Clinical trial results:
A Phase 2, Randomized, Double-Blind, Placebo-Controlled Multiple Center Study to Evaluate the Safety, Tolerability, and Efficacy of Seladelpar Administered for 24 Weeks in Adult Patients with Primary Sclerosing Cholangitis (PSC)

Summary

EudraCT number	2019-001760-30
Trial protocol	GB PL
Global end of trial date	09 January 2020

Results information

Result version number	v1 (current)
This version publication date	03 October 2021
First version publication date	03 October 2021

Trial information

Trial identification

Sponsor protocol code	CB8025-21845

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	IND : Number: 142198

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., +1 510 293-8800, mstanden@cymabay.com
Scientific contact	Elaine Watkins, CymaBay Therapeutics, Inc., +1 510 293-8800, 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	09 January 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 January 2020
Global end of trial reached?	Yes
Global end of trial date	09 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the treatment effect of seladelpar on alkaline phosphatase (AP) in participants with PSC during the study period

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: -

Evidence for comparator: -

Actual start date of recruitment	12 November 2019
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 States: 1
Worldwide total number of subjects	1
EEA total number of subjects	0

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)	0
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted in 60 sites in Australia, Europe, Israel, and North America. Only 1 site in the U.S. enrolled.

Pre-assignment

Screening details:

On Day 1, participants were to be randomized into one of four treatment arms (seladelpar 5 mg, 10 mg, 25 mg, or placebo) in a 1:1:1:1 ratio. Participants stratification at randomization planned per UDCA use (Yes/No) and by averaged Screening total bilirubin values (≤ ULN vs > ULN but ≤ 2 × ULN) to ensure even distribution across treatment groups

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	Investigator, Subject

Arms

Arm title	Placebo

Arm description:

Subjects received matched placebo capsules orally once daily for the study duration

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

Dosage and administration details:

Subjects received matching placebo capsules orally once daily for the study duration

Number of subjects in period 1	Placebo
Started	1
Terminated	1
Completed	0
Not completed	1
Study Termination by Sponsor	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study (overall period)
Reporting group description:	
Subjects received matched placebo capsules orally once daily for the study duration	

Reporting group values	Overall Study (overall period)	Total	
Number of subjects	1	1	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	1	1	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	0	0	
Male	1	1	

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received matched placebo capsules orally once daily for the study duration

Primary: Relative Change from Baseline in Serum Alkaline Phosphatase (ALP) Levels at Week 24 (Endpoint)

End point title	Relative Change from Baseline in Serum Alkaline Phosphatase (ALP) Levels at Week 24 (Endpoint)[1]

End point description:

Relative (percent) change in alkaline phosphatase (ALP) from Baseline to Week 24

End point type	Primary

End point timeframe:

Baseline, Week 24

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The study was terminated early therefore no statistical analyses was done

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Percent Change				
number (not applicable)				

Notes:

[2] - Analysis was not performed due to study termination

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Upto week 24	
Adverse event reporting additional description:	
There were no adverse events reported during the study treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: The study was terminated early and subject’s laboratory values for ALT, AST, GGT, and ALP were slightly elevated at screening and remained essentially the same throughout treatment with slight variations over the 14 days of treatment with placebo.
No Adverse Events were reported in the study.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 June 2019	Version 2.0 *Participants are stratified according to UDCA use (Yes/No) and by averaged Screening total bilirubin (TB) values (≤ ULN vs > ULN but ≤ 2 × ULN). *In the Inclusion Criteria #3: • Platelets were changed from ≥ 120 x 103/µL to ≥ 140 x 103/µL; • Total bilirubin was changed from 2.5 mg/dL to 2.2 mg/dL (2 x ULN); • Add an upper threshold for AP. The criterion is now AP ≥ 1.5 x ULN and ≤ 8 x ULN. *In Inclusion Criteria #4 • Participants taking UDCA must be on a stable dose for 6 months rather than allowing subjects to make some dosing adjustments 8 weeks prior to screening. *Exclusion Criteria # 3 was added to exclude patients with small-duct PSC. *In Exclusion Criteria #10, the following criteria were added: • Historical liver biopsy demonstrating cirrhosis (e.g., Ludwig Stage 4 or Ishak Stage ≥ 5); • Current or prior history of decompensated liver disease, including ascites, hepatic encephalopathy, variceal bleeding or other clinical conditions consistent with cirrhosis and/or portal hypertension; • FibroScan® > 14.4 kPa; • Combined low platelet count (< 140 × 103/µL) with one or more of the following, Albumin < 3.5 g/dL, INR > 1.3 (not due to antithrombotic agent use), or total bilirubin > ULN. *Exclusion Criteria #11 was added to exclude PSC patients whose AP, ALT, AST, or total bilirubin exhibit variability > 40% higher during Screening. *Addition of test for C-terminal pro-peptide of type V collagen (PRO-C5). *Addition of a second screening visit (Screening Visit 2). *Addition of missing pruritis evaluation dispensing at Week 4. *Addition of DILI safety monitoring criteria following the FDA Guidance for Industry: Drug Induced Injury, Premarket Clinical Evaluation. *Addition of the additional stopping criteria for an individual participant

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 until the NASH study (CB8025-21730) histology findings could be understood, a decision was made to terminate this PSC study (CB8025-21845). Investigators were notified and instructed to stop study dosing. Study closure activities were initiated. Only one subject was randomized into the study on November 12, 2019 until study termination.	-

Notes:

Limitations and caveats

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

Only one patient was randomized into the study until the early study termination. On 25-NOV-2019 (Study Day 14) the subject received last dose of placebo. The early termination visit occurred on 09-JAN-2020 (study Day 59).

Notes: