Clinical trial results:
A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate LUM001, an Apical Sodium-Dependent Bile Acid Transporter Inhibitor (ASBTi), in Combination with Ursodeoxycholic Acid (UDCA) in Patients with Primary Biliary Cirrhosis

Summary

EudraCT number	2013-000482-36
Trial protocol	GB
Global end of trial date	09 April 2015

Results information

Result version number	v1 (current)
This version publication date	21 April 2016
First version publication date	21 April 2016

Trial information

Trial identification

Sponsor protocol code	LUM001-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01904058
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Lumena Pharmaceuticals, LLC
Sponsor organisation address	300 Shire Way, Lexington, MA, United States, 02421
Public contact	Study Physician, Shire, 1 866 842 5335,
Scientific contact	Study Physician, Shire, 1 866 842 5335,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 April 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of LUM001 in combination with ursodeoxycholic acid (UDCA) versus UDCA alone on the reduction of pruritus associated with primary biliary cirrhosis (PBC).

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and its revisions as well as with the valid national law(s) of the participating countries, with the International Conference on Harmonisation (ICH) Harmonized Tripartite Guideline for Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 August 2013
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: 1
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	United States: 47
Worldwide total number of subjects	66
EEA total number of subjects	18

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	52
From 65 to 84 years	14

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in 24 centers in the United Kingdom, Canada, and the United States between 19 August 2013 and 09 April 2015.

Pre-assignment

Screening details:

A total of 87 subjects were screened out of which 66 subjects were randomized into the study and the remaining 21 were screen failures.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	LUM001 10 mg + UDCA (Cohort A)

Arm description:

In Cohort A, subjects received LUM001 tablet in combination with ursodeoxycholic acid (UDCA) orally once daily at a dosage of 2.5 up to a maximum of 10 milligram (mg) during the dose-escalation period over a 3 week period. Thereafter, subjects received LUM001 10 mg tablet along with one placebo matched to LUM001 orally once daily for another 10 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.

Arm type	Experimental
Investigational medicinal product name	LUM001
Investigational medicinal product code	SHP625
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received LUM001 tablet in combination with UDCA orally once daily at a dosage of 2.5 up to a maximum of 10 mg during the dose-escalation period over a 3 week period. Thereafter, subjects received LUM001 10 mg tablet along with one placebo matched to LUM001 orally once daily for another 10 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.

Arm title	LUM001 20 mg + UDCA (Cohort B)

Arm description:

In Cohort B, subjects received LUM001 tablets in combination with UDCA orally once daily at a dosage of 2.5 mg up to a maximum of 20 mg during the dose-escalation period over a 4 week period. Thereafter, subjects received LUM001 20 mg (2x10 mg) tablet orally once daily for another 9 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.

Arm type	Experimental
Investigational medicinal product name	LUM001
Investigational medicinal product code	SHP625
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received LUM001 tablets in combination with UDCA orally once daily at a dosage of 2.5 mg up to a maximum of 20 mg during the dose-escalation period over a 4 week period. Thereafter, subjects received LUM001 20 mg (2x10 mg) tablet orally once daily for another 9 weeks, in combination with

UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.

Arm title	Placebo + UDCA (Cohort A)
Arm description:	
In Cohort A, subjects received placebo (matched to LUM001) once daily for a period of 13 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Subjects received placebo (matched to LUM001) once daily for a period of 13 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.	
Arm title	Placebo + UDCA (Cohort B)
Arm description:	
In Cohort B, subjects received placebo (matched to LUM001) for a period of 13 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Subjects received placebo (matched to LUM001) for a period of 13 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.	

Number of subjects in period 1	LUM001 10 mg + UDCA (Cohort A)	LUM001 20 mg + UDCA (Cohort B)	Placebo + UDCA (Cohort A)
Started	21	21	11
Completed	18	21	10
Not completed	3	0	1
Consent withdrawn by subject	1	-	1
Adverse event, non-fatal	2	-	-
Pregnancy	-	-	-

Number of subjects in period 1	Placebo + UDCA (Cohort B)
Started	13
Completed	12
Not completed	1
Consent withdrawn by subject	-
Adverse event, non-fatal	-

Pregnancy	1

Baseline characteristics

Reporting groups	
Reporting group title	LUM001 10 mg + UDCA (Cohort A)
Reporting group description:	
In Cohort A, subjects received LUM001 tablet in combination with ursodeoxycholic acid (UDCA) orally once daily at a dosage of 2.5 up to a maximum of 10 milligram (mg) during the dose-escalation period over a 3 week period. Thereafter, subjects received LUM001 10 mg tablet along with one placebo matched to LUM001 orally once daily for another 10 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.	
Reporting group title	LUM001 20 mg + UDCA (Cohort B)
Reporting group description:	
In Cohort B, subjects received LUM001 tablets in combination with UDCA orally once daily at a dosage of 2.5 mg up to a maximum of 20 mg during the dose-escalation period over a 4 week period. Thereafter, subjects received LUM001 20 mg (2x10 mg) tablet orally once daily for another 9 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.	
Reporting group title	Placebo + UDCA (Cohort A)
Reporting group description:	
In Cohort A, subjects received placebo (matched to LUM001) once daily for a period of 13 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.	
Reporting group title	Placebo + UDCA (Cohort B)
Reporting group description:	
In Cohort B, subjects received placebo (matched to LUM001) for a period of 13 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.	

Reporting group values	LUM001 10 mg + UDCA (Cohort A)	LUM001 20 mg + UDCA (Cohort B)	Placebo + UDCA (Cohort A)
Number of subjects	21	21	11
Age categorical			
Units: Subjects			

Age continuous			
Age continuous description			
Units: years			
arithmetic mean	54.7	53.5	47.5
standard deviation	± 12.74	± 10.53	± 8.14
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	20	17	11
Male	1	4	0

Reporting group values	Placebo + UDCA (Cohort B)	Total	
Number of subjects	13	66	
Age categorical			
Units: Subjects			

Age continuous			
Age continuous description			

Units: years			
arithmetic mean	55.8		
standard deviation	± 8.73	-	

Gender categorical			
Gender categorical description			
Units: Subjects			
Female	12	60	
Male	1	6	

End points

End points reporting groups

Reporting group title	LUM001 10 mg + UDCA (Cohort A)

Reporting group description:

In Cohort A, subjects received LUM001 tablet in combination with ursodeoxycholic acid (UDCA) orally once daily at a dosage of 2.5 up to a maximum of 10 milligram (mg) during the dose-escalation period over a 3 week period. Thereafter, subjects received LUM001 10 mg tablet along with one placebo matched to LUM001 orally once daily for another 10 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.

Reporting group title	LUM001 20 mg + UDCA (Cohort B)

Reporting group description:

In Cohort B, subjects received LUM001 tablets in combination with UDCA orally once daily at a dosage of 2.5 mg up to a maximum of 20 mg during the dose-escalation period over a 4 week period. Thereafter, subjects received LUM001 20 mg (2x10 mg) tablet orally once daily for another 9 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.

Reporting group title	Placebo + UDCA (Cohort A)

Reporting group description:

In Cohort A, subjects received placebo (matched to LUM001) once daily for a period of 13 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.

Reporting group title	Placebo + UDCA (Cohort B)

Reporting group description:

In Cohort B, subjects received placebo (matched to LUM001) for a period of 13 weeks, in combination with UDCA. Subjects continued UDCA alone for an additional period of 4 weeks.

Subject analysis set title	LUM001 5 mg + UDCA
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received LUM001 5 mg tablet orally once daily for a period of 13 weeks in combination with UDCA.

Subject analysis set title	LUM001 10 mg + UDCA
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received LUM001 10 mg tablet orally once daily for a period of 13 weeks in combination with UDCA.

Subject analysis set title	LUM001 20 mg + UDCA
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received LUM001 20 mg (2x 10 mg) tablet for 20 mg daily dose in combination with UDCA orally once daily for a period of 13 weeks.

Subject analysis set title	Placebo + UDCA
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received placebo matched to LUM001 tablet orally once daily for a period of 13 weeks in combination with UDCA.

Primary: Change From Baseline in Pruritus Using Adult Itch Reported Outcome (ItchRO) Weekly Sum Score at Week 13/ Early Termination (ET)

End point title	Change From Baseline in Pruritus Using Adult Itch Reported Outcome (ItchRO) Weekly Sum Score at Week 13/ Early Termination (ET)

End point description:

Pruritus was assessed using ItchRO measure, administered as an electronic diary (eDiary) which was completed by the subjects twice daily (morning and evening). (ItchRO) scores ranged from 0 to 10, with 0 representing no itch and 10 representing very severe itching. The highest score between the morning and evening ItchRO reports represented the daily score: a measure of the worst itching over the previous 24-hour period. The weekly sum score was calculated as the sum of the daily scores for the 7

days prior to the time point being reported:7 days prior to randomization or 7 days prior to Week 13/ET visit. The mITT population included all subjects who were randomized, received at least 1 dose of treatment, and had at least 1 post-baseline ItchRO assessment.

End point type	Primary

End point timeframe:

Baseline and Week 13/ET

End point values	LUM001 10 mg + UDCA (Cohort A)	LUM001 20 mg + UDCA (Cohort B)	Placebo + UDCA (Cohort A)	Placebo + UDCA (Cohort B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	21	11	13
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	48.11 (± 13.363)	52.1 (± 13.78)	54.64 (± 9.157)	49.46 (± 14.11)
Change at Week 13/ET	-24.59 (± 15.24)	-27.67 (± 19.888)	-26.18 (± 18.313)	-22.77 (± 17.123)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference between treatment groups in change from Baseline to Week 13/ET in ItchRO weekly sum score evaluated by analysis of covariance (ANCOVA) using generalized linear model (GLM). The model included terms for treatment group, alkaline phosphatase (ALP) level (strata), treatment group by ALP level interaction and Baseline ItchRO weekly sum score as a covariate. Least squares mean change from Baseline to Week 13/ET, along with 95 percentage (%) confidence interval for mean were presented.

Comparison groups	LUM001 10 mg + UDCA (Cohort A) v Placebo + UDCA (Cohort A) v Placebo + UDCA (Cohort B)
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6603 [1]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-2.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.59
upper limit	8.03

Notes:

[1] - p-value (LUM001 LS Mean = Placebo LS Mean).

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The difference between treatment groups in change from Baseline to Week 13/ET in ItchRO weekly sum score was evaluated by ANCOVA using a GLM. The model included terms for treatment group, ALP level (strata), treatment group by ALP level interaction, and Baseline ItchRO weekly sum score as a covariate.

Least squares mean change from Baseline to Week 13/ET, along with 95% confidence interval for the mean, were presented.

Comparison groups	LUM001 20 mg + UDCA (Cohort B) v Placebo + UDCA (Cohort A) v Placebo + UDCA (Cohort B)
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.438 [2]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-3.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.2
upper limit	6.23

Notes:

[2] - p-value (LUM001 LS Mean = Placebo LS Mean).

Secondary: Change From Baseline in Pruritus Using Adult ItchRO Weekly Sum Scores at Weeks 4, 8 and 13

End point title	Change From Baseline in Pruritus Using Adult ItchRO Weekly Sum Scores at Weeks 4, 8 and 13

End point description:

ItchRO scores had a range from 0 to 10, with 0 representing no itch and 10 representing very severe itching. The highest score between the morning and evening ItchRO reports represented the daily score: a measure of the worst itching over the previous 24-hour period. The weekly sum score was calculated as the sum of the daily scores for the 7 days prior to the time point being reported:7 days prior to randomization or 7 days prior to Week 13/ET visit. Here, "n" signifies the number of subjects evaluable for the respective time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8 and 13

End point values	LUM001 10 mg + UDCA (Cohort A)	LUM001 20 mg + UDCA (Cohort B)	Placebo + UDCA (Cohort A)	Placebo + UDCA (Cohort B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	21	11	13
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=21, 21, 11, 13)	48.11 (± 13.363)	52.1 (± 13.78)	54.64 (± 9.157)	49.46 (± 14.11)
Change at Week 4 (n=20, 21, 11, 13)	-15.62 (± 13.708)	-22.19 (± 18.101)	-10.55 (± 11.103)	-16.23 (± 12.749)
Change at Week 8 (n=20, 21, 10, 13)	-21.92 (± 13.089)	-23.97 (± 20.398)	-23.5 (± 18.585)	-19.15 (± 15.302)
Change at Week 13 (n=18, 21, 10, 12)	-27.41 (± 14.346)	-27.67 (± 19.888)	-28.5 (± 17.52)	-22.92 (± 17.876)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pruritus Using Adult ItchRO Average Daily Scores at Weeks 4, 8, 13, and Last Post-baseline Visit (Week 13/ET)

End point title	Change from Baseline in Pruritus Using Adult ItchRO Average Daily Scores at Weeks 4, 8, 13, and Last Post-baseline Visit (Week 13/ET)

End point description:

ItchRO scores had a range from 0 to 10, with 0 representing no itch and 10 representing very severe itching. The highest score between the morning and evening ItchRO reports represented the daily score: a measure of the worst itching over the previous 24-hour period. Adult ItchRO average daily score was the sum of daily scores divided by the number of days adult ItchRO was completed, using the 7 days prior to the reported visit date. mITT Population. Here, "n" signifies the number of subjects evaluable for the respective time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 13 and Last Post-baseline visit (Week 13/ET)

End point values	LUM001 10 mg + UDCA (Cohort A)	LUM001 20 mg + UDCA (Cohort B)	Placebo + UDCA (Cohort A)	Placebo + UDCA (Cohort B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	21	11	13
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=21, 21, 11, 13)	6.873 (± 1.9091)	7.442 (± 1.9686)	7.805 (± 1.3082)	7.066 (± 2.0158)
Change at Week 4 (n=20, 21, 11, 13)	-2.231 (± 1.9587)	-3.17 (± 2.5859)	-1.506 (± 1.5861)	-2.319 (± 1.8212)
Change at Week 8 (n=20, 21, 10, 13)	-3.131 (± 1.8703)	-3.424 (± 2.9139)	-3.357 (± 2.6549)	-2.736 (± 2.186)
Change at Week 13 (n=18, 21, 10, 12)	-3.915 (± 2.0496)	-3.952 (± 2.8411)	-4.071 (± 2.5028)	-3.274 (± 2.5537)
Change at Week 13/ET (n=21, 21, 11, 13)	-3.512 (± 2.1774)	-3.952 (± 2.8411)	-3.74 (± 2.6161)	-3.253 (± 2.4461)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Alkaline Phosphatase (ALP) at Weeks 4, 8, 13, and Last Post-baseline Visit (Week 13/ET)

End point title	Change From Baseline in Alkaline Phosphatase (ALP) at Weeks 4, 8, 13, and Last Post-baseline Visit (Week 13/ET)

End point description:

Laboratory serum ALP enzyme levels were evaluated using blood samples collected. mITT Population. Here, "n" signifies the number of subjects evaluable for the respective time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 13 and Last Post-baseline (Week 13/ET)

End point values	LUM001 10 mg + UDCA (Cohort A)	LUM001 20 mg + UDCA (Cohort B)	Placebo + UDCA (Cohort A)	Placebo + UDCA (Cohort B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	21	11	13
Units: units per liter (U/L)				
arithmetic mean (standard deviation)				
Baseline (n=21, 21, 11, 13)	288.2 (± 193.91)	257.6 (± 190.38)	253.9 (± 96.83)	274.2 (± 190.85)
Change at Week 4 (n=20, 21, 10, 13)	-22.1 (± 54.94)	13.2 (± 47.76)	20.3 (± 49.68)	-0.7 (± 39.69)
Change at Week 8 (n=20, 21, 10, 12	2.6 (± 53.95)	1.1 (± 41.98)	8.8 (± 38.72)	-4.8 (± 55.7)
Change at Week 13 (n=17, 20, 10, 12)	-15.2 (± 97.19)	18.5 (± 56.21)	24.3 (± 76.48)	-7.2 (± 83.7)
Change at Week 13/ET (n=21, 21, 11, 13)	-8 (± 93.02)	16.4 (± 55.6)	22.9 (± 72.7)	-7.9 (± 80.19)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in 5-D Itch Score at Weeks 4, 8, 13, and Last Post -baseline Visit (Week 13/ET)

End point title	Change from Baseline in 5-D Itch Score at Weeks 4, 8, 13, and Last Post -baseline Visit (Week 13/ET)

End point description:

The 5-D itch (validated instrument to measure pruritus) scale was developed for the multidimensional quantification of pruritus that is sensitive to change over time. The 5-D itch scale included 5 domains (duration, degree, direction, disability, and distribution of pruritus). The total 5-D score was obtained by scoring each of the domains separately and then summing them together. 5-D total scores ranged between 5 (no pruritus) and 25 (most severe pruritus). mITT Population. Here, "n" signifies the number of subjects evaluable for the respective time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 13 and Last Post-baseline visit (Week 13/ET)

End point values	LUM001 10 mg + UDCA (Cohort A)	LUM001 20 mg + UDCA (Cohort B)	Placebo + UDCA (Cohort A)	Placebo + UDCA (Cohort B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	21	11	13
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=21, 21, 11, 13)	18.7 (± 3.47)	19.4 (± 3.49)	19.6 (± 2.94)	19.2 (± 3.32)
Change at Week 4 (n=20, 21, 10, 13)	-4.8 (± 3.91)	-6.3 (± 4.96)	-3.4 (± 3.89)	-4.2 (± 3.81)
Change at Week 8 (n=20, 21, 10, 12)	-6.8 (± 3.16)	-5.9 (± 5.62)	-6.4 (± 6.2)	-4.4 (± 4.27)
Change at Week 13 (n=18, 21, 10, 12)	-7.4 (± 3.68)	-7 (± 5.89)	-7.8 (± 5.94)	-6.1 (± 4.68)

Change at Week 13/ET (n=21, 21, 10, 13)	-6.5 (± 4.11)	-7 (± 5.89)	-7.8 (± 5.94)	-5.6 (± 4.79)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fasting Serum Bile Acid Level at Weeks 4, 8, 13, and Last Post -baseline Visit (Week 13/ET)

End point title	Change From Baseline in Fasting Serum Bile Acid Level at Weeks 4, 8, 13, and Last Post -baseline Visit (Week 13/ET)

End point description:

Laboratory serum bile acid level levels were evaluated using blood samples collected. mITT Population. Here, "n" signifies the number of subjects evaluable for the respective time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 13 and Last Post-baseline visit (Week 13/ET)

End point values	LUM001 10 mg + UDCA (Cohort A)	LUM001 20 mg + UDCA (Cohort B)	Placebo + UDCA (Cohort A)	Placebo + UDCA (Cohort B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	21	11	13
Units: micromoles per liter				
arithmetic mean (standard deviation)				
Baseline (n=21, 21, 11, 13)	33.11 (± 30.5943)	52.46 (± 94.3892)	52.615 (± 64.6162)	58.434 (± 73.9895)
Change at Week 4 (n=20, 21, 10, 13)	-11.204 (± 31.6132)	-14.465 (± 58.5891)	-10.221 (± 50.0398)	14.317 (± 75.1092)
Change at Week 8 (n=20, 21, 10, 12)	-3.968 (± 45.7388)	-21.983 (± 78.6134)	-3.585 (± 52.4398)	34.893 (± 67.7189)
Change at Week 13 (n=18, 21, 10, 12)	-8.122 (± 48.129)	-19.098 (± 81.8452)	11.481 (± 44.0465)	4.123 (± 46.217)
Change at Week 13/ET (n=21, 21, 10, 13)	-4.504 (± 45.7595)	-19.098 (± 81.8452)	11.481 (± 44.0465)	3.69 (± 44.277)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Bile Acid Synthesis as Measured by Serum 7 Alpha-Hydroxy-4-Cholesten-3-One C4 Level [7 Alpha C4]) at Weeks 4, 8, 13, and Last Post -baseline Visit (Week 13/ET)

End point title	Change From Baseline in Bile Acid Synthesis as Measured by Serum 7 Alpha-Hydroxy-4-Cholesten-3-One C4 Level [7 Alpha C4]) at Weeks 4, 8, 13, and Last Post -baseline Visit (Week 13/ET)

End point description:

C4 7 alpha-hydroxy-4-cholesten-3-one is an intermediate in the biochemical synthesis of bile acids from cholesterol and its concentrations reflect the activity of the bile acid synthetic pathway. Elevated levels of C4 indicate bile acid malabsorption. Laboratory C4 levels were evaluated using blood samples collected. mITT Population. Here, "n" signifies the number of subjects evaluable for the respective time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 13 and Last Post-baseline Visit (Week 13/ET)

End point values	LUM001 10 mg + UDCA (Cohort A)	LUM001 20 mg + UDCA (Cohort B)	Placebo + UDCA (Cohort A)	Placebo + UDCA (Cohort B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	21	11	13
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Baseline (n=21, 21, 10, 13)	18.74 (± 16.18)	13.17 (± 11.851)	22.31 (± 20.769)	16.98 (± 33.093)
Change at Week 4 (n=20, 21, 9, 13)	8.66 (± 23.422)	17.03 (± 18.38)	-6.8 (± 6.783)	-0.19 (± 8.856)
Change at Week 8 (n=20, 21, 9, 12)	13.04 (± 17.895)	15.03 (± 31.12)	-12.57 (± 14.63)	3.43 (± 16.666)
Change at Week 13 (n=18, 21, 9, 12)	24.38 (± 38.105)	6.62 (± 10.116)	-12.72 (± 10.374)	4.56 (± 13.61)
Change at Week 13/ET (n=21, 21, 9, 13)	20.56 (± 37.312)	6.62 (± 10.116)	-12.72 (± 10.374)	4.74 (± 13.047)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point description:

An adverse event (AE) was defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational product, whether or not considered related to the product. A serious adverse event (SAE) was defined as an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged in-patient hospitalization; life-threatening; persistent or significant disability/incapacity; congenital anomaly or birth defect; an important medical event that did not meet any of the above criteria but jeopardized the subject or required medical or surgical intervention to prevent one of the outcomes listed above. A TEAE was defined as any AE that occurred during the study, from the start of investigational product dosing through the end of the study [13 weeks of treatment period (or ET) + 14 days], or that worsened since the start of dosing.

End point type	Other pre-specified

End point timeframe:

From the first dose of study drug until the 13 weeks of treatment period (or ET) + 14 days (approximately 15 weeks)

End point values	LUM001 5 mg + UDCA	LUM001 10 mg + UDCA	LUM001 20 mg + UDCA	Placebo + UDCA
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1[3]	20[4]	21[5]	24[6]
Units: subjects				
TEAEs	1	19	21	17
TESAEs	0	2	1	0

Notes:

[3] - The Safety Population included all subjects who randomized, received at least 1dose of study drug.

[4] - The Safety Population included all subjects who randomized, received at least 1dose of study drug.

[5] - The Safety Population included all subjects who randomized, received at least 1dose of study drug.

[6] - The Safety Population included all subjects who randomized, received at least 1dose of study drug.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the first dose of study drug until the 13 weeks of treatment period (or ET) + 14 days (approximately 15 weeks)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	LUM001 10 mg + UDCA
Reporting group description:	
Subjects received LUM001 10 mg tablet orally once daily for a period of 13 weeks in combination with UDCA.	
Reporting group title	LUM001 5 mg + UDCA
Reporting group description:	
Subjects received LUM001 5 mg tablet orally once daily for a period of 13 weeks in combination with UDCA.	
Reporting group title	Placebo + UDCA
Reporting group description:	
Subjects received placebo matched to LUM001 tablet orally once daily for a period of 13 weeks in combination with UDCA.	
Reporting group title	LUM001 20 mg + UDCA
Reporting group description:	
Subjects received LUM001 20 mg (2x 10 mg) tablet for 20 mg daily dose in combination with UDCA orally once daily for a period of 13 weeks.	

Serious adverse events	LUM001 10 mg + UDCA	LUM001 5 mg + UDCA	Placebo + UDCA
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Myocardial Infarction			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (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			
Abdominal Pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	LUM001 20 mg + UDCA		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 21 (4.76%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Myocardial Infarction			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 21 (4.76%)		
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	LUM001 10 mg + UDCA	LUM001 5 mg + UDCA	Placebo + UDCA
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 20 (90.00%)	1 / 1 (100.00%)	16 / 24 (66.67%)
Injury, poisoning and procedural complications			
Anal Injury			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Excoriation			

subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
Sinus Operation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 20 (0.00%)	1 / 1 (100.00%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	8 / 24 (33.33%)
occurrences (all)	3	0	10
Paraesthesia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Fatigue			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Influenza Like Illness			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0

Pyrexia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Dry Eye			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	3 / 24 (12.50%)
occurrences (all)	3	0	4
Abdominal Pain			
subjects affected / exposed	4 / 20 (20.00%)	1 / 1 (100.00%)	1 / 24 (4.17%)
occurrences (all)	4	3	1
Abdominal Pain Upper			
subjects affected / exposed	4 / 20 (20.00%)	0 / 1 (0.00%)	2 / 24 (8.33%)
occurrences (all)	6	0	2
Constipation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	14 / 20 (70.00%)	1 / 1 (100.00%)	6 / 24 (25.00%)
occurrences (all)	16	3	7
Dry Mouth			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	2 / 24 (8.33%)
occurrences (all)	1	0	2
Faeces Discoloured			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	2
Flatulence			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Gastrooesophageal Reflux Disease			

subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Gingival Pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Mouth Ulceration			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	5 / 20 (25.00%)	1 / 1 (100.00%)	4 / 24 (16.67%)
occurrences (all)	6	2	4
Toothache			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 20 (0.00%)	1 / 1 (100.00%)	2 / 24 (8.33%)
occurrences (all)	0	1	2
Reproductive system and breast disorders			
Vaginal Discharge			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 20 (20.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	4	0	0
Laryngeal Inflammation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Nasal Congestion			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal Pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Pharyngeal Erythema			

subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	3 / 24 (12.50%)
occurrences (all)	0	0	3
Rash			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	2
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Muscle Spasms			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Muscular Weakness			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal Chest Pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Pain In Extremity			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Infection			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Urinary Tract Infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1

Non-serious adverse events	LUM001 20 mg + UDCA		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 21 (95.24%)		
Injury, poisoning and procedural complications			
Anal Injury			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Excoriation			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Sinus Operation			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Paraesthesia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			

Asthenia subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Chills subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Fatigue subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Influenza Like Illness subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Pain subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Pyrexia subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Eye disorders Dry Eye subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Gastrointestinal disorders Abdominal Distension subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Abdominal Pain subjects affected / exposed occurrences (all)	5 / 21 (23.81%) 6		
Abdominal Pain Upper subjects affected / exposed occurrences (all)	6 / 21 (28.57%) 9		
Constipation subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Diarrhoea			

subjects affected / exposed	11 / 21 (52.38%)		
occurrences (all)	19		
Dry Mouth			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Faeces Discoloured			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Gastrooesophageal Reflux Disease			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Gingival Pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Mouth Ulceration			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	5		
Toothache			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Vaginal Discharge			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Laryngeal Inflammation			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Nasal Congestion			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Oropharyngeal Pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Pharyngeal Erythema			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Muscle Spasms			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Muscular Weakness			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Musculoskeletal Chest Pain			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Pain In Extremity			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Urinary Tract Infection			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 June 2013	- Clarified inclusion criterion, effective barrier method of contraception, as the combination of condom or diaphragm plus a spermicide. - Clarified excluded screening serum creatinine conventional reference level to 2 decimals 2.00 milligram per deciliter (mg/dL) and corrected reference level 177 micromole per liter (mmoL/L). - Added cholestyramine as example of excluded bile acid resins. - Revised tolerability assessment to be consistent with protocol body. - Added 8-week time point for serum bile acid level and 7alpha-hydroxy-4-cholesten-3-one (7aC4). - Modified section to provide instructions to investigator for unblinding in the event of an emergency situation when knowledge of the treatment assignment will impact the clinical management of the subject. - Added safety monitoring for any subject with an increase in ALP >1.5 x Baseline at any time during the study. - Added stopping rule for any subject with an increase in ALP >2 x baseline at any time during the study. - Added study stopping rules in the event that 10 subjects discontinue dosing for any of the criteria. - Added collection of blood sample for cholestasis biomarkers at Week 8. - Corrected typographical errors in protocol.
28 February 2014	- Revised inclusion criterion, to allow for inclusion of subjects who are on a stable dose of UDCA for greater than equal to (>=) 3 months or are intolerant of UDCA (no UDCA for >=3 months). - Revised Inclusion Criterion, to also include subjects with ability to read and understand Spanish. - Screening period increased to "up to 5 weeks" (was "up to 4 weeks") and total study duration increased to approximately 22 weeks (was approximately 21 weeks). - Corrected time points for evaluation of pruritus using the average daily Adult ItchRO score (4, 8, and 13 weeks) to be consistent with protocol text.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported