Clinical trial results:
MRX-503: An Open-label Extension Study to Evaluate the Long-term Safety and Efficacy of Maralixibat in the Treatment of Subjects with Progressive Familial Intrahepatic Cholestasis (PFIC)

Summary

EudraCT number	2019-003395-39
Trial protocol	DE GB BE PL FR HU AT IT
Global end of trial date	23 April 2025

Results information

Result version number	v2 (current)
This version publication date	09 April 2026
First version publication date	09 November 2025
Version creation reason	• Correction of full data set Adjustment required: ItchRo Scale should follow a 0–4 range instead of the current 1–5.

Trial information

Trial identification

Sponsor protocol code	MRX-503

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04185363
WHO universal trial number (UTN)	-

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)	Yes
EMA paediatric investigation plan number(s)	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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 April 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 April 2025
Global end of trial reached?	Yes
Global end of trial date	23 April 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the long-term safety and tolerability of maralixibat.

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 December 2019
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: 5
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	Brazil: 10
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Colombia: 5
Country: Number of subjects enrolled	Lebanon: 13
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Singapore: 2
Country: Number of subjects enrolled	Türkiye: 2
Country: Number of subjects enrolled	United States: 18
Worldwide total number of subjects	84
EEA total number of subjects	19

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)	18
Children (2-11 years)	62
Adolescents (12-17 years)	4
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 84 participants were enrolled at 28 sites across 17 countries (Argentina, Austria, Belgium, Brazil, Canada, Colombia, France, Germany, Italy, Lebanon, Mexico, Poland, Singapore, Turkey, United Kingdom, United States)

Pre-assignment

Screening details:

MRX-503, screening starts after signing the ICF and confirming eligibility. It overlaps with the MRX-502 end-of-treatment (EOT) visit: if the MRX-503 baseline visit occurs the same day or within 30 days of the MRX-502 EOT visit, those prior evaluations count as the MRX-503 baseline assessments.

Period 1

Period 1 title	Open-Label extension (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Open Label Extension

Arm description:

This open-label, extension study comprised one continuous treatment period, including:
- Dose-escalation (4-6 weeks)
- Stable-dosing (until the sponsor or the subject terminates the study, discontinues/ transitions to commercial product)
- Safety follow-up phases.

Subjects were analyzed in two cohorts:
- The Primary Cohort (non-truncated PFIC2)
- The Secondary Cohort (other PFIC subtypes, including PFIC1, PFIC3, truncated PFIC2, or incomplete response after PEBD)

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

Dosage and administration details:

Maralixibat was administered orally as a ready-to-use oral solution (5, 10, 15, or 20 mg/mL) based on individual body weight, up to 600 µg/kg twice daily (BID).
Dosing followed a weekly escalation schedule over 4–6 weeks as follows:
• Week 1: 150 µg/kg BID
• Week 2: 300 µg/kg BID
• Week 3: 450 µg/kg BID
• Week 4 and onward: 600 µg/kg BID (maximum tolerated dose)

Doses were taken approximately 30 minutes before breakfast and the evening meal.

Subjects unable to tolerate 150 µg/kg BID were discontinued.

The maximum tolerated dose established by Week 6 was maintained for the Stable Dosing period until study termination or transition to commercial product.

Number of subjects in period 1	Open Label Extension
Started	84
Completed	48
Not completed	36
Consent withdrawn by subject	7
Physician decision	3
Disease progression	2
Rolled over under drug interruption.	1
Adverse event, non-fatal	5
Liver transplant	17
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Open-Label extension

Reporting group description: -

Reporting group values	Open-Label extension	Total	
Number of subjects	84	84	
Age categorical Units: Subjects			
1 to <6 years	55	55	
6 to <13 years	25	25	
13 to 18 years	4	4	
Gender categorical Units: Subjects			
Female	48	48	
Male	36	36	

Subject analysis sets	
Subject analysis set title	Primary Cohort
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Primary Cohort in MRX-503 includes subjects with non-truncated PFIC2 (nt-PFIC2) mutations previously enrolled in MRX-502.

Subject analysis set title	PFIC Cohort
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The PFIC (All PFIC) Cohort in MRX-503 combines the nt-PFIC2 primary cohort with other PFIC types to evaluate safety and efficacy across the wider PFIC population.

Subject analysis set title	Primary Cohort Baseline
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Primary Cohort in MRX-503 includes subjects with non-truncated PFIC2 (nt-PFIC2) mutations previously enrolled in MRX-502.

Subject analysis set title	PFIC Cohort Baseline
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The PFIC (All PFIC) Cohort in MRX-503 combines the nt-PFIC2 primary cohort with other PFIC types to evaluate safety and efficacy across the wider PFIC population.

Reporting group values	Primary Cohort	PFIC Cohort	Primary Cohort Baseline
Number of subjects	28	60	28
Age categorical Units: Subjects			
1 to <6 years	17	37	17
6 to <13 years	7	19	7
13 to 18 years	4	4	4

Gender categorical Units: Subjects			
Female	18	33	18
Male	10	27	10

Reporting group values	PFIC Cohort Baseline		
Number of subjects	60		
Age categorical Units: Subjects			
1 to <6 years	37		
6 to <13 years	19		
13 to 18 years	4		
Gender categorical Units: Subjects			
Female	33		
Male	27		

End points

End points reporting groups

Reporting group title	Open Label Extension

Reporting group description:

This open-label, extension study comprised one continuous treatment period, including:
- Dose-escalation (4-6 weeks)
- Stable-dosing (until the sponsor or the subject terminates the study, discontinues/ transitions to commercial product)
- Safety follow-up phases.

Subjects were analyzed in two cohorts:
- The Primary Cohort (non-truncated PFIC2)
- The Secondary Cohort (other PFIC subtypes, including PFIC1, PFIC3, truncated PFIC2, or incomplete response after PEBD)

Subject analysis set title	Primary Cohort
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Primary Cohort in MRX-503 includes subjects with non-truncated PFIC2 (nt-PFIC2) mutations previously enrolled in MRX-502.

Subject analysis set title	PFIC Cohort
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The PFIC (All PFIC) Cohort in MRX-503 combines the nt-PFIC2 primary cohort with other PFIC types to evaluate safety and efficacy across the wider PFIC population.

Subject analysis set title	Primary Cohort Baseline
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Primary Cohort in MRX-503 includes subjects with non-truncated PFIC2 (nt-PFIC2) mutations previously enrolled in MRX-502.

Subject analysis set title	PFIC Cohort Baseline
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The PFIC (All PFIC) Cohort in MRX-503 combines the nt-PFIC2 primary cohort with other PFIC types to evaluate safety and efficacy across the wider PFIC population.

Primary: Mean change from baseline over time in the average morning ItchRO(Obs) severity score

End point title	Mean change from baseline over time in the average morning ItchRO(Obs) severity score

End point description:

End point type	Primary

End point timeframe:

From Baseline to Weeks 75-78 (MRX-503)

End point values	Primary Cohort	PFIC Cohort	Primary Cohort Baseline	PFIC Cohort Baseline
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	42	28	60
Units: ItchRO score (1-4)				
arithmetic mean (standard deviation)	0.839 (± 1.0767)	0.943 (± 1.1075)	2.473 (± 1.1444)	2.537 (± 1.1096)

Statistical analyses

Statistical analysis title	Primary Cohort: Change from Baseline Over Time
Comparison groups	Primary Cohort v Primary Cohort Baseline
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-1.613
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.275
upper limit	-0.95
Variability estimate	Standard deviation
Dispersion value	1.4936

Statistical analysis title	PFIC Cohort: Change from Baseline Over Time
Comparison groups	PFIC Cohort v PFIC Cohort Baseline
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-1.701
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.138
upper limit	-1.264
Variability estimate	Standard deviation
Dispersion value	1.4022

Secondary: Maintenance of ItchRO(Obs) response (Weeks 15 – 26)

End point title	Maintenance of ItchRO(Obs) response (Weeks 15 – 26)

End point description:

Maintenance of treatment effect described as the proportion of participants in the MRX-MRX treatment group who obtain ItchRO(Obs) response from Week 15 to Week 26 in Study MRX-503 in the primary cohort and PFIC cohort.

End point type	Secondary

End point timeframe:

Week 15 - 26

End point values	Primary Cohort	PFIC Cohort		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	33		
Units: %				
number (not applicable)				
Week 15 - 18	71.4	69.7		
Week 19-22	64.3	72.7		
Week 23-26	64.3	69.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of ItchRO(Obs) responders over time

End point title	Proportion of ItchRO(Obs) responders over time

End point description:

Proportion of ItchRO responders over time at each study visit using the 4-week study period prior to the visit as per ItchRO(Obs) responder definition.

End point type	Secondary

End point timeframe:

Baseline to EOT

End point values	Primary Cohort	PFIC Cohort		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	60		
Units: %				
number (not applicable)				
Week 1-6	57.1	50		
Week 7-10	67.9	65		
Week 11-14	67.9	63.3		
Week 15-18	75	66.7		
Week 19-22	67.9	68.3		
Week 23-26	64.3	63.3		
Week 39-42	78.6	71.7		
Week 51-54	71.4	66.7		

Week 63-66	57.1	58.3		
Week 75-78	57.1	53.3		
Week 87-90	50	48.3		
Week 99-102	57.1	46.7		
Week 111-114	21.4	26.7		
Week 123-126	14.3	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline over time in the average morning ItchRO(Obs) frequency score

End point title	Mean change from baseline over time in the average morning ItchRO(Obs) frequency score
End point description:	
End point type	Secondary
End point timeframe:	
From Baseline (MRX-502) to Weeks 75-78 (MRX-503)	

End point values	Primary Cohort	PFIC Cohort	Primary Cohort Baseline	PFIC Cohort Baseline
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	41	28	60
Units: Ordinal Scale (0-4)				
arithmetic mean (standard deviation)	0.842 (± 0.8522)	0.878 (± 0.9447)	2.522 (± 1.1043)	2.525 (± 1.0973)

Statistical analyses

Statistical analysis title	Primary Cohort Change from Baseline
Comparison groups	Primary Cohort v Primary Cohort Baseline
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-1.644
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.302
upper limit	-0.986

Variability estimate	Standard deviation
Dispersion value	1.4451

Statistical analysis title	PFIC Cohort Change from Baseline
Comparison groups	PFIC Cohort v PFIC Cohort Baseline
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-1.598
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.036
upper limit	-1.159
Variability estimate	Standard deviation
Dispersion value	1.3893

Secondary: Mean change from baseline over time in total serum bile acid (sBA) levels

End point title	Mean change from baseline over time in total serum bile acid (sBA) levels
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to week 70	

End point values	Primary Cohort	PFIC Cohort	Primary Cohort Baseline	PFIC Cohort Baseline
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	46	26	58
Units: umol/L				
arithmetic mean (standard deviation)	128.822 (± 182.6239)	127.987 (± 159.9969)	312.932 (± 163.8795)	262.139 (± 145.9310)

Statistical analyses

Statistical analysis title	Primary Cohort Change from Baseline
Comparison groups	Primary Cohort Baseline v Primary Cohort

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0054
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-150.064
Confidence interval	
level	95 %
sides	2-sided
lower limit	-250.1
upper limit	-50.029
Variability estimate	Standard deviation
Dispersion value	213.7437

Statistical analysis title	PFIC Cohort Change from Baseline
Comparison groups	PFIC Cohort v PFIC Cohort Baseline
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0003
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-111.473
Confidence interval	
level	95 %
sides	2-sided
lower limit	-168.687
upper limit	-54.258
Variability estimate	Standard deviation
Dispersion value	188.188

Secondary: Proportion of subjects who experience an sBA control over time from Week 18 to Week 26

End point title	Proportion of subjects who experience an sBA control over time from Week 18 to Week 26

End point description:

End point type	Secondary

End point timeframe:

From Week 18 to Week 26

End point values	Primary Cohort	PFIC Cohort		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	60		
Units: % of subjects				
number (not applicable)				
Week 18	42.9	40		
Week 22	42.9	38.3		
Week 26	46.4	43.3		
Average of Weeks 18,22,26	42.9	40		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in height z-score

End point title	Change from baseline in height z-score

End point description:

End point type	Secondary

End point timeframe:

From baseline to Week 70

End point values	Primary Cohort	PFIC Cohort	Primary Cohort Baseline	PFIC Cohort Baseline
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	47	28	60
Units: Z-Score				
arithmetic mean (standard deviation)	-1.425 (± 1.5057)	-1.671 (± 1.5503)	-2.061 (± 1.3016)	-2.107 (± 1.3061)

Statistical analyses

Statistical analysis title	Primary Cohort Change from Baseline
Comparison groups	Primary Cohort v Primary Cohort Baseline
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0026
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.486

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.161
upper limit	0.782
Variability estimate	Standard deviation
Dispersion value	0.6665

Statistical analysis title	PFIC Cohort Change from Baseline
Comparison groups	PFIC Cohort v PFIC Cohort Baseline
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0006
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.335
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.152
upper limit	0.518
Variability estimate	Standard deviation
Dispersion value	0.6229

Secondary: Change from baseline in weight z-score

End point title	Change from baseline in weight z-score
End point description:	

End point type	Secondary
End point timeframe:	
From Baseline to Week 70	

End point values	Primary Cohort	PFIC Cohort	Primary Cohort Baseline	PFIC Cohort Baseline
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	46	28	60
Units: Z-Score				
arithmetic mean (standard deviation)	-0.364 (± 1.3123)	-1.051 (± 1.4540)	-1.127 (± 1.3173)	-1.459 (± 1.2806)

Statistical analyses

Statistical analysis title	Primary Cohort Change from Baseline
Comparison groups	Primary Cohort v Primary Cohort Baseline
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0194
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.518
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.093
upper limit	0.944
Variability estimate	Standard deviation
Dispersion value	0.9349

Statistical analysis title	PFIC Cohort Change from Baseline
Comparison groups	PFIC Cohort v PFIC Cohort Baseline
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0042
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.109
upper limit	0.55
Variability estimate	Standard deviation
Dispersion value	0.7421

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose through 14 days after the last dose of maralixibat.

Adverse event reporting additional description:

Adverse events were systematically collected from all participants at each scheduled visit and through continuous monitoring from first dose to 14 days after last dose. Investigators were required to actively elicit and record all new or worsening events, with assessment of severity, relationship, and outcome.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Open Label Extension

Reporting group description:

This open-label, extension study comprised one continuous treatment period, including:
- Dose-escalation (4-6 weeks)
- Stable-dosing (until the sponsor or the subject terminates the study, discontinues/ transitions to commercial product)
- Safety follow-up phases.

Subjects were analyzed in two cohorts:
- The Primary Cohort (non-truncated PFIC2)
- The Secondary Cohort (other PFIC subtypes, including PFIC1, PFIC3, truncated PFIC2, or incomplete response after PEBD)

Serious adverse events	Open Label Extension		
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 84 (29.76%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Injury, poisoning and procedural complications			
Accidental exposure to product			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Accidental overdose			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur fracture			

subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Postoperative renal failure				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Stoma site haemorrhage				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Progressive familial intrahepatic cholestasis				
subjects affected / exposed	2 / 84 (2.38%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Haematoma				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Biliary tract operation				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Disease progression				

subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Diarrhoea				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematochezia				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal varices haemorrhage				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Biliary colic				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholangitis				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	2 / 84 (2.38%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				

subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic function abnormal				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Jaundice				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Epistaxis				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nasal obstruction				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Skin and subcutaneous tissue disorders				
Pruritus				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Adenovirus infection				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Bacterial translocation			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronavirus infection			
subjects affected / exposed	2 / 84 (2.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Enterovirus infection			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	4 / 84 (4.76%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis viral			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nasopharyngitis			

subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rhinovirus infection				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Open Label Extension		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	84 / 84 (100.00%)		
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	5 / 84 (5.95%)		
occurrences (all)	9		
Alanine aminotransferase increased			
subjects affected / exposed	14 / 84 (16.67%)		
occurrences (all)	27		
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 84 (7.14%)		
occurrences (all)	8		
Blood bilirubin increased			
subjects affected / exposed	16 / 84 (19.05%)		
occurrences (all)	23		
International normalised ratio increased			
subjects affected / exposed	11 / 84 (13.10%)		
occurrences (all)	14		
Prothrombin time prolonged			
subjects affected / exposed	4 / 84 (4.76%)		
occurrences (all)	5		
Vitamin A increased			
subjects affected / exposed	5 / 84 (5.95%)		
occurrences (all)	5		
Vitamin D decreased			
subjects affected / exposed	14 / 84 (16.67%)		
occurrences (all)	28		
Vitamin E decreased			
subjects affected / exposed	9 / 84 (10.71%)		
occurrences (all)	12		
Injury, poisoning and procedural complications			
Skin abrasion			

subjects affected / exposed occurrences (all)	5 / 84 (5.95%) 5		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 6 / 84 (7.14%) 9		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Coagulopathy subjects affected / exposed occurrences (all)	 7 / 84 (8.33%) 9 4 / 84 (4.76%) 10		
General disorders and administration site conditions Influenza like illness subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 4 / 84 (4.76%) 4 40 / 84 (47.62%) 77		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Dental caries subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	 23 / 84 (27.38%) 37 5 / 84 (5.95%) 6 8 / 84 (9.52%) 9 4 / 84 (4.76%) 5 39 / 84 (46.43%) 82		

Vomiting subjects affected / exposed occurrences (all)	13 / 84 (15.48%) 20		
Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all) Jaundice subjects affected / exposed occurrences (all)	 5 / 84 (5.95%) 6 6 / 84 (7.14%) 8		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	 28 / 84 (33.33%) 61 8 / 84 (9.52%) 31 5 / 84 (5.95%) 7 6 / 84 (7.14%) 8 12 / 84 (14.29%) 16		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	 21 / 84 (25.00%) 35 4 / 84 (4.76%) 4 5 / 84 (5.95%) 6		

Infections and infestations			
Conjunctivitis			
subjects affected / exposed	6 / 84 (7.14%)		
occurrences (all)	7		
Coronavirus infection			
subjects affected / exposed	12 / 84 (14.29%)		
occurrences (all)	12		
Ear infection			
subjects affected / exposed	11 / 84 (13.10%)		
occurrences (all)	12		
Gastroenteritis			
subjects affected / exposed	11 / 84 (13.10%)		
occurrences (all)	17		
Gastrointestinal viral infection			
subjects affected / exposed	4 / 84 (4.76%)		
occurrences (all)	4		
Influenza			
subjects affected / exposed	16 / 84 (19.05%)		
occurrences (all)	23		
Nasopharyngitis			
subjects affected / exposed	21 / 84 (25.00%)		
occurrences (all)	45		
Otitis media			
subjects affected / exposed	9 / 84 (10.71%)		
occurrences (all)	10		
Otitis media acute			
subjects affected / exposed	6 / 84 (7.14%)		
occurrences (all)	9		
Pharyngitis			
subjects affected / exposed	8 / 84 (9.52%)		
occurrences (all)	11		
Respiratory tract infection			
subjects affected / exposed	5 / 84 (5.95%)		
occurrences (all)	6		
Rhinitis			

subjects affected / exposed	9 / 84 (10.71%)		
occurrences (all)	18		
Tonsillitis			
subjects affected / exposed	6 / 84 (7.14%)		
occurrences (all)	8		
Upper respiratory tract infection			
subjects affected / exposed	16 / 84 (19.05%)		
occurrences (all)	53		
Viral infection			
subjects affected / exposed	7 / 84 (8.33%)		
occurrences (all)	9		
Viral upper respiratory tract infection			
subjects affected / exposed	4 / 84 (4.76%)		
occurrences (all)	4		
Metabolism and nutrition disorders			
Vitamin A deficiency			
subjects affected / exposed	6 / 84 (7.14%)		
occurrences (all)	6		
Vitamin D deficiency			
subjects affected / exposed	10 / 84 (11.90%)		
occurrences (all)	10		
Vitamin E deficiency			
subjects affected / exposed	4 / 84 (4.76%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 June 2020	This amendment clarified the study design and baseline transition from MRX-502 to MRX-503, refined dosing and packaging details, and aligned the safety-monitoring baseline with the previous study to ensure consistency. It introduced provisions for home or remote visits to maintain study conduct during COVID-19 restrictions and added the Work Productivity and Activity Impairment Questionnaire (WPAI:PFIC) to capture quality-of-life data. Secondary endpoints were expanded to include serum bile acid control and time to liver-associated events, and Appendix 9 was added to guide pandemic-related procedures. These changes were made to improve operational flexibility, maintain patient safety and data integrity during public-health disruptions, and refine the efficacy assessments based on emerging clinical experience and regulatory feedback.
18 November 2021	This amendment updated the protocol to reflect maralixibat's approval and evolving regulatory standards. Terminology was revised from ASBT to IBAT, and background sections were aligned with the current Investigator's Brochure. The stable dosing period was extended indefinitely to allow continued treatment until study termination or transition to commercial supply. A new "All PFIC" analysis cohort was introduced, and efficacy and safety sections were reorganized with updated endpoints and statistical methods. Electronic SAE reporting via the EDC system was implemented, safety monitoring and liver-function follow-up were strengthened, and new guidance for dose interruptions, PEBD, and COVID-19 vaccination was added. These updates were made to expand patient access, modernize safety oversight, and align the study with post-approval and electronic data-capture requirements.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported