibat chloride oral solution orally twice daily Up to 1.2* mg/kg/day), and according to indication. *equivalent to 1.14 mg/kg/day maralixibat. Doses reported here are in maralixibat chloride. Participants with ALGS received maralixibat doses in the range of 0.15 mg/kg QD to 0.45 mg/kg BID. Participants with PFIC received maralixibat doses in the range of 0.3 mg/kg QD to 0.6 mg/kg BID.	

Reporting group values	Maralixibat	Total	
Number of subjects	52	52	
Age categorical			
Age at time of the baseline visit.			
Units: Subjects			
5 to 8 years	12	12	
9 to 12 years	25	25	
13 to 18 years	10	10	
> 18 years	5	5	
Age continuous			
Age at time of the baseline visit.			
Units: years			
arithmetic mean	11.3		
standard deviation	± 4.19	-	
Gender categorical			
Units: Subjects			
Female	26	26	
Male	26	26	

Subject analysis sets	
Subject analysis set title	ALGS
Subject analysis set type	Safety 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	Safety 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	40	12	
Age categorical			
Age at time of the baseline visit.			
Units: Subjects			
5 to 8 years	8	4	
9 to 12 years	18	7	
13 to 18 years	9	1	

> 18 years	5	0	

Age continuous			
Age at time of the baseline visit.			
Units: years			
arithmetic mean	12	8.8	
standard deviation	± 4.28	± 2.82	
Gender categorical			
Units: Subjects			
Female	19	7	
Male	21	5	

End points

End points reporting groups

Reporting group title	Maralixibat

Reporting group description:

Maralixibat chloride oral solution orally twice daily Up to 1.2* mg/kg/day), and according to indication. *equivalent to 1.14 mg/kg/day maralixibat. Doses reported here are in maralixibat chloride.

Participants with ALGS received maralixibat doses in the range of 0.15 mg/kg QD to 0.45 mg/kg BID. Participants with PFIC received maralixibat doses in the range of 0.3 mg/kg QD to 0.6 mg/kg BID.

Subject analysis set title	ALGS
Subject analysis set type	Safety 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	Safety 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

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

End point description:

TEAE = Treatment-emergent Adverse Event; AESI = Adverse Event of Special Interest.

End point type	Primary

End point timeframe:

From Baseline through End of Treatment (up to approximately 4 years)

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: The primary endpoint data was a count of occurrences, and no statistical analysis was performed.

End point values	Maralixibat	ALGS	PFIC	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	52	40	12	
Units: Number of participants				
At least one TEAE	48	36	12	
TEAE ≥ 3	13	9	4	
Serious TEAE	13	10	3	
Serious Treatment-Related Adverse Event	0	0	0	
Serious Treatment-Related TEAE	0	0	0	
TEAE Leading to Discontinuation of Study Drug	4	3	1	
TEAE Leading to Death	1	1	0	
Treatment-emergent AESI	1	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Long-Term Effect on Pruritus

End point title	Long-Term Effect on Pruritus

End point description:

Change from Baseline in Pruritus Severity assessed using the Clinician Scratch Score (CSS), a 5-point scale where 0 indicates no evidence of scratching and 4 indicates cutaneous mutilation with bleeding, hemorrhage, and scarring.

End point type	Secondary

End point timeframe:

From Baseline through Week 160, including Change from Baseline values.

End point values	ALGS	PFIC		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40	12		
Units: Pruritus severity score				
arithmetic mean (standard deviation)	-0.4 (± 0.89)	-0.3 (± 1.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Long-Term Effect on Serum Bile Acid Levels

End point title	Long-Term Effect on Serum Bile Acid Levels

End point description:

End point type	Secondary

End point timeframe:

From Baseline through Week 160, including Change from Baseline values.

End point values	Maralixibat	ALGS	PFIC	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	52	40	12	
Units: Serum bile acid levels (µmol/L)				
arithmetic mean (standard deviation)	-56.994 (± 111.0334)	-15.948 (± 31.4239)	-82.647 (± 136.4354)	

Statistical analyses

No statistical analyses for this end point

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	PFIC
Reporting group description:	
All participants in the PFIC arm who received maralixibat and were included in the AE analysis.	
Reporting group title	ALGS
Reporting group description:	
All participants in the ALGS arm who received maralixibat and were included in the AE analysis.	

Serious adverse events	PFIC	ALGS	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 12 (25.00%)	11 / 40 (27.50%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Nodular lymphocyte predominant Hodgkin lymphoma			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	1 / 12 (8.33%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Oedema peripheral			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Fibrinous bronchitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatopulmonary syndrome			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
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			
Gastrointestinal procedural complication			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Congenital, familial and genetic disorders			
Coarctation of the aorta			

subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alagille syndrome			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arteriovenous malformation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			

subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal mass			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			

subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 12 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pruritus			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (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			
Lung abscess			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (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	PFIC	ALGS	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	39 / 40 (97.50%)	
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 12 (16.67%)	8 / 40 (20.00%)	
occurrences (all)	4	11	
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Oedema peripheral			
subjects affected / exposed	0 / 12 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	3	
Peripheral swelling			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 12 (8.33%)	5 / 40 (12.50%)	
occurrences (all)	1	7	
Allergy to arthropod sting			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Hypersensitivity			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 12 (16.67%)	3 / 40 (7.50%)	
occurrences (all)	2	3	
Epistaxis			
subjects affected / exposed	0 / 12 (0.00%)	6 / 40 (15.00%)	
occurrences (all)	0	13	
Nasal congestion			
subjects affected / exposed	3 / 12 (25.00%)	1 / 40 (2.50%)	
occurrences (all)	3	1	

Oropharyngeal pain			
subjects affected / exposed	2 / 12 (16.67%)	4 / 40 (10.00%)	
occurrences (all)	2	4	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 12 (8.33%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Rhinorrhoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 12 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	3	
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	3	
Executive dysfunction			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Attention deficit/hyperactivity disorder			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Anxiety			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	3 / 40 (7.50%)	
occurrences (all)	1	3	
Blood bilirubin increased			
subjects affected / exposed	2 / 12 (16.67%)	2 / 40 (5.00%)	
occurrences (all)	4	2	
Ultrasound liver abnormal			
subjects affected / exposed	1 / 12 (8.33%)	4 / 40 (10.00%)	
occurrences (all)	1	4	
Vitamin D decreased			

subjects affected / exposed	1 / 12 (8.33%)	3 / 40 (7.50%)	
occurrences (all)	1	4	
Weight decreased			
subjects affected / exposed	0 / 12 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	3	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Vitamin A decreased			
subjects affected / exposed	0 / 12 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Blood calcium decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Blood phosphorus decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Hepatic enzyme increased			
subjects affected / exposed	2 / 12 (16.67%)	0 / 40 (0.00%)	
occurrences (all)	6	0	
Spleen scan abnormal			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Bilirubin conjugated increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Anti-transglutaminase antibody increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 12 (8.33%)	2 / 40 (5.00%)	
occurrences (all)	1	2	
Radius fracture			

subjects affected / exposed	1 / 12 (8.33%)	2 / 40 (5.00%)	
occurrences (all)	1	2	
Vaccination complication			
subjects affected / exposed	0 / 12 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	5	
Skin abrasion			
subjects affected / exposed	1 / 12 (8.33%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Stress fracture			
subjects affected / exposed	1 / 12 (8.33%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Femur fracture			
subjects affected / exposed	1 / 12 (8.33%)	1 / 40 (2.50%)	
occurrences (all)	1	2	
Sunburn			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Arthropod bite			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Face injury			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Oral contusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Hand fracture			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Stoma site haemorrhage			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 12 (8.33%)	4 / 40 (10.00%)	
occurrences (all)	1	4	

Lethargy			
subjects affected / exposed	0 / 12 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	3	
Head discomfort			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Splenomegaly			
subjects affected / exposed	0 / 12 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	4	
Anaemia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 12 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 12 (25.00%)	8 / 40 (20.00%)	
occurrences (all)	7	12	
Abdominal pain upper			
subjects affected / exposed	1 / 12 (8.33%)	3 / 40 (7.50%)	
occurrences (all)	1	3	
Constipation			
subjects affected / exposed	2 / 12 (16.67%)	1 / 40 (2.50%)	
occurrences (all)	2	2	
Dental caries			
subjects affected / exposed	2 / 12 (16.67%)	1 / 40 (2.50%)	
occurrences (all)	3	1	
Diarrhoea			
subjects affected / exposed	4 / 12 (33.33%)	3 / 40 (7.50%)	
occurrences (all)	7	3	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 12 (8.33%)	2 / 40 (5.00%)	
occurrences (all)	2	2	
Nausea			

subjects affected / exposed	1 / 12 (8.33%)	2 / 40 (5.00%)	
occurrences (all)	1	6	
Toothache			
subjects affected / exposed	3 / 12 (25.00%)	2 / 40 (5.00%)	
occurrences (all)	4	2	
Vomiting			
subjects affected / exposed	2 / 12 (16.67%)	2 / 40 (5.00%)	
occurrences (all)	2	2	
Pancreatic failure			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Food poisoning			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Aphthous ulcer			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hepatic mass			
subjects affected / exposed	1 / 12 (8.33%)	5 / 40 (12.50%)	
occurrences (all)	1	5	
Biliary colic			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Liver injury			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Cholelithiasis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 12 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	3	
Alopecia			

subjects affected / exposed	2 / 12 (16.67%)	2 / 40 (5.00%)	
occurrences (all)	2	2	
Pruritus			
subjects affected / exposed	3 / 12 (25.00%)	3 / 40 (7.50%)	
occurrences (all)	6	3	
Rash			
subjects affected / exposed	3 / 12 (25.00%)	2 / 40 (5.00%)	
occurrences (all)	3	2	
Rash erythematous			
subjects affected / exposed	1 / 12 (8.33%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Xanthoma			
subjects affected / exposed	0 / 12 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Dry skin			
subjects affected / exposed	0 / 12 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Rash papular			
subjects affected / exposed	1 / 12 (8.33%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Erythema			
subjects affected / exposed	1 / 12 (8.33%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Urticaria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Milia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Delayed puberty			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	1 / 12 (8.33%)	4 / 40 (10.00%)	
occurrences (all)	1	4	
Pain in extremity			
subjects affected / exposed	3 / 12 (25.00%)	4 / 40 (10.00%)	
occurrences (all)	4	6	
Myalgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Epiphyses delayed fusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Growing pains			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Ear infection			
subjects affected / exposed	2 / 12 (16.67%)	2 / 40 (5.00%)	
occurrences (all)	2	3	
Nasopharyngitis			
subjects affected / exposed	4 / 12 (33.33%)	8 / 40 (20.00%)	
occurrences (all)	6	17	
Upper respiratory tract infection			
subjects affected / exposed	5 / 12 (41.67%)	4 / 40 (10.00%)	
occurrences (all)	8	6	
Otitis media			
subjects affected / exposed	0 / 12 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	4	
Corona virus infection			
subjects affected / exposed	9 / 12 (75.00%)	9 / 40 (22.50%)	
occurrences (all)	14	10	
Gastroenteritis viral			
subjects affected / exposed	1 / 12 (8.33%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Lower respiratory tract infection			

subjects affected / exposed	1 / 12 (8.33%)	1 / 40 (2.50%)	
occurrences (all)	1	2	
Urinary tract infection			
subjects affected / exposed	1 / 12 (8.33%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Tonsillitis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 40 (0.00%)	
occurrences (all)	2	0	
Viral infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Body tinea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Otitis externa			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal viral infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Impetigo			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Fungal skin infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Large intestine infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	3 / 12 (25.00%)	4 / 40 (10.00%)	
occurrences (all)	4	4	
Vitamin E deficiency			
subjects affected / exposed	1 / 12 (8.33%)	3 / 40 (7.50%)	
occurrences (all)	2	3	

Vitamin A deficiency subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 40 (5.00%) 2	
Vitamin K deficiency subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 40 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 November 2020	Released in 2020, this amendment expanded the MRX-800 study to include participants with biliary atresia, in addition to those with Alagille syndrome (ALGS) and progressive familial intrahepatic cholestasis (PFIC). The study continued to focus on evaluating the long-term safety of maralixibat in individuals with rare cholestatic liver diseases. Key changes made: - Expanded Population: Inclusion criteria were revised to allow enrolment of participants with biliary atresia and those who had previously discontinued maralixibat studies for non-safety reasons. - Study Objectives: Primary, secondary, and exploratory objectives were updated to reflect the inclusion of biliary atresia and new outcome measures. - New Assessments: Growth and neurodevelopmental evaluations were added for participants with biliary atresia. Pharmacokinetic testing was removed to reduce participant burden. - Dose Adjustments: The protocol allowed for higher maralixibat dosing in some cases, based on individual response and safety. - Safety Monitoring: Additional monitoring and liver safety guidelines were introduced for biliary atresia, including criteria for treatment interruption and investigation of cholangitis. - Outcome Measures: New endpoints included changes in bilirubin levels and growth parameters specific to biliary atresia. - Other Updates: Adjustments were made to pregnancy testing procedures, geographic scope of study sites, drug packaging, and data collection processes. Provisions for study conduct during events such as pandemics were also added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported