Clinical trial results:
An Open Label Long-Term Study to Evaluate the Safety and Tolerability of Seladelpar in Subjects with Primary Biliary Cholangitis (PBC)

Summary

EudraCT number	2017-003910-16
Trial protocol	GB DE
Global end of trial date	11 February 2020

Results information

Result version number	v1 (current)
This version publication date	06 May 2021
First version publication date	06 May 2021

Trial information

Trial identification

Sponsor protocol code	CB8025-31731

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03301506
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CymaBay Therapeutics, Inc.
Sponsor organisation address	7575 Gateway Blvd, Suite 110, Newark, United States, 94560
Public contact	Mary Standen, CymaBay Therapeutics, Inc., 1 5102938800, mstanden@cymabay.com
Scientific contact	Elaine Watkins, CymaBay Therapeutics, Inc., 1 5102938800, ewatkins@cymabay.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 February 2020
Global end of trial reached?	Yes
Global end of trial date	11 February 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of seladelpar.
In this long-term (~5 year) interventional study of PBC, subjects who completed a previous study with seladelpar (CB8025-21629, CB8025-31735, or CB8025-21838) were invited to continue treatment. The primary endpoint was safety, and secondary endpoint was efficacy. The End of Treatment Visit for the subjects from the prior PBC study was meant to be coincident with the Day 1 visit of this study. Subjects from prior study participation (CB8025-21629 and CB8025-31735) with a study drug interruption ≤4 weeks prior to Day 1, did not require evaluation for exclusion criteria, and the screening period could be omitted. Subjects with study drug interruption from prior study >4 weeks prior to Day 1 entered the screening period and could not have met any of the exclusion criteria. Subjects participating in CB8025-21838 were to undergo screening period, but none were enrolled into the study .

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and its revisions and the International Conference on Harmonisation (ICH) Harmonized Tripartite Guideline for Good Clinical Practice (GCP). The study was also in compliance with the applicable local regulatory requirements and laws of each country in which the study was conducted, as well as with any applicable guidelines.

Background therapy:

Standard of care ursodeoxycholic acid (UDCA) was administered in subjects who could tolerate it and seladelpar was administered as an add-on. For subjects with UDCA intolerance, seladelpar was administered as a monotherapy.

Evidence for comparator: -

Actual start date of recruitment	01 December 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 17
Country: Number of subjects enrolled	Germany: 12
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	United States: 72
Worldwide total number of subjects	106
EEA total number of subjects	12

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)	72
From 65 to 84 years	34
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at a total of 31 clinical sites in North America (United States and Canada) and Europe (United Kingdom and Germany) between 11 December 2017 to 11 February 2020.

Pre-assignment

Screening details:

Total of 106 subjects from parental seladelpar PBC studies were enrolled and analyzed - 104 (CB8025-21629) and 2 (CB8025-31735). All 106 subjects rolled over at approximately Week 52 visit and entered study while on seladelpar dose 2 mg (1), 5 mg (18), 10 mg (87). Subject on 2 mg was included in safety analysis but excluded from efficacy analysis

Period 1

Period 1 title	Seladelpar Total (Initial Dose) (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Seladelpar 2 mg (initial dose)

Arm description:

One subject received two 1 mg seladelpar capsules orally once daily for the study duration

Arm type	Experimental
Investigational medicinal product name	Seladelpar
Investigational medicinal product code	MBX-8025
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One subject received two 1 mg seladelpar capsules orally once daily for the study duration

Arm title	Seladelpar 5 mg (initial dose)

Arm description:

Subjects received 5 mg seladelpar capsule orally once daily for the study duration

Arm type	Experimental
Investigational medicinal product name	Seladelpar
Investigational medicinal product code	MBX-8025
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received 5 mg seladelpar capsule orally once daily for the study duration

Arm title	Seladelpar 10 mg (initial dose)

Arm description:

Subjects received 10 mg seladelpar capsule orally once daily for the study duration

Arm type	Experimental

Investigational medicinal product name	Seladelpar
Investigational medicinal product code	MBX-8025
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received 10 mg seladelpar capsule orally once daily for the study duration

Number of subjects in period 1	Seladelpar 2 mg (initial dose)	Seladelpar 5 mg (initial dose)	Seladelpar 10 mg (initial dose)
Started	1	18	87
Completed	0	0	0
Not completed	1	18	87
Other - Study Closure	1	18	80
Other - Prohibitive concomitant Medication Use	-	-	1
Other - Administrative Decision	-	-	1
Adverse event, non-fatal	-	-	3
Other - Lack of response withdrawl	-	-	1
Lost to follow-up	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Seladelpar 2 mg (initial dose)
Reporting group description:	
One subject received two 1 mg seladelpar capsules orally once daily for the study duration	
Reporting group title	Seladelpar 5 mg (initial dose)
Reporting group description:	
Subjects received 5 mg seladelpar capsule orally once daily for the study duration	
Reporting group title	Seladelpar 10 mg (initial dose)
Reporting group description:	
Subjects received 10 mg seladelpar capsule orally once daily for the study duration	

Reporting group values	Seladelpar 2 mg (initial dose)	Seladelpar 5 mg (initial dose)	Seladelpar 10 mg (initial dose)
Number of subjects	1	18	87
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1	11	60
>65 years	0	7	27
Age continuous Units: years			
arithmetic mean	63	61.2	58.1
standard deviation	± 0	± 8.57	± 9.24
Gender categorical Units: Subjects			
Female	1	18	81
Male	0	0	6
Race Units: Subjects			
White	1	18	79
Black or African-American	0	0	3
Asian	0	0	2
American Indian or Alaska Native	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0
Other	0	0	2
Multiple (White, Turkish)	0	0	1

Reporting group values	Total		
Number of subjects	106		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	72		
>65 years	34		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	100		
Male	6		
Race Units: Subjects			
White	98		
Black or African-American	3		
Asian	2		
American Indian or Alaska Native	0		
Native Hawaiian or other Pacific Islander	0		
Other	2		
Multiple (White, Turkish)	1		

Subject analysis sets

Subject analysis set title	Seladelpar Total (initial dose)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received 2 mg, 5 mg, 10 mg seladelpar capsule (s) orally once daily for the study duration

Reporting group values	Seladelpar Total (initial dose)		
Number of subjects	106		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	72		
>65 years	34		

Age continuous Units: years			
arithmetic mean	58.7		
standard deviation	± 9.13		
Gender categorical Units: Subjects			
Female	100		
Male	6		
Race Units: Subjects			
White	98		
Black or African-American	3		
Asian	2		
American Indian or Alaska Native	0		
Native Hawaiian or other Pacific Islander	0		
Other	2		
Multiple (White, Turkish)	1		

End points

End points reporting groups

Reporting group title	Seladelpar 2 mg (initial dose)
Reporting group description:	
One subject received two 1 mg seladelpar capsules orally once daily for the study duration	
Reporting group title	Seladelpar 5 mg (initial dose)
Reporting group description:	
Subjects received 5 mg seladelpar capsule orally once daily for the study duration	
Reporting group title	Seladelpar 10 mg (initial dose)
Reporting group description:	
Subjects received 10 mg seladelpar capsule orally once daily for the study duration	
Subject analysis set title	Seladelpar Total (initial dose)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received 2 mg, 5 mg, 10 mg seladelpar capsule (s) orally once daily for the study duration	

Primary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)[1][2]
End point description:	
The primary endpoint of the study was safety analysis of Treatment-emergent adverse events (TEAEs) (National Cancer Institute [NCI] Common Terminology Criteria for Adverse Events [CTCAE] Version 5.0) results. Adverse events were coded by SOC and preferred term using MedDRA 22.0. The severity of AEs was graded from 1 to 5 based on NCI CTCAE, Version 5.0. The safety data were analyzed for seladelpar 5 mg, 10 mg, and the overall population, which included subjects who received seladelpar 2 mg dose.	
End point type	Primary
End point timeframe:	
Over 21 months	

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: Statistical analysis was descriptive (summary statistics), with no formal statistical testing performed.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The overall population represented by the Seladelpar Total (initial dose) includes the single subject who received seladelpar 2 mg dose, therefore the 2 mg arm from baseline period is not reported here. Statistical analysis was descriptive (summary statistics), with no formal statistical testing performed.

End point values	Seladelpar 5 mg (initial dose)	Seladelpar 10 mg (initial dose)	Seladelpar Total (initial dose)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	87	106	
Units: Subjects with at least one				
TEAE	11	72	84	
Serious TEAE (S-TEAE)	0	14	14	
Grade 3 or Higher TEAE	0	14	14	
Treatment-related TEAE (T-R-TEAE)	3	9	13	
T-R Serious TEAE	0	0	0	
T-R Grade 3 or Higher TEAE	0	1	1	
TEAE Leading to Treatment Discontinuation	0	4	4	

T-R TEAE Leading to Treatment Discontinuation	0	1	1	
TEAE Leading to Dose Interruption or Adjustment	1	7	9	
TEAE with Fatal Outcome	0	1	1	
T-R TEAE with Fatal Outcome	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Study duration	
Adverse event reporting additional description:	
Adverse events	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	Seladelpar 5 mg (initial Dose)
Reporting group description:	
Subjects received seladelpar 5 mg capsules orally once daily for the study duration	
Reporting group title	Seladelpar 10 mg (initial dose)
Reporting group description:	
Subjects received seladelpar 10 mg capsules orally once daily for the study duration	
Reporting group title	Seladelpar Total (initial dose)
Reporting group description:	
Subjects received any seladelpar capsules for the study duration	

Serious adverse events	Seladelpar 5 mg (initial Dose)	Seladelpar 10 mg (initial dose)	Seladelpar Total (initial dose)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	14 / 87 (16.09%)	14 / 106 (13.21%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm of unknown primary site			
subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			

subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
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			
Toxic encephalopathy			
subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Microcytic anaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Complication associated with device			
subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Upper gastrointestinal haemorrhage			

subjects affected / exposed	0 / 18 (0.00%)	2 / 87 (2.30%)	2 / 106 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Systemic scleroderma			
subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 87 (1.15%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	Seladelpar 5 mg (initial Dose)	Seladelpar 10 mg (initial dose)	Seladelpar Total (initial dose)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 18 (61.11%)	71 / 87 (81.61%)	83 / 106 (78.30%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 18 (5.56%)	4 / 87 (4.60%)	5 / 106 (4.72%)
occurrences (all)	2	5	7
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 18 (11.11%)	5 / 87 (5.75%)	7 / 106 (6.60%)
occurrences (all)	2	5	7
Headache			
subjects affected / exposed	2 / 18 (11.11%)	5 / 87 (5.75%)	7 / 106 (6.60%)
occurrences (all)	3	5	8
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 18 (5.56%)	9 / 87 (10.34%)	10 / 106 (9.43%)
occurrences (all)	1	10	11
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 18 (5.56%)	8 / 87 (9.20%)	9 / 106 (8.49%)
occurrences (all)	1	9	10
Abdominal pain			
subjects affected / exposed	2 / 18 (11.11%)	4 / 87 (4.60%)	7 / 106 (6.60%)
occurrences (all)	2	4	7
Diarrhoea			
subjects affected / exposed	1 / 18 (5.56%)	4 / 87 (4.60%)	6 / 106 (5.66%)
occurrences (all)	5	4	10
Skin and subcutaneous tissue disorders			
Pruritus generalised			
subjects affected / exposed	1 / 18 (5.56%)	9 / 87 (10.34%)	10 / 106 (9.43%)
occurrences (all)	1	9	10
Pruritus			
subjects affected / exposed	0 / 18 (0.00%)	6 / 87 (6.90%)	6 / 106 (5.66%)
occurrences (all)	0	6	6
Psychiatric disorders			

Depression			
subjects affected / exposed	0 / 18 (0.00%)	5 / 87 (5.75%)	5 / 106 (4.72%)
occurrences (all)	0	5	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 18 (0.00%)	7 / 87 (8.05%)	7 / 106 (6.60%)
occurrences (all)	0	7	7
Myalgia			
subjects affected / exposed	2 / 18 (11.11%)	4 / 87 (4.60%)	6 / 106 (5.66%)
occurrences (all)	2	5	7
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 18 (5.56%)	8 / 87 (9.20%)	9 / 106 (8.49%)
occurrences (all)	1	8	9
Bronchitis			
subjects affected / exposed	0 / 18 (0.00%)	5 / 87 (5.75%)	5 / 106 (4.72%)
occurrences (all)	0	5	5
Nasopharyngitis			
subjects affected / exposed	1 / 18 (5.56%)	4 / 87 (4.60%)	5 / 106 (4.72%)
occurrences (all)	1	4	5
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	0 / 18 (0.00%)	5 / 87 (5.75%)	5 / 106 (4.72%)
occurrences (all)	0	5	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2017	Protocol amendment (version 1.1) for United Kingdom •Required subjects to have participated in a prior seladelpar study for at least 8 weeks. •Required that, in the Investigator's opinion, subjects had to have derived a net benefit from participation in a prior PBC study with seladelpar. •Required that female subjects of childbearing potential have a serum pregnancy test performed at every On-Treatment Visit, and between On-Treatment Visits, perform a urine pregnancy test at home monthly (every 30 days).
04 January 2018	Protocol amendment (version 1.2) for Germany •Required subjects to have participated in a prior seladelpar study for at least 8 weeks. •Required that, in the Investigator's opinion, subjects had to have derived a net benefit from participation in a prior PBC study with seladelpar. •Required that female subjects of childbearing potential have a serum pregnancy test performed at every On-Treatment Visit.
16 July 2019	Protocol Amendment 1 (version 2.0) •Enrollment into the study was expanded to allow subjects who completed PBC Studies CB8025-31735 (double-blind placebo-controlled study) and CB8025-21838 (single dose hepatic impairment study in PBC population). •Clinical data from Phase 1 and Phase 2 studies was updated. •The study design was updated to add partial randomization. •A secondary objective was added to collect data to support pruritis that was also assessed in study CB8025-31735 and to support future population PK analysis. •The composite response endpoint of ALP and total bilirubin and normalization of ALP were added to analyze similar data collected in a Phase 3 study. •Secondary measures were added to include PBC clinical events to be collected to evaluate the long-term effect of seladelpar. •Patient-reported outcome (pruritus NRS) was added to evaluate the effect of seladelpar based on similar data collected in Phase 3 study. •PK of seladelpar and its metabolites and exposure-response relationship to seladelpar were added to expand seladelpar PK profile in PBC population. •Exclusion criteria was modified for consistency with study CB8025-31735 and with other clinical studies. •The 1 mg dose was removed based on the data collected in study CB8025-21629. •Clearer instructions were added on how to handle safety issues when dose down-titration occurred. •Study assessments were modified to align with updated study measures and with data collected in Phase 3 study. Month 1 visit was added to evaluate safety of the subjects after initiation of seladelpar (specifically, for placebo subjects from Phase 3 and for subjects from Study CB8025-21838). •A dose adjustment during the first year was added to protect the blinding of the Phase 3 study. Dose adjustment criteria were updated to match the Phase 3 study. •Clarification on the liver, muscle, and pancreatic safety monitoring, and serum creatinine monitoring were added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
25 November 2019	On 25 November 2019, as a precautionary measure due to unexpected histology observations in an ongoing study in subjects with nonalcoholic steatohepatitis (NASH) study CB8025-21730; study CB8025-31731 was put on-hold, and subject enrollment or treatment with study drug was stopped. At that time, a total of 106 subjects were enrolled - 104 subjects from study CB8025-21629 and 2 subjects from study CB8025-31735. No subjects were enrolled from study CB8025-21838. Given the time needed to conduct an investigation, the study was terminated on 20 December 2019. The study design was amended in 2019 to implement changes relevant for subjects rolling over from CB8025-31735 e.g., pruritus data collection, PK collection, liver biopsy collection, dose adjustment at specific timepoints (Month 6 and Month 12). Since, study was discontinued when 2 subjects from CB8025-31735 were enrolled and were in the study for a limited time while still on the study drug (<1 month), none of the changes from protocol amendment of 2019 were implemented. The duration of exposure to seladelpar in this study is from Day 1 to over 21 months and when combined with that of the parental study is up to 33 months (12 months in a parental PBC study).	-

Notes:

Limitations and caveats

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

The study results for primary endpoint (safety) are presented. Study was terminated early, therefore secondary efficacy endpoints are not presented.

Notes: