Clinical trial results:
A Phase 4, Double Blind, Randomized, Placebo Controlled, Multicenter Study Evaluating the Effect of Obeticholic Acid on Clinical Outcomes in Subjects with Primary Biliary Cholangitis.
The COBALT Study Clinical Outcomes with Obeticholic Acid in Liver Treatment (COBALT)

Summary

EudraCT number	2014-005012-42
Trial protocol	HU LT AT BE DK FI GB EE ES NL FR DE BG PT
Global end of trial date	23 December 2021

Results information

Result version number	v1 (current)
This version publication date	05 January 2023
First version publication date	05 January 2023

Trial information

Trial identification

Sponsor protocol code	747-302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02308111
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Intercept Pharmaceuticals, Inc.
Sponsor organisation address	305 Madison Avenue, Morristown, New Jersey, United States, 07960
Public contact	Steven Lauder, Intercept Pharmaceuticals, Inc., steven.lauder@interceptpharma.com
Scientific contact	Medical Information, Intercept Pharmaceuticals, Inc., medinfo@interceptpharma.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	28 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 December 2021
Global end of trial reached?	Yes
Global end of trial date	23 December 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to assess the long-term efficacy of obeticholic acid (OCA) compared to placebo, in conjunction with the established local standard of care, on clinical outcomes in participants with primary biliary cholangitis (PBC) as measured by time to the first occurrence of any of the following adjudicated events, derived as composite event endpoints of death (all-cause), liver transplant, model of end-stage liver disease (MELD) ≥15, uncontrolled ascites, or hospitalization for new onset or recurrence of variceal bleed, hepatic encephalopathy, or spontaneous bacterial peritonitis; and as expanded composite event endpoints (including events mentioned above with additional events of MELD-Na ≥15, portal hypertension syndromes, progression to decompensated liver disease, and Progression to clinical evidence of portal hypertension without decompensation).

Protection of trial subjects:

This study was conducted in accordance with the International Council on Harmonisation (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the countries in which the study was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 December 2014
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	United States: 61
Country: Number of subjects enrolled	Argentina: 38
Country: Number of subjects enrolled	Canada: 31
Country: Number of subjects enrolled	Australia: 16
Country: Number of subjects enrolled	Hong Kong: 9
Country: Number of subjects enrolled	Israel: 12
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Switzerland: 7
Country: Number of subjects enrolled	Chile: 3
Country: Number of subjects enrolled	Brazil: 3
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	Turkey: 2

Country: Number of subjects enrolled	Netherlands: 11
Country: Number of subjects enrolled	Poland: 19
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	United Kingdom: 26
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Denmark: 9
Country: Number of subjects enrolled	Estonia: 4
Country: Number of subjects enrolled	Finland: 5
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	Italy: 24
Country: Number of subjects enrolled	Lithuania: 9
Worldwide total number of subjects	334
EEA total number of subjects	119

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)	280
From 65 to 84 years	54
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 334 participant were randomised into the study. The study was terminated early as the Data Monitoring Committee made the recommendation to not pursue further enrollment given the lack of feasibility for this post-marketing study as designed. At termination, the study randomised <80% of planned enrollment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Obeticholic Acid

Arm description:

Participants received obeticholic acid (OCA) 5 mg for a minimum of 3 months and titrating up to 10 mg for the remainder of the study (based on tolerability and Child-Pugh [CP] Score).

Non-cirrhotic and classified as CP Class A: 5 mg tablet of OCA once daily, titrating up to a maximum of 10 mg OCA once daily based on tolerability at 3 months for the duration of the study (majority of participants).

Cirrhotic and classified as CP Class B and C: 5 mg tablet of OCA once weekly for at least 3 months, titrating up to a maximum dose and frequency of 10 mg twice weekly based on tolerability and biochemical response for the duration of the study.

Arm type	Experimental
Investigational medicinal product name	Obeticholic Acid
Investigational medicinal product code	747-302
Other name	6alpha-ethylchenodeoxycholic acid (6-ECDCA), INT-747
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Non-cirrhotic and classified as CP Class A: 5 mg tablet of OCA once daily, titrating up to a maximum of 10 mg OCA once daily based on tolerability at 3 months for the duration of the study (majority of participants). Cirrhotic and classified as CP Class B and C: 5 mg tablet of OCA once weekly for at least 3 months, subsequently titrating up to a maximum dose and frequency of 10 mg OCA twice weekly based on tolerability and biochemical response for the duration of the study.

Arm title	Placebo

Arm description:

Participants received one tablet daily (or a lower frequency depending on CP score) for the remainder of the study.

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:

Participant received one tablet of placebo daily (or a lower frequency depending on CP score) for the remainder of the study.

Number of subjects in period 1	Obeticholic Acid	Placebo
Started	168	166
Completed	0	0
Not completed	168	166
Adverse event, serious fatal	9	6
Physician decision	6	17
Liver transplant	3	3
Study Terminated by Sponsor	72	61
Site closure	3	3
Consent withdrawn by subject	28	38
Initiated Commercial OCALIVA	6	8
Adverse event, non-fatal	31	19
Liver transplant waitlist	2	2
Non-compliance with study drug	3	1
Lost to follow-up	2	7
COVID-19 pandemic limitation	2	-
Early termination as subject not met criteria	1	-
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Obeticholic Acid

Reporting group description:

Participants received obeticholic acid (OCA) 5 mg for a minimum of 3 months and titrating up to 10 mg for the remainder of the study (based on tolerability and Child-Pugh [CP] Score).

Non-cirrhotic and classified as CP Class A: 5 mg tablet of OCA once daily, titrating up to a maximum of 10 mg OCA once daily based on tolerability at 3 months for the duration of the study (majority of participants).

Cirrhotic and classified as CP Class B and C: 5 mg tablet of OCA once weekly for at least 3 months, titrating up to a maximum dose and frequency of 10 mg twice weekly based on tolerability and biochemical response for the duration of the study.

Reporting group title	Placebo

Reporting group description:

Participants received one tablet daily (or a lower frequency depending on CP score) for the remainder of the study.

Reporting group values	Obeticholic Acid	Placebo	Total
Number of subjects	168	166	334
Age categorical Units: Subjects			
Between 18 and 65 years	140	140	280
>=65 years	28	26	54
Age continuous Units: years			
arithmetic mean	53.4	53.9	
standard deviation	± 10.28	± 10.41	-
Gender categorical Units: Subjects			
Female	151	149	300
Male	17	17	34
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	24	18	42
Not Hispanic or Latino	138	139	277
Unknown or Not Reported	6	9	15
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	2	3
Asian	11	9	20
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	2	4
White	146	143	289
More than one race	4	1	5
Unknown or Not Reported	4	9	13

End points reporting groups

Reporting group title	Obeticholic Acid

Reporting group description:

Participants received obeticholic acid (OCA) 5 mg for a minimum of 3 months and titrating up to 10 mg for the remainder of the study (based on tolerability and Child-Pugh [CP] Score).

Non-cirrhotic and classified as CP Class A: 5 mg tablet of OCA once daily, titrating up to a maximum of 10 mg OCA once daily based on tolerability at 3 months for the duration of the study (majority of participants).

Cirrhotic and classified as CP Class B and C: 5 mg tablet of OCA once weekly for at least 3 months, titrating up to a maximum dose and frequency of 10 mg twice weekly based on tolerability and biochemical response for the duration of the study.

Reporting group title	Placebo

Reporting group description:

Participants received one tablet daily (or a lower frequency depending on CP score) for the remainder of the study.

Subject analysis set title	Obeticholic Acid (ITT)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intent-to-Treat (ITT) population consisted of all randomized participants who received at least 1 dose of OCA.

Subject analysis set title	Placebo (ITT)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

ITT population consisted of all randomized participants who received at least 1 dose of placebo.

Subject analysis set title	Obeticholic Acid (Safety)
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population consisted of all participants who received any amount of OCA. Treatment assignment based on the treatment received before any initiation of commercial OCA.

Subject analysis set title	Placebo (Safety)
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population consisted of all participants who received any amount of placebo.

Subject analysis set title	Obeticholic Acid (PK)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The pharmacokinetic (PK) population consisted of all OCA participants who had at least 1 confirmed fasted analyzable sample. Participants fasted for approximately 8 hours prior to the visit and had no major protocol deviations that potentially affected exposure levels.

Primary: Time to the First Occurrence of Composite Endpoint

End point title	Time to the First Occurrence of Composite Endpoint

End point description:

To assess the effect of OCA, compared to placebo in conjunction with the established local standard of care, on clinical outcomes in participants with PBC as measured by time to the first occurrence of any of the following adjudicated events, derived as a composite event endpoint of death, liver transplant, model of end-stage liver disease (MELD) ≥15, uncontrolled ascites, or hospitalization for new onset or recurrence of variceal bleed, hepatic encephalopathy (as defined by a West Haven score of >=2), or spontaneous bacterial peritonitis. The clinical events distribution was estimated using the Kaplan-Meier methodology. Point estimates and 95% confidence intervals (CIs) for the clinical events distribution percentiles (25th and 50th) are provided.

Here 9999 represents the data that was not calculable due to insufficient clinical events. The 95% CI limits were not estimable due to an insufficient number of participants with clinical events, as indicated by 9999.

End point type	Primary

End point timeframe:

Time to accrue approximately 127 primary endpoint events, up to End of Study (EOS)

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: days				
number (confidence interval 95%)				
25th Percentile	1092 (670 to 1464)	970 (688 to 1342)		
50th Percentile	9999 (1910 to 9999)	9999 (9999 to 9999)		

Statistical analyses

Statistical analysis title	Time to the First Occurrence of Composite Endpoint
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.954
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.51

Primary: Time to the First Occurrence of Primary Clinical Event (Expanded Endpoint)

End point title	Time to the First Occurrence of Primary Clinical Event (Expanded Endpoint)

End point description:

Primary clinical outcome event is the first occurrence of the following events: death, liver transplant, MELD score >=15 (MELD-Na score >=12 baseline), MELD-Na score >=15 (MELD-Na score <12 baseline), hospitalization for new onset or recurrence of variceal bleed, hepatic encephalopathy, spontaneous bacterial peritonitis (confirmed by diagnostic paracentesis), or bacterial empyema, uncontrolled or refractory ascites (requiring large volume paracentesis), portal hypertension syndromes, progression to decompensated liver disease, and progression to clinical evidence of portal hypertension without decompensation (for participants without decompensation or clinical evidence of portal hypertension at baseline). 71 endpoint events were observed in the OCA arm, and 80 were observed in the Placebo arm. The clinical events distribution was estimated using the Kaplan-Meier methodology.

Point estimates and 95% CIs for the clinical events distribution percentiles (25th and 50th) are provided.

End point type	Primary

End point timeframe:

Time to accrue approximately 127 primary endpoint events, up to EOS

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168[1]	166[2]		
Units: days				
number (confidence interval 95%)				
25th Percentile	370 (261 to 638)	450 (358 to 569)		
50th Percentile	1827 (1198 to 9999)	1102 (841 to 9999)		

Notes:

[1] - 9999 = Upper 95% CI not estimated due to an insufficient number of participants with clinical events

[2] - 9999 = Upper 95% CI not estimated due to an insufficient number of participants with clinical events

Statistical analyses

Statistical analysis title	Primary Clinical Event (Expanded Endpoint)
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.304
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.16

Secondary: Time to First Occurrence of Fatal Event (All-Cause)

End point title	Time to First Occurrence of Fatal Event (All-Cause)

End point description:

The results represent the ratio of OCA to placebo. The fatal events distribution was estimated using the Kaplan-Meier methodology. Point estimates and 95% CIs for the fatal events distribution percentiles (25th and 50th) are provided.

Here 9999 represents the data that was not calculable due to insufficient clinical events. The 95% CI limits were not estimable due to an insufficient number of participants with clinical events, as indicated by 9999.

End point type	Secondary

End point timeframe:

Time to first occurrence from date of randomisation until the date of death from any cause, up to EOS

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: days				
number (confidence interval 95%)				
25th Percentile	9999 (9999 to 9999)	9999 (9999 to 9999)		
50th Percentile	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

Statistical analysis title	Time to First Occurrence Fatal Event (All-Cause)
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.568
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	2.78

Secondary: Time to First Occurrence of Liver Transplant

End point title	Time to First Occurrence of Liver Transplant

End point description:

The effect of OCA compared to placebo on time to occurrence of a liver transplant was assessed. The results represented the ratio of OCA to placebo. A hazard ratio <1 indicated an advantage for OCA. The event of interest was summarized through Cumulative Incidence Function (CIF) estimate at 5 years.

End point type	Secondary

End point timeframe:

Time to first occurrence from date of randomisation until the date of first documented liver transplant or date of death from any cause, whichever came first, up to EOS

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: score on a scale				
number (confidence interval 95%)	0.18 (0.11 to 0.26)	0.16 (0.09 to 0.23)		

Statistical analyses

Statistical analysis title	Time to First Occurrence of Liver Transplant
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.769
Method	Gray's Test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	2.07

Secondary: Time to First Occurrence of Hospitalization Due to Hepatic Events

End point title	Time to First Occurrence of Hospitalization Due to Hepatic Events

End point description:

Hospitalization events include new onset or recurrent variceal bleed, hepatic encephalopathy (as defined by a West Haven score of >=2), spontaneous bacterial peritonitis (confirmed by diagnostic paracentesis OR presence of >250/mm^3 polymorph leucocytes [PMNs] in the ascitic fluid), bacterial empyema is confirmed by diagnostic thoracentesis OR presence of >250/mm^3 PMNs in the pleural fluid. The event of interest was summarized through CIF estimate at 5 years.

End point type	Secondary

End point timeframe:

Time to first occurrence from date of randomisation until the date of hospitalization, liver transplant or death from any cause, whichever came first, up to EOS

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: score on a scale				
number (confidence interval 95%)	0.11 (0.06 to 0.17)	0.18 (0.10 to 0.26)		

Statistical analyses

Statistical analysis title	Occurrence of Hospitalization Due to Hepatic Event
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.599
Method	Gray's Test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	1.67

Secondary: Time to First Occurrence of Uncontrolled or Refractory Ascites

End point title	Time to First Occurrence of Uncontrolled or Refractory Ascites

End point description:

Uncontrolled or refractory ascites are defined as diuretic-resistant ascites requiring large-volume paracentesis. The effect of OCA compared to placebo on time to the first occurrence of uncontrolled or refractory ascites was assessed. The event of interest was summarized through CIF estimate at 5 years.

End point type	Secondary

End point timeframe:

Time to first occurrence from date of randomization until the date of first documented uncontrolled or refractory ascites, liver transplant, or date of death from any cause, whichever came first, up to EOS

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: score on a scale				
number (confidence interval 95%)	0.02 (0.01 to 0.05)	0.04 (0.01 to 0.08)		

Statistical analyses

Statistical analysis title	Occurrence of Uncontrolled or Refractory Ascites
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.745
Method	Gray's Test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	3.43

Secondary: Time to First Occurrence of MELD Score ≥15

End point title	Time to First Occurrence of MELD Score ≥15

End point description:

The MELD score is useful in assessing participants with significant decompensation, and the MELD score is now used by the United Network for Organ Sharing in the United States and Eurotransplants to manage organ allocation for liver transplantation. The MELD score is derived from the participant's serum total bilirubin, serum creatinine, and International Normalized Ratio (INR), as appropriate, to predict survival. The event of interest was summarized through CIF estimate at 5 years.

End point type	Secondary

End point timeframe:

Time to first occurrence from date of randomization until the date of first documented MELD Score ≥15, liver transplant or date of death from any cause, whichever came first, up to EOS

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: score on a scale				
number (confidence interval 95%)	0.13 (0.07 to 0.19)	0.18 (0.11 to 0.25)		

Statistical analyses

Statistical analysis title	Time to First Occurrence of MELD Score ≥15
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)

Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.437
Method	Gray's Test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.44

Secondary: Time To First Occurrence Of Severe Decompensating Events of Expanded Composite Endpoint

End point title	Time To First Occurrence Of Severe Decompensating Events of Expanded Composite Endpoint

End point description:

The first occurrence of the key secondary clinical event refers to the first occurrence of the following events: death, liver transplant, MELD-Na score >=15 if MELD-Na< 12 at baseline, MELD score >=15 if MELD-Na >=12 at baseline, uncontrolled or refractory ascites, portal hypertension syndromes (hepatorenal syndrome, portopulmonary syndrome, hepatopulmonary syndrome) or hospitalization for new onset or recurrence of variceal bleed, hepatic encephalopathy, spontaneous bacterial peritonitis, or bacterial empyema. The clinical events distribution was estimated using the Kaplan-Meier methodology. Point estimates and 95% CIs for the clinical events distribution percentiles (25th and 50th) are provided.

Here 9999 represents the data that was not calculable due to insufficient clinical events. The 95% CI limits were not estimable due to an insufficient number of participants with clinical events, as indicated by 9999.

End point type	Secondary

End point timeframe:

Time to first occurrence from date of randomization until the date of first documented progression or date of death from any cause, whichever came first, up to EOS

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: days				
number (confidence interval 95%)				
25th Percentile	1092 (670 to 1408)	929 (679 to 1342)		
50th Percentile	9999 (1910 to 9999)	9999 (9999 to 9999)		

Statistical analyses

Statistical analysis title	Severe Decompensating Events Expanded Composite
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.898
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.52

Secondary: Time To Liver Transplant Or Death (All-Cause)

End point title	Time To Liver Transplant Or Death (All-Cause)

End point description:

The effect of OCA compared to placebo on time to liver transplant or death (all-cause) was assessed. The events distribution was estimated using the Kaplan-Meier methodology. Point estimates and 95% CIs for the clinical events distribution percentiles (25th and 50th) are provided.

Here 9999 represents the data that was not calculable due to insufficient clinical events. The 95% CI limits were not estimable due to an insufficient number of participants with clinical events, as indicated by 9999

End point type	Secondary

End point timeframe:

Time to first occurrence from date of randomisation until the date of first documented liver transplant or date of death from any cause, whichever came first, up to EOS

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: days				
number (confidence interval 95%)				
25th Percentile	1580 (1275 to 9999)	1803 (1206 to 9999)		
50th Percentile	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

Statistical analysis title	Time To Liver Transplant Or Death (All-cause)
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)

Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.594
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.91

Secondary: Time To Development Of Varix/Varices

End point title	Time To Development Of Varix/Varices

End point description:

The effect of OCA compared to placebo on time to development of varix/varices was assessed. The event of interest was summarized through CIF estimate at 5 years.

End point type	Secondary

End point timeframe:

Time to first occurrence from date of randomization until the date of first documented development of varix/varices, liver transplant or death from any cause, whichever came first, up to EOS

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: score on a scale				
number (confidence interval 95%)	0.07 (0.03 to 0.12)	0.09 (0.04 to 0.17)		

Statistical analyses

Statistical analysis title	Time To Development Of Varix/Varices
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.838
Method	Gray's Test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	2.24

Secondary: Time To Liver-Related Death

End point title	Time To Liver-Related Death

End point description:

The effect of OCA compared to placebo on time to liver-related death was assessed. The event of interest was summarized through CIF estimate at 5 years.

End point type	Secondary

End point timeframe:

Time to first occurrence from date of randomization until the date of first liver-related or non-liver-related death, whichever came first, up to EOS

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: score on a scale				
number (confidence interval 95%)	0.03 (0.01 to 0.07)	0.04 (0.01 to 0.09)		

Statistical analyses

Statistical analysis title	Time To Liver-Related Death
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.98
Method	Gray's Test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	4.04

Secondary: Time To Liver-Related Death Or Liver Transplant

End point title	Time To Liver-Related Death Or Liver Transplant

End point description:

The effect of OCA compared to placebo on time to liver-related death or liver transplant was assessed. The event of interest was summarized through CIF estimate at 5 years.

End point type	Secondary

End point timeframe:

Time to first occurrence from date of randomization until the date of liver transplant, liver-related death or non-liver-related death from any cause, whichever came first, up to EOS

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: score on a scale				
number (confidence interval 95%)	0.20 (0.13 to 0.29)	0.19 (0.12 to 0.27)		

Statistical analyses

Statistical analysis title	Time To Liver-Related Death Or Liver Transplant
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.933
Method	Gray's Test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	1.83

Secondary: Time To Liver-Related Death, Liver Transplant, Or MELD Score ≥15

End point title	Time To Liver-Related Death, Liver Transplant, Or MELD Score ≥15

End point description:

The effect of OCA compared to placebo on time to liver-related death, liver transplant, or MELD Score ≥15 was assessed. The event of interest was summarized through CIF estimate at 5 years.

End point type	Secondary

End point timeframe:

Time to first occurrence from date of randomization until the date of liver transplant, liver-related death, non-liver-related death from any cause or MELD Score ≥15, whichever came first, up to EOS

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: score on a scale				
number (confidence interval 95%)	0.25 (0.17 to 0.33)	0.29 (0.21 to 0.37)		

Statistical analyses

Statistical analysis title	Liver-related death, transplant, MELD Score ≥15
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.468
Method	Gray's Test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.34

Secondary: Progression To Cirrhosis (for Noncirrhotic Subjects at Baseline)

End point title	Progression To Cirrhosis (for Noncirrhotic Subjects at Baseline)

End point description:

When a participant is identified as noncirrhotic at the Baseline and exhibited any signs or symptoms associated with progression to cirrhosis, the participant was assessed by Fibroscan® TE where available. The event of interest was summarized through CIF estimate at 5 years.

End point type	Secondary

End point timeframe:

Time to first occurrence from date of randomization until the date of cirrhosis, liver transplant or death from any cause, whichever came first, up to EOS

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	78	62		
Units: score on a scale				
number (confidence interval 95%)	0.07 (0.02 to 0.16)	0.15 (0.06 to 0.27)		

Statistical analyses

Statistical analysis title	Progression To Cirrhosis (Noncirrhotic Subject)
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.19
Method	Cochran-Mantel-Haenszel
Parameter estimate	Hazard ratio (HR)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	1.41

Statistical analysis title	Progression To Cirrhosis (Noncirrhotic Subject)
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.178
Method	Gray’s Test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	1.41

Secondary: Time To Occurrence Of Hepatocellular Carcinoma (HCC)

End point title	Time To Occurrence Of Hepatocellular Carcinoma (HCC)

End point description:

The effect of OCA compared to placebo on time to occurrence of HCC was assessed. The event of interest was summarized through CIF estimate at 5 years.

Here 9999 represents the data that was not calculable due to insufficient clinical events. The 95% CI limits were not estimable due to an insufficient number of participants with clinical events, as indicated by 9999.

End point type	Secondary

End point timeframe:

Time to first occurrence from date of randomisation until the date of HCC diagnosis, liver transplant or death from any cause, whichever came first, up to EOS

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168[3]	166		
Units: score on a scale				
number (confidence interval 95%)	9999 (9999 to 9999)	0.01 (0 to 0.05)		

Notes:

[3] - 9999 = 95% CI limits not estimated due to an insufficient number of participants with clinical event

Statistical analyses

Statistical analysis title	Time To Occurrence Of Hepatocellular Carcinoma
Comparison groups	Obeticholic Acid (ITT) v Placebo (ITT)
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.443
Method	Gray's Test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	3.54

Secondary: Change From Baseline To Month 24 Of Total Bilirubin

End point title	Change From Baseline To Month 24 Of Total Bilirubin

End point description:

Liver biochemistry, which includes total bilirubin, was assessed to evaluate biochemical triggers that would prompt an immediate reevaluation of participants for potential hepatic injury or hepatic decompensation. Analysis was performed using mixed model repeated measures (MMRM), including treatment group, time, treatment group by time interaction, and randomization stratification factors as entered in the interactive web review board (IWRS) as fixed effects and baseline values as a covariate.

Month 6: OCA (n=149); Placebo (n=153)
Month 12: OCA (n=126); Placebo (n=138)
Month 24: OCA (n=97); Placebo (n=101)

End point type	Secondary

End point timeframe:

Baseline up to Month 24

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: mg/dL				
least squares mean (standard error)				
Month 6	0.10 (± 0.069)	0.17 (± 0.069)		
Month 12	0.26 (± 0.113)	0.29 (± 0.111)		
Month 24	0.30 (± 0.141)	0.63 (± 0.138)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 24 Of Direct Bilirubin

End point title	Change From Baseline To Month 24 Of Direct Bilirubin

End point description:

Liver biochemistry, which includes direct bilirubin, was assessed to evaluate biochemical triggers that would prompt an immediate reevaluation of participants for potential hepatic injury or hepatic decompensation. Analysis was performed using MMRM, including treatment group, time, treatment group by time interaction, and randomization stratification factors as entered in the IWRS as fixed effects and baseline values as a covariate.

Month 6: OCA (n=147); Placebo (n=147)
Month 12: OCA (n=121); Placebo (n=138)
Month 24: OCA (n=96); Placebo (n=97)

End point type	Secondary

End point timeframe:

Baseline up to Month 24

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: mg/dL				
least squares mean (standard error)				
Month 6	0.11 (± 0.054)	0.14 (± 0.054)		
Month 12	0.13 (± 0.073)	0.22 (± 0.071)		
Month 24	0.19 (± 0.107)	0.48 (± 0.106)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 24 Of Aspartate Aminotransferase (AST)

End point title	Change From Baseline To Month 24 Of Aspartate Aminotransferase (AST)

End point description:

Liver biochemistry, which includes AST, was assessed to evaluate biochemical triggers that would prompt an immediate reevaluation of participants for potential hepatic injury or hepatic decompensation. Analysis was performed using MMRM, including treatment group, time, treatment group by time interaction, and randomization stratification factors as entered in the IWRS as fixed effects and baseline values as a covariate.

Month 6: OCA (n=147); Placebo (n=150)
Month 12: OCA (n=124); Placebo (n=138)
Month 24: OCA (n=97); Placebo (n=102)

End point type	Secondary

End point timeframe:

Baseline up to Month 24

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: U/L				
least squares mean (standard error)				
Month 6	-14.5 (± 2.21)	-0.6 (± 2.19)		
Month 12	-11.8 (± 2.36)	-5.4 (± 2.27)		
Month 24	-14.8 (± 2.78)	-6.0 (± 2.72)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 24 Of Alanine Aminotransferase (ALT)

End point title	Change From Baseline To Month 24 Of Alanine Aminotransferase (ALT)

End point description:

Liver biochemistry, which includes ALT, was assessed to evaluate biochemical triggers that would prompt an immediate reevaluation of participants for potential hepatic injury or hepatic decompensation. Analysis was performed using MMRM, including treatment group, time, treatment group by time interaction, and randomization stratification factors as entered in the IWRS as fixed effects and baseline values as a covariate.

Month 6: OCA (n=149); Placebo (n=153)
Month 12: OCA (n=126); Placebo (n=138)
Month 24: OCA (n=97); Placebo (n=100)

End point type	Secondary

End point timeframe:

Baseline up to Month 24

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: U/L				
least squares mean (standard error)				
Month 6	-24.3 (± 2.62)	-7.4 (± 2.59)		
Month 12	-20.5 (± 3.49)	-12.8 (± 3.37)		
Month 24	-28.5 (± 2.92)	-19.4 (± 2.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 24 Of Alkaline Phosphatase (ALP)

End point title	Change From Baseline To Month 24 Of Alkaline Phosphatase (ALP)

End point description:

Liver biochemistry, which includes ALP, was assessed to evaluate biochemical triggers that would prompt an immediate reevaluation of participants for potential hepatic injury or hepatic decompensation. Analysis was performed using MMRM, including treatment group, time, treatment group by time interaction, and randomization stratification factors as entered in the IWRS as fixed effects and baseline values as a covariate.

Month 6: OCA (n=150); Placebo (n=152)
Month 12: OCA (n=126); Placebo (n=138)
Month 24: OCA (n=98); Placebo (n=102)

End point type	Secondary

End point timeframe:

Baseline up to Month 24

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: U/L				
least squares mean (standard error)				
Month 6	-134.3 (± 10.86)	-37.4 (± 10.85)		
Month 12	-144.8 (± 12.05)	-68.8 (± 11.72)		
Month 24	-156.4 (± 14.93)	-113.1 (± 14.60)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 24 Of Gamma-glutamyl Transferase (GGT)

End point title	Change From Baseline To Month 24 Of Gamma-glutamyl Transferase (GGT)

End point description:

Liver biochemistry, which includes GGT, was assessed to evaluate biochemical triggers that would prompt an immediate reevaluation of participants for potential hepatic injury or hepatic decompensation. Analysis was performed using MMRM, including treatment group, time, treatment group by time interaction, and randomization stratification factors as entered in the IWRS as fixed effects and baseline values as a covariate.

Month 6: OCA (n=150); Placebo (n=152)
Month 12: OCA (n=126); Placebo (n=138)
Month 24: OCA (n=98); Placebo (n=102)

End point type	Secondary

End point timeframe:

Baseline up to Month 24

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: U/L				
least squares mean (standard error)				
Month 6	-155.5 (± 15.04)	-47.0 (± 14.99)		
Month 12	-152.2 (± 18.24)	-63.4 (± 17.71)		
Month 24	-175.6 (± 22.49)	-127.7 (± 22.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 24 Of Albumin

End point title	Change From Baseline To Month 24 Of Albumin

End point description:

Liver biochemistry, which includes albumin, was assessed to evaluate biochemical triggers that would prompt an immediate reevaluation of participants for potential hepatic injury or hepatic decompensation. Analysis was performed using MMRM, including treatment group, time, treatment group by time interaction, and randomization stratification factors as entered in the IWRS as fixed effects and baseline values as a covariate.

Month 6: OCA (n=150); Placebo (n=153)
Month 12: OCA (n=126); Placebo (n=138)
Month 24: OCA (n=98); Placebo (n=102)

End point type	Secondary

End point timeframe:

Baseline up to Month 24

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: g/L				
least squares mean (standard error)				
Month 6	-0.4 (± 0.19)	-0.1 (± 0.19)		
Month 12	-0.3 (± 0.23)	-0.3 (± 0.22)		
Month 24	-0.1 (± 0.29)	-1.1 (± 0.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 24 Of INR

End point title	Change From Baseline To Month 24 Of INR

End point description:

The coagulation test, which includes INR, was assessed to evaluate biochemical triggers that would prompt an immediate reevaluation of participants for potential hepatic injury or hepatic decompensation. Analysis was performed using MMRM, including treatment group, time, treatment group by time interaction, and randomization stratification factors as entered in the IWRS as fixed effects and baseline values as a covariate.

Month 6: OCA (n=148); Placebo (n=146)
Month 12: OCA (n=124); Placebo (n=136)
Month 24: OCA (n=93); Placebo (n=98)

End point type	Secondary

End point timeframe:

Baseline up to Month 24

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: units on a scale				
least squares mean (standard error)				
Month 6	0.02 (± 0.014)	0.02 (± 0.014)		
Month 12	0.01 (± 0.009)	0.02 (± 0.008)		
Month 24	0.03 (± 0.014)	0.06 (± 0.014)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 72 Of MELD Score

End point title	Change From Baseline To Month 72 Of MELD Score

End point description:

The MELD score is useful in assessing participants with significant decompensation, and the MELD score is now used by the United Network for Organ Sharing in the United States and Eurotransplants to manage organ allocation for liver transplantation. The MELD score is derived from the participant's serum total bilirubin, serum creatinine, and INR, as appropriate, to predict survival.

Month 12: OCA (n=121); Placebo (n=134)
Month 24: OCA (n=91); Placebo (n=97)
Month 36: OCA (n=71); Placebo (n=59)
Month 48: OCA (n=48); Placebo (n=34)
Month 60: OCA (n=31); Placebo (n=20)
Month 72: OCA (n=7); Placebo (n=4)

End point type	Secondary

End point timeframe:

Baseline up to Month 72

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: score on a scale				
median (inter-quartile range (Q1-Q3))				
Month 12	0 (-0.60 to 0.60)	0 (-0.50 to 1.30)		
Month 24	0 (-1.00 to 0.70)	0.20 (-0.50 to 1.70)		
Month 36	0 (-1.00 to 0.50)	0.60 (-0.50 to 2.90)		
Month 48	0 (-0.95 to 1.45)	0.40 (-0.80 to 1.60)		
Month 60	0 (-1.30 to 0.40)	0 (-1.20 to 1.85)		
Month 72	0 (-0.80 to 5.20)	1.95 (-1.40 to 3.10)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 72 Of MELD-Na Score

End point title	Change From Baseline To Month 72 Of MELD-Na Score

End point description:

The MELD score is useful in assessing participants with significant decompensation, and the MELD score is now used by the United Network for Organ Sharing in the United States and Eurotransplants to manage organ allocation for liver transplantation. The MELD score is derived from the participant's serum total bilirubin, serum creatinine, and INR, as appropriate, to predict survival.

Month 12: OCA (n=121); Placebo (n=132)
Month 24: OCA (n=91); Placebo (n=97)
Month 36: OCA (n=71); Placebo (n=59)
Month 48: OCA (n=48); Placebo (n=34)
Month 60: OCA (n=31); Placebo (n=20)
Month 72: OCA (n=6); Placebo (n=4)

End point type	Secondary

End point timeframe:

Baseline up to Month 72

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: score on a scale				
median (inter-quartile range (Q1-Q3))				
Month 12	0 (-1.0 to 0.0)	0 (-1.0 to 1.0)		
Month 24	0 (-2.0 to 0)	0 (-1.0 to 1.0)		
Month 36	0 (-2.0 to 0)	0 (-1.0 to 2.0)		
Month 48	0 (-2.0 to 2.0)	0 (-2.0 to 2.0)		
Month 60	-1.0 (-3.0 to 0)	0 (-2.5 to 1.5)		
Month 72	0 (-2.0 to 0)	0.5 (-3.5 to 1.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 72 Of CP Score

End point title	Change From Baseline To Month 72 Of CP Score

End point description:

Child-Pugh Score (Pugh 1973, Lucey 1997) was calculated and reported within the electronic data capture (EDC) system based on data entered into the CRF by adding the scores from the 5 factors and could have ranged from 5 to15. A total score of 5 to 6 was considered Grade A (mild, well-compensated disease); 7 to 9 was Grade B (moderate, significant functional compromise); and 10 and above was Grade C (severe, decompensated disease).

Month 12: OCA (n=126); Placebo (n=135)
Month 24: OCA (n=93); Placebo (n=97)
Month 36: OCA (n=71); Placebo (n=57)
Month 48: OCA (n=47); Placebo (n=35)
Month 60: OCA (n=31); Placebo (n=20)
Month 72: OCA (n=7); Placebo (n=4)

End point type	Secondary

End point timeframe:

Baseline up to Month 72

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: score on a scale				
median (inter-quartile range (Q1-Q3))				
Month 12	0 (0 to 0)	0 (0 to 1.0)		
Month 24	0 (0 to 0)	0 (0 to 1.0)		
Month 36	0 (0 to 0)	0 (0 to 1.0)		
Month 48	0 (0 to 0)	0 (0 to 1.0)		
Month 60	0 (0 to 0)	0 (0 to 1.0)		
Month 72	0 (0 to 2.0)	1.0 (0 to 1.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 72 Of Mayo Risk Score (MRS)

End point title	Change From Baseline To Month 72 Of Mayo Risk Score (MRS)

End point description:

Mayo Risk Score (MRS) was calculated and reported within the EDC system. Calculation of MRS included Investigator assessment of peripheral edema and the use of diuretic therapy, which was assessed during the adverse event and concomitant medicine review at the scheduled visits and entered into the CRF, as well as total bilirubin, albumin, and prothrombin time results obtained from the central laboratory data.

Month 12: OCA (n=117); Placebo (n=128)
Month 24: OCA (n=80); Placebo (n=91)
Month 36: OCA (n=65); Placebo (n=53)
Month 48: OCA (n=43); Placebo (n=29)
Month 60: OCA (n=28); Placebo (n=18)
Month 72: OCA (n=6); Placebo (n=4)

End point type	Secondary

End point timeframe:

Baseline up to Month 72

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: score on a scale				
median (inter-quartile range (Q1-Q3))				
Month 12	0 (-0.380 to 0.320)	0.080 (-0.205 to 0.535)		
Month 24	-0.080 (-0.270 to 0.390)	0.140 (-0.170 to 0.660)		
Month 36	-0.040 (-0.410 to 0.280)	0.050 (-0.240 to 0.650)		
Month 48	0.030 (-0.430 to 0.620)	0.210 (-0.240 to 0.810)		
Month 60	-0.145 (-0.575 to 0.160)	-0.060 (-0.490 to 0.790)		

Month 72	-0.130 (-0.460 to 0.320)	0.990 (0.240 to 1.165)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 72 Of Immunoglobulin-M (IgM)

End point title	Change From Baseline To Month 72 Of Immunoglobulin-M (IgM)

End point description:

Markers of inflammation, which include IgM, were assessed.

Month 12: OCA (n=124); Placebo (n=135)
Month 24: OCA (n=97); Placebo (n=101)
Month 36: OCA (n=72); Placebo (n=59)
Month 48: OCA (n=48); Placebo (n=35)
Month 60: OCA (n=32); Placebo (n=21)
Month 72: OCA (n=7); Placebo (n=4)

End point type	Secondary

End point timeframe:

Baseline up to Month 72

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: g/L				
median (inter-quartile range (Q1-Q3))				
Month 12	-0.305 (-0.955 to 0.025)	-0.160 (-0.720 to 0.200)		
Month 24	-0.470 (-1.250 to -0.090)	-0.230 (-0.630 to 0.170)		
Month 36	-0.700 (-1.440 to -0.025)	-0.330 (-1.270 to 0)		
Month 48	-0.525 (-1.615 to 0.005)	-0.690 (-1.540 to 0.090)		
Month 60	-0.745 (-1.545 to -0.075)	-0.350 (-1.050 to -0.150)		
Month 72	-1.590 (-4.100 to 0.050)	-0.640 (-1.060 to 0.645)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 72 Of C-reactive Protein (CRP)

End point title	Change From Baseline To Month 72 Of C-reactive Protein (CRP)

End point description:

Markers of inflammation, which include CRP, were assessed.

Month 12: OCA (n=127); Placebo (n=137)
Month 24: OCA (n=98); Placebo (n=101)
Month 36: OCA (n=74); Placebo (n=59)
Month 48: OCA (n=51); Placebo (n=36)
Month 60: OCA (n=33); Placebo (n=22)
Month 72: OCA (n=7); Placebo (n=4)

End point type	Secondary

End point timeframe:

Baseline up to Month 72

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: mg/L				
median (inter-quartile range (Q1-Q3))				
Month 12	-0.140 (-1.320 to 1.360)	0.400 (-0.760 to 2.720)		
Month 24	-0.280 (-1.210 to 1.110)	0.290 (-1.450 to 2.950)		
Month 36	-0.525 (-2.160 to 0.630)	0.340 (-1.460 to 3.830)		
Month 48	-0.260 (-1.700 to 2.180)	-0.180 (-1.200 to 2.025)		
Month 60	-0.720 (-3.020 to 0.740)	-0.730 (-2.700 to 1.650)		
Month 72	-0.100 (-2.740 to 2.570)	0.765 (-2.630 to 4.715)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 72 Of Tumor Necrosis Factor-α (TNF-α)

End point title	Change From Baseline To Month 72 Of Tumor Necrosis Factor-α (TNF-α)

End point description:

Markers of inflammation, which include TNF-α, were assessed.

Month 12: OCA (n=117); Placebo (n=123)
Month 24: OCA (n=91); Placebo (n=95)
Month 36: OCA (n=66); Placebo (n=56)
Month 48: OCA (n=46); Placebo (n=33)
Month 60: OCA (n=29); Placebo (n=19)
Month 72: OCA (n=6); Placebo (n=3)

End point type	Secondary

End point timeframe:

Baseline up to Month 72

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
Month 12	0 (-0.362 to 0.580)	0.058 (-0.236 to 0.791)		
Month 24	0.203 (-0.213 to 0.758)	0.323 (-0.039 to 0.654)		
Month 36	0.055 (-0.304 to 0.627)	0.296 (-0.078 to 0.750)		
Month 48	0.165 (-0.195 to 0.814)	0.539 (0.113 to 0.918)		
Month 60	-0.009 (-0.765 to 0.596)	0.419 (-0.153 to 0.753)		
Month 72	0.046 (-0.390 to 0.175)	0.616 (-1.318 to 0.788)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 72 Of Fibroblast Growth Factor-19 (FGF-19)

End point title	Change From Baseline To Month 72 Of Fibroblast Growth Factor-19 (FGF-19)

End point description:

Markers of hepatic fibrosis, which include FGF-19, were assessed.

Month 12: OCA (n=124); Placebo (n=132)
Month 24: OCA (n=95); Placebo (n=97)
Month 36: OCA (n=69); Placebo (n=59)
Month 48: OCA (n=47); Placebo (n=34)
Month 60: OCA (n=31); Placebo (n=22)
Month 72: OCA (n=5); Placebo (n=4)

End point type	Secondary

End point timeframe:

Baseline up to Month 72

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
Month 12	73.50 (2.85 to 208.00)	-2.80 (-57.65 to 36.50)		
Month 24	72.00 (1.00 to 211.00)	-0.40 (-63.00 to 61.40)		
Month 36	39.90 (-17.70 to 132.00)	-2.00 (-51.00 to 50.80)		
Month 48	56.00 (-24.00 to 219.00)	-9.45 (-59.90 to 39.30)		
Month 60	14.40 (-30.00 to 183.00)	-1.45 (-83.40 to 156.00)		
Month 72	-106.90 (-172.30 to -1.00)	-62.00 (-239.00 to -26.50)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 72 Of Cytokeratin-18 (CK-18)

End point title	Change From Baseline To Month 72 Of Cytokeratin-18 (CK-18)

End point description:

Markers of inflammation, which include CK-18, were assessed.

Month 12: OCA (n=126); Placebo (n=133)
Month 24: OCA (n=97); Placebo (n=100)
Month 36: OCA (n=72); Placebo (n=59)
Month 48: OCA (n=50); Placebo (n=35)
Month 60: OCA (n=33); Placebo (n=21)
Month 72: OCA (n=7); Placebo (n=4)

End point type	Secondary

End point timeframe:

Baseline up to Month 72

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: U/L				
median (inter-quartile range (Q1-Q3))				
Month 12	-34.450 (-138.010 to 45.800)	9.100 (-78.540 to 123.770)		
Month 24	-57.660 (-158.960 to 8.470)	17.545 (-54.630 to 165.835)		

Month 36	-45.935 (-171.225 to 18.715)	6.680 (-112.010 to 76.110)		
Month 48	-81.035 (-158.900 to 33.550)	0.290 (-130.710 to 79.410)		
Month 60	-117.660 (-232.770 to 0)	-56.390 (-159.780 to 77.020)		
Month 72	-182.590 (-207.020 to 17.060)	-32.745 (-199.555 to 78.070)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 72 Of 7α-hydroxy-4-cholesten-3-one (C4)

End point title	Change From Baseline To Month 72 Of 7α-hydroxy-4-cholesten-3-one (C4)

End point description:

Markers of hepatic fibrosis, which include C4, were assessed.

Month 12: OCA (n=116); Placebo (n=132)
Month 24: OCA (n=96); Placebo (n=98)
Month 36: OCA (n=71); Placebo (n=60)
Month 48: OCA (n=49); Placebo (n=34)
Month 60: OCA (n=33); Placebo (n=22)
Month 72: OCA (n=7); Placebo (n=4)

End point type	Secondary

End point timeframe:

Baseline up to Month 72

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: ng/mL				
median (inter-quartile range (Q1-Q3))				
Month 12	-2.222 (-8.110 to 0.002)	-0.250 (-2.691 to 1.523)		
Month 24	-3.700 (-10.119 to -0.885)	-0.861 (-5.500 to 0.900)		
Month 36	-3.826 (-9.380 to 0.182)	-1.225 (-5.620 to 1.161)		
Month 48	-4.220 (-9.870 to 0)	-1.168 (-12.240 to 1.691)		
Month 60	-3.250 (-10.334 to -0.110)	-1.161 (-9.591 to 0.660)		

Month 72	-7.500 (-10.914 to -0.690)	-0.947 (-15.281 to -0.277)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 72 Of Enhanced Liver Fibrosis (ELF)

End point title	Change From Baseline To Month 72 Of Enhanced Liver Fibrosis (ELF)

End point description:

Liver fibrosis was assessed using ELF test. The ELF test assessed: hyaluronic acid, procollagen3 N-terminal peptide, and a tissue inhibitor of metalloproteinase 1.

Month 12: OCA (n=126); Placebo (n=127)
Month 24: OCA (n=95); Placebo (n=95)
Month 36: OCA (n=71); Placebo (n=59)
Month 48: OCA (n=48); Placebo (n=34)
Month 60: OCA (n=33); Placebo (n=21)
Month 72: OCA (n=7); Placebo (n=4)

End point type	Secondary

End point timeframe:

Baseline up to Month 72

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: score on a scale				
median (inter-quartile range (Q1-Q3))				
Month 12	0.10 (-0.50 to 0.60)	0.10 (-0.20 to 0.70)		
Month 24	0 (-0.70 to 0.60)	0.20 (-0.40 to 1.00)		
Month 36	-0.20 (-0.90 to 0.70)	0 (-0.60 to 0.70)		
Month 48	0.25 (-0.45 to 0.80)	0.10 (-0.70 to 1.10)		
Month 60	-0.20 (-1.20 to 0.60)	0.10 (-1.00 to 1.00)		
Month 72	0 (-0.80 to 2.80)	-0.20 (-1.10 to 0.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To Month 72 Of Liver Stiffness - Transient Elastography

End point title	Change From Baseline To Month 72 Of Liver Stiffness - Transient Elastography

End point description:

Hepatic stiffness was measured using non-invasive transient Elastography with a Fibroscan® TE device.

Month 12: OCA (n=88); Placebo (n=90)
Month 24: OCA (n=67); Placebo (n=67)
Month 36: OCA (n=49); Placebo (n=41)
Month 48: OCA (n=31); Placebo (n=19)
Month 60: OCA (n=19); Placebo (n=14)
Month 72: OCA (n=5); Placebo (n=3)

End point type	Secondary

End point timeframe:

Baseline up to Month 72

End point values	Obeticholic Acid (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: kPa				
median (inter-quartile range (Q1-Q3))				
Month 12	0.25 (-2.40 to 4.05)	0.90 (-1.80 to 7.30)		
Month 24	-0.60 (-2.60 to 3.60)	1.50 (-2.20 to 15.60)		
Month 36	0.30 (-3.40 to 5.50)	2.00 (-1.60 to 9.10)		
Month 48	0.70 (-2.20 to 4.00)	1.00 (-2.80 to 11.90)		
Month 60	0.20 (-2.50 to 6.00)	-1.35 (-4.70 to 1.90)		
Month 72	-2.40 (-2.50 to 2.70)	3.20 (-2.20 to 8.70)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point description:

An adverse event (AE) was defined as any unfavorable and unintended sign (for example, including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product or procedure, whether or not considered related to the medicinal product or procedure, which occurred during the course of the clinical study. TEAEs were defined as AEs that occurred on or after the date and time of study drug administration, or those that first occurred before dosing but worsened in frequency or severity after study drug administration. A summary of all Serious Adverse Events and Other Adverse Events (nonserious) regardless of causality is located in the 'Reported Adverse Events' Section.

End point type	Secondary

End point timeframe:

Baseline up to the last IP dose plus 30 days and prior to commercial OCA initiation date

End point values	Obeticholic Acid (Safety)	Placebo (Safety)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	166		
Units: participants				
TEAEs	162	158		
SAE	53	53		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) Population: Fasting Trough Concentrations Of OCA By Dose Regimen

End point title	Pharmacokinetic (PK) Population: Fasting Trough Concentrations Of OCA By Dose Regimen

End point description:

The fasting trough PK concentrations of OCA of different dose regimens taken throughout the study are reported.

Here 9999 represents data that were not available.

End point type	Secondary

End point timeframe:

Months 3, 6, 9, 12, 24, 36, 48, and 60

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	149			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
5 mg QD (Month 3)	119 (± 185)			
5 mg QD (Month 6)	102 (± 186)			
5 mg QD (Month 9)	175 (± 33.0)			
5 mg QD (Month 12)	117 (± 153)			
5 mg QD (Month 24)	113 (± 121)			
5 mg QD (Month 36)	84.5 (± 169)			
5 mg QD (Month 48)	203 (± 181)			
5 mg QD (Month 60)	7.96 (± 173)			
5 mg QOD (Month 3)	123 (± 191)			
5 mg QOD (Month 6)	103 (± 232)			

5 mg QOD (Month 9)	396 (± 9999)			
5 mg QOD (Month 12)	103 (± 97.2)			
5 mg QOD (Month 24)	134 (± 17.1)			
5 mg QOD (Month 48)	307 (± 9999)			
5 mg QW (Month 3)	57.3 (± 199)			
5 mg QW (Month 6)	31.0 (± 125)			
5 mg QW (Month 12)	73.5 (± 302)			
5 mg QW (Month 24)	171 (± 109)			
5 mg QW (Month 36)	245 (± 34.8)			
5 mg QW (Month 48)	141 (± 216)			
5 mg Q2W (Month 3)	61.9 (± 54.7)			
5 mg Q2W (Month 6)	108 (± 57.1)			
5 mg Q2W (Month 12)	187 (± 30.8)			
5 mg Q2W (Month 24)	208 (± 61.0)			
5 mg Q2W (Month 36)	225 (± 159)			
5 mg Q2W (Month 48)	502 (± 59.6)			
5 mg Q2W (Month 60)	7.32 (± 9999)			
5 mg other regimens (Month 3)	50.3 (± 1730)			
5 mg other regimens (Month 6)	79.6 (± 68.2)			
5 mg other regimens (Month 12)	20.6 (± 500)			
5 mg other regimens (Month 24)	91.1 (± 236)			
10 mg QD (Month 6)	126 (± 161)			
10 mg QD (Month 9)	51.1 (± 167)			
10 mg QD (Month 12)	86.9 (± 188)			
10 mg QD (Month 24)	85.6 (± 152)			
10 mg QD (Month 36)	79.9 (± 143)			
10 mg QD (Month 48)	81.2 (± 161)			
10 mg QD (Month 60)	48.6 (± 323)			
10 mg QOD (Month 12)	102 (± 576)			
10 mg QOD (Month 24)	25.5 (± 9999)			
10 mg QOD (Month 48)	9.08 (± 9999)			
10 mg Q2W (Month 6)	538 (± 9999)			
10 mg Q2W (Month 9)	566 (± 9999)			
10 mg Q2W (Month 12)	41.7 (± 45.6)			
10 mg Q2W (Month 24)	62.5 (± 35.9)			
10 mg Q2W (Month 36)	96.3 (± 132)			
10 mg Q2W (Month 48)	70.9 (± 218)			
10 mg Q2W (Month 60)	83.8 (± 9999)			
10 mg Q3D (Month 12)	0.861 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Serial Concentration of OCA By Dose Regimen

End point title	PK Population: Serial Concentration of OCA By Dose Regimen

End point description:

On Month 9, blood samples were collected at predose, 0.5 h, 0.75 h, 1 h, 1.5 h, 2 h, 2.5 h, 3 h, 4h, 5 h, and 6 h and PK serial concentrations at different dose regimen are reported.

Here 9999 represents data that were not available.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
5 mg QD (Predose)	61.2 (± 315)			
5 mg QD (0.5 h)	109 (± 66.1)			
5 mg QD (0.75 h)	158 (± 35.6)			
5 mg QD (1 h)	173 (± 56.4)			
5 mg QD (1.5 h)	137 (± 53.2)			
5 mg QD (2 h)	100 (± 100)			
5 mg QD (2.5 h)	90.1 (± 93.0)			
5 mg QD (3 h)	64.7 (± 47.1)			
5 mg QD (4 h)	71.6 (± 179)			
5 mg QD (5 h)	193 (± 150)			
5 mg QD (6 h)	199 (± 203)			
5 mg QOD (Predose)	396 (± 9999)			
5 mg QOD (0.5 h)	236 (± 9999)			
5 mg QOD (0.75 h)	211 (± 9999)			
5 mg QOD (1 h)	217 (± 9999)			
5 mg QOD (1.5 h)	232 (± 9999)			
5 mg QOD (2 h)	243 (± 9999)			
5 mg QOD (2.5 h)	240 (± 9999)			
5 mg QOD (3 h)	171 (± 9999)			
5 mg QOD (4 h)	117 (± 9999)			
5 mg QOD (5 h)	282 (± 9999)			
5 mg QOD (6 h)	544 (± 9999)			
10 mg QD (Predose)	64.2 (± 139)			
10 mg QD (0.5 h)	142 (± 55.8)			
10 mg QD (0.75 h)	176 (± 55.5)			
10 mg QD (1 h)	196 (± 65.5)			
10 mg QD (1.5 h)	254 (± 64.0)			
10 mg QD (2 h)	233 (± 54.0)			
10 mg QD (2.5 h)	206 (± 80.2)			
10 mg QD (3 h)	217 (± 90.7)			
10 mg QD (4 h)	151 (± 74.4)			
10 mg QD (5 h)	180 (± 80.0)			
10 mg QD (6 h)	214 (± 77.9)			
10 mg Q2W (Predose)	370 (± 65.8)			
10 mg Q2W (0.5 h)	490 (± 52.6)			
10 mg Q2W (P0.75 h)	593 (± 68.2)			
10 mg Q2W (1 h)	633 (± 69.5)			

10 mg Q2W (1.5 h)	425 (± 9999)			
10 mg Q2W (2 h)	769 (± 64.5)			
10 mg Q2W (2.5 h)	716 (± 75.1)			
10 mg Q2W (3 h)	602 (± 77.2)			
10 mg Q2W (4 h)	422 (± 116)			
10 mg Q2W (5 h)	758 (± 84.4)			
10 mg Q2W (6 h)	728 (± 169)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Area Under The Concentration-Time Curve (AUC) From 0 to 6 Hours Post-dose (AUC0-6h) Of Participants Who Received 5 mg QD OCA and With CP Score=Non-Cirrhotic (NC)

End point title	PK Population: Area Under The Concentration-Time Curve (AUC) From 0 to 6 Hours Post-dose (AUC0-6h) Of Participants Who Received 5 mg QD OCA and With CP Score=Non-Cirrhotic (NC)

End point description:

On Month 9, blood samples were collected at predose, 0.5h, 0.75 h, 1 h, 1.5 h, 2 h, 2.5 h, 3 h, 4h, 5 h, and 6 h for PK analysis in participants who received 5 mg QD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[4]			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	758 (± 9999)			

Notes:

[4] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC From 0 to 24 Hours Post-dose (AUC0-24h) Of Participants Who Received 5 mg QD OCA and With CP Score=NC

End point title	PK Population: AUC From 0 to 24 Hours Post-dose (AUC0-24h) Of Participants Who Received 5 mg QD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose, 0.5h, 0.75 h, 1 h, 1.5 h, 2 h, 2.5 h, 3 h, 4h, 5 h, and 6 h for PK analysis in participants who received 5 mg QD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[5]			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	3710 (± 9999)			

Notes:

[5] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Maximum Observed Concentration (Cmax) Of Participants Who Received 5mg QD OCA and With CP Score=NC

End point title	PK Population: Maximum Observed Concentration (Cmax) Of Participants Who Received 5mg QD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	317 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Time to Cmax (Tmax) Of Participants Who Received 5mg QD OCA and With CP Score=NC

End point title	PK Population: Time to Cmax (Tmax) Of Participants Who Received 5mg QD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: hours				
median (full range (min-max))	6.0 (6.0 to 6.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Metabolite to Parent Ratio of AUC0-6h (MRAUC) Of Participants Who Received 5mg QD OCA and With CP Score=NC

End point title	PK Population: Metabolite to Parent Ratio of AUC0-6h (MRAUC) Of Participants Who Received 5mg QD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	15.9 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Metabolite to Parent Ration of Cmax (MRCmax) Of

Participants Who Received 5mg QD OCA and With CP Score=NC	
End point title	PK Population: Metabolite to Parent Ration of Cmax (MRCmax) Of Participants Who Received 5mg QD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	8.93 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-6h Of Participants Who Received 5 mg QD OCA and With CP Score=A	
End point title	PK Population: AUC0-6h Of Participants Who Received 5 mg QD OCA and With CP Score=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with CP Score=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	889 (± 133)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-24h Of Participants Who Received 5 mg QD OCA and With CP Score=A

End point title	PK Population: AUC0-24h Of Participants Who Received 5 mg QD OCA and With CP Score=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with CP Score=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	4040 (± 129)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Cmax Of Participants Who Received 5mg QD OCA and With CP Score=A

End point title	PK Population: Cmax Of Participants Who Received 5mg QD OCA and With CP Score=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with CP Score=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	275 (± 117)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Tmax Of Participants Who Received 5mg QD OCA and With CP Score=A

End point title	PK Population: Tmax Of Participants Who Received 5mg QD OCA and With CP Score=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with CP Score=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: hours				
median (full range (min-max))	3.38 (0.750 to 6.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Concentration at 24 Hours Post-dose (Ctrough) Of Participants Who Received 5mg QD OCA and With CP Score=A

End point title	PK Population: Concentration at 24 Hours Post-dose (Ctrough) Of Participants Who Received 5mg QD OCA and With CP Score=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with CP Score=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	149 (± 22.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRAUC Of Participants Who Received 5mg QD OCA and With CP Score=A

End point title	PK Population: MRAUC Of Participants Who Received 5mg QD OCA and With CP Score=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with CP Score=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	8.41 (± 50.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Ctrough Of Participants Who Received 5mg QD OCA and With CP Score=B

End point title	PK Population: Ctrough Of Participants Who Received 5mg QD OCA and With CP Score=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with CP Score=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	242 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-6h Of Participants Who Received 5 mg QOD OCA and With CP Score=NC

End point title	PK Population: AUC0-6h Of Participants Who Received 5 mg QOD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QOD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[6]			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	1480 (± 9999)			

Notes:

[6] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-24h Of Participants Who Received 5 mg QOD OCA and With CP Score=NC

End point title	PK Population: AUC0-24h Of Participants Who Received 5 mg QOD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QOD OCA with CP Score=NC

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	9940 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Cmax Of Participants Who Received 5mg QOD OCA and With CP Score=NC

End point title	PK Population: Cmax Of Participants Who Received 5mg QOD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QOD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[7]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	544 (± 9999)			

Notes:

[7] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Tmax Of Participants Who Received 5mg QOD OCA and With CP Score=NC

End point title	PK Population: Tmax Of Participants Who Received 5mg QOD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received

5 mg QOD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: hours				
median (full range (min-max))	6.0 (6.0 to 6.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Ctrough Of Participants Who Received 5mg QOD OCA and With CP Score=NC

End point title	PK Population: Ctrough Of Participants Who Received 5mg QOD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QOD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[8]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	396 (± 9999)			

Notes:

[8] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRAUC Of Participants Who Received 5mg QOD OCA and With CP Score=NC

End point title	PK Population: MRAUC Of Participants Who Received 5mg QOD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QOD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[9]			
Units: unit on a scale				
geometric mean (geometric coefficient of variation)	26.6 (± 9999)			

Notes:

[9] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRCmax Of Participants Who Received 5mg QOD OCA and With CP Score=NC

End point title	PK Population: MRCmax Of Participants Who Received 5mg QOD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QOD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[10]			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	15.8 (± 9999)			

Notes:

[10] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-6h Of Participants Who Received 10 mg QD OCA

and With CP Score=NC	
End point title	PK Population: AUC0-6h Of Participants Who Received 10 mg QD OCA and With CP Score=NC
End point description:	
On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QOD OCA with CP Score=NC.	
End point type	Secondary
End point timeframe:	
Month 9	

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	1090 (± 98.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-24h Of Participants Who Received 10 mg QD OCA and With CP Score=NC	
End point title	PK Population: AUC0-24h Of Participants Who Received 10 mg QD OCA and With CP Score=NC
End point description:	
On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QOD OCA with CP Score=NC.	
End point type	Secondary
End point timeframe:	
Month 9	

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	3820 (± 91.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Cmax Of Participants Who Received 10 mg QD OCA and With CP Score=NC

End point title	PK Population: Cmax Of Participants Who Received 10 mg QD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QOD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	289 (± 74.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Tmax Of Participants Who Received 10 mg QD OCA and With CP Score=NC

End point title	PK Population: Tmax Of Participants Who Received 10 mg QD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QOD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: hours				
median (full range (min-max))	1.50 (1.50 to 3.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Ctrough Of Participants Who Received 10 mg QD OCA and With CP Score=NC

End point title	PK Population: Ctrough Of Participants Who Received 10 mg QD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QOD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	50.6 (± 148)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRAUC Of Participants Who Received 10 mg QD OCA and With CP Score=NC

End point title	PK Population: MRAUC Of Participants Who Received 10 mg QD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QOD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	13.8 (± 151)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRCmax Of Participants Who Received 10 mg QD OCA and With CP Score=NC

End point title	PK Population: MRCmax Of Participants Who Received 10 mg QD OCA and With CP Score=NC

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QOD OCA with CP Score=NC.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	4.02 (± 107)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-6h Of Participants Who Received 10 mg QD OCA and With CP Score=A

End point title	PK Population: AUC0-6h Of Participants Who Received 10 mg QD OCA and With CP Score=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with CP Score=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	1310 (± 11.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-24h Of Participants Who Received 10 mg QD OCA and With CPS Score=A

End point title	PK Population: AUC0-24h Of Participants Who Received 10 mg QD OCA and With CPS Score=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with CP Score=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	4280 (± 26.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Cmax Of Participants Who Received 10 mg QD OCA and With CP Score=A

End point title	PK Population: Cmax Of Participants Who Received 10 mg QD OCA and With CP Score=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with CP Score=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	334 (± 6.71)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Tmax Of Participants Who Received 10 mg QD OCA and With CPS Score=A On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with CP Score=A. Month 9

End point title	PK Population: Tmax Of Participants Who Received 10 mg QD OCA and With CPS Score=A On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with CP Score=A. Month 9

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with CP Score=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: hours				
median (full range (min-max))	1.50 (0.750 to 2.50)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Ctrough Of Participants Who Received 10 mg QD OCA and With CP Score=A

End point title	PK Population: Ctrough Of Participants Who Received 10 mg

	QD OCA and With CP Score=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with CP Score=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	55.2 (± 414)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRAUC Of Participants Who Received 10 mg QD OCA and With CP Score=A

End point title	PK Population: MRAUC Of Participants Who Received 10 mg QD OCA and With CP Score=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with CP Score=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	2.94 (± 15.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRCmax Of Participants Who Received 10 mg QD OCA and With CP Score=A

End point title	PK Population: MRCmax Of Participants Who Received 10 mg QD OCA and With CP Score=A

End point description:

PK Population: MRCmax Of Participants Who Received 10 mg QD OCA and With CP Score=A

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	1.48 (± 21.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-6h Of Participants Who Received 10 mg Q2W OCA and With CP Score=B

End point title	PK Population: AUC0-6h Of Participants Who Received 10 mg Q2W OCA and With CP Score=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg Q2W OCA with CP Score=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	3770 (± 84.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-24h Of Participants Who Received 10 mg Q2W OCA and With CP Score=B

End point title	PK Population: AUC0-24h Of Participants Who Received 10 mg Q2W OCA and With CP Score=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg Q2W OCA with CP Score=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	13900 (± 113)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Cmax Of Participants Who Received 10 mg Q2W OCA and With CP Score=B

End point title	PK Population: Cmax Of Participants Who Received 10 mg Q2W OCA and With CP Score=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg Q2W OCA with CP Score=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	916 (± 101)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Tmax Of Participants Who Received 10 mg Q2W OCA and With CP Score=B

End point title	PK Population: Tmax Of Participants Who Received 10 mg Q2W OCA and With CP Score=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg Q2W OCA with CP Score=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: hour				
median (full range (min-max))	4.0 (2.0 to 6.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Ctrough Of Participants Who Received 10 mg Q2W OCA and With CP Score=B

End point title	PK Population: Ctrough Of Participants Who Received 10 mg Q2W OCA and With CP Score=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg Q2W OCA with CP Score=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[11]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	566 (± 9999)			

Notes:

[11] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRAUC Of Participants Who Received 10 mg Q2W OCA and With CP Score=B

End point title	PK Population: MRAUC Of Participants Who Received 10 mg Q2W OCA and With CP Score=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg Q2W OCA with CP Score=B

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	12.6 (± 450)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRCmax Of Participants Who Received 10 mg Q2W OCA and With CP Score=B

End point title	PK Population: MRCmax Of Participants Who Received 10 mg Q2W OCA and With CP Score=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg Q2W OCA with CP Score=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	7.13 (± 315)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-6h Of Participants Who Received 5 mg QD OCA and With MELD Category=A

End point title	PK Population: AUC0-6h Of Participants Who Received 5 mg QD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	1170 (± 68.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-24h Of Participants Who Received 5 mg QD OCA and With MELD Category=A

End point title	PK Population: AUC0-24h Of Participants Who Received 5 mg QD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	5490 (± 60.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Cmax Of Participants Who Received 5 mg QD OCA and With MELD Category=A

End point title	PK Population: Cmax Of Participants Who Received 5 mg QD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	410 (± 37.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Tmax Of Participants Who Received 5 mg QD OCA and With MELD Category=A

End point title	PK Population: Tmax Of Participants Who Received 5 mg QD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received

5 mg QD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: hour				
median (full range (min-max))	6.0 (6.0 to 6.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Ctrough Of Participants Who Received 5 mg QD OCA and With MELD Category=A

End point title	PK Population: Ctrough Of Participants Who Received 5 mg QD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[12]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	174 (± 9999)			

Notes:

[12] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRAUC Of Participants Who Received 5 mg QD OCA and With MELD Category=A

End point title	PK Population: MRAUC Of Participants Who Received 5 mg QD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	13.7 (± 21.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRCmax Of Participants Who Received 5 mg QD OCA and With MELD Category=A

End point title	PK Population: MRCmax Of Participants Who Received 5 mg QD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	7.15 (± 32.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-6h Of Participants Who Received 5 mg QD OCA and With MELD Category=B

End point title	PK Population: AUC0-6h Of Participants Who Received 5 mg QD OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[13]			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	436 (± 9999)			

Notes:

[13] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-24h Of Participants Who Received 5 mg QD OCA and With MELD Category=B

End point title	PK Population: AUC0-24h Of Participants Who Received 5 mg QD OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[14]			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	2000 (± 9999)			

Notes:

[14] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Cmax Of Participants Who Received 5 mg QD OCA and With MELD Category=B

End point title	PK Population: Cmax Of Participants Who Received 5 mg QD OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[15]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	143 (± 9999)			

Notes:

[15] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Tmax Of Participants Who Received 5 mg QD OCA and With MELD Category=B

End point title	PK Population: Tmax Of Participants Who Received 5 mg QD OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: hour				
median (full range (min-max))	0.750 (0.750 to 0.750)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Ctrough Of Participants Who Received 5 mg QD OCA and With MELD Category=B

End point title	PK Population: Ctrough Of Participants Who Received 5 mg QD OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	176 (± 47.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRAUC Of Participants Who Received 5 mg QD OCA and With MELD Category=B

End point title	PK Population: MRAUC Of Participants Who Received 5 mg QD OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[16]			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	5.99 (± 9999)			

Notes:

[16] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRCmax Of Participants Who Received 5 mg QD OCA and With MELD Category=B

End point title	PK Population: MRCmax Of Participants Who Received 5 mg QD OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QD OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[17]			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	2.48 (± 9999)			

Notes:

[17] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-6h Of Participants Who Received 5 mg QOD OCA and With MELD Category=A

End point title	PK Population: AUC0-6h Of Participants Who Received 5 mg QOD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QOD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[18]			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	1480 (± 9999)			

Notes:

[18] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-24h Of Participants Who Received 5 mg QOD OCA and With MELD Category=A

End point title	PK Population: AUC0-24h Of Participants Who Received 5 mg QOD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QOD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[19]			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	9940 (± 9999)			

Notes:

[19] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Cmax Of Participants Who Received 5 mg QOD OCA and With MELD Category=A

End point title	PK Population: Cmax Of Participants Who Received 5 mg QOD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QOD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[20]			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	544 (± 9999)			

Notes:

[20] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Tmax Of Participants Who Received 5 mg QOD OCA and With MELD Category=A

End point title	PK Population: Tmax Of Participants Who Received 5 mg QOD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QOD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: hour				
median (full range (min-max))	6.0 (6.0 to 6.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Ctrough Of Participants Who Received 5 mg QOD OCA and With MELD Category=A

End point title	PK Population: Ctrough Of Participants Who Received 5 mg QOD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QOD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[21]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	396 (± 9999)			

Notes:

[21] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRAUC Of Participants Who Received 5 mg QOD OCA and With MELD Category=A

End point title	PK Population: MRAUC Of Participants Who Received 5 mg QOD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 5 mg QOD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[22]			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	26.6 (± 9999)			

Notes:

[22] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRCmax Of Participants Who Received 5 mg QOD OCA and With MELD Category=A

End point title	PK Population: MRCmax Of Participants Who Received 5 mg QOD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received

5 mg QOD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[23]			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	15.8 (± 9999)			

Notes:

[23] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-6h Of Participants Who Received 10 mg QD OCA and With MELD Category=A

End point title	PK Population: AUC0-6h Of Participants Who Received 10 mg QD OCA and With MELD Category=A

End point description:

PK Population: AUC0-6h Of Participants Who Received 10 mg QD OCA and With MELD Category=A

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	886 (± 55.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-24h Of Participants Who Received 10 mg QD OCA and With MELD Category=A

End point title	PK Population: AUC0-24h Of Participants Who Received 10 mg QD OCA and With MELD Category=A

End point description:	
On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with MELD Category=A.	
End point type	Secondary
End point timeframe:	
Month 9	

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	2860 (± 35.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Cmax Of Participants Who Received 10 mg QD OCA and With MELD Category=A

End point title	PK Population: Cmax Of Participants Who Received 10 mg QD OCA and With MELD Category=A
End point description:	
On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with MELD Category=A	
End point type	Secondary
End point timeframe:	
Month 9	

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	240 (± 35.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Tmax Of Participants Who Received 10 mg QD OCA and With MELD Category=A

End point title	PK Population: Tmax Of Participants Who Received 10 mg QD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: hour				
median (full range (min-max))	1.50 (1.50 to 3.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Ctrough Of Participants Who Received 10 mg QD OCA and With MELD Category=A

End point title	PK Population: Ctrough Of Participants Who Received 10 mg QD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	25.8 (± 188)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRAUC Of Participants Who Received 10 mg QD OCA and With MELD Category=A

End point title	PK Population: MRAUC Of Participants Who Received 10 mg QD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	6.04 (± 162)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRCmax Of Participants Who Received 10 mg QD OCA and With MELD Category=A

End point title	PK Population: MRCmax Of Participants Who Received 10 mg QD OCA and With MELD Category=A

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with MELD Category=A.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	1.92 (± 50.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-6h Of Participants Who Received 10 mg QD OCA and With MELD Category=B

End point title	PK Population: AUC0-6h Of Participants Who Received 10 mg QD OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	1610 (± 44.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-24h Of Participants Who Received 10 mg QD OCA and With MELD Category=B

End point title	PK Population: AUC0-24h Of Participants Who Received 10 mg QD OCA and With MELD Category=B

End point description:

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	5700 (± 48.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Cmax Of Participants Who Received 10 mg QD OCA and With MELD Category=B

End point title	PK Population: Cmax Of Participants Who Received 10 mg QD OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	403 (± 39.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Tmax Of Participants Who Received 10 mg QD OCA and With MELD Category=B

End point title	PK Population: Tmax Of Participants Who Received 10 mg QD OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: hours				
median (full range (min-max))	1.50 (0.750 to 2.50)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Ctrough Of Participants Who Received 10 mg QD OCA and With MELD Category=B

End point title	PK Population: Ctrough Of Participants Who Received 10 mg QD OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	136 (± 14.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRAUC Of Participants Who Received 10 mg QD OCA and With MELD Category=B

End point title	PK Population: MRAUC Of Participants Who Received 10 mg QD OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	6.73 (± 212)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRCmax Of Participants Who Received 10 mg QD OCA and With MELD Category=B

End point title	PK Population: MRCmax Of Participants Who Received 10 mg QD OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg QD OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	3.11 (± 147)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-6h Of Participants Who Received 10 mg Q2W OCA and With MELD Category=B

End point title	PK Population: AUC0-6h Of Participants Who Received 10 mg Q2W OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg Q2W OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	3770 (± 84.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: AUC0-24h Of Participants Who Received 10 mg Q2W OCA and With MELD Category=B

End point title	PK Population: AUC0-24h Of Participants Who Received 10 mg Q2W OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg Q2W OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	13900 (± 113)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Cmax Of Participants Who Received 10 mg Q2W OCA and With MELD Category=B

End point title	PK Population: Cmax Of Participants Who Received 10 mg Q2W OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg Q2W OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	916 (± 101)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Tmax Of Participants Who Received 10 mg Q2W OCA and With MELD Category=B

End point title	PK Population: Tmax Of Participants Who Received 10 mg Q2W OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg Q2W OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: hour				
median (full range (min-max))	4.0 (2.0 to 6.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Ctrough Of Participants Who Received 10 mg Q2W OCA and With MELD Category=B

End point title	PK Population: Ctrough Of Participants Who Received 10 mg Q2W OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg Q2W OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[24]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	566 (± 9999)			

Notes:

[24] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRAUC Of Participants Who Received 10 mg Q2W OCA and With MELD Category=B

End point title	PK Population: MRAUC Of Participants Who Received 10 mg Q2W OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg Q2W OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	12.6 (± 450)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: MRCmax Of Participants Who Received 10 mg Q2W OCA and With MELD Category=B

End point title	PK Population: MRCmax Of Participants Who Received 10 mg Q2W OCA and With MELD Category=B

End point description:

On Month 9, blood samples were collected at predose to 6 h for PK analysis in participants who received 10 mg Q2W OCA with MELD Category=B.

End point type	Secondary

End point timeframe:

Month 9

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: units on a scale				
geometric mean (geometric coefficient of variation)	7.13 (± 315)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Trough Concentrations Of Cirrhotic Participants Who Received 5 mg QD OCA

End point title	PK Population: Trough Concentrations Of Cirrhotic Participants Who Received 5 mg QD OCA

End point description:

The trough concentration of OCA in the cirrhotic participants who received 5 mg QD OCA was reported.

End point type	Secondary

End point timeframe:

Months 3, 6, 12, 24, and 48

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	149[25]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Month 3	295 (± 9999)			
Month 6	291 (± 166)			
Month 12	227 (± 127)			
Month 24	127 (± 9999)			
Month 48	849 (± 9999)			

Notes:

[25] - No variation was calculated for Months 3, 24, and 48.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Trough Concentrations Of Non-Cirrhotic Participants Who Received 5 mg QD OCA

End point title	PK Population: Trough Concentrations Of Non-Cirrhotic Participants Who Received 5 mg QD OCA

End point description:

The trough concentration of OCA in the non-cirrhotic participants who received 5 mg QD OCA was reported.

End point type	Secondary

End point timeframe:

Months 3, 6, 9, 12, and 24

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	149[26]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Month 3	77.4 (± 157)			
Month 6	55.9 (± 85.1)			
Month 9	127 (± 9999)			
Month 12	96.0 (± 94.7)			
Month 24	45.4 (± 693)			

Notes:

[26] - No variation was calculated on Month 9.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Trough Concentrations Of Cirrhotic Participants Who Received 5 mg QOD OCA

End point title	PK Population: Trough Concentrations Of Cirrhotic Participants Who Received 5 mg QOD OCA

End point description:

The trough concentration of OCA in the cirrhotic participants who received 5 mg QOD OCA was reported.

End point type	Secondary

End point timeframe:

Months 6, 12, and 24

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	149[27]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Month 6	1050 (± 9999)			
Month 12	48.0 (± 9999)			
Month 24	134 (± 17.1)			

Notes:

[27] - No variation was calculated on Months 6 and 12.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Trough Concentrations Of Non-Cirrhotic Participants Who Received 5 mg QOD OCA

End point title	PK Population: Trough Concentrations Of Non-Cirrhotic Participants Who Received 5 mg QOD OCA

End point description:

The trough concentration of OCA in the non-cirrhotic participants who received 5 mg QOD OCA was reported.

End point type	Secondary

End point timeframe:

Months 3, 6, and 12

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	149[28]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Month 3	97.2 (± 53.9)			
Month 6	85.4 (± 9999)			
Month 12	200 (± 184)			

Notes:

[28] - No variation was calculated on Month 6.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Trough Concentrations Of Cirrhotic Participants Who Received 5 mg QW OCA

End point title	PK Population: Trough Concentrations Of Cirrhotic Participants Who Received 5 mg QW OCA

End point description:

The trough concentration of OCA in the cirrhotic participants who received 5 mg QW OCA was reported.

End point type	Secondary

End point timeframe:

Months 6 and 12

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	149[29]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Month 6 Month 12	56.7 (± 9999) 116 (± 395)			

Notes:

[29] - No variation was calculated on Month 6.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Trough Concentrations Of Non-Cirrhotic Participants Who Received 5 mg QW OCA

End point title	PK Population: Trough Concentrations Of Non-Cirrhotic Participants Who Received 5 mg QW OCA

End point description:

At month 12, the trough concentration of OCA in the non-cirrhotic participants who received 5 QW QOD OCA was reported.

End point type	Secondary

End point timeframe:

Month 12

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[30]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	179 (± 9999)			

Notes:

[30] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Trough Concentrations Of Cirrhotic Participants Who Received 5 mg Q2W OCA

End point title	PK Population: Trough Concentrations Of Cirrhotic Participants Who Received 5 mg Q2W OCA

End point description:

At Month 6, the trough concentration of OCA in the cirrhotic participants who received 5 mg Q2W OCA was reported.

End point type	Secondary

End point timeframe:

Month 6

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[31]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	131 (± 9999)			

Notes:

[31] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Trough Concentrations Of Non-Cirrhotic Participants Who Received 5 mg Q2W OCA

End point title	PK Population: Trough Concentrations Of Non-Cirrhotic Participants Who Received 5 mg Q2W OCA

End point description:

The trough concentration of OCA in the non-cirrhotic participants who received 5 Q2W QOD OCA was reported.

End point type	Secondary

End point timeframe:

Months 3, 6, 12, 24, 36, and 48

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	149[32]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Month 3	86.0 (± 9999)			
Month 6	122 (± 9999)			
Month 12	250 (± 9999)			
Month 24	497 (± 9999)			
Month 36	117 (± 9999)			

Month 48	271 (± 9999)			

Notes:

[32] - No variation was calculated at all timepoints.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Trough Concentrations Of Cirrhotic Participants Who Received 10 mg QD OCA

End point title	PK Population: Trough Concentrations Of Cirrhotic Participants Who Received 10 mg QD OCA

End point description:

The trough concentration of OCA in the cirrhotic participants who received 10 mg QD OCA was reported.

End point type	Secondary

End point timeframe:

Months 6, 9, 12, 24, 36, and 60

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	149[33]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Month 6	142 (± 242)			
Month 9	7.74 (± 9999)			
Month 12	133 (± 489)			
Month 24	396 (± 61.7)			
Month 36	346 (± 9999)			
Month 60	290 (± 9999)			

Notes:

[33] - No variation was calculated on Months 9, 36, and 60.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Trough Concentrations Of Non-Cirrhotic Participants Who Received 10 mg QD OCA

End point title	PK Population: Trough Concentrations Of Non-Cirrhotic Participants Who Received 10 mg QD OCA

End point description:

The trough concentration of OCA in the non-cirrhotic participants who received 10 QD QOD OCA was reported.

End point type	Secondary

End point timeframe:

Months 6, 9, 12, 24, and 36

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	149			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Month 6	127 (± 601)			
Month 9	74.5 (± 10.6)			
Month 12	73.3 (± 102)			
Month 24	100 (± 216)			
Month 36	98.5 (± 1730)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Trough Concentrations Of Cirrhotic Participants Who Received 10 mg QOD OCA

End point title	PK Population: Trough Concentrations Of Cirrhotic Participants Who Received 10 mg QOD OCA

End point description:

The trough concentration of OCA in the Cirrhotic participants who received 10 mg QOD OCA was reported.

End point type	Secondary

End point timeframe:

Months 3, 6, 9, 12, 24, 36, 48, and 60

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	149[34]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	0 (± 0)			

Notes:

[34] - No participants was tested for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Trough Concentrations Of Non-Cirrhotic Participants Who Received 10 mg QOD OCA

End point title	PK Population: Trough Concentrations Of Non-Cirrhotic Participants Who Received 10 mg QOD OCA

End point description:

At Month 12, the trough concentration of OCA in the non-cirrhotic participants who received 10 mg OCA QOD was reported.

End point type	Secondary

End point timeframe:

Month 12

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[35]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	26.9 (± 9999)			

Notes:

[35] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Trough Concentrations Of Cirrhotic Participants Who Received 10 mg Q2W OCA

End point title	PK Population: Trough Concentrations Of Cirrhotic Participants Who Received 10 mg Q2W OCA

End point description:

At Month 6, the trough concentration of OCA in the cirrhotic participants who received 10 mg Q2W OCA was reported.

End point type	Secondary

End point timeframe:

Month 6

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[36]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	538 (± 9999)			

Notes:

[36] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Population: Trough Concentrations Of Non-Cirrhotic Participants Who Received 10 mg Q2W OCA

End point title	PK Population: Trough Concentrations Of Non-Cirrhotic Participants Who Received 10 mg Q2W OCA

End point description:

At Month 6, the trough concentration of OCA in the non-cirrhotic participants who received 10 mg Q2W OCA was reported.

End point type	Secondary

End point timeframe:

Month 6

End point values	Obeticholic Acid (PK)			
Subject group type	Subject analysis set			
Number of subjects analysed	1[37]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	566 (± 9999)			

Notes:

[37] - No variation was calculated.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline up to the last IP dose plus 30 days and prior to commercial OCA initiation date	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Obeticholic Acid
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Obeticholic Acid	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	53 / 168 (31.55%)	53 / 166 (31.93%)	
number of deaths (all causes)	5	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign ovarian tumour			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 168 (0.00%)	2 / 166 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Desmoid tumour			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	0 / 168 (0.00%)	2 / 166 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	

Lymphoma			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Oesophageal variceal ligation			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	2 / 168 (1.19%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	2 / 168 (1.19%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometriosis			

subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heavy menstrual bleeding			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	2 / 168 (1.19%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Asthma			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic hydrothorax			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			

subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal stenosis			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 168 (0.60%)	2 / 166 (1.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 168 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Investigations			
Blood bicarbonate decreased			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			

subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour marker increased			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight increased			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Acetabulum fracture			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 168 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured sacrum			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			

subjects affected / exposed	0 / 168 (0.00%)	2 / 166 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural bile leak			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pneumothorax			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural vomiting			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			

subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			

subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	2 / 168 (1.19%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	2 / 168 (1.19%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical cord compression			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Demyelination			

subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic encephalopathy			
subjects affected / exposed	3 / 168 (1.79%)	5 / 166 (3.01%)	
occurrences causally related to treatment / all	1 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorder			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraplegia			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Syncope			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			

subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	2 / 168 (1.19%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Uveitis			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 168 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ascites			
subjects affected / exposed	2 / 168 (1.19%)	4 / 166 (2.41%)	
occurrences causally related to treatment / all	1 / 3	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 168 (0.00%)	3 / 166 (1.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			

subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric vein thrombosis			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	4 / 168 (2.38%)	5 / 166 (3.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 168 (0.00%)	2 / 166 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 168 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varices oesophageal			
subjects affected / exposed	1 / 168 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			

subjects affected / exposed	0 / 168 (0.00%)	2 / 166 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder polyp			
subjects affected / exposed	1 / 168 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	2 / 168 (1.19%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	2 / 168 (1.19%)	2 / 166 (1.20%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice hepatocellular			

subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 168 (1.19%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 168 (1.19%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Secondary adrenocortical insufficiency			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin pain			

subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcopenia			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 168 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corynebacterium bacteraemia			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			

subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peritonitis bacterial			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 168 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 168 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 168 (1.19%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Spinal cord abscess			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			

subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	3 / 168 (1.79%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 168 (0.00%)	3 / 166 (1.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral pericarditis			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 168 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 168 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Obeticholic Acid	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	156 / 168 (92.86%)	146 / 166 (87.95%)	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	19 / 168 (11.31%)	25 / 166 (15.06%)	
occurrences (all)	27	31	
Vascular disorders			

Hypertension			
subjects affected / exposed	9 / 168 (5.36%)	7 / 166 (4.22%)	
occurrences (all)	11	10	
Nervous system disorders			
Headache			
subjects affected / exposed	23 / 168 (13.69%)	21 / 166 (12.65%)	
occurrences (all)	33	30	
Dizziness			
subjects affected / exposed	10 / 168 (5.95%)	14 / 166 (8.43%)	
occurrences (all)	12	16	
Hepatic encephalopathy			
subjects affected / exposed	7 / 168 (4.17%)	9 / 166 (5.42%)	
occurrences (all)	8	12	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	31 / 168 (18.45%)	18 / 166 (10.84%)	
occurrences (all)	44	28	
Fatigue			
subjects affected / exposed	18 / 168 (10.71%)	25 / 166 (15.06%)	
occurrences (all)	32	27	
Pyrexia			
subjects affected / exposed	12 / 168 (7.14%)	8 / 166 (4.82%)	
occurrences (all)	19	11	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	10 / 168 (5.95%)	13 / 166 (7.83%)	
occurrences (all)	13	13	
Splenomegaly			
subjects affected / exposed	3 / 168 (1.79%)	9 / 166 (5.42%)	
occurrences (all)	3	9	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	25 / 168 (14.88%)	12 / 166 (7.23%)	
occurrences (all)	36	17	
Nausea			

subjects affected / exposed	25 / 168 (14.88%)	21 / 166 (12.65%)	
occurrences (all)	28	28	
Abdominal pain			
subjects affected / exposed	21 / 168 (12.50%)	17 / 166 (10.24%)	
occurrences (all)	27	19	
Diarrhoea			
subjects affected / exposed	21 / 168 (12.50%)	26 / 166 (15.66%)	
occurrences (all)	40	33	
Varices oesophageal			
subjects affected / exposed	20 / 168 (11.90%)	27 / 166 (16.27%)	
occurrences (all)	30	29	
Constipation			
subjects affected / exposed	19 / 168 (11.31%)	10 / 166 (6.02%)	
occurrences (all)	20	11	
Ascites			
subjects affected / exposed	18 / 168 (10.71%)	20 / 166 (12.05%)	
occurrences (all)	29	30	
Abdominal distension			
subjects affected / exposed	15 / 168 (8.93%)	8 / 166 (4.82%)	
occurrences (all)	23	8	
Portal hypertensive gastropathy			
subjects affected / exposed	14 / 168 (8.33%)	7 / 166 (4.22%)	
occurrences (all)	15	7	
Vomiting			
subjects affected / exposed	14 / 168 (8.33%)	12 / 166 (7.23%)	
occurrences (all)	17	13	
Gastrooesophageal reflux disease			
subjects affected / exposed	11 / 168 (6.55%)	6 / 166 (3.61%)	
occurrences (all)	12	6	
Dyspepsia			
subjects affected / exposed	9 / 168 (5.36%)	8 / 166 (4.82%)	
occurrences (all)	9	9	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	15 / 168 (8.93%)	9 / 166 (5.42%)	
occurrences (all)	18	11	
Cough			
subjects affected / exposed	13 / 168 (7.74%)	6 / 166 (3.61%)	
occurrences (all)	19	8	
Oropharyngeal pain			
subjects affected / exposed	11 / 168 (6.55%)	3 / 166 (1.81%)	
occurrences (all)	13	3	
Hepatobiliary disorders			
Hepatic cirrhosis			
subjects affected / exposed	9 / 168 (5.36%)	8 / 166 (4.82%)	
occurrences (all)	9	8	
Jaundice			
subjects affected / exposed	8 / 168 (4.76%)	10 / 166 (6.02%)	
occurrences (all)	8	11	
Hyperbilirubinaemia			
subjects affected / exposed	4 / 168 (2.38%)	11 / 166 (6.63%)	
occurrences (all)	5	11	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	131 / 168 (77.98%)	85 / 166 (51.20%)	
occurrences (all)	358	139	
Rash			
subjects affected / exposed	10 / 168 (5.95%)	6 / 166 (3.61%)	
occurrences (all)	16	7	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	12 / 168 (7.14%)	16 / 166 (9.64%)	
occurrences (all)	13	16	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	23 / 168 (13.69%)	29 / 166 (17.47%)	
occurrences (all)	32	42	
Back pain			
subjects affected / exposed	12 / 168 (7.14%)	11 / 166 (6.63%)	
occurrences (all)	15	11	

Muscle spasms			
subjects affected / exposed	12 / 168 (7.14%)	5 / 166 (3.01%)	
occurrences (all)	14	5	
Pain in extremity			
subjects affected / exposed	9 / 168 (5.36%)	7 / 166 (4.22%)	
occurrences (all)	12	13	
Osteoporosis			
subjects affected / exposed	5 / 168 (2.98%)	11 / 166 (6.63%)	
occurrences (all)	6	12	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	20 / 168 (11.90%)	30 / 166 (18.07%)	
occurrences (all)	30	43	
Nasopharyngitis			
subjects affected / exposed	18 / 168 (10.71%)	14 / 166 (8.43%)	
occurrences (all)	31	16	
Upper respiratory tract infection			
subjects affected / exposed	14 / 168 (8.33%)	10 / 166 (6.02%)	
occurrences (all)	20	15	
Sinusitis			
subjects affected / exposed	11 / 168 (6.55%)	9 / 166 (5.42%)	
occurrences (all)	17	11	
Bronchitis			
subjects affected / exposed	10 / 168 (5.95%)	8 / 166 (4.82%)	
occurrences (all)	11	9	
Influenza			
subjects affected / exposed	9 / 168 (5.36%)	10 / 166 (6.02%)	
occurrences (all)	12	11	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 April 2015	The Protocol was amended to modify the dose titration schedule based on observed efficacy and tolerability of OCA, address advice provided by regulatory agencies, and clarify questions raised by study site personnel currently using original protocol version.
12 November 2015	The changes to Amendment 1 of the protocol generated specifically for regulatory authority requests, include an additional exclusion criteria and changes to text precluding UDCA naïve participants from entering the study and clarifying information showing that OCA may increase the exposure of narrow therapeutic index drugs that are substrates for CYP1A2, thus answering questions raised by regulatory authorities.
07 September 2016	The changes to amendment 3 of the protocol, included dosing adjustments based on Child-Pugh scoring, additional exclusion criteria, changes to text precluding UDCA-naïve participants from entering the study.
10 May 2017	Amendment 4 included the following major revision in the protocol: - HCC was redefined as a secondary endpoint - Added a commitment to enroll a minimum of 30% of participants with abnormal bilirubin - Incorporated clarifications throughout the protocol based on the addition of a biopsy substudy in Addendum 2 - Modified statistical language and added to clarify statistical assumptions and analyses including the addition of a PP Population - Updated the background rationale to reflect the current approval status of Ocaliva - Updated the safety language throughout the protocol to reflect the updating of Sponsor standards. - Added relevant references

04 January 2018	Amendment 5 included the following major revisions: - Revised the introduction to highlight the need for close monitoring specifically in participants with clinical evidence of hepatic decompensation and other complications due to advanced cirrhosis. Reference is made to sections describing specific criteria for investigational product adjustment, interruption, or discontinuation based on adverse events or laboratory values. This language also emphasizes the need for careful observation and evaluation of the entire clinical picture over and above system-generated alerts and flags for lab values. - Updated the dosing regimens to modify dosing to one regimen for participants with moderate and severe hepatic impairment (eg, same for CP-B and CP-C), not to exceed 10 mg twice weekly, to align with USPI dosing guidelines. Titration is now only based on tolerability and not CP score. - Updated the discontinuation criteria for decompensation events and biochemical thresholds. A plan for monitoring and drug-induced liver injury algorithm has been included to ensure careful monitoring and drug interruption/discontinuation. Analysis of decompensation events as adverse events of interest has been added. Additionally, "Close Observation" per FDA Guidance for Industry on Drug Induced Liver Injury has been clearly defined in the protocol to ensure that participants who experience a potential DILI undergo a full evaluation. - Added guidance that the participants should be instructed to contact the site promptly upon awareness if they develop signs and symptoms of potential hepatic decompensation. - Added guidance that the Investigator should contact the study Medical Monitor upon awareness when any signs and symptoms of hepatic decompensation are observed in any participant. - Added guidance for monitoring amylase and lipase levels in participants with diagnosed acute pancreatitis. - Added gallbladder assessments at Screening or Day 1.
05 November 2019	Amendment 6 included the following major revisions: - Updated contraception language to align with CTFG guidelines for highly effective methods - Updated the section on the total number of participants exposed to OCA as of 26 May 2019 - Updated the section on known potential risks of OCA - Updated the section on reporting adverse events to include instructions for reporting SUSARs - Included various options for retaining participants in the study and emphasized the critical importance of collecting clinical outcomes data - Provided guidance for Investigators on the importance of documenting specific reasons in the EDC for participants who discontinue treatment and/or the study, especially for participants who discontinue due to adverse events - Provided guidance for Investigators on study procedures for subjects who reconsent to participate in the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The estimated effect of treatment from the ITT population was underpowered and potentially biased, resulting in difficulties in the interpretation of the tests of hypotheses for the primary and key secondary endpoints.

Notes: