



Clinical trial results:

An Open-label Extension Study to Evaluate Long-term Efficacy and Safety of A4250 in Children with Progressive Familial Intrahepatic Cholestasis Types 1 and 2 (PEDFIC 2)

Summary

EudraCT number	2017-002325-38
Trial protocol	DE FR SE GB NL BE ES IT PL
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	A4250-008
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03659916
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen Pharma
Sponsor organisation address	Arvid Wallgrens backe 20, Gteborg, Sweden, 41346
Public contact	Medical Director, Ipsen Pharma, clinical.trials@ipsen.com
Scientific contact	Medical Director, Ipsen Pharma, clinical.trials@ipsen.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-002054-PIP01-16
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	15 February 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 February 2024
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate a sustained effect of odevixibat on serum bile acid (s-BAs) and pruritus in children with progressive familial intrahepatic cholestasis (PFIC) Types 1 and 2 and to evaluate the effect of odevixibat on serum bile acids and pruritus in participants with PFIC who either did not meet eligibility criteria for Study A4250-005 (2017-002338-21) or who did meet the eligibility criteria for Study A4250-005 (2017-002338-21) after recruitment of Study A4250-005 (2017-002338-21) had been completed.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and with Good Clinical Practice guidelines as denoted in the International Council for Harmonization E6 requirements. These practices include Independent Ethics Committee/Institutional Review Board procedures, informed consent, protocol adherence, administrative documents, drug-supply accountability, data collection, participant records (source documents), adverse event (AE) recording and reporting, inspection and audit preparation, and record retention. All participant identities were kept confidential.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 September 2018
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	Canada: 2
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Netherlands: 11
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Saudi Arabia: 5
Country: Number of subjects enrolled	Türkiye: 21
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	United States: 17
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Belgium: 2
Worldwide total number of subjects	116
EEA total number of subjects	47

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)	39
Children (2-11 years)	56
Adolescents (12-17 years)	14
Adults (18-64 years)	7
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase III, open-label extension was conducted in participants with PFIC at 43 centers in 13 countries. The first participant was enrolled on 28 September 2018 and data cut-off (DCO) date was 15 February 2024.

Pre-assignment

Screening details:

This study consisted of a 72-week treatment period and a 4-week follow-up period. An optional extension period for continued treatment until commercial availability of odevixibat followed the 72-week treatment period. A total of 116 participants were enrolled in the study. Results are presented up to DCO of 15 February 2024.

Period 1

Period 1 title	Treatment Period (72 Weeks)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Placebo/Odevixibat

Arm description:

Participants who previously received placebo in study A4250-005 for 24 weeks received odevixibat capsule orally at a dose of 120 microgram/kilogram/day (mcg/kg/day) for 72 weeks, unless they required down-titration to the 40 mcg/kg/day due to tolerability issues.

Arm type	Experimental
Investigational medicinal product name	Odevixibat
Investigational medicinal product code	A4250
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

120 mcg/kg/day odevixibat was administered once daily for 72 weeks, if participant was unable to swallow the capsules, capsules were opened and the content sprinkled on soft foods.

Arm title	Cohort 1: Odevixibat/Odevixibat
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Arm description:

Participants who previously received odevixibat capsule orally at a dose of 40 or 120 mcg/kg/day in study A4250-005 for 24 weeks received odevixibat capsule orally at a dose of 120 mcg/kg/day for 72 weeks, unless they required down-titration to the 40 mcg/kg/day due to tolerability issues.

Arm type	Experimental
Investigational medicinal product name	Odevixibat
Investigational medicinal product code	A4250
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

120 mcg/kg/day odevixibat was administered once daily for 72 weeks, if participant was unable to swallow the capsules, capsules were opened and the content sprinkled on soft foods.

Arm title	Cohort 2: Odevixibat
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Arm description:

Participants any age with any type of PFIC who either did not meet eligibility criteria for study A4250-005 or were eligible for enrolment in A4250-005 after recruitment was complete received odevixibat at a

dose of 120 mcg/kg/day or following protocol amendment 6.0, initiated at a dose of 40 mcg/kg/day with the possibility to dose escalate to 120 mcg/kg/day after 12 weeks if there was no improvement in pruritus based on investigator judgement, up to 72 weeks.

Arm type	Experimental
Investigational medicinal product name	Odevixibat
Investigational medicinal product code	A4250
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Starting with 40 mcg/kg/day and escalate to 120 mcg/kg/day odevixibat was administered once daily for 72 weeks, if participant was unable to swallow the capsules, capsules were opened and the content sprinkled on soft foods.

Number of subjects in period 1	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat
Started	19	37	60
Completed	15	28	40
Not completed	4	9	20
Consent withdrawn by subject	1	4	4
Physician decision	-	1	-
Adverse event, non-fatal	2	1	6
Unspecified	1	3	9
Lost to follow-up	-	-	1

Period 2

Period 2 title	Optional Extension Treatment (176 Weeks)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Placebo/Odevixibat

Arm description:

Participants who previously received placebo in study A4250-005 for 24 weeks received odevixibat capsule orally at a dose of 120 microgram/kilogram/day (mcg/kg/day) for 72 weeks, unless they required down-titration to the 40 mcg/kg/day due to tolerability issues. Participants continued receiving study treatment until commercial availability of odevixibat.

Arm type	Experimental
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Investigational medicinal product name	Odevixibat
Investigational medicinal product code	A4250
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

120 mcg/kg/day odevixibat was administered once daily for 72 weeks, if participant was unable to swallow the capsules, capsules were opened and the content sprinkled on soft foods.

Arm title	Cohort 1: Odevixibat/Odevixibat
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Arm description:

Participants who previously received odevixibat capsule orally at a dose of 40 or 120 mcg/kg/day in study A4250-005 for 24 weeks received odevixibat capsule orally at a dose of 120 mcg/kg/day for 72 weeks, unless they required down-titration to the 40 mcg/kg/day due to tolerability issues. Participants continued receiving study treatment until commercial availability of odevixibat.

Arm type	Experimental
Investigational medicinal product name	Odevixibat
Investigational medicinal product code	A4250
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

120 mcg/kg/day odevixibat was administered once daily for 72 weeks, if participant was unable to swallow the capsules, capsules were opened and the content sprinkled on soft foods.

Arm title	Cohort 2: Odevixibat
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Arm description:

Participants any age with any type of PFIC who either did not meet eligibility criteria for study A4250-005 or were eligible for enrolment in A4250-005 after recruitment was complete received odevixibat at a dose of 120 mcg/kg/day or following protocol amendment 6.0, initiated at a dose of 40 mcg/kg/day with the possibility to dose escalate to 120 mcg/kg/day after 12 weeks if there was no improvement in pruritus based on investigator judgement, up to 72 weeks. Participants continued receiving study treatment until commercial availability of odevixibat.

Arm type	Experimental
Investigational medicinal product name	Odevixibat
Investigational medicinal product code	A4250
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Starting with 40 mcg/kg/day and escalate to 120 mcg/kg/day odevixibat was administered once daily for 72 weeks, if participant was unable to swallow the capsules, capsules were opened and the content sprinkled on soft foods.

Number of subjects in period 2^[1]	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat
Started	14	27	33
Completed	0	0	0
Not completed	14	27	33
Consent withdrawn by subject	-	1	-
Physician decision	-	-	1
Adverse event, non-fatal	-	-	1

Transition to Commercial Drug	5	17	11
Unspecified	4	-	3
Ongoing Optional Extension Period	5	9	17

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: One participant each from Cohort 1: Placebo/Odevixibat and Cohort 1: Odevixibat/Odevixibat, and 7 participants from Cohort 2: Odevixibat did not enter optional extension treatment period.

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: Placebo/Odevixibat
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Reporting group description:

Participants who previously received placebo in study A4250-005 for 24 weeks received odevixibat capsule orally at a dose of 120 microgram/kilogram/day (mcg/kg/day) for 72 weeks, unless they required down-titration to the 40 mcg/kg/day due to tolerability issues.

Reporting group title	Cohort 1: Odevixibat/Odevixibat
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Reporting group description:

Participants who previously received odevixibat capsule orally at a dose of 40 or 120 mcg/kg/day in study A4250-005 for 24 weeks received odevixibat capsule orally at a dose of 120 mcg/kg/day for 72 weeks, unless they required down-titration to the 40 mcg/kg/day due to tolerability issues.

Reporting group title	Cohort 2: Odevixibat
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Reporting group description:

Participants any age with any type of PFIC who either did not meet eligibility criteria for study A4250-005 or were eligible for enrolment in A4250-005 after recruitment was complete received odevixibat at a dose of 120 mcg/kg/day or following protocol amendment 6.0, initiated at a dose of 40 mcg/kg/day with the possibility to dose escalate to 120 mcg/kg/day after 12 weeks if there was no improvement in pruritus based on investigator judgement, up to 72 weeks.

Reporting group values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat
Number of subjects	19	37	60
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	4.34 ± 3.962	4.75 ± 3.711	7.62 ± 7.208
Gender categorical Units: Subjects			
Female	7	20	25
Male	12	17	35
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	2
Not Hispanic or Latino	18	37	50
Unknown or Not Reported	0	0	8
Race Units: Subjects			
White	16	31	53
Black/African American	0	1	2
Asian	2	3	2
Other	1	2	3

Reporting group values	Total		
Number of subjects	116		

Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	52		
Male	64		
Ethnicity			
Units: Subjects			
Hispanic or Latino	3		
Not Hispanic or Latino	105		
Unknown or Not Reported	8		
Race			
Units: Subjects			
White	100		
Black/African American	3		
Asian	7		
Other	6		

End points

End points reporting groups

Reporting group title	Cohort 1: Placebo/Odevixibat
Reporting group description: Participants who previously received placebo in study A4250-005 for 24 weeks received odevixibat capsule orally at a dose of 120 microgram/kilogram/day (mcg/kg/day) for 72 weeks, unless they required down-titration to the 40 mcg/kg/day due to tolerability issues.	
Reporting group title	Cohort 1: Odevixibat/Odevixibat
Reporting group description: Participants who previously received odevixibat capsule orally at a dose of 40 or 120 mcg/kg/day in study A4250-005 for 24 weeks received odevixibat capsule orally at a dose of 120 mcg/kg/day for 72 weeks, unless they required down-titration to the 40 mcg/kg/day due to tolerability issues.	
Reporting group title	Cohort 2: Odevixibat
Reporting group description: Participants any age with any type of PFIC who either did not meet eligibility criteria for study A4250-005 or were eligible for enrolment in A4250-005 after recruitment was complete received odevixibat at a dose of 120 mcg/kg/day or following protocol amendment 6.0, initiated at a dose of 40 mcg/kg/day with the possibility to dose escalate to 120 mcg/kg/day after 12 weeks if there was no improvement in pruritus based on investigator judgement, up to 72 weeks.	
Reporting group title	Cohort 1: Placebo/Odevixibat
Reporting group description: Participants who previously received placebo in study A4250-005 for 24 weeks received odevixibat capsule orally at a dose of 120 microgram/kilogram/day (mcg/kg/day) for 72 weeks, unless they required down-titration to the 40 mcg/kg/day due to tolerability issues. Participants continued receiving study treatment until commercial availability of odevixibat.	
Reporting group title	Cohort 1: Odevixibat/Odevixibat
Reporting group description: Participants who previously received odevixibat capsule orally at a dose of 40 or 120 mcg/kg/day in study A4250-005 for 24 weeks received odevixibat capsule orally at a dose of 120 mcg/kg/day for 72 weeks, unless they required down-titration to the 40 mcg/kg/day due to tolerability issues. Participants continued receiving study treatment until commercial availability of odevixibat.	
Reporting group title	Cohort 2: Odevixibat
Reporting group description: Participants any age with any type of PFIC who either did not meet eligibility criteria for study A4250-005 or were eligible for enrolment in A4250-005 after recruitment was complete received odevixibat at a dose of 120 mcg/kg/day or following protocol amendment 6.0, initiated at a dose of 40 mcg/kg/day with the possibility to dose escalate to 120 mcg/kg/day after 12 weeks if there was no improvement in pruritus based on investigator judgement, up to 72 weeks. Participants continued receiving study treatment until commercial availability of odevixibat.	

Primary: Change From Baseline in Serum Bile Acids

End point title	Change From Baseline in Serum Bile Acids ^[1]
End point description: Blood samples for analysis of fasting total s-BAs were drawn at specified timepoints. Participants were to fast (water intake only) for at least 4 hours prior to the collection of samples for s-BAs. Exceptions were made for infants <12 months of age if unable to fast for the full 4 hours. Baseline for Cohort 1 placebo/odevixibat and Cohort 2 groups was defined as the average of last 2 values before the first dose of study treatment in the study. Baseline for Cohort 1 odevixibat/odevixibat group was defined as average of last 2 values before the first dose of study treatment in study A4250-005 (2017-002338-21). The Full Analysis Set (FAS) consisted of all participants who had received at least 1 dose of the study treatment. Only participants with data collected at specified timepoints are reported.	
End point type	Primary
End point timeframe: Baseline and Week 72	

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: No additional statistical analysis was prespecified for this endpoint.

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	28	43	
Units: micromole per liter (mcmol/L)				
arithmetic mean (standard deviation)	-104.00 (± 167.318)	-139.84 (± 172.070)	-57.97 (± 137.990)	

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of Positive Pruritus Assessments at the Participant Level Over 72-Week Using the Albireo Observer-Reported Outcome (ObsRo) Instrument

End point title	Proportion of Positive Pruritus Assessments at the Participant Level Over 72-Week Using the Albireo Observer-Reported Outcome (ObsRo) Instrument ^[2]
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End point description:

A positive pruritus assessment was defined as a scratching score of ≤ 1 or at least a 1-point drop from baseline on the Albireo ObsRO instrument. The proportion of positive pruritus assessment was calculated as the number of positive pruritus assessments divided by the total number of reported assessments only when more than 50% of planned assessment recorded by each participant. The FAS consisted of all participants who had received at least 1 dose of the study treatment. Only participants with data collected at Baseline and Week 72 are reported.

End point type	Primary
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End point timeframe:

Baseline and Week 72

Notes:

[2] - 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: No additional statistical analysis was prespecified for this endpoint.

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	26	31	
Units: proportion of pruritus-participant-level				
arithmetic mean (standard deviation)	55.20 (± 38.733)	38.58 (± 34.877)	77.28 (± 28.084)	

Statistical analyses

Secondary: Proportion of Positive Pruritus Assessments at the Participant Level Using the Albireo ObsRo Instrument From Weeks 0-4, 0-12, 0-22, 0-24, 0-36, 0-46, 0-48, 0-60, and 0-70

End point title	Proportion of Positive Pruritus Assessments at the Participant Level Using the Albireo ObsRo Instrument From Weeks 0-4, 0-12, 0-22, 0-24, 0-36, 0-46, 0-48, 0-60, and 0-70
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End point description:

A positive pruritus assessment was defined as a scratching score of ≤ 1 or at least a 1-point drop from baseline on the Albireo ObsRO instrument. The proportion of positive pruritus assessment was calculated as the number of positive pruritus assessments divided by the total number of reported assessments only when more than 50% of planned assessment recorded by each participant. The FAS consisted of all participants who had received at least 1 dose of the study treatment. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary
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End point timeframe:

Weeks 0-4, Weeks 0-12, Weeks 0-22, Weeks 0-24, Weeks 0-36, Weeks 0-46, Weeks 0-48, Weeks 0-60, and Weeks 0-70

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	37	53	
Units: proportion of pruritus-participant-level				
arithmetic mean (standard deviation)				
Weeks 0-4 (n = 19,37,53)	45.72 (\pm 34.300)	23.64 (\pm 27.005)	60.14 (\pm 33.985)	
Weeks 0-12 (n = 19,37,50)	51.05 (\pm 37.670)	27.34 (\pm 28.687)	67.63 (\pm 33.645)	
Weeks 0-22 (n = 17,36,48)	56.01 (\pm 38.537)	31.09 (\pm 31.859)	70.05 (\pm 33.858)	
Weeks 0-24 (n = 17,36,45)	56.00 (\pm 38.331)	31.45 (\pm 32.324)	68.55 (\pm 34.116)	
Weeks 0-36 (n = 16,31,43)	54.63 (\pm 38.243)	33.66 (\pm 33.704)	69.97 (\pm 33.872)	
Weeks 0-46 (n = 14,28,37)	60.41 (\pm 39.491)	34.70 (\pm 35.593)	75.46 (\pm 29.801)	
Weeks 0-48 (n = 14,29,41)	61.61 (\pm 39.936)	33.56 (\pm 35.668)	74.79 (\pm 30.843)	
Weeks 0-60 (n = 13,31,35)	57.80 (\pm 38.873)	33.18 (\pm 34.935)	74.89 (\pm 30.434)	
Weeks 0-70 (n = 13,22,29)	58.18 (\pm 38.766)	40.59 (\pm 34.928)	75.60 (\pm 29.514)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Bile Acids at Weeks 4, 12, 22, 24, 36, 46, 48, 60, 70, and 72

End point title	Change From Baseline in Serum Bile Acids at Weeks 4, 12, 22, 24, 36, 46, 48, 60, 70, and 72
End point description:	
Blood samples for analysis of fasting total s-BAs were drawn at specified timepoints. Participants were to fast (water intake only) for at least 4 hours prior to the collection of samples for s-BAs. Exceptions were made for infants <12 months of age if unable to fast for the full 4 hours. Baseline for Cohort 1 placebo/odevixibat, and Cohort 2 groups was defined as the average of last 2 values before the first dose of study treatment in the study. Baseline for Cohort 1 odevixibat/odevixibat group was defined as average of last 2 values before the first dose of study treatment in study A4250-005 (2017-002338-21). The FAS consisted of all participants who had received at least 1 dose of the study treatment. Here, 'n' = number of participants analyzed at specific time point.	
End point type	Secondary
End point timeframe:	
Baseline and Weeks 4, 12, 22, 24, 36, 46, 48, 60, 70, and 72	

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	35	54	
Units: mcmol/L				
arithmetic mean (standard deviation)				
Week 4 (n = 17,34,53)	-115.76 (± 151.014)	-118.78 (± 172.353)	-76.92 (± 94.662)	
Week 12 (n = 18,35,54)	-98.39 (± 149.118)	-109.90 (± 176.472)	-65.01 (± 136.303)	
Week 22 (n = 15,25,38)	-138.67 (± 147.069)	-125.18 (± 165.395)	-73.24 (± 126.319)	
Week 24 (n = 14,30,50)	-112.96 (± 175.107)	-133.52 (± 191.550)	-65.37 (± 128.580)	
Week 36 (n = 17,29,49)	-129.41 (± 179.357)	-114.19 (± 200.789)	-60.90 (± 128.520)	
Week 46 (n = 11,25,38)	-166.05 (± 195.963)	-156.88 (± 157.687)	-63.80 (± 128.199)	
Week 48 (n = 13,26,45)	-145.65 (± 177.520)	-121.73 (± 114.214)	-57.90 (± 143.238)	
Week 60 (n = 13,27,47)	-86.46 (± 159.360)	-133.17 (± 162.933)	-43.31 (± 125.923)	
Week 70 (n = 10,23,33)	-149.02 (± 186.918)	-146.43 (± 196.501)	-50.08 (± 140.232)	
Week 72 (n = 13,26,40)	-101.31 (± 169.631)	-123.44 (± 143.220)	-52.39 (± 156.473)	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Positive Pruritus Assessments at the Participant Level Using the Albireo ObsRo Instrument From Weeks 1-4, 5-8, 9-12, 13-16, 17-20, 21-24, 34-36, 44-46, 47-48, 58-60, 68-70, 71-72, 73-76

End point title	Proportion of Positive Pruritus Assessments at the Participant Level Using the Albireo ObsRo Instrument From Weeks 1-4, 5-8, 9-12, 13-16, 17-20, 21-24, 34-36, 44-46, 47-48, 58-60, 68-70, 71-72, 73-76
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End point description:

A positive pruritus assessment was defined as a scratching score of ≤ 1 or at least a 1-point drop from baseline on the Albireo ObsRO instrument. The proportion of positive pruritus assessment was calculated as the number of positive pruritus assessments divided by the total number of reported assessments only when more than 50% of planned assessment recorded by each participant. The FAS consisted of all participants who had received at least 1 dose of the study treatment. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary
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End point timeframe:

Weeks 1-4, 5-8, 9-12, 13-16, 17-20, 21-24, 34-36, 44-46, 47-48, 58-60, 68-70, 71-72, 73-76
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End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	37	53	
Units: proportion of pruritus-participant-level				
arithmetic mean (standard deviation)				
Weeks 1-4 (n = 19,37,53)	45.72 (± 34.300)	23.64 (± 27.005)	60.14 (± 33.985)	
Weeks 5-8 (n = 19,37,51)	53.75 (± 39.894)	28.76 (± 32.349)	71.14 (± 34.866)	
Weeks 9-12 (n = 19,37,50)	54.01 (± 41.345)	29.64 (± 35.594)	71.03 (± 36.961)	
Weeks 13-16 (n = 18,37,50)	57.47 (± 42.420)	31.78 (± 36.364)	72.19 (± 39.221)	
Weeks 17-20 (n = 18,36,48)	55.28 (± 41.441)	36.15 (± 38.564)	73.95 (± 38.051)	
Weeks 21-24 (n = 17,36,45)	55.62 (± 42.927)	35.83 (± 40.132)	73.11 (± 37.875)	
Weeks 34-36 (n = 16,31,43)	58.24 (± 41.117)	32.79 (± 39.066)	72.39 (± 35.581)	
Weeks 44-46 (n = 14,28,37)	67.33 (± 39.242)	38.40 (± 43.144)	77.11 (± 31.712)	
Weeks 47-48 (n = 14,29,41)	67.31 (± 43.702)	34.71 (± 42.594)	71.86 (± 39.020)	
Weeks 58-60 (n = 13,31,35)	65.82 (± 40.745)	44.22 (± 43.534)	72.31 (± 38.008)	
Weeks 68-70 (n = 13,22,29)	62.43 (± 40.321)	56.79 (± 42.935)	69.40 (± 39.034)	
Weeks 71-72 (n = 12,26,31)	57.65 (± 39.797)	55.75 (± 45.076)	72.26 (± 38.680)	
Weeks 73-76 (n = 3,8,9)	41.59 (± 39.923)	63.48 (± 29.003)	69.23 (± 33.797)	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Positive Pruritus Assessments at the Participant Level Using the Albireo ObsRo Instrument (AM Score)

End point title	Proportion of Positive Pruritus Assessments at the Participant
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End point description:

A positive pruritus assessment was defined as a scratching score of ≤ 1 or at least a 1-point drop from baseline on the Albireo ObsRO instrument. The proportion of positive pruritus assessment was calculated as the number of positive pruritus assessments divided by the total number of reported assessments only when more than 50% of planned assessment recorded by each participant. AM score represents night-time itching/scratching and sleep disturbance. The FAS consisted of all participants who had received at least 1 dose of the study treatment. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary
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End point timeframe:

Weeks 1-4, 5-8, 9-12, 13-16, 17-20, 21-24, 34-36, 44-46, 47-48, 58-60, 68-70, 71-72, and 73-76
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End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	36	53	
Units: proportion of pruritus-participant-level				
arithmetic mean (standard deviation)				
Weeks 1-4 (n = 19,36,53)	42.38 (\pm 36.177)	23.72 (\pm 29.373)	58.19 (\pm 36.799)	
Weeks 5-8 (n = 19,36,51)	48.16 (\pm 42.655)	27.70 (\pm 34.144)	69.00 (\pm 38.199)	
Weeks 9-12 (n = 19,36,49)	50.57 (\pm 42.880)	28.41 (\pm 37.802)	68.96 (\pm 38.876)	
Weeks 13-16 (n = 18,36,48)	53.47 (\pm 43.689)	31.70 (\pm 38.438)	69.03 (\pm 41.902)	
Weeks 17-20 (n = 18,36,47)	53.94 (\pm 42.837)	35.37 (\pm 40.673)	71.30 (\pm 40.934)	
Weeks 21-24 (n = 17,36,45)	55.52 (\pm 44.798)	35.15 (\pm 41.940)	69.63 (\pm 40.353)	
Weeks 34-36 (n = 16,29,43)	57.49 (\pm 43.512)	34.80 (\pm 39.644)	69.92 (\pm 37.610)	
Weeks 44-46 (n = 14,27,36)	67.07 (\pm 42.321)	40.11 (\pm 43.580)	73.62 (\pm 37.122)	
Weeks 47-48 (n = 14,28,41)	63.67 (\pm 46.870)	35.60 (\pm 42.748)	69.18 (\pm 42.923)	
Weeks 58-60 (n = 13,30,33)	59.54 (\pm 45.249)	46.44 (\pm 44.871)	70.83 (\pm 40.675)	
Weeks 68-70 (n = 13,21,28)	62.42 (\pm 42.359)	63.21 (\pm 43.450)	64.35 (\pm 44.147)	
Weeks 71-72 (n = 12,27,30)	60.18 (\pm 41.743)	60.74 (\pm 43.254)	71.45 (\pm 41.406)	
Weeks 73-76 (n = 3,8,10)	33.22 (\pm 52.059)	62.66 (\pm 29.530)	69.93 (\pm 36.023)	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Positive Pruritus Assessments at the Participant Level

Using the Albireo ObsRo Instrument (PM Score)

End point title	Proportion of Positive Pruritus Assessments at the Participant Level Using the Albireo ObsRo Instrument (PM Score)
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End point description:

A positive pruritus assessment was defined as a scratching score of ≤ 1 or at least a 1-point drop from baseline on the Albireo ObsRO instrument. The proportion of positive pruritus assessment was calculated as the number of positive pruritus assessments divided by the total number of reported assessments only when more than 50% of planned assessment recorded by each participant. PM score represents daytime itching/scratching and tiredness. The FAS consisted of all participants who had received at least 1 dose of the study treatment. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary
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End point timeframe:

Weeks 1-4, 5-8, 9-12, 13-16, 17-20, 21-24, 34-36, 44-46, 47-48, 58-60, 68-70, 71-72, and 73-76

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	37	53	
Units: proportion of pruritus-participant-level				
arithmetic mean (standard deviation)				
Weeks 1-4 (n = 19,37,53)	49.01 (\pm 35.687)	24.13 (\pm 30.344)	62.08 (\pm 34.404)	
Weeks 5-8 (n = 19,37,51)	60.03 (\pm 39.300)	30.45 (\pm 35.987)	73.11 (\pm 36.284)	
Weeks 9-12 (n = 19,37,50)	57.77 (\pm 42.435)	31.73 (\pm 38.223)	72.42 (\pm 37.687)	
Weeks 13-16 (n = 18,37,50)	61.36 (\pm 41.530)	33.08 (\pm 39.999)	74.13 (\pm 38.607)	
Weeks 17-20 (n = 18,37,48)	56.49 (\pm 41.590)	36.22 (\pm 41.689)	76.12 (\pm 36.907)	
Weeks 21-24 (n = 17,36,46)	55.78 (\pm 43.495)	36.28 (\pm 41.318)	77.23 (\pm 37.626)	
Weeks 34-36 (n = 16,31,43)	58.75 (\pm 39.774)	30.28 (\pm 39.297)	75.11 (\pm 36.650)	
Weeks 44-46 (n = 14,28,37)	67.01 (\pm 39.601)	38.02 (\pm 43.252)	81.00 (\pm 30.974)	
Weeks 47-48 (n = 14,29,41)	71.08 (\pm 41.878)	34.98 (\pm 43.148)	74.62 (\pm 38.856)	
Weeks 58-60 (n = 13,31,33)	72.28 (\pm 38.149)	43.53 (\pm 43.694)	73.17 (\pm 38.473)	
Weeks 68-70 (n = 13,21,28)	62.63 (\pm 40.626)	55.65 (\pm 42.883)	74.85 (\pm 38.702)	
Weeks 71-72 (n = 12,26,32)	55.12 (\pm 42.336)	53.97 (\pm 45.611)	75.38 (\pm 39.038)	
Weeks 73-76 (n = 3,8,10)	49.36 (\pm 36.671)	63.35 (\pm 31.538)	68.11 (\pm 32.377)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Responders for Pruritus Assessments Bi-Weekly (AM and PM)

End point title	Percentage of Responders for Pruritus Assessments Bi-Weekly (AM and PM)
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End point description:

A responder is defined as a participant who reports a decrease in pruritus score from unrounded baseline equivalent to or greater than the threshold of meaningful change estimated from the blinded psychometric analysis. The averaged pruritus score was used to calculate the percentage of participants achieving meaningful reduction at specified Week against the thresholds value of 1.00 based on bi-weekly scores at specified Week obtained from blinded psychometric analysis across all anchors support a threshold of 1.0 point for AM, PM and AM and PM scratching scores. ObsRO instrument was used to assess severity of observed scratching twice a day (AM and PM) with score from 0 to 4 where 0 is no scratching and 4 is worst possible scratching. The FAS consisted of all participants who had received at least 1 dose of the study treatment. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary
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End point timeframe:

Weeks 1-2, 3-4, 5-6, 7-8, 9-10, 11-12, 13-14, 15-16, 17-18, 19-20, 21-22, 23-24, 35-36, 47-48, 59-60, and 71-72

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	36	53	
Units: percentage of participants				
number (confidence interval 95%)				
Weeks 1-2 (n = 19,36,53)	15.8 (3.38 to 39.58)	2.8 (0.07 to 14.53)	28.3 (16.79 to 42.35)	
Weeks 3-4 (n = 19,36,53)	36.8 (16.29 to 61.64)	2.8 (0.07 to 14.53)	52.8 (38.64 to 66.70)	
Weeks 5-6 (n = 19,36,52)	36.8 (16.29 to 61.64)	5.6 (0.68 to 18.66)	55.8 (41.33 to 69.53)	
Weeks 7-8 (n = 19,36,51)	36.8 (16.29 to 61.64)	13.9 (4.67 to 29.50)	54.9 (40.34 to 68.87)	
Weeks 9-10 (n = 19,36,50)	31.6 (12.58 to 56.55)	8.3 (1.75 to 22.47)	58.0 (43.21 to 71.81)	
Weeks 11-12 (n = 18,36,50)	33.3 (13.34 to 59.01)	13.9 (4.67 to 29.50)	56.0 (41.25 to 70.01)	
Weeks 13-14 (n = 18,36,50)	50.0 (26.02 to 73.98)	11.1 (3.11 to 26.06)	58.0 (43.21 to 71.81)	
Weeks 15-16 (n = 18,36,49)	50.0 (26.02 to 73.98)	13.9 (4.67 to 29.50)	57.1 (42.21 to 71.18)	
Weeks 17-18 (n = 18,36,47)	44.4 (21.53 to 69.24)	16.7 (6.37 to 32.81)	55.3 (40.12 to 69.83)	
Weeks 19-20 (n = 16,36,48)	50.0 (24.65 to 75.35)	22.2 (10.12 to 39.15)	56.3 (41.18 to 70.52)	
Weeks 21-22 (n = 17,36,45)	41.2 (18.44 to 67.08)	16.7 (6.37 to 32.81)	57.8 (42.15 to 72.34)	
Weeks 23-24 (n = 17,36,46)	41.2 (18.44 to 67.08)	19.4 (8.19 to 36.02)	56.5 (41.11 to 71.07)	
Weeks 35-36 (n = 15,27,39)	33.3 (11.82 to 61.62)	18.5 (6.30 to 38.08)	56.4 (39.62 to 72.19)	
Weeks 47-48 (n = 14,28,39)	57.1 (28.86 to 82.34)	25.0 (10.69 to 44.87)	64.1 (47.18 to 78.80)	
Weeks 59-60 (n = 11,30,30)	36.4 (10.93 to 69.21)	30.0 (14.73 to 49.40)	60.0 (40.60 to 77.34)	

Weeks 71-72 (n = 12,26,31)	41.7 (15.17 to 72.33)	34.6 (17.21 to 55.67)	61.3 (42.19 to 78.15)	
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Responders for Pruritus Assessments Monthly (AM and PM)

End point title	Percentage of Responders for Pruritus Assessments Monthly (AM and PM)
End point description:	
A responder is defined as a participant who reports a decrease in pruritus score from unrounded baseline equivalent to or greater than the threshold of meaningful change estimated from the blinded psychometric analysis. The averaged pruritus score was used to calculate the percentage of participants achieving meaningful reduction at specified Week against the thresholds value of 1.00 based on monthly scores at specified Week obtained from blinded psychometric analysis across all anchors support a threshold of 1.0 point for AM, PM and AM and PM scratching scores. ObsRO instrument was used to assess severity of observed scratching twice a day (AM and PM) with score from 0 to 4 where 0 is no scratching and 4 is worst possible scratching. The FAS consisted of all participants who had received at least 1 dose of the study treatment. Here, 'n' = number of participants analyzed at specific time point.	
End point type	Secondary
End point timeframe:	
Weeks 1-4, 5-8, 9-12, 13-16, 17-20, 21-24, 34-36, 45-48, 58-60, and 68-72	

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	36	53	
Units: percentage of participants				
number (confidence interval 95%)				
Weeks 1-4 (n = 19,36,53)	21.1 (6.05 to 45.57)	2.8 (0.07 to 14.53)	43.4 (29.84 to 57.72)	
Weeks 5-8 (n = 19,36,51)	36.8 (16.29 to 61.64)	8.3 (1.75 to 22.47)	54.9 (40.34 to 68.87)	
Weeks 9-12 (n = 19,36,50)	36.8 (16.29 to 61.64)	11.1 (3.11 to 26.06)	56.0 (41.25 to 70.01)	
Weeks 13-16 (n = 18,36,50)	50.0 (26.02 to 73.98)	13.9 (4.67 to 29.50)	60.0 (45.18 to 73.59)	
Weeks 17-20 (n = 18,36,48)	38.9 (17.30 to 64.25)	16.7 (6.37 to 32.81)	56.3 (41.18 to 70.52)	
Weeks 21-24 (n = 17,36,45)	35.3 (14.21 to 61.67)	16.7 (6.37 to 32.81)	53.3 (37.87 to 68.34)	
Weeks 34-36 (n = 16,30,43)	43.8 (19.75 to 70.12)	23.3 (9.93 to 42.28)	58.1 (42.13 to 72.99)	
Weeks 45-48 (n = 15,29,39)	53.3 (26.59 to 78.73)	24.1 (10.30 to 43.54)	64.1 (47.18 to 78.80)	
Weeks 58-60 (n = 13,31,35)	46.2 (19.22 to 74.87)	29.0 (14.22 to 48.04)	57.1 (39.35 to 73.68)	
Weeks 68-72 (n = 13,24,31)	53.8 (25.13 to 80.78)	37.5 (18.80 to 59.41)	64.5 (45.37 to 80.77)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving a Positive Pruritus Assessment for >50% of the Time Based on the Albireo ObsRO (AM and PM)

End point title	Percentage of Participants Achieving a Positive Pruritus Assessment for >50% of the Time Based on the Albireo ObsRO (AM and PM)
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End point description:

The percentage of participants who achieved positive pruritus assessment for more than 50% of the time for Weeks 0-72 is reported. A positive pruritus assessment is defined as a scratching score of ≤ 1 or at least a 1-point decrease from baseline on the Albireo ObsRO instrument based on rounded baseline and was calculated based on reported eDiary data. At each assessment, the AM score was compared to the baseline AM average, and the PM score was compared to the baseline PM average. All assessments after intercurrent events (premature treatment discontinuation, death, or initiation of rescue treatments such as biliary diversion surgery or liver transplantation) or follow-up assessments (\geq last dose day + 15 days) were excluded from analysis. The FAS consisted of all participants who had received at least 1 dose of the study treatment. Only participants with non-missing value when $>50\%$ were included.

End point type	Secondary
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End point timeframe:

Week 72

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	26	31	
Units: percentage of participants				
number (confidence interval 95%)	58.3 (27.67 to 84.83)	34.6 (17.21 to 55.67)	83.9 (66.27 to 94.55)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Underwent Biliary Diversion Surgery and Liver Transplantation

End point title	Number of Participants Who Underwent Biliary Diversion Surgery and Liver Transplantation
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End point description:

Participants who underwent biliary diversion surgery and or liver transplantation data has been reported. The FAS consisted of all participants who had received at least 1 dose of the study treatment.

End point type	Secondary
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End point timeframe:

Baseline and Weeks 24, 48, and 72

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	37	60	
Units: participants				
number (not applicable)				
Weeks 0-24: Biliary Diversion Surgery	0	0	0	
Weeks 0-24: Liver Transplantation	1	0	0	
Weeks 0-48: Biliary Diversion Surgery	1	0	1	
Weeks 0-48: Liver Transplantation	2	0	2	
Weeks 0-72: Biliary Diversion Surgery	1	0	1	
Weeks 0-72: Liver Transplantation	2	0	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Height Z-Scores

End point title	Change From Baseline in Height Z-Scores
End point description: Growth factors like height was measured by standardized assessments outlined in US food and drug administration (FDA) guidance document. Height was measured using certified stadiometer. Change in growth parameters was assessed using linear growth compared to standard growth curve (Z-score) calculated by using software/methods from centers for disease control(CDC) website for participants with age ≥ 2 years old and from world health organization (WHO) website for participants with age < 2 years old. Participants whose accurate age was not available, Z-score was not calculated. Baseline is last available assessment prior to first dose of study treatment. A Z-score indicates how many standard deviation's (SD) a participant's measurement, was from average for their age and sex. A Z-score of 0 represents median or 50th percentile, while positive or negative values show how far above or below average a measurement was. FAS. n=participants with data collected specified timepoints are reported.	
End point type	Secondary
End point timeframe: Baseline and Weeks 24, 48, 70 and 72	

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	28	46	
Units: Z-score				
median (full range (min-max))				
Week 24 (n = 14,28,46)	0.181 (-0.28 to 1.53)	0.341 (-1.04 to 2.26)	0.089 (-1.34 to 1.97)	

Week 48 (n = 14,27,41)	0.485 (0.02 to 1.42)	0.662 (-0.75 to 2.08)	0.095 (-1.46 to 2.03)	
Average of Weeks 70-72 (n = 15,28,39)	0.556 (-0.01 to 1.57)	0.543 (-0.83 to 2.12)	0.224 (-1.42 to 2.62)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weight Z-Scores

End point title	Change From Baseline in Weight Z-Scores
End point description:	
Growth factors like weight was measured by the standardized assessments outlined in the US FDA guidance document. Weight was measured using certified weight scale. Change in growth parameters was assessed using linear growth (weight) compared to standard growth curve (Z-score), calculated by using the software or methods from the CDC website for participants with age ≥ 2 years old and from the WHO website for participants with age < 2 years old. Participants whose accurate age was not available, Z-score was not calculated. Baseline is the last available assessment prior to the first dose of study treatment. The Z-score indicates how many SDs a participant's measurement (like weight), was from the average for their age and sex. A Z-score of 0 represents the median or 50th percentile, while positive or negative values show how far above or below the average a measurement was. FAS. Here, 'n'= participants with data collected at specified timepoints are reported.	
End point type	Secondary
End point timeframe:	
Baseline and Weeks 24, 48, 70 and 72	

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	29	48	
Units: Z-score				
median (full range (min-max))				
Week 24 (n = 14,29,48)	0.155 (-0.49 to 1.40)	0.383 (-0.75 to 1.57)	0.169 (-0.68 to 1.74)	
Week 48 (n = 14,27,42)	0.544 (-1.15 to 1.43)	0.494 (-1.04 to 2.14)	0.246 (-0.54 to 1.29)	
Average of Weeks 70-72 (n = 15,28,40)	0.098 (-1.13 to 2.17)	0.389 (-1.21 to 2.11)	0.400 (-0.86 to 2.27)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Mass Index (BMI) Z-Scores

End point title	Change From Baseline in Body Mass Index (BMI) Z-Scores
End point description:	

Growth factors like BMI was measured by the standardized assessments outlined in the US FDA guidance document. BMI was calculated by weight (kg) / height (m²). Change in growth parameters

was assessed using linear growth (BMI) compared to standard growth curve (Z-score), calculated by using the software or methods from the CDC website for participants with age ≥ 2 years old and from the WHO website for participants with age < 2 years old. Participants whose accurate age was not available, Z-score was not calculated. Baseline is the last available assessment prior to the first dose of study treatment. The Z-score indicates how many SDs a participant's measurement (like BMI), was from the average for their age and sex. A Z-score of 0 represents the median or 50th percentile, while positive or negative values show how far above or below the average a measurement was. FAS. Here, 'n' = participants with data collected at specified timepoints are reported.

End point type	Secondary
End point timeframe:	
Baseline and Weeks 24, 48, 70 and 72	

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	28	46	
Units: Z-score				
median (full range (min-max))				
Week 24 (n = 14,28,46)	-0.106 (-0.66 to 1.86)	0.150 (-2.00 to 2.21)	0.202 (-1.60 to 2.08)	
Week 48 (n = 14,27,41)	0.028 (-0.88 to 1.23)	-0.135 (-2.44 to 2.59)	0.129 (-1.34 to 2.45)	
Average of Weeks 70-72 (n = 15,28,39)	-0.059 (-1.24 to 3.12)	-0.007 (-1.64 to 2.25)	0.182 (-0.99 to 2.68)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Use of Ursodeoxycholic Acid (UDCA) and/or Rifampicin at Weeks 24, 48, and 72

End point title	Number of Participants With Use of Ursodeoxycholic Acid (UDCA) and/or Rifampicin at Weeks 24, 48, and 72
End point description:	
Data for the number of participants with use of UDCA and rifampicin are reported. The FAS consisted of all participants who had received at least 1 dose of the study treatment. Here, 'n' = number of participants collected at specific time point.	
End point type	Secondary
End point timeframe:	
Weeks 24, 48, and 72	

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	37	60	
Units: participants				
number (not applicable)				
Week 24: Use of UDCA (n=19,37,60)	17	29	43	
Week 24: Use of Rifampicin (n=19,37,60)	17	19	37	
Week 24: Use of UDCA or Rifampicin (n=19,37,60)	19	33	50	
Week 24: Use of UDCA and Rifampicin(n=19,37,60)	15	15	30	
Week 48: Use of UDCA (n=18,35,56)	16	27	39	
Week 48: Use of Rifampicin (n=18,35,56)	16	20	31	
Week 48: Use of UDCA or Rifampicin (n=18,35,56)	18	33	46	
Week 48: Use of UDCA and Rifampicin (n=18,35,56)	14	14	24	
Week 72: Use of UDCA (n=16,31,50)	14	24	34	
Week 72: Use of Rifampicin (n=16,31,50)	14	15	26	
Week 72: Use of UDCA or Rifampicin (n=16,31,50)	16	29	41	
Week 72: Use of UDCA and Rifampicin (n=16,31,50)	12	10	19	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Week 72 in Pediatric End-Stage Liver Disease (PELD) Score

End point title	Change From Baseline to Week 72 in Pediatric End-Stage Liver Disease (PELD) Score
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End point description:

PELD score was calculated for children under 12 years of age, ranged across negative to positive values. Calculation of PELD score was done by converting laboratory parameters: total bilirubin in milligram/deciliter (mg/dL), albumin in gram (g)/dL, and creatinine in mg/dL laboratory parameters were converted to units. PELD score was calculated as $4.80 \cdot \ln(\text{total bilirubin}) + 18.57 \cdot \ln[\text{international normalized ratio (INR)}] - 6.87 \cdot \ln(\text{albumin}) + 4.36$ (if participant <1 year: scores for participants listed for liver transplantation before participant's first birthday continued to include value assigned for age (<1 year) until participant reached the age of 24 months) + 6.67 (if participant has growth failure [<-2 SD]). Laboratory values <1.0 were set to 1.0 for calculation of PELD score. Lower scores represent less severe hepatic disease. Baseline is last available assessment prior to first dose of study treatment. FAS. Only participants with data collected at specified timepoint reported.

End point type	Secondary
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End point timeframe:

Baseline and Week 72

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	20	23	
Units: score on a scale				
arithmetic mean (standard deviation)	-0.397 (± 3.6168)	1.361 (± 2.5083)	-0.303 (± 9.4631)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Week 72 in Model for End-stage Liver Disease (MELD) Score for Children 12 Years of Age or Older

End point title	Change From Baseline to Week 72 in Model for End-stage Liver Disease (MELD) Score for Children 12 Years of Age or Older
End point description: The calculation of MELD score was done by converting laboratory parameters in following units: total bilirubin in mg/dL, albumin in g/dL, and creatinine in mg/dL laboratory parameters were converted to units. MELD score for children 12 years of age or older ranges from 6 to 40 was calculated as $9.57 \times \ln(\text{creatinine}) + 3.78 \times \ln(\text{total bilirubin}) + 11.2 \times \ln(\text{INR}) + 6.43$. Laboratory values <1.0 were set to 1.0 and serum creatinine values >4.0 mg/dL were set to 4.0 for calculation of MELD score. Lower scores represent less severe hepatic disease. Baseline is last available assessment prior to first dose of study treatment. FAS. Only participants 12 years of age or older are included in this analysis and reported. For Cohort 1: Placebo/Odevixibat change from baseline data was not collected as participant was under 12 years old, that aligns with MELD score calculation. n=number of participants with data collected. 9999=standard deviation not calculated for 1 participant. 99999=0 participant analyzed.	
End point type	Secondary
End point timeframe: Baseline and Week 72	

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	3	17	
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n = 1,3,17)	6.869 (± 9999)	9.795 (± 2.4694)	11.574 (± 4.0801)	
Change from Baseline (n = 0,1,9)	99999 (± 99999)	1.286 (± 9999)	-2.221 (± 5.7744)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Week 72 in Aspartate Aminotransferase (AST)

to Platelet Ratio Index (APRI) Score

End point title	Change From Baseline to Week 72 in Aspartate Aminotransferase (AST) to Platelet Ratio Index (APRI) Score
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End point description:

AST to APRI score was calculated as $[(\text{AST in units per liter } \{U/L\}) / (\text{AST upper limit of normal } \{ULN\} \text{ in } U/L)] * 100 / (\text{platelets in } 10^9/L)$. The APRI score is a way to assess fibrosis of the liver. The lower the APRI score (< 0.5), the greater the negative predictive value and ability to rule out cirrhosis; the higher the value (> 1.5) the greater the positive predictive value and ability to rule in cirrhosis. Lower values indicate less severe hepatic fibrosis. Baseline is the last available assessment prior to the first dose of study treatment. The FAS consisted of all participants who had received at least 1 dose of the study treatment. Only participants with data collected at Baseline and Week 72 are reported.

End point type	Secondary
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End point timeframe:

Baseline and Week 72

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	21	22	
Units: score on a scale				
arithmetic mean (standard deviation)	0.044 (\pm 0.3435)	0.071 (\pm 0.3951)	0.411 (\pm 0.9690)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Week 72 in Fibrosis-4 (Fib-4) Score

End point title	Change From Baseline to Week 72 in Fibrosis-4 (Fib-4) Score
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End point description:

Fib-4 score was calculated as $(\text{age} * \text{AST in } U/L) / (\text{platelets in } 10^9/L * \text{square root of (alanine aminotransferase [ALT] in } U/L))$. The FIB-4 score estimates the amount of scarring in the liver. A FIB-4 score < 1.45 has a negative predictive value of 90% for advanced fibrosis (Ishak fibrosis score 4-6 which includes early bridging fibrosis to cirrhosis). In contrast, a FIB-4 > 3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis. Lower values indicate less severe hepatic fibrosis. Baseline is the last available assessment prior to the first dose of study treatment. The FAS consisted of all participants who had received at least 1 dose of the study treatment. Only participants with data collected at Baseline and Week 72 are reported.

End point type	Secondary
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End point timeframe:

Baseline and Week 72

End point values	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	21	21	
Units: score on a scale				
arithmetic mean (standard deviation)	0.050 (± 0.1187)	0.106 (± 0.2696)	0.113 (± 0.2820)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All treatment emergent AEs were collected from the start of study treatment administration (Day 1) up to 28 days after last dose of study treatment (248 weeks) and death was assessed from signing of informed consent form till DCO (281 weeks).

Adverse event reporting additional description:

The FAS consisted of all participants who had received at least 1 dose of the study treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	Cohort 1: Placebo/Odevixibat
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Reporting group description:

Participants who previously received placebo in study A4250-005 for 24 weeks received odevixibat capsule orally at a dose of 120 mcg/kg/day for 72 weeks, unless they required down-titration to the 40 mcg/kg/day due to tolerability issues. Participants continued receiving study treatment until commercial availability of odevixibat.

Reporting group title	Cohort 1: Odevixibat/Odevixibat
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Reporting group description:

Participants who previously received odevixibat capsule orally at a dose of 40 or 120 mcg/kg/day in study A4250-005 for 24 weeks received odevixibat capsule orally at a dose of 120 mcg/kg/day for 72 weeks, unless they required down-titration to the 40 mcg/kg/day due to tolerability issues. Participants continued receiving study treatment until commercial availability of odevixibat.

Reporting group title	Cohort 2: Odevixibat
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Reporting group description:

Participants any age with any type of PFIC who either did not meet eligibility criteria for study A4250-005 or were eligible for enrolment in A4250-005 after recruitment was complete received odevixibat at a dose of 120 mcg/kg/day or following protocol amendment 6.0, initiated at a dose of 40 mcg/kg/day with the possibility to dose escalate to 120 mcg/kg/day after 12 weeks if there was no improvement in pruritus based on investigator judgement, up to 72 weeks. Participants continued receiving study treatment until commercial availability of odevixibat.

Serious adverse events	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 19 (26.32%)	7 / 37 (18.92%)	23 / 60 (38.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	2 / 60 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Anaphylactic reaction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alpha 1 foetoprotein increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood sodium decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fracture displacement			

subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Progressive familial intrahepatic cholestasis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coagulopathy			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	2 / 60 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolysis			

subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocutaneous fistula			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			

subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varices oesophageal			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	2 / 60 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic hepatic failure			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic arthritis streptococcal			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	2 / 60 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	2 / 60 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cohort 1: Placebo/Odevixibat	Cohort 1: Odevixibat/Odevixibat	Cohort 2: Odevixibat
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 19 (94.74%)	35 / 37 (94.59%)	57 / 60 (95.00%)
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed occurrences (all)	7 / 19 (36.84%) 17	12 / 37 (32.43%) 25	16 / 60 (26.67%) 29
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2	0 / 37 (0.00%) 0	1 / 60 (1.67%) 1
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	4 / 19 (21.05%) 6	13 / 37 (35.14%) 23	10 / 60 (16.67%) 14
Epistaxis subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 2	3 / 37 (8.11%) 5	6 / 60 (10.00%) 12
Nasal congestion subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	2 / 60 (3.33%) 2
Oropharyngeal pain subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 6	2 / 37 (5.41%) 3	1 / 60 (1.67%) 1
Respiratory disorder subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	1 / 37 (2.70%) 1	0 / 60 (0.00%) 0
Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	3 / 37 (8.11%) 3	2 / 60 (3.33%) 2
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Autism spectrum disorder subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	2 / 37 (5.41%) 2	0 / 60 (0.00%) 0
Irritability			

subjects affected / exposed	1 / 19 (5.26%)	2 / 37 (5.41%)	0 / 60 (0.00%)
occurrences (all)	1	2	0
Sleep disorder			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1
Tic			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 19 (10.53%)	3 / 37 (8.11%)	6 / 60 (10.00%)
occurrences (all)	3	3	10
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 19 (5.26%)	2 / 37 (5.41%)	5 / 60 (8.33%)
occurrences (all)	1	2	10
Bile acids increased			
subjects affected / exposed	0 / 19 (0.00%)	2 / 37 (5.41%)	2 / 60 (3.33%)
occurrences (all)	0	2	2
Bilirubin conjugated increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	3 / 60 (5.00%)
occurrences (all)	1	0	6
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 19 (0.00%)	3 / 37 (8.11%)	0 / 60 (0.00%)
occurrences (all)	0	4	0
Blood bilirubin increased			
subjects affected / exposed	4 / 19 (21.05%)	10 / 37 (27.03%)	13 / 60 (21.67%)
occurrences (all)	6	17	20
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 19 (10.53%)	1 / 37 (2.70%)	1 / 60 (1.67%)
occurrences (all)	2	1	1
Blood sodium increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			

subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 19 (0.00%)	2 / 37 (5.41%)	0 / 60 (0.00%)
occurrences (all)	0	2	0
International normalised ratio increased			
subjects affected / exposed	3 / 19 (15.79%)	5 / 37 (13.51%)	11 / 60 (18.33%)
occurrences (all)	3	7	13
Lymph node palpable			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Platelet count increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Prothrombin time prolonged			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1
Transaminases increased			
subjects affected / exposed	0 / 19 (0.00%)	2 / 37 (5.41%)	3 / 60 (5.00%)
occurrences (all)	0	2	4
Vitamin A increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Vitamin D decreased			
subjects affected / exposed	1 / 19 (5.26%)	2 / 37 (5.41%)	2 / 60 (3.33%)
occurrences (all)	1	4	2
Vitamin E decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	3 / 60 (5.00%)
occurrences (all)	2	0	3
Injury, poisoning and procedural complications			

Accidental overdose subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 2	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Foot fracture subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Immunisation reaction subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Limb injury subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Post vaccination fever subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Scar subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Scratch subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	1 / 37 (2.70%) 1	0 / 60 (0.00%) 0
Nervous system disorders			
Dyslexia subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 2	0 / 37 (0.00%) 0	2 / 60 (3.33%) 3
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	4 / 60 (6.67%)
occurrences (all)	0	1	4
Coagulopathy			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	3 / 60 (5.00%)
occurrences (all)	0	0	3
Iron deficiency anaemia			
subjects affected / exposed	1 / 19 (5.26%)	2 / 37 (5.41%)	0 / 60 (0.00%)
occurrences (all)	1	2	0
Splenomegaly			
subjects affected / exposed	2 / 19 (10.53%)	3 / 37 (8.11%)	4 / 60 (6.67%)
occurrences (all)	2	3	4
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	2	0	0
Ear haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)	1 / 37 (2.70%)	0 / 60 (0.00%)
occurrences (all)	1	1	0
Ear pain			
subjects affected / exposed	1 / 19 (5.26%)	3 / 37 (8.11%)	1 / 60 (1.67%)
occurrences (all)	3	3	1
Otorrhoea			
subjects affected / exposed	0 / 19 (0.00%)	2 / 37 (5.41%)	0 / 60 (0.00%)
occurrences (all)	0	4	0
Eye disorders			
Keratoconus			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 19 (5.26%)	1 / 37 (2.70%)	0 / 60 (0.00%)
occurrences (all)	1	1	0
Abdominal pain			
subjects affected / exposed	1 / 19 (5.26%)	3 / 37 (8.11%)	2 / 60 (3.33%)
occurrences (all)	1	4	4
Abdominal pain upper			

subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1
Constipation			
subjects affected / exposed	2 / 19 (10.53%)	3 / 37 (8.11%)	4 / 60 (6.67%)
occurrences (all)	2	6	4
Dental caries			
subjects affected / exposed	1 / 19 (5.26%)	3 / 37 (8.11%)	1 / 60 (1.67%)
occurrences (all)	1	3	1
Diarrhoea			
subjects affected / exposed	2 / 19 (10.53%)	8 / 37 (21.62%)	16 / 60 (26.67%)
occurrences (all)	3	16	20
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 19 (5.26%)	1 / 37 (2.70%)	0 / 60 (0.00%)
occurrences (all)	1	1	0
Faeces soft			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorder			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 19 (5.26%)	1 / 37 (2.70%)	0 / 60 (0.00%)
occurrences (all)	1	1	0
Nausea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	3 / 60 (5.00%)
occurrences (all)	0	0	4
Tooth impacted			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	2 / 60 (3.33%)
occurrences (all)	1	0	3
Umbilical hernia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Vomiting			

subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2	2 / 37 (5.41%) 2	10 / 60 (16.67%) 15
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 19 (5.26%)	1 / 37 (2.70%)	0 / 60 (0.00%)
occurrences (all)	1	1	0
Hepatomegaly			
subjects affected / exposed	1 / 19 (5.26%)	4 / 37 (10.81%)	1 / 60 (1.67%)
occurrences (all)	1	4	1
Hepatosplenomegaly			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1
Jaundice			
subjects affected / exposed	0 / 19 (0.00%)	2 / 37 (5.41%)	3 / 60 (5.00%)
occurrences (all)	0	2	3
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1
Dermatitis allergic			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	2	0	0
Dermatitis atopic			
subjects affected / exposed	0 / 19 (0.00%)	2 / 37 (5.41%)	0 / 60 (0.00%)
occurrences (all)	0	2	0
Eczema			
subjects affected / exposed	1 / 19 (5.26%)	2 / 37 (5.41%)	2 / 60 (3.33%)
occurrences (all)	1	3	2
Pruritus			
subjects affected / exposed	3 / 19 (15.79%)	7 / 37 (18.92%)	7 / 60 (11.67%)
occurrences (all)	4	10	8
Psoriasis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Urticaria			

subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	2 / 37 (5.41%) 2	0 / 60 (0.00%) 0
Renal and urinary disorders Bladder dysfunction subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	1 / 60 (1.67%) 1
Trigger finger subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Infections and infestations Boston exanthema subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 37 (0.00%) 0	0 / 60 (0.00%) 0
Bronchitis subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	1 / 37 (2.70%) 4	2 / 60 (3.33%) 4
COVID-19 subjects affected / exposed occurrences (all)	3 / 19 (15.79%) 3	3 / 37 (8.11%) 3	15 / 60 (25.00%) 17
Conjunctivitis subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	3 / 37 (8.11%) 3	0 / 60 (0.00%) 0
Ear infection subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 4	2 / 37 (5.41%) 2	3 / 60 (5.00%) 3
Gastroenteritis subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 2	5 / 37 (13.51%) 5	6 / 60 (10.00%) 6
Gastroenteritis viral			

subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	2 / 60 (3.33%)
occurrences (all)	1	0	2
Gastrointestinal candidiasis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 19 (0.00%)	3 / 37 (8.11%)	1 / 60 (1.67%)
occurrences (all)	0	3	1
Influenza			
subjects affected / exposed	0 / 19 (0.00%)	7 / 37 (18.92%)	8 / 60 (13.33%)
occurrences (all)	0	10	11
Lower respiratory tract infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	2 / 60 (3.33%)
occurrences (all)	2	0	2
Nasopharyngitis			
subjects affected / exposed	3 / 19 (15.79%)	9 / 37 (24.32%)	9 / 60 (15.00%)
occurrences (all)	4	16	10
Oral candidiasis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Otitis externa			
subjects affected / exposed	2 / 19 (10.53%)	0 / 37 (0.00%)	2 / 60 (3.33%)
occurrences (all)	2	0	2
Otitis media			
subjects affected / exposed	2 / 19 (10.53%)	3 / 37 (8.11%)	2 / 60 (3.33%)
occurrences (all)	3	9	2
Paronychia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	1 / 19 (5.26%)	1 / 37 (2.70%)	1 / 60 (1.67%)
occurrences (all)	1	1	1
Pneumonia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	2 / 60 (3.33%)
occurrences (all)	1	0	4
Postoperative wound infection			

subjects affected / exposed	1 / 19 (5.26%)	1 / 37 (2.70%)	0 / 60 (0.00%)
occurrences (all)	1	1	0
Respiratory tract infection			
subjects affected / exposed	1 / 19 (5.26%)	2 / 37 (5.41%)	1 / 60 (1.67%)
occurrences (all)	1	2	1
Rhinitis			
subjects affected / exposed	2 / 19 (10.53%)	3 / 37 (8.11%)	0 / 60 (0.00%)
occurrences (all)	2	4	0
Tonsillitis			
subjects affected / exposed	3 / 19 (15.79%)	3 / 37 (8.11%)	1 / 60 (1.67%)
occurrences (all)	4	4	1
Upper respiratory tract infection			
subjects affected / exposed	7 / 19 (36.84%)	10 / 37 (27.03%)	12 / 60 (20.00%)
occurrences (all)	21	19	17
Varicella			
subjects affected / exposed	3 / 19 (15.79%)	2 / 37 (5.41%)	3 / 60 (5.00%)
occurrences (all)	3	2	3
Viral infection			
subjects affected / exposed	1 / 19 (5.26%)	4 / 37 (10.81%)	5 / 60 (8.33%)
occurrences (all)	2	5	5
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 19 (10.53%)	0 / 37 (0.00%)	1 / 60 (1.67%)
occurrences (all)	2	0	1
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 19 (0.00%)	2 / 37 (5.41%)	1 / 60 (1.67%)
occurrences (all)	0	2	1
Vitamin D deficiency			
subjects affected / exposed	1 / 19 (5.26%)	2 / 37 (5.41%)	8 / 60 (13.33%)
occurrences (all)	1	2	9
Vitamin E deficiency			
subjects affected / exposed	0 / 19 (0.00%)	2 / 37 (5.41%)	3 / 60 (5.00%)
occurrences (all)	0	2	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 April 2018	Protocol Amendment 1 was the initial protocol submitted to regulatory and competent authorities.
18 January 2019	Cohort 2 added for participant enrollment. Revision of inclusion and exclusion criteria. Secondary and exploratory endpoints added. Removal of exploratory endpoint "proportion of patients achieving meaningful reduction in caregiver reported observed scratching". Baseline definitions revised. Sample size determination added. Clarification added for data review and dose titration guidelines. Liver biopsy text revised and criteria for withdrawal from study revised. List of food items that can be mixed with study treatment expanded. Amendment of derived variable calculation for primary endpoint. Definition of FAS updated, and safety analysis set removed. Revision of concomitant medication guidelines. Pediatric quality of life inventory for participants ages 18 to 25 added.
11 March 2019	Cohort 2 participant population revised. The secondary objective revised for additional clarification. Exclusion criteria revised. The list of genes analyzed to confirm PFIC diagnosis added.
25 October 2019	Clarification added for primary analysis performed after the last participant from either Cohort 1 or 2. Addition of optional extension period. Revision of inclusion and exclusion criteria. Revision of concomitant medication guidelines. Voluntary photography assessment removed. Estimated blood volumes required for optional extension period added.
18 March 2020	Addition of collection of a blood sample for pharmacokinetic analysis as close to onset as possible for hepatic AEs including liver decompensation
21 December 2021	Clarification added for participant population. Starting dose for participant in Cohort 2 revised. Clarification added for follow-up requirements for participants. Use of certified stadiometer for height and length measurements added. Clarification added for autotaxin, plasma 7-alpha-hydroxy-4-cholesten-3-one concentration (p-C4), pharmacokinetic samples added. Home nursing and local lab collection added. Extended screening period due to Coronavirus Disease 2019 (COVID-19) added. Baseline data requirements for participants added. Inclusion and exclusion criteria modified. Clarification added for end of treatment visit for optional extension period. Addition of allowance for participants vaccinated against COVID-19 while in the study added. Follow-up requirements added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported