Clinical trial results:
A Phase 4, Double-Blind, Randomized, Placebo-Controlled Study Evaluating the Pharmacokinetics and Safety of Obeticholic Acid in Patients with Primary Biliary Cholangitis and Moderate to Severe Hepatic Impairment

Summary

EudraCT number	2017-001762-13
Trial protocol	ES DE BE HU EE LT IT
Global end of trial date	09 July 2021

Results information

Result version number	v1 (current)
This version publication date	24 July 2022
First version publication date	24 July 2022

Trial information

Trial identification

Sponsor protocol code	747-401

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03633227
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Intercept Pharmaceuticals, Inc.
Sponsor organisation address	305 Madison Avenue, Morristown, NJ, United States, 07960
Public contact	Medical Information, Intercept Pharmaceuticals, Inc., +1 844-782-4278, medinfo@interceptpharma.com
Scientific contact	Medical Information, Intercept Pharmaceuticals, Inc., +1 844-782-4278, 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	20 June 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 July 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the pharmacokinetics (PK) of Obeticholic acid (OCA) and its conjugates, glycine 6α-ethyl chenodeoxycholic acid (glyco-OCA) and taurine 6α-ethyl chenodeoxycholic acid (tauro-OCA), and OCA metabolite glucuronide (OCA-glucuronide) compared with placebo. To evaluate the safety and tolerability of OCA treatment compared with placebo.

Protection of trial subjects:

The study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Council for Harmonisation (ICH)/Good Clinical Practice (GCP), applicable regulatory requirements and the Sponsor’s policies.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 June 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Estonia: 1
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Lithuania: 2
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Brazil: 2
Country: Number of subjects enrolled	Argentina: 4
Worldwide total number of subjects	22
EEA total number of subjects	7

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)	12
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at study sites in the United States, Argentina, Belgium, Spain, Lithuania, Brazil, Australia, Germany, Estonia, Italy, Canada, and Hungary.

Pre-assignment

Screening details:

A total of 31 participants were screened and 22 participants were randomized.

Period 1

Period 1 title	Double Blind (DB), up to Week 48
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	Placebo

Arm description:

Participants received OCA matching placebo tablets orally once weekly or twice weekly for the duration of at least 48 Weeks.

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

Dosage and administration details:

OCA matching placebo was administered per schedule specified in the arm description.

Arm title	Obeticholic Acid (OCA)

Arm description:

Participants initiated treatment with OCA 5 milligrams (mg) tablets orally once weekly. At Week 12, if there were no safety concerns, the dose was up-titrated to OCA 5 mg twice weekly. Every 6 weeks thereafter, based on tolerability assessments, further up-titration of dose was considered. At each titration visit, the participants started the higher dose regimen no earlier than 2 days after the prior dose. The maximum dose titration was OCA 10 mg twice weekly at least 3 days apart. The minimum treatment duration was 48 Weeks.

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

Dosage and administration details:

OCA was administered per dose and schedule specified in the arm description.

Number of subjects in period 1	Placebo	Obeticholic Acid (OCA)
Started	12	10
Completed	4	6
Not completed	8	4
Physician decision	1	-
Consent withdrawn by subject	1	1
Adverse event, non-fatal	-	1
Death	2	1
Multiple Serious AE and Drug Interruptions	1	-
Study Terminated by Sponsor	2	1
Liver Transplant During the Course of the Study	1	-

Period 2

Period 2 title	DB Extension, Week 48 up to 3 Years
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants, who had completed their 48-week treatment, could continue the treatment until all randomized participants had completed their 48-week treatment period and the database for that period was locked (total duration: approximately up to 3 years).

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:

OCA matching placebo was administered per the schedule specified in the arm description.

Arm title	Obeticholic Acid (OCA)

Arm description:

Participants, who had completed their 48-week treatment, could continue the treatment until all randomized participants had completed their 48-week treatment period and the database for that period was locked (total duration: approximately up to 3 years).

Arm type	Experimental

Investigational medicinal product name	Obeticholic Acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

OCA was administered per dose and schedule specified in the arm description.

Number of subjects in period 2	Placebo	Obeticholic Acid (OCA)
Started	4	6
Completed	0	0
Not completed	4	6
Consent withdrawn by subject	-	2
Physician decision	-	1
Death	-	1
Study Terminated by Sponsor	3	2
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received OCA matching placebo tablets orally once weekly or twice weekly for the duration of at least 48 Weeks.	
Reporting group title	Obeticholic Acid (OCA)
Reporting group description:	
Participants initiated treatment with OCA 5 milligrams (mg) tablets orally once weekly. At Week 12, if there were no safety concerns, the dose was up-titrated to OCA 5 mg twice weekly. Every 6 weeks thereafter, based on tolerability assessments, further up-titration of dose was considered. At each titration visit, the participants started the higher dose regimen no earlier than 2 days after the prior dose. The maximum dose titration was OCA 10 mg twice weekly at least 3 days apart. The minimum treatment duration was 48 Weeks.	

Reporting group values	Placebo	Obeticholic Acid (OCA)	Total
Number of subjects	12	10	22
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	62.5	60.5	
standard deviation	± 9.10	± 10.19	-
Gender categorical Units: Subjects			
Female	10	6	16
Male	2	4	6
Ethnicity Units: Subjects			
Hispanic or Latino	6	4	10
Not Hispanic or Latino	6	6	12
Unknown or Not Reported	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	11	10	21
Child-Pugh Score Component Category (Ascites Categories)			
Number of participants with Child-Pugh component - ascites categories of none, mild, and moderate-severe has been reported. The assessment of ascites was based on the investigator's discretion.			
Units: Subjects			
None	6	5	11
Mild	5	3	8
Moderate to Severe	1	2	3
Child-Pugh Score Component Category			

(Prothrombin Time Categories)			
Number of participants with Child-Pugh component - prothrombin time (measured as INR) in categories of <1.7, 1.7 - 2.3, and >2.3 has been reported.			
Units: Subjects			
<1.7	12	10	22
1.7-2.3	0	0	0
>2.3	0	0	0
Child-Pugh Score Component Category (Serum Albumin Categories)			
Number of participants with Child-Pugh component - serum albumin levels in categories of >35 gram per liter (g/L), 28-35 g/L, or <28 g/L has been reported.			
Units: Subjects			
>35 gram per liter (g/L)	3	4	7
28 - 35 g/L	8	5	13
<28 g/L	1	1	2
Child-Pugh Score Component Category (Total Bilirubin Categories)			
Number of participants with Child-Pugh component - total bilirubin levels in categories of <34 micromole per liter (µmol/L), 34-50 µmol/L, and >50 µmol/L has been reported.			
Units: Subjects			
<34 micromole per liter (µmol/L)	3	5	8
34-50 µmol/L	5	0	5
>50 µmol/L	4	5	9
Child-Pugh Score Component Category (Hepatic Encephalopathy Categories)			
Grade 0: normal consciousness, normal personality, normal neurological examination, normal electroencephalogram. Grade 1: restless, sleep disturbed, irritable/agitated, tremor, impaired handwriting, 5 cycles, per second (cps) waves. Grade 2: lethargic, time-disoriented, inappropriate, asterixis, ataxia, slow triphasic waves. Grade 3: somnolent, stuporous, place-disoriented, hyperactive reflexes, rigidity, slower waves. Grade 4: unrousable coma, no personality/behavior, decerebrate, slow 2-3 cps delta activity.			
Units: Subjects			
Grade 0	7	7	14
Grade 1 or 2	5	3	8
Grade 3 or 4	0	0	0
Model of End-stage Liver Disease (MELD) Score			
The MELD scoring system is used to assess the severity of chronic liver disease. The MELD score is derived from the participant's serum total bilirubin, serum creatinine, and prothrombin international normalized ratio (INR): 3.78×log normal (ln) [total bilirubin (mg/deciliter [dL])] + 11.2×ln[INR] + 9.57×ln[serum creatinine (mg/dL)] + 6.43. The MELD score ranges from 6 to 40 with higher scores indicating more severe liver disease and a worse outcome.			
Units: Score on a scale			
median	11.75	12.75	
inter-quartile range (Q1-Q3)	10.60 to 13.50	9.50 to 16.00	-
MELD-Sodium (Na) Score			
The MELD-Na scoring system is used to assess the severity of chronic liver disease in the participants with an initial MELD(i) score greater than 11. MELD-Na score is derived from the participant's serum total bilirubin, serum creatinine, INR, and sodium. The MELD-Na score is re-calculated as follows: MELD-Na = MELD(i) + 1.32*(137-Na) – [0.033*MELD(i)*(137-Na)]. MELD score ranges from 6-40 with higher scores indicating more severe liver disease and a worse outcome.			
Units: score on a scale			
median	11.75	13.25	
inter-quartile range (Q1-Q3)	10.60 to 14.25	9.50 to 16.00	-
Child-Pugh Score			
The Child-Pugh classification was a scoring system used for the classification of the severity of cirrhosis. It included three continuous variables (bilirubin, albumin, and INR) and two discrete variables (ascites			

and encephalopathy). Each variable was scored 1-3 with 3 indicating most severe derangement. The determination of Child-Pugh score ranged from 5 to 15. The higher the score, the sicker the participant.			
Units: score on a scale			
median	8.0	8.0	
inter-quartile range (Q1-Q3)	7.0 to 8.0	7.0 to 8.0	-
Total Bilirubin			
Units: µmol/L			
median	45.38	41.50	
inter-quartile range (Q1-Q3)	34.57 to 55.79	19.00 to 106.88	-
Direct Bilirubin			
Units: µmol/L			
median	21.58	25.50	
inter-quartile range (Q1-Q3)	15.37 to 37.18	8.00 to 76.00	-
Alkaline Phosphatase			
Units: unit per liter (U/L)			
median	216.0	267.5	
inter-quartile range (Q1-Q3)	144.5 to 290.0	151.0 to 381.0	-
Alanine Aminotransferase			
Units: U/L			
median	47.5	38.0	
inter-quartile range (Q1-Q3)	31.0 to 60.5	27.0 to 56.0	-
Aspartate Aminotransferase			
Units: U/L			
median	60.0	65.5	
inter-quartile range (Q1-Q3)	45.5 to 95.5	46.0 to 104.0	-
Gamma Glutamyl Transferase			
Units: U/L			
median	98.0	103.0	
inter-quartile range (Q1-Q3)	36.0 to 152.0	53.0 to 191.0	-
Prothrombin INR			
Units: INR			
median	1.15	1.23	
inter-quartile range (Q1-Q3)	1.10 to 1.20	1.10 to 1.30	-
Creatinine			
Units: µmol/L			
median	60.000	60.172	
inter-quartile range (Q1-Q3)	51.000 to 96.732	55.000 to 95.472	-
Albumin			
Units: gram per liter (g/L)			
median	34.50	33.00	
inter-quartile range (Q1-Q3)	33.00 to 36.75	30.00 to 36.50	-
Platelets			
Number analyzed (n) for Placebo arm = 11 Number analyzed (n) for OCA arm = 9			
Units: 10^9/L			
median	141.5	132.5	
inter-quartile range (Q1-Q3)	80.0 to 160.5	84.5 to 158.5	-
Total Bile Acids Concentration			
Total bile acids (micromole [µM]) = total ursodeoxycholic acid (unconjugated, glyco-conjugate, tauro-conjugate) in µM + total chenodeoxycholic acid (unconjugated, glyco-conjugate, tauro-conjugate) in µM + total deoxycholic acid (unconjugated, glyco-conjugate, tauro-conjugate) in µM + total cholic acid (unconjugated, glyco-conjugate, tauro-conjugate) in µM + total lithocholic acid (unconjugated, glyco-conjugate, tauro-conjugate) in µM.			

Number analyzed (n) for Placebo arm = 11			
Units: µM			
median	149	127	
inter-quartile range (Q1-Q3)	90.3 to 307	65.3 to 176	-
Total Endogenous Bile Acids Concentration			
Number analyzed (n) for Placebo arm = 11			
Units: µM			
median	64.7	42.1	
inter-quartile range (Q1-Q3)	29.4 to 75.2	18.6 to 69.6	-
7α-hydroxy-4-cholesten-3-one (C4)			
Number analyzed (n) for Placebo arm = 11			
Units: ng/mL			
median	0.708	0.814	
inter-quartile range (Q1-Q3)	0.372 to 5.16	0.472 to 2.09	-
Fibroblast Growth Factor-19 (FGF-19)			
Number analyzed (n) for Placebo arm = 11			
Units: picograms per milliliter (pg/mL)			
median	278	163	
inter-quartile range (Q1-Q3)	105 to 618	139 to 359	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received OCA matching placebo tablets orally once weekly or twice weekly for the duration of at least 48 Weeks.	
Reporting group title	Obeticholic Acid (OCA)
Reporting group description:	
Participants initiated treatment with OCA 5 milligrams (mg) tablets orally once weekly. At Week 12, if there were no safety concerns, the dose was up-titrated to OCA 5 mg twice weekly. Every 6 weeks thereafter, based on tolerability assessments, further up-titration of dose was considered. At each titration visit, the participants started the higher dose regimen no earlier than 2 days after the prior dose. The maximum dose titration was OCA 10 mg twice weekly at least 3 days apart. The minimum treatment duration was 48 Weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants, who had completed their 48-week treatment, could continue the treatment until all randomized participants had completed their 48-week treatment period and the database for that period was locked (total duration: approximately up to 3 years).	
Reporting group title	Obeticholic Acid (OCA)
Reporting group description:	
Participants, who had completed their 48-week treatment, could continue the treatment until all randomized participants had completed their 48-week treatment period and the database for that period was locked (total duration: approximately up to 3 years).	
Subject analysis set title	OCA 5 mg Once Weekly
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received OCA 5 mg tablets orally once weekly.	
Subject analysis set title	OCA 5 mg Twice Weekly
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received OCA 5 mg tablets orally twice weekly.	
Subject analysis set title	OCA 10 mg Twice Weekly
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received OCA 10 mg tablets orally twice weekly.	
Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants received OCA matching placebo tablets orally once weekly or twice weekly for the duration of at least 48 Weeks. Participants, who had completed their 48-Week treatment, could continue the treatment until all randomized participants had completed their 48-Week treatment period and the database for that period was locked (total duration: approximately up to 3 years).	
Subject analysis set title	Obeticholic Acid (OCA)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants initiated treatment with OCA 5 mg tablets orally once weekly. At Week 12, if there were no safety concerns, the dose was up-titrated to OCA 5 mg twice weekly. Every 6 weeks thereafter, based on tolerability assessments, further up-titration of dose was considered. At each titration visit, the participants started the higher dose regimen no earlier than 2 days after the prior dose. The maximum dose titration was OCA 10 mg twice weekly at least 3 days apart. The minimum treatment duration was 48 Weeks. Participants, who had completed their 48-Week treatment, could continue the treatment until all randomized participants had completed their 48-Week treatment period and the database for that period was locked (total duration: approximately up to 3 years).	

Primary: Maximum Observed Concentration (Cmax) of Total OCA at Week 12

End point title	Maximum Observed Concentration (Cmax) of Total OCA at Week 12[1]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA.

Analysis population description (APD): PK Population: participants who received OCA and had adequate concentration-time profile to characterize OCA and its conjugates and must not have had any major protocol deviations that potentially affect exposure level. Results of PK were planned to be listed by dose regimen. Participants who received planned dose regimen and had available data were included. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	0[2]	0[3]	
Units: Nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	293 (± 189)	()	()	

Notes:

[2] - No participant started OCA 5 mg twice weekly at Week 12.

[3] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Time to Maximum Concentration (Tmax) of Total OCA at Week 12

End point title	Time to Maximum Concentration (Tmax) of Total OCA at Week 12[4]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	0[5]	0[6]	
Units: hours				
median (full range (min-max))	2.02 (2.00 to 3.00)	(to)	(to)	

Notes:

[5] - No participant started OCA 5 mg twice weekly at Week 12.

[6] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Trough Concentration (Ctrough) of Total OCA at Week 12

End point title	Trough Concentration (Ctrough) of Total OCA at Week 12[7]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 12. Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 12

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	0[8]	0[9]	
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	77.6 (± 49.7)	()	()	

Notes:

[8] - No participant started OCA 5 mg twice weekly at week 12.

[9] - No participant started OCA 10 mg twice weekly at week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration Versus Time Curve From Zero Time to 24 Hours (AUC0-24h) of Total OCA at Week 12

End point title	Area Under the Concentration Versus Time Curve From Zero Time to 24 Hours (AUC0-24h) of Total OCA at Week 12[10]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA. AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5

mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	0[11]	0[12]	
Units: ng*h/mL				
arithmetic mean (standard deviation)	2970 (± 1650)	()	()	

Notes:

[11] - No participant started OCA 5 mg twice weekly at Week 12.

[12] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Total OCA at Week 18

End point title	Cmax of Total OCA at Week 18[13]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[14]	
Units: ng/mL				
arithmetic mean (standard deviation)	136 (± 77.6)	406 (± 120)	()	

Notes:

[14] - No participant started OCA 10 mg twice weekly at Week 18.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Total OCA at Week 18

End point title	Tmax of Total OCA at Week 18[15]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[16]	
Units: hours				
median (full range (min-max))	0.750 (0.500 to 1.00)	2.52 (2.00 to 3.03)	(to)	

Notes:

[16] - No participant started OCA 10 mg twice weekly at Week 18.

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Total OCA at Week 18

End point title	Ctrough of Total OCA at Week 18[17]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 18. Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 18

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[18]	
Units: ng/mL				
arithmetic mean (standard deviation)	28.7 (± 13.6)	187 (± 147)	()	

Notes:

[18] - No participant started OCA 10 mg twice weekly at Week 18.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Total OCA at Week 18

End point title	AUC0-24h of Total OCA at Week 18[19]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA. AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[20]	
Units: ng*h/mL				
arithmetic mean (standard deviation)	1380 (± 776)	5810 (± 3600)	()	

Notes:

[20] - No participant started OCA 10 mg twice weekly at Week 18.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Total OCA at Week 24

End point title	Cmax of Total OCA at Week 24[21]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA and tauro-OCA.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[22]	2	
Units: ng/mL				
arithmetic mean (standard deviation)	263 (± 261)	195 (± 99999)	622 (± 117)	

Notes:

[22] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Total OCA at Week 24

End point title	Tmax of Total OCA at Week 24[23]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1	2	
Units: hours				
median (full range (min-max))	5.04 (4.00 to 6.08)	0.750 (0.750 to 0.750)	2.27 (2.00 to 2.53)	

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Total OCA at Week 24

End point title	Ctrough of Total OCA at Week 24[24]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 24. Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 24

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[25]	2	
Units: ng/mL				
arithmetic mean (standard deviation)	132 (± 163)	41.4 (± 99999)	435 (± 28.6)	

Notes:

[25] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Total OCA at Week 24

End point title	AUC0-24h of Total OCA at Week 24[26]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA. AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[27]	2	
Units: ng*h/mL				
arithmetic mean (standard deviation)	4500 (± 4910)	2020 (± 99999)	11300 (± 2950)	

Notes:

[27] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Total OCA at Week 30

End point title	Cmax of Total OCA at Week 30[28]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[28] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[29]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	125 (± 99999)	277 (± 64.7)	674 (± 310)	

Notes:

[29] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Total OCA at Week 30

End point title	Tmax of Total OCA at Week 30[30]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[30] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1	2	2	
Units: hours				
median (full range (min-max))	1.00 (1.00 to 1.00)	4.52 (4.03 to 5.00)	3.77 (2.53 to 5.00)	

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Total OCA at Week 30

End point title	Ctrough of Total OCA at Week 30[31]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 30. Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 30

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[32]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	22.3 (± 99999)	217 (± 15.7)	317 (± 248)	

Notes:

[32] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Total OCA at Week 30

End point title	AUC0-24h of Total OCA at Week 30[33]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA. AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[34]	2	2	
Units: ng*h/mL				
arithmetic mean (standard deviation)	1260 (± 99999)	5040 (± 855)	10500 (± 7000)	

Notes:

[34] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Total OCA at Week 48

End point title	Cmax of Total OCA at Week 48[35]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[35] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[36]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	()	200 (± 15.1)	728 (± 27.5)	

Notes:

[36] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Total OCA at Week 48

End point title	Tmax of Total OCA at Week 48[37]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[37] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[38]	2	2	
Units: hours				
median (full range (min-max))	(to)	1.73 (1.47 to 2.00)	4.03 (2.00 to 6.05)	

Notes:

[38] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Total OCA at Week 48

End point title	Ctrough of Total OCA at Week 48[39]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 48. Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 48

Notes:

[39] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[40]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	()	88.3 (± 29.9)	497 (± 135)	

Notes:

[40] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Total OCA at Week 48

End point title	AUC0-24h of Total OCA at Week 48[41]

End point description:

Total OCA is molar sum of unconjugated OCA, glyco-OCA, and tauro-OCA. AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[41] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[42]	2	2	
Units: ng*h/mL				
arithmetic mean (standard deviation)	()	3210 (± 56.7)	13900 (± 452)	

Notes:

[42] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Unconjugated OCA at Week 12

End point title	Cmax of Unconjugated OCA at Week 12[43]

End point description:

APD: Results of PK were planned to be listed by dose regimen. Participants who received planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[43] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	0[44]	0[45]	
Units: ng/mL				
arithmetic mean (standard deviation)	107 (± 62.0)	()	()	

Notes:

[44] - No participant started OCA 5 mg twice weekly at Week 12.

[45] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Unconjugated OCA at Week 12

End point title	Tmax of Unconjugated OCA at Week 12[46]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[46] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	0[47]	0[48]	
Units: hours				
median (full range (min-max))	1.43 (1.00 to 1.50)	(to)	(to)	

Notes:

[47] - No participant started OCA 5 mg twice weekly at Week 12.

[48] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Unconjugated OCA at Week 12

End point title	Ctrough of Unconjugated OCA at Week 12[49]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 12.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 12

Notes:

[49] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	0[50]	0[51]	
Units: ng/mL				
arithmetic mean (standard deviation)	2.92 (± 2.51)	()	()	

Notes:

[50] - No participant started OCA 5 mg twice weekly at Week 12.

[51] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Unconjugated OCA at Week 12

End point title	AUC0-24h of Unconjugated OCA at Week 12[52]

End point description:

AUC0-24 was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[52] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	0[53]	0[54]	
Units: ng*h/mL				
arithmetic mean (standard deviation)	278 (± 142)	()	()	

Notes:

[53] - No participant started OCA 5 mg twice weekly at Week 12.

[54] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Unconjugated OCA at Week 18

End point title	Cmax of Unconjugated OCA at Week 18[55]

End point description:

Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[55] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[56]	
Units: ng/mL				
arithmetic mean (standard deviation)	107 (± 47.4)	109 (± 90.3)	()	

Notes:

[56] - No participant started OCA 10 mg twice weekly at Week 18.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Unconjugated OCA at Week 18

End point title	Tmax of Unconjugated OCA at Week 18[57]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[57] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[58]	
Units: hours				
median (full range (min-max))	0.750 (0.500 to 1.00)	1.24 (1.00 to 1.48)	(to)	

Notes:

[58] - No participant started OCA 10 mg twice weekly at Week 18.

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Unconjugated OCA at Week 18

End point title	Ctrough of Unconjugated OCA at Week 18[59]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 18.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 18

Notes:

[59] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[60]	
Units: ng/mL				
arithmetic mean (standard deviation)	3.38 (± 0.262)	3.56 (± 4.01)	()	

Notes:

[60] - No participant started OCA 10 mg twice weekly at Week 18.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Unconjugated OCA at Week 18

End point title	AUC0-24h of Unconjugated OCA at Week 18[61]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[61] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[62]	
Units: ng*h/mL				
arithmetic mean (standard deviation)	191 (± 125)	263 (± 247)	()	

Notes:

[62] - No participant started OCA 10 mg twice weekly at Week 18.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Unconjugated OCA at Week 24

End point title	Cmax of Unconjugated OCA at Week 24[63]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[63] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[64]	2	
Units: ng/mL				
arithmetic mean (standard deviation)	115 (± 98.2)	157 (± 99999)	168 (± 92.6)	

Notes:

[64] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Unconjugated OCA at Week 24

End point title	Tmax of Unconjugated OCA at Week 24[65]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[65] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1	2	
Units: hours				
median (full range (min-max))	1.13 (0.750 to 1.50)	0.500 (0.500 to 0.500)	1.63 (1.58 to 1.67)	

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Unconjugated OCA at Week 24

End point title	Ctrough of Unconjugated OCA at Week 24[66]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 24.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 24

Notes:

[66] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[67]	2	
Units: ng/mL				
arithmetic mean (standard deviation)	2.46 (± 2.05)	5.18 (± 99999)	8.77 (± 11.4)	

Notes:

[67] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Unconjugated OCA at Week 24

End point title	AUC0-24h of Unconjugated OCA at Week 24[68]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[68] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[69]	2	
Units: ng*h/mL				
arithmetic mean (standard deviation)	235 (± 130)	345 (± 99999)	480 (± 414)	

Notes:

[69] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Unconjugated OCA at Week 30

End point title	Cmax of Unconjugated OCA at Week 30[70]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[70] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[71]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	92.6 (± 99999)	132 (± 24.0)	115 (± 40.9)	

Notes:

[71] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Unconjugated OCA at Week 30

End point title	Tmax of Unconjugated OCA at Week 30[72]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24

hours post-dose at Week 30

Notes:

[72] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1	2	2	
Units: hours				
median (full range (min-max))	0.750 (0.750 to 0.750)	1.17 (1.00 to 1.33)	1.75 (0.500 to 3.00)	

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Unconjugated OCA at Week 30

End point title	Ctrough of Unconjugated OCA at Week 30[73]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 30.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 30

Notes:

[73] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[74]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	3.03 (± 99999)	4.27 (± 4.85)	3.20 (± 3.14)	

Notes:

[74] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Unconjugated OCA at Week 30

End point title	AUC0-24h of Unconjugated OCA at Week 30[75]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who

received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[75] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[76]	2	2	
Units: ng*h/mL				
arithmetic mean (standard deviation)	176 (± 99999)	304 (± 82.3)	473 (± 397)	

Notes:

[76] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Unconjugated OCA at Week 48

End point title	Cmax of Unconjugated OCA at Week 48[77]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[77] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[78]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	()	131 (± 31.8)	284 (± 177)	

Notes:

[78] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Unconjugated OCA at Week 48

End point title	Tmax of Unconjugated OCA at Week 48[79]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[79] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[80]	2	2	
Units: hours				
median (full range (min-max))	(to)	1.10 (0.700 to 1.50)	0.500 (0.500 to 0.500)	

Notes:

[80] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Unconjugated OCA at Week 48

End point title	Ctrough of Unconjugated OCA at Week 48[81]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 48.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 48

Notes:

[81] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[82]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	()	3.43 (± 3.90)	4.72 (± 6.67)	

Notes:

[82] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Unconjugated OCA at Week 48

End point title	AUC0-24h of Unconjugated OCA at Week 48[83]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[83] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[84]	2	1[85]	
Units: ng*h/mL				
arithmetic mean (standard deviation)	()	376 (± 118)	1190 (± 99999)	

Notes:

[84] - No participant received OCA 5 mg once weekly at Week 48.

[85] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Glyco-OCA at Week 12

End point title	Cmax of Glyco-OCA at Week 12[86]

End point description:

APD: Results of PK were planned to be listed by dose regimen. Participants who received planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[86] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	0[87]	0[88]	
Units: ng/mL				
arithmetic mean (standard deviation)	117 (± 55.0)	()	()	

Notes:

[87] - No participant started OCA 5 mg twice weekly at Week 12.

[88] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Glyco-OCA at Week 12

End point title	Tmax of Glyco-OCA at Week 12[89]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[89] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	0[90]	0[91]	
Units: hours				
median (full range (min-max))	5.00 (3.92 to 5.00)	(to)	(to)	

Notes:

[90] - No participant started OCA 5 mg twice weekly at Week 12.

[91] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Glyco-OCA at Week 12

End point title	Ctrough of Glyco-OCA at Week 12[92]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 12.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 12

Notes:

[92] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	0[93]	0[94]	
Units: ng/mL				
arithmetic mean (standard deviation)	47.1 (± 31.1)	()	()	

Notes:

[93] - No participant started OCA 5 mg twice weekly at Week 12.

[94] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Glyco-OCA at Week 12

End point title	AUC0-24h of Glyco-OCA at Week 12[95]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[95] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	0[96]	0[97]	
Units: ng*h/mL				
arithmetic mean (standard deviation)	1690 (± 947)	()	()	

Notes:

[96] - No participant started OCA 5 mg twice weekly at Week 12.

[97] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Metabolite to Parent Ratio of AUC-0-24h (MRAUC) of Glyco-OCA at Week 12

End point title	Metabolite to Parent Ratio of AUC-0-24h (MRAUC) of Glyco-OCA at Week 12[98]

End point description:

MRAUC was the ratio of AUC0-24h of Glyco-OCA (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Glyco-OCA, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[98] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	0[99]	0[100]	
Units: ratio				
arithmetic mean (standard deviation)	4.36 (± 1.03)	()	()	

Notes:

[99] - No participant started OCA 5 mg twice weekly at Week 12.

[100] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Metabolite to Parent Ratio of Cmax (MRCmax) of Glyco-OCA at Week 12

End point title	Metabolite to Parent Ratio of Cmax (MRCmax) of Glyco-OCA at Week 12[101]

End point description:

MRCmax was the ratio of Cmax of Glyco-OCA (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Glyco-OCA, where Cmax is the maximum observed concentration.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[101] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	0[102]	0[103]	
Units: ratio				
arithmetic mean (standard deviation)	1.39 (± 1.38)	()	()	

Notes:

[102] - No participant started OCA 5 mg twice weekly at Week 12.

[103] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Glyco-OCA at Week 18

End point title	Cmax of Glyco-OCA at Week 18[104]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[104] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[105]	
Units: ng/mL				
arithmetic mean (standard deviation)	52.7 (± 4.31)	213 (± 22.6)	()	

Notes:

[105] - No participant started OCA 10 mg twice weekly at Week 18.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Glyco-OCA at Week 18

End point title	Tmax of Glyco-OCA at Week 18[106]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[106] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[107]	
Units: hours				
median (full range (min-max))	4.25 (2.50 to 6.00)	2.52 (2.00 to 3.03)	(to)	

Notes:

[107] - No participant started OCA 10 mg twice weekly at Week 18.

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Glyco-OCA at Week 18

End point title	Ctrough of Glyco-OCA at Week 18[108]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 18.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 18

Notes:

[108] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[109]	
Units: ng/mL				
arithmetic mean (standard deviation)	13.3 (± 5.03)	98.1 (± 53.7)	()	

Notes:

[109] - No participant started OCA 10 mg twice weekly at Week 18.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Glyco-OCA at Week 18

End point title	AUC0-24h of Glyco-OCA at Week 18[110]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who

received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[110] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[111]	
Units: ng*h/mL				
arithmetic mean (standard deviation)	625 (± 147)	3020 (± 1120)	()	

Notes:

[111] - No participant started OCA 10 mg twice weekly at Week 18.

Statistical analyses

No statistical analyses for this end point

Primary: MRAUC of Glyco-OCA at Week 18

End point title	MRAUC of Glyco-OCA at Week 18[112]

End point description:

MRAUC was the ratio of AUC0-24h of Glyco-OCA (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Glyco-OCA, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[112] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[113]	
Units: ratio				
arithmetic mean (standard deviation)	3.39 (± 1.55)	21.2 (± 23.6)	()	

Notes:

[113] - No participant started OCA 10 mg twice weekly at Week 18.

Statistical analyses

No statistical analyses for this end point

Primary: MRCmax of Glyco-OCA at Week 18

End point title	MRCmax of Glyco-OCA at Week 18[114]

End point description:

MRCmax was the ratio of Cmax of Glyco-OCA (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Glyco-OCA, where Cmax is the maximum observed concentration.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[114] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[115]	
Units: ratio				
arithmetic mean (standard deviation)	0.487 (± 0.250)	2.73 (± 2.44)	()	

Notes:

[115] - No participant started OCA 10 mg twice weekly at Week 18.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Glyco-OCA at Week 24

End point title	Cmax of Glyco-OCA at Week 24[116]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[116] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[117]	2	
Units: ng/mL				
arithmetic mean (standard deviation)	166 (± 163)	56.2 (± 99999)	294 (± 70.0)	

Notes:

[117] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Glyco-OCA at Week 24

End point title	Tmax of Glyco-OCA at Week 24[118]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[118] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1	2	
Units: hours				
median (full range (min-max))	5.04 (4.00 to 6.08)	5.00 (5.00 to 5.00)	4.54 (4.08 to 5.00)	

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Glyco-OCA at Week 24

End point title	Ctrough of Glyco-OCA at Week 24[119]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 24.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 24

Notes:

[119] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[120]	2	
Units: ng/mL				
arithmetic mean (standard deviation)	83.0 (± 106)	22.0 (± 99999)	239 (± 7.07)	

Notes:

[120] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Glyco-OCA at Week 24

End point title	AUC0-24h of Glyco-OCA at Week 24[121]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[121] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[122]	2	
Units: ng*h/mL				
arithmetic mean (standard deviation)	2710 (± 3030)	936 (± 99999)	5550 (± 878)	

Notes:

[122] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRAUC of Glyco-OCA at Week 24

End point title	MRAUC of Glyco-OCA at Week 24[123]

End point description:

MRAUC was the ratio of AUC0-24h of Glyco-OCA (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Glyco-OCA, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[123] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[124]	2	
Units: ratio				
arithmetic mean (standard deviation)	8.26 (± 6.80)	2.39 (± 99999)	17.3 (± 16.5)	

Notes:

[124] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRCmax of Glyco-OCA at Week 24

End point title	MRCmax of Glyco-OCA at Week 24[125]

End point description:

MRCmax was the ratio of Cmax of Glyco-OCA (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Glyco-OCA, where Cmax is the maximum observed concentration.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[125] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[126]	2	
Units: ratio				
arithmetic mean (standard deviation)	1.17 (± 0.253)	0.315 (± 99999)	1.94 (± 1.44)	

Notes:

[126] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Glyco-OCA at Week 30

End point title	Cmax of Glyco-OCA at Week 30[127]

End point description:

APD: Results of PK were planned to be listed by dose regimen. Participants who received planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[127] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[128]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	83.0 (± 99999)	174 (± 75.0)	301 (± 86.3)	

Notes:

[128] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Glyco-OCA at Week 30

End point title	Tmax of Glyco-OCA at Week 30[129]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[129] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1	2	2	
Units: hours				
median (full range (min-max))	6.00 (6.00 to 6.00)	14.0 (4.03 to 24.0)	4.51 (4.02 to 5.00)	

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Glyco-OCA at Week 30

End point title	Ctrough of Glyco-OCA at Week 30[130]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 30.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 30

Notes:

[130] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[131]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	14.4 (± 99999)	143 (± 30.4)	156 (± 79.4)	

Notes:

[131] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Glyco-OCA at Week 30

End point title	AUC0-24h of Glyco-OCA at Week 30[132]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[132] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[133]	2	2	
Units: ng*h/mL				
arithmetic mean (standard deviation)	863 (± 99999)	3180 (± 1080)	5050 (± 2260)	

Notes:

[133] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRAUC of Glyco-OCA at Week 30

End point title	MRAUC of Glyco-OCA at Week 30[134]

End point description:

MRAUC was the ratio of AUC0-24h of Glyco-OCA (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Glyco-OCA, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[134] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[135]	2	2	
Units: ratio				
arithmetic mean (standard deviation)	4.31 (± 99999)	10.0 (± 5.84)	17.2 (± 18.7)	

Notes:

[135] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRCmax of Glyco-OCA at Week 30

End point title	MRCmax of Glyco-OCA at Week 30[136]

End point description:

MRCmax was the ratio of Cmax of Glyco-OCA (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Glyco-OCA, where Cmax is the maximum observed concentration.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[136] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[137]	2	2	
Units: ratio				
arithmetic mean (standard deviation)	0.789 (± 99999)	1.23 (± 0.723)	2.58 (± 1.58)	

Notes:

[137] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Glyco-OCA at Week 48

End point title	Cmax of Glyco-OCA at Week 48[138]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[138] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[139]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	()	123 (± 34.0)	354 (± 37.5)	

Notes:

[139] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Glyco-OCA at Week 48

End point title	Tmax of Glyco-OCA at Week 48[140]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10

mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[140] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[141]	2	2	
Units: hours				
median (full range (min-max))	(to)	5.00 (5.00 to 5.00)	4.03 (2.00 to 6.05)	

Notes:

[141] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Glyco-OCA at Week 48

End point title	Ctrough of Glyco-OCA at Week 48[142]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 48.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 48

Notes:

[142] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[143]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	()	65.9 (± 10.2)	280 (± 62.2)	

Notes:

[143] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Glyco-OCA at Week 48

End point title	AUC0-24h of Glyco-OCA at Week 48[144]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[144] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[145]	2	2	
Units: ng*h/mL				
arithmetic mean (standard deviation)	()	2120 (± 442)	6950 (± 648)	

Notes:

[145] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: MRAUC of Glyco-OCA at Week 48

End point title	MRAUC of Glyco-OCA at Week 48[146]

End point description:

MRAUC was the ratio of AUC0-24h of Glyco-OCA (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Glyco-OCA, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[146] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[147]	2	1[148]	
Units: ratio				
arithmetic mean (standard deviation)	()	5.39 (± 2.69)	4.79 (± 99999)	

Notes:

[147] - No participant received OCA 5 mg once weekly at Week 48.

[148] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRCmax of Glyco-OCA at Week 48

End point title	MRCmax of Glyco-OCA at Week 48[149]

End point description:

MRCmax was the ratio of Cmax of Glyco-OCA (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Glyco-OCA, where Cmax is the maximum observed concentration.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[149] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[150]	2	2	
Units: ratio				
arithmetic mean (standard deviation)	()	0.826 (± 0.0280)	1.41 (± 1.00)	

Notes:

[150] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Tauro-OCA at Week 12

End point title	Cmax of Tauro-OCA at Week 12[151]

End point description:

APD: Results of PK were planned to be listed by dose regimen. Participants who received planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[151] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	0[152]	0[153]	
Units: ng/mL				
arithmetic mean (standard deviation)	201 (± 213)	()	()	

Notes:

[152] - No participant started OCA 5 mg twice weekly at Week 12.

[153] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Tauro-OCA at Week 12

End point title	Tmax of Tauro-OCA at Week 12[154]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[154] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	0[155]	0[156]	
Units: hours				
median (full range (min-max))	5.00 (3.00 to 5.00)	(to)	(to)	

Notes:

[155] - No participant started OCA 5 mg twice weekly at Week 12.

[156] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Tauro-OCA at Week 12

End point title	Ctrough of Tauro-OCA at Week 12[157]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 12.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 12

Notes:

[157] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	0[158]	0[159]	
Units: ng/mL				
arithmetic mean (standard deviation)	41.6 (± 33.0)	()	()	

Notes:

[158] - No participant started OCA 5 mg twice weekly at Week 12.

[159] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Tauro-OCA at Week 12

End point title	AUC0-24h of Tauro-OCA at Week 12[160]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[160] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	0[161]	0[162]	
Units: ng*h/mL				
arithmetic mean (standard deviation)	1580 (± 1260)	()	()	

Notes:

[161] - No participant started OCA 5 mg twice weekly at Week 12.

[162] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: MRAUC of Tauro-OCA at Week 12

End point title	MRAUC of Tauro-OCA at Week 12[163]

End point description:

MRAUC was the ratio of AUC0-24h of Tauro-OCA (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Tauro-OCA, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[163] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	0[164]	0[165]	
Units: ratio				
arithmetic mean (standard deviation)	3.13 (± 1.08)	()	()	

Notes:

[164] - No participant started OCA 5 mg twice weekly at Week 12.

[165] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: MRCmax of Tauro-OCA at Week 12

End point title	MRCmax of Tauro-OCA at Week 12[166]

End point description:

MRCmax was the ratio of Cmax of Tauro-OCA (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Tauro-OCA, where Cmax is the maximum observed concentration.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[166] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	0[167]	0[168]	
Units: ratio				
arithmetic mean (standard deviation)	2.24 (± 2.46)	()	()	

Notes:

[167] - No participant started OCA 5 mg twice weekly at Week 12.

[168] - No participant started OCA 10 mg twice weekly at Week 12.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Tauro-OCA at Week 18

End point title	Cmax of Tauro-OCA at Week 18[169]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[169] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[170]	
Units: ng/mL				
arithmetic mean (standard deviation)	63.2 (± 46.9)	221 (± 188)	()	

Notes:

[170] - No participant started OCA 10 mg twice weekly at Week 18

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Tauro-OCA at Week 18

End point title	Tmax of Tauro-OCA at Week 18[171]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who

received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[171] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[172]	
Units: hours				
median (full range (min-max))	5.00 (5.00 to 5.00)	2.52 (2.00 to 3.03)	(to)	

Notes:

[172] - No participant started OCA 10 mg twice weekly at Week 18

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Tauro-OCA at Week 18

End point title	Ctrough of Tauro-OCA at Week 18[173]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 18.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 18

Notes:

[173] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[174]	
Units: ng/mL				
arithmetic mean (standard deviation)	17.0 (± 11.2)	122 (± 130)	()	

Notes:

[174] - No participant started OCA 10 mg twice weekly at Week 18

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Tauro-OCA at Week 18

End point title	AUC0-24h of Tauro-OCA at Week 18[175]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[175] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[176]	
Units: ng*h/mL				
arithmetic mean (standard deviation)	799 (± 654)	3630 (± 3600)	()	

Notes:

[176] - No participant started OCA 10 mg twice weekly at Week 18

Statistical analyses

No statistical analyses for this end point

Primary: MRAUC of Tauro-OCA at Week 18

End point title	MRAUC of Tauro-OCA at Week 18[177]

End point description:

MRAUC was the ratio of AUC0-24h of Tauro-OCA (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Tauro-OCA, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[177] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[178]	
Units: ratio				
arithmetic mean (standard deviation)	3.11 (± 0.685)	28.8 (± 37.9)	()	

Notes:

[178] - No participant started OCA 10 mg twice weekly at Week 18

Statistical analyses

No statistical analyses for this end point

Primary: MRCmax of Tauro-OCA at Week 18

End point title	MRCmax of Tauro-OCA at Week 18[179]

End point description:

MRCmax was the ratio of Cmax of Tauro-OCA (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Tauro-OCA, where Cmax is the maximum observed concentration.

Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[179] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[180]	
Units: ratio				
arithmetic mean (standard deviation)	0.434 (± 0.156)	3.32 (± 4.12)	()	

Notes:

[180] - No participant started OCA 10 mg twice weekly at Week 18

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Tauro-OCA at Week 24

End point title	Cmax of Tauro-OCA at Week 24[181]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[181] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[182]	2	
Units: ng/mL				
arithmetic mean (standard deviation)	142 (± 144)	65.5 (± 99999)	430 (± 142)	

Notes:

[182] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Tauro-OCA at Week 24

End point title	Tmax of Tauro-OCA at Week 24[183]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[183] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1	2	
Units: hours				
median (full range (min-max))	5.54 (5.00 to 6.08)	9.00 (9.00 to 9.00)	4.05 (3.10 to 5.00)	

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Tauro-OCA at Week 24

End point title	Ctrough of Tauro-OCA at Week 24[184]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 24.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 24

Notes:

[184] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[185]	2	
Units: ng/mL				
arithmetic mean (standard deviation)	71.0 (± 90.5)	21.2 (± 99999)	271 (± 58.0)	

Notes:

[185] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Tauro-OCA at Week 24

End point title	AUC0-24h of Tauro-OCA at Week 24[186]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[186] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[187]	2	
Units: ng*h/mL				
arithmetic mean (standard deviation)	2360 (± 2650)	1060 (± 99999)	7470 (± 3260)	

Notes:

[187] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRAUC of Tauro-OCA at Week 24

End point title	MRAUC of Tauro-OCA at Week 24[188]

End point description:

MRAUC was the ratio of AUC0-24h of Tauro-OCA (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Tauro-OCA, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[188] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[189]	2	
Units: ratio				
arithmetic mean (standard deviation)	6.51 (± 5.40)	2.46 (± 99999)	23.4 (± 25.6)	

Notes:

[189] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRCmax of Tauro-OCA at Week 24

End point title	MRCmax of Tauro-OCA at Week 24[190]

End point description:

MRCmax was the ratio of Cmax of Tauro-OCA (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Tauro-OCA, where Cmax is the maximum observed concentration.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[190] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[191]	2	
Units: ratio				
arithmetic mean (standard deviation)	0.881 (± 0.249)	0.332 (± 99999)	2.63 (± 2.13)	

Notes:

[191] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Tauro-OCA at Week 30

End point title	Cmax of Tauro-OCA at Week 30[192]

End point description:

APD: Results of PK were planned to be listed by dose regimen. Participants who received planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[192] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[193]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	38.6 (± 99999)	141 (± 13.4)	460 (± 342)	

Notes:

[193] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Tauro-OCA at Week 30

End point title	Tmax of Tauro-OCA at Week 30[194]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[194] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1	2	2	
Units: hours				
median (full range (min-max))	6.00 (6.00 to 6.00)	4.52 (4.03 to 5.00)	4.03 (3.05 to 5.00)	

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Tauro-OCA at Week 30

End point title	Ctrough of Tauro-OCA at Week 30[195]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 30.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 30

Notes:

[195] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[196]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	8.21 (± 99999)	110 (± 7.78)	222 (± 228)	

Notes:

[196] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Tauro-OCA at Week 30

End point title	AUC0-24h of Tauro-OCA at Week 30[197]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[197] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[198]	2	2	
Units: ng*h/mL				
arithmetic mean (standard deviation)	408 (± 99999)	2430 (± 18.1)	7020 (± 6780)	

Notes:

[198] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRAUC of Tauro-OCA at Week 30

End point title	MRAUC of Tauro-OCA at Week 30[199]

End point description:

MRAUC was the ratio of AUC0-24h of Tauro-OCA (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Tauro-OCA, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[199] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[200]	2	2	
Units: ratio				
arithmetic mean (standard deviation)	1.84 (± 99999)	6.61 (± 1.74)	25.7 (± 33.0)	

Notes:

[200] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRCmax of Tauro-OCA at Week 30

End point title	MRCmax of Tauro-OCA at Week 30[201]

End point description:

MRCmax was the ratio of Cmax of Tauro-OCA (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Tauro-OCA, where Cmax is the maximum observed

concentration.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[201] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[202]	2	2	
Units: ratio				
arithmetic mean (standard deviation)	0.332 (± 99999)	0.855 (± 0.0746)	3.85 (± 3.73)	

Notes:

[202] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Tauro-OCA at Week 48

End point title	Cmax of Tauro-OCA at Week 48[203]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[203] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[204]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	()	72.5 (± 15.1)	485 (± 20.5)	

Notes:

[204] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of Tauro-OCA at Week 48

End point title	Tmax of Tauro-OCA at Week 48[205]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[205] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[206]	2	2	
Units: hours				
median (full range (min-max))	(to)	6.50 (6.00 to 7.00)	2.57 (2.00 to 3.13)	

Notes:

[206] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of Tauro-OCA at Week 48

End point title	Ctrough of Tauro-OCA at Week 48[207]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 48.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 48

Notes:

[207] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[208]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	()	33.7 (± 21.4)	309 (± 109)	

Notes:

[208] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of Tauro-OCA at Week 48

End point title	AUC0-24h of Tauro-OCA at Week 48[209]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[209] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[210]	2	2	
Units: ng*h/mL				
arithmetic mean (standard deviation)	()	1220 (± 389)	8890 (± 696)	

Notes:

[210] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: MRAUC of Tauro-OCA at Week 48

End point title	MRAUC of Tauro-OCA at Week 48[211]

End point description:

MRAUC was the ratio of AUC0-24h of Tauro-OCA (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Tauro-OCA, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[211] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[212]	2	1[213]	
Units: ratio				
arithmetic mean (standard deviation)	()	2.59 (± 0.00903)	5.60 (± 99999)	

Notes:

[212] - No participant received OCA 5 mg once weekly at Week 48.

[213] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRCmax of Tauro-OCA at Week 48

End point title	MRCmax of Tauro-OCA at Week 48[214]

End point description:

MRCmax was the ratio of Cmax of Tauro-OCA (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of Tauro-OCA, where Cmax is the maximum observed concentration.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[214] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[215]	2	2	
Units: ratio				
arithmetic mean (standard deviation)	()	0.468 (± 0.206)	1.67 (± 0.989)	

Notes:

[215] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of OCA-glucuronide at Week 12

End point title	Cmax of OCA-glucuronide at Week 12[216]

End point description:

APD: Results of PK were planned to be listed by dose regimen. Participants who received planned dose regimen and had available data were included. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[216] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	0[217]	0[218]	
Units: ng/mL				
arithmetic mean (standard deviation)	47.0 (± 24.7)	()	()	

Notes:

[217] - No participant started OCA 5 mg Twice Weekly at Week 12

[218] - No participant started OCA 10 mg Twice Weekly at Week 12

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of OCA-glucuronide at Week 12

End point title	Tmax of OCA-glucuronide at Week 12[219]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.
Pharmacokinetic of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[219] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	0[220]	0[221]	
Units: hours				
median (full range (min-max))	2.50 (1.50 to 3.00)	(to)	(to)	

Notes:

[220] - No participant started OCA 5 mg Twice Weekly at Week 12

[221] - No participant started OCA 10 mg Twice Weekly at Week 12

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of OCA-glucuronide at Week 12

End point title	Ctrough of OCA-glucuronide at Week 12[222]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 12.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 12

Notes:

[222] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	0[223]	0[224]	
Units: ng/mL				
arithmetic mean (standard deviation)	20.7 (± 15.4)	()	()	

Notes:

[223] - No participant started OCA 5 mg Twice Weekly at Week 12

[224] - No participant started OCA 10 mg Twice Weekly at Week 12

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of OCA-glucuronide at Week 12

End point title	AUC0-24h of OCA-glucuronide at Week 12[225]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.
Pharmacokinetic of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[225] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	0[226]	0[227]	
Units: ng*h/mL				
arithmetic mean (standard deviation)	593 (± 388)	()	()	

Notes:

[226] - No participant started OCA 5 mg Twice Weekly at Week 12

[227] - No participant started OCA 10 mg Twice Weekly at Week 12

Statistical analyses

No statistical analyses for this end point

Primary: MRAUC of OCA-glucuronide at Week 12

End point title	MRAUC of OCA-glucuronide at Week 12[228]

End point description:

MRAUC was the ratio of AUC0-24h of OCA-glucuronide (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of OCA-glucuronide, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[228] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	0[229]	0[230]	
Units: ratio				
arithmetic mean (standard deviation)	1.17 (± 0.638)	()	()	

Notes:

[229] - No participant started OCA 5 mg Twice Weekly at Week 12

[230] - No participant started OCA 10 mg Twice Weekly at Week 12

Statistical analyses

No statistical analyses for this end point

Primary: MRCmax of OCA-glucuronide at Week 12

End point title	MRCmax of OCA-glucuronide at Week 12[231]

End point description:

MRCmax was the ratio of Cmax of OCA-glucuronide (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of OCA-glucuronide, where Cmax is the maximum observed concentration.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg twice weekly or 10 mg twice weekly at Week 12 are not applicable as no participant started 5 mg twice weekly or 10 mg twice weekly at Week 12.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 12

Notes:

[231] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	0[232]	0[233]	
Units: ratio				
arithmetic mean (standard deviation)	0.384 (± 0.275)	()	()	

Notes:

[232] - No participant started OCA 5 mg Twice Weekly at Week 12

[233] - No participant started OCA 10 mg Twice Weekly at Week 12

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of OCA-glucuronide at Week 18

End point title	Cmax of OCA-glucuronide at Week 18[234]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[234] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[235]	
Units: ng/mL				
arithmetic mean (standard deviation)	39.2 (± 30.3)	74.9 (± 38.4)	()	

Notes:

[235] - No participant started OCA 10 mg Twice Weekly at Week 18

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of OCA-glucuronide at Week 18

End point title	Tmax of OCA-glucuronide at Week 18[236]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[236] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[237]	
Units: hours				
median (full range (min-max))	1.25 (1.00 to 1.50)	2.73 (1.50 to 3.97)	(to)	

Notes:

[237] - No participant started OCA 10 mg Twice Weekly at Week 18

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of OCA-glucuronide at Week 18

End point title	Ctrough of OCA-glucuronide at Week 18[238]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 18.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 18

Notes:

[238] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[239]	
Units: ng/mL				
arithmetic mean (standard deviation)	11.7 (± 7.55)	40.9 (± 43.9)	()	

Notes:

[239] - No participant started OCA 10 mg Twice Weekly at Week 18

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of OCA-glucuronide at Week 18

End point title	AUC0-24h of OCA-glucuronide at Week 18[240]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[240] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[241]	
Units: ng*h/mL				
arithmetic mean (standard deviation)	390 (± 278)	1120 (± 989)	()	

Notes:

[241] - No participant started OCA 10 mg Twice Weekly at Week 18

Statistical analyses

No statistical analyses for this end point

Primary: MRAUC of OCA-glucuronide at Week 18

End point title	MRAUC of OCA-glucuronide at Week 18[242]

End point description:

MRAUC was the ratio of AUC0-24h of OCA-glucuronide (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of OCA-glucuronide, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[242] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[243]	
Units: ratio				
arithmetic mean (standard deviation)	1.41 (± 0.101)	7.58 (± 9.76)	()	

Notes:

[243] - No participant started OCA 10 mg Twice Weekly at Week 18

Statistical analyses

No statistical analyses for this end point

Primary: MRCmax of OCA-glucuronide at Week 18

End point title	MRCmax of OCA-glucuronide at Week 18[244]

End point description:

MRCmax was the ratio of Cmax of OCA-glucuronide (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of OCA-glucuronide, where Cmax is the maximum observed concentration.

Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 10 mg twice weekly at Week 18 is not applicable as no participant started 10 mg twice weekly at Week 18.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 18

Notes:

[244] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	2	0[245]	
Units: ratio				
arithmetic mean (standard deviation)	0.236 (± 0.0942)	0.891 (± 0.985)	()	

Notes:

[245] - No participant started OCA 10 mg Twice Weekly at Week 18

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of OCA-glucuronide at Week 24

End point title	Cmax of OCA-glucuronide at Week 24[246]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[246] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[247]	2	
Units: ng/mL				
arithmetic mean (standard deviation)	20.2 (± 7.42)	58.1 (± 99999)	127 (± 71.0)	

Notes:

[247] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of OCA-glucuronide at Week 24

End point title	Tmax of OCA-glucuronide at Week 24[248]

End point description:

Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[248] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1	2	
Units: hours				
median (full range (min-max))	2.54 (2.08 to 3.00)	1.00 (1.00 to 1.00)	2.27 (2.00 to 2.53)	

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of OCA-glucuronide at Week 24

End point title	Ctrough of OCA-glucuronide at Week 24[249]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 24.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 24

Notes:

[249] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[250]	2	
Units: ng/mL				
arithmetic mean (standard deviation)	11.6 (± 6.43)	14.5 (± 99999)	84.2 (± 81.7)	

Notes:

[250] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of OCA-glucuronide at Week 24

End point title	AUC0-24h of OCA-glucuronide at Week 24[251]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[251] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[252]	2	
Units: ng*h/mL				
arithmetic mean (standard deviation)	330 (± 191)	602 (± 99999)	2120 (± 1920)	

Notes:

[252] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRAUC of OCA-glucuronide at Week 24

End point title	MRAUC of OCA-glucuronide at Week 24[253]

End point description:

MRAUC was the ratio of AUC0-24h of OCA-glucuronide (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of OCA-glucuronide, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[253] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[254]	2	
Units: ratio				
arithmetic mean (standard deviation)	0.983 (± 0.0286)	1.23 (± 99999)	6.87 (± 8.74)	

Notes:

[254] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRCmax of OCA-glucuronide at Week 24

End point title	MRCmax of OCA-glucuronide at Week 24[255]

End point description:

MRCmax was the ratio of Cmax of OCA-glucuronide (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of OCA-glucuronide, where Cmax is the maximum observed concentration.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 24

Notes:

[255] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	1[256]	2	
Units: ratio				
arithmetic mean (standard deviation)	0.165 (± 0.0959)	0.261 (± 99999)	0.727 (± 0.701)	

Notes:

[256] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of OCA-glucuronide at Week 30

End point title	Cmax of OCA-glucuronide at Week 30[257]

End point description:

APD: Results of PK were planned to be listed by dose regimen. Participants who received planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[257] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[258]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	13.7 (± 99999)	51.9 (± 49.4)	148 (± 117)	

Notes:

[258] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of OCA-glucuronide at Week 30

End point title	Tmax of OCA-glucuronide at Week 30[259]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[259] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1	2	2	
Units: hours				
median (full range (min-max))	1.50 (1.50 to 1.50)	2.26 (1.50 to 3.02)	4.51 (4.02 to 5.00)	

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of OCA-glucuronide at Week 30

End point title	Ctrough of OCA-glucuronide at Week 30[260]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 30.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 30

Notes:

[260] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[261]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	5.57 (± 99999)	19.7 (± 13.8)	89.0 (± 107)	

Notes:

[261] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of OCA-glucuronide at Week 30

End point title	AUC0-24h of OCA-glucuronide at Week 30[262]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[262] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[263]	2	2	
Units: ng*h/mL				
arithmetic mean (standard deviation)	170 (± 99999)	641 (± 482)	2200 (± 2100)	

Notes:

[263] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRAUC of OCA-glucuronide at Week 30

End point title	MRAUC of OCA-glucuronide at Week 30[264]

End point description:

MRAUC was the ratio of AUC0-24h of OCA-glucuronide (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of OCA-glucuronide, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[264] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[265]	2	2	
Units: ratio				
arithmetic mean (standard deviation)	0.680 (± 99999)	1.39 (± 0.742)	7.10 (± 9.09)	

Notes:

[265] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRCmax of OCA-glucuronide at Week 30

End point title	MRCmax of OCA-glucuronide at Week 30[266]

End point description:

MRCmax was the ratio of Cmax of OCA-glucuronide (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of OCA-glucuronide, where Cmax is the maximum observed concentration.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 30

Notes:

[266] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1[267]	2	2	
Units: ratio				
arithmetic mean (standard deviation)	0.104 (± 99999)	0.257 (± 0.217)	1.11 (± 1.11)	

Notes:

[267] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of OCA-glucuronide at Week 48

End point title	Cmax of OCA-glucuronide at Week 48[268]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[268] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[269]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	()	66.0 (± 63.6)	134 (± 71.3)	

Notes:

[269] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of OCA-glucuronide at Week 48

End point title	Tmax of OCA-glucuronide at Week 48[270]

End point description:

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[270] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[271]	2	2	
Units: hours				
median (full range (min-max))	(to)	1.73 (1.47 to 2.00)	1.54 (1.50 to 1.58)	

Notes:

[271] - No participant OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: Ctrough of OCA-glucuronide at Week 48

End point title	Ctrough of OCA-glucuronide at Week 48[272]

End point description:

Ctrough was considered as the concentration at 24-hours post-dose at Week 48.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

24 hours post-dose at Week 48

Notes:

[272] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[273]	2	2	
Units: ng/mL				
arithmetic mean (standard deviation)	()	39.2 (± 35.7)	89.2 (± 73.3)	

Notes:

[273] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24h of OCA-glucuronide at Week 48

End point title	AUC0-24h of OCA-glucuronide at Week 48[274]

End point description:

AUC0-24h was calculated using the linear/linear trapezoidal rule.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[274] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[275]	2	2	
Units: ng*h/mL				
arithmetic mean (standard deviation)	()	952 (± 833)	2490 (± 1520)	

Notes:

[275] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: MRAUC of OCA-glucuronide at Week 48

End point title	MRAUC of OCA-glucuronide at Week 48[276]

End point description:

MRAUC was the ratio of AUC0-24h of OCA-glucuronide (metabolite) to AUC0-24h of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of OCA-glucuronide, where AUC0-24 is the area under the plasma concentration time profile from time 0 to 24 hours.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[276] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[277]	2	1[278]	
Units: ratio				
arithmetic mean (standard deviation)	()	1.62 (± 1.05)	0.833 (± 99999)	

Notes:

[277] - No participant received OCA 5 mg once weekly at Week 48.

[278] - 99999: Standard deviation is not estimable as there is only one participant.

Statistical analyses

No statistical analyses for this end point

Primary: MRCmax of OCA-glucuronide at Week 48

End point title	MRCmax of OCA-glucuronide at Week 48[279]

End point description:

MRCmax was the ratio of Cmax of OCA-glucuronide (metabolite) to Cmax of OCA (parent drug) * ratio of molecular weight of OCA to molecular weight of OCA-glucuronide, where Cmax is the maximum observed concentration.

APD: Results of PK were planned to be listed by the dose regimen. Participants in the PK population who received the planned dose regimen and had available data were included in the analysis. PK of OCA 5 mg once weekly at Week 48 is not applicable as participants received either OCA 5 mg twice daily or 10 mg twice daily and no participant received OCA 5 mg once weekly at Week 48.

End point type	Primary

End point timeframe:

Pre-dose (30 minutes before administration) and 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, and 24 hours post-dose at Week 48

Notes:

[279] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	OCA 5 mg Once Weekly	OCA 5 mg Twice Weekly	OCA 10 mg Twice Weekly	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[280]	2	2	
Units: ratio				
arithmetic mean (standard deviation)	()	0.411 (± 0.444)	0.482 (± 0.479)	

Notes:

[280] - No participant received OCA 5 mg once weekly at Week 48.

Statistical analyses

No statistical analyses for this end point

Primary: 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)[281]

End point description:

An adverse event (AE) was any unfavorable & unintended sign (including abnormal laboratory finding), symptom, or disease temporally associated with use of study drug, whether or not related to study drug. An SAE was any AE that resulted in death, was life-threatening, resulted in a persistent or significant disability/incapacity, resulted in in-patient hospitalization or prolonged an existing hospitalization, was a congenital anomaly/birth defect, or was an important medical event that could jeopardize participant or could have required medical intervention to prevent one of the outcomes listed above. TEAE was defined as any AE if it met one or more of the following criteria: 1)An AE started on or after first study drug dose & within 30 days after last dose of study drug, 2)An AE occurred prior to first study drug dose that worsens after the first study drug dose.
APD: Safety Population included all participants who received at least 1 dose of investigational product (OCA or placebo)

End point type	Primary

End point timeframe:

Baseline up to approximately 3 years

Notes:

[281] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	10		
Units: Participants				
Any TEAE	12	10		
SAE	9	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Model of End-stage Liver Disease (MELD) Score at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point title	Change From Baseline in the Model of End-stage Liver Disease

	(MELD) Score at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point description:

The MELD scoring system is used to assess the severity of chronic liver disease. The MELD score is derived from the participant's serum total bilirubin, serum creatinine, and prothrombin international normalized ratio (INR): 3.78× log normal (ln) [total bilirubin (mg/deciliter [dL])] + 11.2×ln[INR] + 9.57×ln[serum creatinine (mg/dL)] + 6.43. The MELD score ranges from 6 to 40 with higher scores indicating more severe liver disease and a worse outcome.

APD: Intent-to-treat (ITT) population included all randomized participants who received any amount of investigational product (OCA or placebo). Participants with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[282]	10[283]		
Units: Score on a scale				
median (inter-quartile range (Q1-Q3))				
Change at Week 3 (n = 11, 10)	0.50 (-0.50 to 1.00)	0.00 (-1.50 to 2.00)		
Change at Week 6 (n = 9, 8)	0.50 (0.00 to 2.50)	0.00 (-0.75 to 1.25)		
Change at Week 12 (n = 6, 7)	0.75 (0.00 to 2.50)	0.00 (-1.00 to 1.00)		
Change at Week 18 (n = 8, 8)	0.65 (-0.25 to 3.00)	-0.75 (-2.00 to 1.00)		
Change at Week 24 (n = 4, 5)	0.15 (0.00 to 0.40)	-1.50 (-2.00 to 0.00)		
Change at Week 30 (n = 6, 6)	0.15 (-0.50 to 0.50)	-1.25 (-2.00 to 0.00)		
Change at Week 36 (n = 6, 6)	0.15 (-1.00 to 1.50)	0.25 (-1.50 to 1.00)		
Change at Week 42 (n = 6, 6)	0.65 (-0.50 to 1.50)	0.50 (0.00 to 1.50)		
Change at Week 48 (n = 6, 4)	0.65 (0.00 to 1.50)	-1.75 (-2.50 to -0.50)		
Change at Extension Month 3 (n = 5, 5)	0.50 (0.50 to 4.30)	-1.00 (-1.50 to -0.50)		
Change at Extension Month 6 (n = 3, 2)	0.00 (-1.00 to 3.50)	0.25 (0.00 to 0.50)		
Change at Extension Month 9 (n = 0, 2)	99999 (99999 to 99999)	0.75 (-1.00 to 2.50)		
Change at Extension Month 12 (n = 1, 1)	-1.00 (-1.00 to -1.00)	4.50 (4.50 to 4.50)		
Change at Extension Month 15 (n = 1, 0)	-1.00 (-1.00 to -1.00)	99999 (99999 to 99999)		

Notes:

[282] - 99999 denotes data not available as there were no participants at specified timepoint.

[283] - 99999 denotes data not available as there were no participants at specified timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in MELD-Sodium (Na) Score at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point title	Change From Baseline in MELD-Sodium (Na) Score at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point description:

The MELD-Na scoring system is used to assess the severity of chronic liver disease in the participants with an initial MELD(i) score greater than 11. MELD-Na score is derived from the participant's serum total bilirubin, serum creatinine, INR, and sodium. The MELD-Na score is re-calculated as follows: MELD-Na = MELD(i) + 1.32*(137-Na) – [0.033*MELD(i)*(137-Na)]. MELD score ranges from 6-40 with higher scores indicating more severe liver disease and a worse outcome.

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11[284]	10[285]		
Units: Score on a Scale				
median (inter-quartile range (Q1-Q3))				
Change at Week 3 (n = 11, 10)	0.00 (-0.50 to 1.00)	0.50 (-1.50 to 2.00)		
Change at Week 6 (n = 9, 8)	0.50 (0.00 to 2.00)	-0.25 (-0.75 to 1.50)		
Change at Week 12 (n = 6, 7)	0.50 (0.00 to 3.50)	0.50 (-1.50 to 2.00)		
Change at Week 18 (n = 8, 8)	0.65 (-0.25 to 2.75)	-0.75 (-2.50 to 0.50)		
Change at Week 24 (n = 4, 5)	0.15 (0.00 to 0.40)	-2.00 (-2.50 to 1.00)		
Change at Week 30 (n = 6, 6)	0.15 (-0.50 to 0.50)	-0.75 (-2.00 to 0.50)		
Change at Week 36 (n = 6, 6)	0.15 (-1.00 to 1.50)	-0.25 (-1.50 to 1.00)		
Change at Week 42 (n = 5, 6)	0.00 (-0.50 to 1.30)	0.50 (0.00 to 0.50)		
Change at Week 48 (n = 6, 4)	0.65 (0.00 to 2.50)	-1.75 (-3.00 to 0.00)		
Change at Extension Month 3 (n = 5, 5)	2.50 (0.50 to 4.30)	-1.00 (-2.50 to -0.50)		
Change at Extension Month 6 (n = 3, 2)	0.00 (-1.00 to 3.50)	1.75 (0.50 to 3.00)		
Change at Extension Month 9 (n = 0, 2)	99999 (99999 to 99999)	0.75 (-1.00 to 2.50)		
Change at Extension Month 12 (n = 1, 1)	-1.00 (-1.00 to -1.00)	4.50 (4.50 to 4.50)		
Change at Extension Month 15 (n = 1, 0)	-1.00 (-1.00 to -1.00)	99999 (99999 to 99999)		

Notes:

[284] - 99999 denotes data not available as there were no participants.

[285] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Child-Pugh Score at Day 1, Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Months 3, 6, 9, 12, and 15

End point title	Change From Baseline in Child-Pugh Score at Day 1, Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Months 3, 6, 9, 12, and 15

End point description:

The Child-Pugh classification was a scoring system used for the classification of the severity of cirrhosis. It included three continuous variables (bilirubin, albumin, and INR) and two discrete variables (ascites and encephalopathy). Each variable was scored 1-3 with 3 indicating most severe derangement. The determination of child-pugh score ranged from 5 to 15. The higher the score, the sicker the participant.

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Day 1, Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12[286]	10[287]		
Units: Score on a Scale				
median (inter-quartile range (Q1-Q3))				
Change at Day 1 (n = 12, 10)	0.0 (-0.5 to 0.0)	0.0 (0.0 to 0.0)		
Change at Week 6 (n = 9, 8)	0.0 (-1.0 to 0.0)	0.0 (-0.5 to 0.5)		
Change at Week 12 (n = 6, 7)	-0.5 (-1.0 to 1.0)	0.0 (-1.0 to 1.0)		
Change at Week 18 (n = 8, 8)	0.0 (-1.0 to 0.0)	-0.5 (-2.0 to 0.0)		
Change at Week 24 (n = 5, 5)	-1.0 (-1.0 to 0.0)	0.0 (-1.0 to 0.0)		
Change at Week 30 (n = 6, 6)	-0.5 (-1.0 to 0.0)	-1.0 (-2.0 to 0.0)		
Change at Week 36 (n = 6, 6)	-1.0 (-1.0 to 0.0)	-0.5 (-1.0 to 0.0)		
Change at Week 48 (n = 6, 6)	-0.5 (-1.0 to 0.0)	0.0 (-2.0 to 0.0)		
Change at Extension Month 3 (n = 6, 5)	0.0 (-1.0 to 0.0)	0.0 (-1.0 to 1.0)		
Change at Extension Month 6 (n = 3, 2)	1.0 (-2.0 to 3.0)	0.0 (0.0 to 0.0)		
Change at Extension Month 9 (n = 0, 2)	99999 (99999 to 99999)	0.0 (-1.0 to 1.0)		
Change at Extension Month 12 (n = 1, 1)	1.0 (1.0 to 1.0)	0.0 (0.0 to 0.0)		
Change at Extension Month 15 (n = 1, 0)	1.0 (1.0 to 1.0)	99999 (99999 to 99999)		

Notes:

[286] - 99999 denotes data not available as there were no participants.

[287] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants by Child-Pugh Score Component (Ascites Categories)

End point title	Number of Participants by Child-Pugh Score Component (Ascites Categories)

End point description:

Number of participants with Child-Pugh component - ascites categories of none, mild, and moderate-severe has been reported. The ascites categories were defined per investigator's discretion.

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Day 1, Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	10		
Units: Participants				
Day 1: None (n =12, 10)	6	5		
Day 1: Mild (n =12, 10)	5	4		
Day 1: Moderate-Severe (n =12, 10)	1	1		
Week 6: None (n = 9, 9)	7	4		
Week 6: Mild (n = 9, 9)	2	5		
Week 6: Moderate-Severe (n = 9, 9)	0	0		
Week 12: None (n = 6, 7)	4	4		
Week 12: Mild (n = 6, 7)	2	3		
Week 12: Moderate-Severe (n = 6, 7)	0	0		
Week 18: None (n = 8, 8)	6	5		
Week 18: Mild (n = 8, 8)	2	3		
Week 18: Moderate-Severe (n = 8, 8)	0	0		
Week 24: None (n = 6, 6)	6	3		
Week 24: Mild (n = 6, 6)	0	3		
Week 24: Moderate-Severe (n = 6, 6)	0	0		
Week 30: None (n = 6, 6)	6	4		
Week 30: Mild (n = 6, 6)	0	2		
Week 30: Moderate-Severe (n = 6, 6)	0	0		
Week 36: None (n = 6, 6)	6	4		
Week 36: Mild (n = 6, 6)	0	2		
Week 36: Moderate-Severe (n = 6, 6)	0	0		
Week 48: None (n = 6, 6)	6	4		
Week 48: Mild (n = 6, 6)	0	1		
Week 48: Moderate-Severe (n = 6, 6)	0	1		
Extension Month 3: None (n = 6, 5)	6	2		
Extension Month 3: Mild (n = 6, 5)	0	1		
Extension Month 3: Moderate-Severe (n = 6, 5)	0	2		
Extension Month 6: None (n = 3, 2)	1	1		
Extension Month 6: Mild (n = 3, 2)	1	1		

Extension Month 6: Moderate-Severe (n = 3, 2)	1	0		
Extension Month 9: None (n = 0, 2)	0	1		
Extension Month 9: Mild (n = 0, 2)	0	1		
Extension Month 9: Moderate-Severe (n = 0, 2)	0	0		
Extension Month 12: None (n = 1, 1)	0	0		
Extension Month 12: Mild (n = 1, 1)	1	1		
Extension Month 12: Moderate-Severe (n = 1, 1)	0	0		
Extension Month 15: None (n = 1, 1)	0	0		
Extension Month 15: Mild (n = 1, 1)	1	1		
Extension Month 15: Moderate-Severe (n = 1, 1)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants by Child-Pugh Score Component (Prothrombin Time Categories)

End point title	Number of Participants by Child-Pugh Score Component (Prothrombin Time Categories)

End point description:

Number of participants with Child-Pugh component - prothrombin time (measured as INR) in categories of <1.7, 1.7 - 2.3, and >2.3 has been reported.

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Day 1, Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	10		
Units: Participants				
Day 1: <1.7 (n = 12, 10)	12	10		
Day 1: 1.7 - 2.3 (n = 12, 10)	0	0		
Day 1: >2.3 (n = 12, 10)	0	0		
Week 6: <1.7 (n = 9, 9)	9	9		
Week 6: 1.7 - 2.3 (n = 9, 9)	0	0		
Week 6: >2.3 (n = 9, 9)	0	0		
Week 12: <1.7 (n = 6, 7)	6	7		
Week 12: 1.7 - 2.3 (n = 6, 7)	0	0		
Week 12: >2.3 (n = 6, 7)	0	0		
Week 18: <1.7 (n = 8, 8)	8	8		
Week 18: 1.7 - 2.3 (n = 8, 8)	0	0		
Week 18: >2.3 (n = 8, 8)	0	0		

Week 24: <1.7 (n = 5, 5)	4	5		
Week 24: 1.7 - 2.3 (n = 5, 5)	1	0		
Week 24: >2.3 (n = 5, 5)	0	0		
Week 30: <1.7 (n = 6, 6)	6	6		
Week 30: 1.7 - 2.3 (n = 6, 6)	0	0		
Week 30: >2.3 (n = 6, 6)	0	0		
Week 36: <1.7 (n = 6, 6)	6	6		
Week 36: 1.7 - 2.3 (n = 6, 6)	0	0		
Week 36: >2.3 (n = 6, 6)	0	0		
Week 48: <1.7 (n = 6, 6)	6	6		
Week 48: 1.7 - 2.3 (n = 6, 6)	0	0		
Week 48: >2.3 (n = 6, 6)	0	0		
Extension Month 3: <1.7 (n = 6, 5)	6	5		
Extension Month 3: 1.7 - 2.3 (n = 6, 5)	0	0		
Extension Month 3: >2.3 (n = 6, 5)	0	0		
Extension Month 6: <1.7 (n = 3, 2)	3	2		
Extension Month 6: 1.7 - 2.3 (n = 3, 2)	0	0		
Extension Month 6: >2.3 (n = 3, 2)	0	0		
Extension Month 9: <1.7 (n = 0, 2)	0	2		
Extension Month 9: 1.7 - 2.3 (n = 0, 2)	0	0		
Extension Month 9: >2.3 (n = 0, 2)	0	0		
Extension Month 12: <1.7 (n = 1, 1)	1	1		
Extension Month 12: 1.7 - 2.3 (n = 1, 1)	0	0		
Extension Month 12: >2.3 (n = 1, 1)	0	0		
Extension Month 15: <1.7 (n = 1, 0)	1	0		
Extension Month 15: 1.7 - 2.3 (n = 1, 0)	0	0		
Extension Month 12: >2.3 (n = 1, 0)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants by Child-Pugh Score Component (Serum Albumin Categories)

End point title	Number of Participants by Child-Pugh Score Component (Serum Albumin Categories)

End point description:

Number of participants with Child-Pugh component - serum albumin levels in categories of >35 gram per liter (g/L), 28-35 g/L, or <28 g/L has been reported.

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Day 1, Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	10		
Units: Participants				
Day 1: >35 g/L (n = 12, 10)	3	4		
Day 1: 28-35 g/L (n = 12, 10)	9	4		
Day 1: <28 g/L (n = 12, 10)	0	2		
Week 6: >35 g/L (n = 9, 9)	2	4		
Week 6: 28-35 g/L (n = 9, 9)	7	3		
Week 6: <28 g/L (n = 9, 9)	0	2		
Week 12: >35 g/L (n = 6, 7)	1	3		
Week 12: 28-35 g/L (n = 6, 7)	5	3		
Week 12: <28 g/L (n = 6, 7)	0	1		
Week 18: >35 g/L (n = 8, 8)	2	5		
Week 18: 28-35 g/L (n = 8, 8)	6	3		
Week 18: <28 g/L (n = 8, 8)	0	0		
Week 24: >35 g/L (n = 6, 6)	1	3		
Week 24: 28-35 g/L (n = 6, 6)	5	3		
Week 24: <28 g/L (n = 6, 6)	0	0		
Week 30: >35 g/L (n = 6, 6)	1	3		
Week 30: 28-35 g/L (n = 6, 6)	5	3		
Week 30: <28 g/L (n = 6, 6)	0	0		
Week 36: >35 g/L (n = 6, 6)	1	2		
Week 36: 28-35 g/L (n = 6, 6)	5	4		
Week 36: <28 g/L (n = 6, 6)	0	0		
Week 48: >35 g/L (n = 6, 6)	2	3		
Week 48: 28-35 g/L (n = 6, 6)	4	3		
Week 48: <28 g/L (n = 6, 6)	0	0		
Extension Month 3: >35 g/L (n = 6, 5)	1	2		
Extension Month 3: 28-35 g/L (n = 6, 5)	5	3		
Extension Month 3: <28 g/L (n = 6, 5)	0	0		
Extension Month 6: >35 g/L (n = 3, 2)	1	1		
Extension Month 6: 28-35 g/L (n = 3, 2)	2	1		
Extension Month 6: <28 g/L (n = 3, 2)	0	0		
Extension Month 9: >35 g/L (n = 0, 2)	0	0		
Extension Month 9: 28-35 g/L (n = 0, 2)	0	2		
Extension Month 9: <28 g/L (n = 0, 2)	0	0		
Extension Month 12: >35 g/L (n = 1, 1)	0	1		
Extension Month 12: 28-35 g/L (n = 1, 1)	1	0		
Extension Month 12: <28 g/L (n = 1, 1)	0	0		
Extension Month 15: >35 g/L (n = 1, 1)	0	0		
Extension Month 15: 28-35 g/L (n = 1, 1)	1	1		
Extension Month 15: <28 g/L (n = 1, 1)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants by Child-Pugh Score Component (Total Bilirubin Categories)

End point title	Number of Participants by Child-Pugh Score Component (Total Bilirubin Categories)

End point description:

Number of participants with Child-Pugh component - total bilirubin levels in categories of <34 micromole per liter (µmol/ L), 34-50 µmol/L, and >50 µmol/L has been reported.

End point type	Secondary

End point timeframe:

Day 1, Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	10		
Units: Participants				
Day 1: <34 µmol/L (n = 12, 10)	3	5		
Day 1: 34-50 µmol/L (n = 12, 10)	5	0		
Day 1: >50 µmol/L (n = 12, 10)	4	5		
Week 6: <34 µmol/L (n = 9, 8)	4	4		
Week 6: 34-50 µmol/L (n = 9, 8)	1	0		
Week 6: >50 µmol/L (n = 9, 8)	4	4		
Week 12: <34 µmol/L (n = 6, 7)	2	4		
Week 12: 34-50 µmol/L (n = 6, 7)	3	0		
Week 12: >50 µmol/L (n = 6, 7)	1	3		
Week 18: <34 µmol/L (n = 8, 8)	2	5		
Week 18: 34-50 µmol/L (n = 8, 8)	3	0		
Week 18: >50 µmol/L (n = 8, 8)	3	3		
Week 24: <34 µmol/L (n = 6, 6)	2	4		
Week 24: 34-50 µmol/L (n = 6, 6)	3	0		
Week 24: >50 µmol/L (n = 6, 6)	1	2		
Week 30: <34 µmol/L (n = 6, 6)	3	4		
Week 30: 34-50 µmol/L (n = 6, 6)	1	1		
Week 30: >50 µmol/L (n = 6, 6)	2	1		
Week 36: <34 µmol/L (n = 6, 6)	3	4		
Week 36: 34-50 µmol/L (n = 6, 6)	1	0		
Week 36: >50 µmol/L (n = 6, 6)	2	2		
Week 48: <34 µmol/L (n = 6, 6)	2	4		
Week 48: 34-50 µmol/L (n = 6, 6)	1	0		
Week 48: >50 µmol/L (n = 6, 6)	3	2		
Extension Month 3: <34 µmol/L (n = 6, 5)	2	3		
Extension Month 3: 34-50 µmol/L (n = 6, 5)	1	1		
Extension Month 3: >50 µmol/L (n = 6, 5)	3	1		
Extension Month 6: <34 µmol/L (n = 3, 2)	1	1		

Extension Month 6: 34-50 µmol/L (n = 3, 2)	1	0		
Extension Month 6: >50 µmol/L (n = 3, 2)	1	1		
Extension Month 9: <34 µmol/L (n = 0, 2)	0	1		
Extension Month 9: 34-50 µmol/L (n = 0, 2)	0	1		
Extension Month 9: >50 µmol/L (n = 0, 2)	0	0		
Extension Month 12: <34 µmol/L (n = 1, 1)	0	1		
Extension Month 12: 34-50 µmol/L (n = 1, 1)	1	0		
Extension Month 12: >50 µmol/L (n = 1, 1)	0	0		
Extension Month 15: <34 µmol/L (n = 1, 1)	0	1		
Extension Month 15: 34-50 µmol/L (n = 1, 1)	1	0		
Extension Month 15: >50 µmol/L (n = 1, 1)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants by Child-Pugh Score Component (Hepatic Encephalopathy Categories)

End point title	Number of Participants by Child-Pugh Score Component (Hepatic Encephalopathy Categories)

End point description:

Number of participants with Child-Pugh component - Hepatic encephalopathy in categories of Grade 0, Grade 1 or 2, and Grade 3 and 4 has been reported.
Grade 0: normal consciousness, normal personality, normal neurological examination, normal electroencephalogram.
Grade 1: restless, sleep disturbed, irritable/agitated, tremor, impaired handwriting, 5 cycles, per second (cps) waves.
Grade 2: lethargic, time-disoriented, inappropriate, asterixis, ataxia, slow triphasic waves.
Grade 3: somnolent, stuporous, place-disoriented, hyperactive reflexes, rigidity, slower waves.
Grade 4: unrousable coma, no personality/behavior, decerebrate, slow 2-3 cps delta activity.

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Day 1, Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	10		
Units: Participants				
Day 1: Grade 0 (n = 12, 10)	8	8		
Day 1: Grade 1 or 2 (n = 12, 10)	4	2		
Day 1: Grade 3 or 4 (n = 12, 10)	0	0		
Week 6: Grade 0 (n = 9, 9)	6	6		
Week 6: Grade 1 or 2 (n = 9, 9)	3	3		
Week 6: Grade 3 or 4 (n = 9, 9)	0	0		
Week 12: Grade 0 (n = 6, 7)	4	5		
Week 12: Grade 1 or 2 (n = 6, 7)	2	2		
Week 12: Grade 3 or 4 (n = 6, 7)	0	0		
Week 18: Grade 0 (n = 8, 8)	6	7		
Week 18: Grade 1 or 2 (n = 8, 8)	2	1		
Week 18: Grade 3 or 4 (n = 8, 8)	0	0		
Week 24: Grade 0 (n = 6, 6)	6	5		
Week 24: Grade 1 or 2 (n = 6, 6)	0	1		
Week 24: Grade 3 or 4 (n = 6, 6)	0	0		
Week 30: Grade 0 (n = 6, 6)	5	5		
Week 30: Grade 1 or 2 (n = 6, 6)	1	1		
Week 30: Grade 3 or 4 (n = 6, 6)	0	0		
Week 36: Grade 0 (n = 6, 6)	6	5		
Week 36: Grade 1 or 2 (n = 6, 6)	0	1		
Week 36: Grade 3 or 4 (n = 6, 6)	0	0		
Week 48: Grade 0 (n = 6, 6)	5	5		
Week 48: Grade 1 or 2 (n = 6, 6)	1	1		
Week 48: Grade 3 or 4 (n = 6, 6)	0	0		
Extension Month 3: Grade 0 (n = 6, 5)	5	4		
Extension Month 3: Grade 1 or 2 (n = 6, 5)	1	1		
Extension Month 3: Grade 3 or 4 (n = 6, 5)	0	0		
Extension Month 6: Grade 0 (n = 3, 2)	3	1		
Extension Month 6: Grade 1 or 2 (n = 3, 2)	0	1		
Extension Month 6: Grade 3 or 4 (n = 3, 2)	0	0		
Extension Month 9: Grade 0 (n = 0, 2)	0	1		
Extension Month 9: Grade 1 or 2 (n = 0, 2)	0	1		
Extension Month 9: Grade 3 or 4 (n = 0, 2)	0	0		
Extension Month 12: Grade 0 (n = 1, 1)	1	0		
Extension Month 12: Grade 1 or 2 (n = 1, 1)	0	1		
Extension Month 12: Grade 3 or 4 (n = 1, 1)	0	0		
Extension Month 15: Grade 0 (n = 1, 1)	1	0		
Extension Month 15: Grade 1 or 2 (n = 1, 1)	0	1		
Extension Month 15: Grade 3 or 4 (n = 1, 1)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Bilirubin at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point title	Change From Baseline in Total Bilirubin at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point description:

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11[288]	10		
Units: µmol/L				
median (inter-quartile range (Q1-Q3))				
Change at Week 3 (n = 11, 10)	0.86 (-13.0 to 6.50)	-3.25 (-4.00 to 24.00)		
Change at Week 6 (n = 9, 8)	3.00 (-1.50 to 5.99)	-2.14 (-3.43 to 26.75)		
Change at Week 12 (n = 7, 7)	0.86 (-4.28 to 9.00)	-1.71 (-6.00 to 17.96)		
Change at Week 18 (n = 8, 8)	1.08 (-4.70 to 16.05)	-4.03 (-9.00 to 3.21)		
Change at Week 24 (n = 5, 7)	2.67 (-1.50 to 20.40)	-3.50 (-10.00 to 1.71)		
Change at Week 30 (n = 6, 6)	2.08 (-2.57 to 31.34)	-8.49 (-9.00 to -5.50)		
Change at Week 36 (n = 6, 6)	4.25 (-11.12 to 9.67)	-3.53 (-7.00 to 3.42)		
Change at Week 42 (n = 6, 7)	6.58 (-7.70 to 12.00)	1.71 (-2.85 to 6.00)		
Change at Week 48 (n = 6, 6)	6.25 (-2.57 to 23.67)	-3.75 (-6.27 to -0.57)		
Change at Extension Month 3 (n = 6, 5)	2.25 (0.86 to 60.67)	0.50 (-16.00 to 0.57)		
Change at Extension Month 6 (n = 3, 2)	-1.50 (-12.83 to 21.38)	-0.22 (-1.00 to 0.57)		
Change at Extension Month 9 (n = 0, 2)	99999 (99999 to 99999)	-7.86 (-18.00 to 2.28)		
Change at Extension Month 12 (n = 1, 1)	-14.54 (-14.54 to -14.54)	9.12 (9.12 to 9.12)		

Change at Extension Month 15 (n = 1, 1)	-12.83 (-12.83 to -12.83)	24.51 (24.51 to 24.51)		

Notes:

[288] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Direct Bilirubin at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point title	Change From Baseline in Direct Bilirubin at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point description:

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11[289]	10		
Units: µmol/L				
median (inter-quartile range (Q1-Q3))				
Change at Week 3 (n = 11, 10)	0.00 (-6.04 to 1.50)	-1.07 (-1.50 to 15.00)		
Change at Week 6 (n = 8, 8)	2.53 (0.00 to 7.25)	-1.32 (-4.61 to 18.50)		
Change at Week 12 (n = 7, 7)	4.28 (0.00 to 12.50)	-1.14 (-3.00 to 1.71)		
Change at Week 18 (n = 8, 8)	2.99 (0.50 to 14.20)	-1.82 (-3.25 to 2.00)		
Change at Week 24 (n = 5, 6)	1.00 (-1.00 to 15.00)	-1.75 (-2.85 to 0.00)		
Change at Week 30 (n = 6, 5)	0.93 (-1.00 to 6.10)	-2.50 (-4.00 to -1.71)		
Change at Week 36 (n = 6, 6)	0.00 (-4.28 to 3.37)	-1.57 (-2.50 to 0.00)		
Change at Week 42 (n = 6, 7)	2.50 (-2.57 to 9.37)	-1.71 (-2.66 to 1.50)		
Change at Week 48 (n = 6, 6)	3.61 (-1.00 to 15.00)	-2.36 (-6.08 to -1.14)		
Change at Extension Month 3 (n = 5, 5)	3.37 (0.00 to 4.28)	-2.00 (-15.00 to 1.50)		
Change at Extension Month 6 (n = 3, 2)	0.00 (-5.99 to 19.67)	-1.00 (-6.00 to 3.99)		
Change at Extension Month 9 (n = 0, 2)	99999 (99999 to 99999)	-3.79 (-15.00 to 7.41)		
Change at Extension Month 12 (n = 1, 1)	-9.41 (-9.41 to -9.41)	7.41 (7.41 to 7.41)		

Change at Extension Month 15 (n = 1, 1)	-5.99 (-5.99 to -5.99)	12.54 (12.54 to 12.54)		

Notes:

[289] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Alkaline Phosphatase at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point title	Change From Baseline in Alkaline Phosphatase at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point description:

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11[290]	10		
Units: unit per liter (U/ L)				
median (inter-quartile range (Q1-Q3))				
Change at Week 3 (n = 11, 10)	-21.0 (-48.0 to 6.0)	-9.0 (-48.0 to 0.0)		
Change at Week 6 (n = 9, 9)	-7.0 (-22.0 to 19.0)	5.0 (-12.0 to 15.0)		
Change at Week 12 (n = 7, 7)	-1.0 (-54.0 to 12.0)	-17.0 (-32.0 to 6.0)		
Change at Week 18 (n = 8, 8)	-20.5 (-35.5 to 16.5)	-4.5 (-37.5 to 1.5)		
Change at Week 24 (n = 5, 7)	-30.0 (-66.0 to 16.0)	-5.0 (-100.0 to 4.0)		
Change at Week 30 (n = 6, 6)	-34.5 (-76.0 to -19.0)	-20.0 (-33.0 to -7.0)		
Change at Week 36 (n = 6, 8)	-26.0 (-64.0 to -6.0)	-4.0 (-89.5 to 4.0)		
Change at Week 42 (n = 6, 7)	-24.0 (-45.0 to -17.0)	5.0 (-87.0 to 9.0)		
Change at Week 48 (n = 6, 5)	-29.0 (-63.0 to -17.0)	8.0 (-3.0 to 13.0)		
Change at Extension Month 3 (n = 6, 5)	-24.0 (-48.0 to -7.0)	10.0 (-14.0 to 26.0)		
Change at Extension Month 6 (n = 3, 2)	6.0 (-33.0 to 7.0)	-46.0 (-133.0 to 41.0)		
Change at Extension Month 9 (n = 0, 2)	99999 (99999 to 99999)	-66.5 (-148.0 to 15.0)		
Change at Extension Month 12 (n = 1, 1)	-72.0 (-72.0 to -72.0)	122.0 (122.0 to 122.0)		

Change at Extension Month 15 (n = 1, 1)	-83.0 (-83.0 to -83.0)	10.0 (10.0 to 10.0)		

Notes:

[290] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Alanine Aminotransferase at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point title	Change From Baseline in Alanine Aminotransferase at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point description:

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11[291]	10		
Units: U/L				
median (inter-quartile range (Q1-Q3))				
Change at Week 3 (n = 11, 10)	-5.0 (-9.0 to -1.0)	-2.0 (-9.0 to 1.0)		
Change at Week 6 (n = 9, 8)	-5.0 (-9.0 to 1.0)	2.5 (-1.0 to 12.5)		
Change at Week 12 (n = 7, 7)	1.0 (-9.0 to 5.0)	10.0 (1.0 to 19.0)		
Change at Week 18 (n = 8, 8)	-6.5 (-12.5 to -3.5)	-0.5 (-5.0 to 1.5)		
Change at Week 24 (n = 5, 6)	-4.0 (-5.0 to 4.0)	-4.0 (-8.0 to 3.0)		
Change at Week 30 (n = 6, 6)	-6.0 (-12.0 to 3.0)	1.5 (-2.0 to 3.0)		
Change at Week 36 (n = 6, 7)	11.5 (-6.0 to 24.0)	-3.0 (-5.0 to 5.0)		
Change at Week 42 (n = 6, 7)	-9.0 (-12.0 to -3.0)	-1.0 (-6.0 to 1.0)		
Change at Week 48 (n = 6, 6)	-6.0 (-7.0 to -2.0)	1.0 (-1.0 to 2.0)		
Change at Extension Month 3 (n = 6, 5)	-8.0 (-12.0 to -3.0)	-1.0 (-7.0 to 7.0)		
Change at Extension Month 6 (n = 3, 2)	-12.0 (-27.0 to -1.0)	-1.5 (-6.0 to 3.0)		
Change at Extension Month 9 (n = 0, 2)	99999 (99999 to 99999)	-6.0 (-11.0 to -1.0)		
Change at Extension Month 12 (n = 1, 1)	-34.0 (-34.0 to -34.0)	-2.0 (-2.0 to -2.0)		

Change at Extension Month 15 (n = 1, 1)	-32.0 (-32.0 to -32.0)	1.0 (1.0 to 1.0)		

Notes:

[291] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Aspartate Aminotransferase at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point title	Change From Baseline in Aspartate Aminotransferase at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point description:

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11[292]	10		
Units: U/L				
median (inter-quartile range (Q1-Q3))				
Change at Week 3 (n = 11, 10)	-4.0 (-11.0 to 3.0)	-1.0 (-13.0 to 6.0)		
Change at Week 6 (n = 8, 8)	-4.0 (-12.0 to 0.5)	10.5 (-3.5 to 23.5)		
Change at Week 12 (n = 7, 7)	0.0 (-5.0 to 19.0)	18.0 (-3.0 to 29.0)		
Change at Week 18 (n = 8, 8)	-1.5 (-7.5 to 5.5)	-5.0 (-10.5 to 4.5)		
Change at Week 24 (n = 5, 6)	-7.0 (-13.0 to -2.0)	-2.0 (-7.0 to 1.0)		
Change at Week 30 (n = 6, 6)	-10.0 (-12.0 to -3.0)	1.0 (-2.0 to 9.0)		
Change at Week 36 (n = 6, 7)	19.5 (-10.0 to 34.0)	2.0 (-4.0 to 15.0)		
Change at Week 42 (n = 6, 7)	-3.5 (-14.0 to 8.0)	1.0 (-2.0 to 39.0)		
Change at Week 48 (n = 6, 6)	-12.0 (-22.0 to 7.0)	0.5 (-15.0 to 20.0)		
Change at Extension Month 3 (n = 6, 5)	-6.5 (-11.0 to 6.0)	-12.0 (-15.0 to 6.0)		
Change at Extension Month 6 (n = 3, 2)	-16.0 (-32.0 to 1.0)	-0.5 (-21.0 to 20.0)		
Change at Extension Month 9 (n = 0, 2)	99999 (99999 to 99999)	-8.5 (-33.0 to 16.0)		
Change at Extension Month 12 (n = 1, 1)	-33.0 (-33.0 to -33.0)	19.0 (19.0 to 19.0)		

Change at Extension Month 15 (n = 1, 1)	-34.0 (-34.0 to -34.0)	16.0 (16.0 to 16.0)		

Notes:

[292] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Gamma Glutamyl Transferase at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point title	Change From Baseline in Gamma Glutamyl Transferase at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point description:

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10[293]	10		
Units: U/L				
median (inter-quartile range (Q1-Q3))				
Change at Week 3 (n = 10, 10)	-12.5 (-27.0 to -2.0)	-13.5 (-54.0 to -1.0)		
Change at Week 6 (n = 9, 9)	-11.0 (-28.0 to -3.0)	0.0 (-31.0 to 4.0)		
Change at Week 12 (n = 7, 7)	-13.0 (-32.0 to -3.0)	-2.0 (-44.0 to 7.0)		
Change at Week 18 (n = 8, 8)	-9.5 (-28.0 to -0.5)	-3.5 (-38.5 to 1.5)		
Change at Week 24 (n = 5, 7)	8.0 (-37.0 to 25.0)	-14.0 (-70.0 to -5.0)		
Change at Week 30 (n = 5, 6)	-9.0 (-22.0 to -5.0)	-12.5 (-27.0 to 5.0)		
Change at Week 36 (n = 6, 8)	-5.5 (-12.0 to 24.0)	-10.5 (-90.0 to 4.5)		
Change at Week 42 (n = 6, 7)	-12.0 (-26.0 to 5.0)	-4.0 (-154.0 to 17.0)		
Change at Week 48 (n = 6, 6)	-9.0 (-21.0 to -6.0)	-15.0 (-112.0 to 9.0)		
Change at Extension Month 3 (n = 6, 5)	-9.5 (-48.0 to 1.0)	9.0 (-14.0 to 22.0)		
Change at Extension Month 6 (n = 3, 2)	-10.0 (-35.0 to -9.0)	-58.5 (-137.0 to 20.0)		
Change at Extension Month 9 (n = 0, 2)	99999 (99999 to 99999)	-57.0 (-128.0 to 14.0)		
Change at Extension Month 12 (n = 1, 1)	-74.0 (-74.0 to -74.0)	8.0 (8.0 to 8.0)		

Change at Extension Month 15 (n = 1, 1)	-63.0 (-63.0 to -63.0)	2.0 (2.0 to 2.0)		

Notes:

[293] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Prothrombin INR at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point title	Change From Baseline in Prothrombin INR at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point description:

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	10[294]		
Units: INR				
median (inter-quartile range (Q1-Q3))				
Change at Week 3 (n = 11, 10)	0.00 (0.00 to 0.10)	0.00 (0.00 to 0.10)		
Change at Week 6 (n = 9, 9)	0.00 (-0.03 to 0.00)	0.00 (-0.05 to 0.00)		
Change at Week 12 (n = 6, 7)	0.08 (0.00 to 0.15)	-0.05 (-0.10 to 0.00)		
Change at Week 18 (n = 8, 8)	0.09 (0.00 to 0.10)	-0.05 (-0.13 to 0.05)		
Change at Week 24 (n = 4, 5)	0.03 (-0.02 to 0.08)	-0.05 (-0.10 to 0.05)		
Change at Week 30 (n = 6, 6)	0.03 (-0.03 to 0.10)	0.00 (-0.10 to 0.00)		
Change at Week 36 (n = 6, 8)	0.05 (0.00 to 0.10)	-0.10 (-0.18 to 0.03)		
Change at Week 42 (n = 6, 7)	0.05 (0.00 to 0.07)	0.00 (-0.10 to 0.05)		
Change at Week 48 (n = 6, 5)	0.00 (-0.03 to 0.05)	-0.10 (-0.15 to 0.00)		
Change at Extension Month 3 (n = 6, 5)	0.06 (0.00 to 0.10)	-0.10 (-0.10 to -0.10)		
Change at Extension Month 6 (n = 3, 2)	0.05 (-0.10 to 0.15)	-0.05 (-0.10 to 0.00)		
Change at Extension Month 9 (n = 1, 2)	0.15 (0.15 to 0.15)	0.00 (0.00 to 0.00)		
Change at Extension Month 12 (n = 1, 1)	0.05 (0.05 to 0.05)	0.10 (0.10 to 0.10)		

Change at Extension Month 15 (n = 1, 0)	0.05 (0.05 to 0.05)	99999 (99999 to 99999)		

Notes:

[294] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Creatinine at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point title	Change From Baseline in Creatinine at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point description:

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11[295]	10		
Units: µmol/L				
median (inter-quartile range (Q1-Q3))				
Change at Week 3 (n = 11, 10)	0.884 (-3.000 to 5.000)	-0.308 (-2.000 to 1.768)		
Change at Week 6 (n = 9, 9)	5.000 (0.388 to 5.746)	0.884 (-1.000 to 4.000)		
Change at Week 12 (n = 7, 7)	-0.496 (-4.000 to 13.500)	2.500 (-1.000 to 5.000)		
Change at Week 18 (n = 8, 8)	-2.431 (-4.958 to 7.250)	0.942 (-6.170 to 5.036)		
Change at Week 24 (n = 5, 7)	-1.000 (-4.000 to -0.496)	-2.652 (-11.492 to 5.000)		
Change at Week 30 (n = 6, 6)	-0.663 (-4.032 to 1.768)	-2.250 (-6.188 to 3.000)		
Change at Week 36 (n = 6, 8)	1.500 (-1.326 to 7.000)	2.466 (-1.960 to 33.586)		
Change at Week 42 (n = 6, 7)	2.000 (-1.326 to 4.000)	6.236 (-2.652 to 28.000)		
Change at Week 48 (n = 6, 6)	2.221 (-3.536 to 6.000)	0.466 (-3.000 to 20.000)		
Change at Extension Month 3 (n = 6, 5)	3.884 (0.000 to 6.630)	0.000 (-1.500 to 12.000)		
Change at Extension Month 6 (n = 3, 2)	2.652 (-4.000 to 12.818)	4.648 (-7.500 to 16.796)		
Change at Extension Month 9 (n = 0, 2)	99999 (99999 to 99999)	15.068 (4.500 to 25.636)		
Change at Extension Month 12 (n = 1, 1)	10.608 (10.608 to 10.608)	27.404 (27.404 to 27.404)		

Change at Extension Month 15 (n = 1, 1)	4.420 (4.420 to 4.420)	29.172 (29.172 to 29.172)		

Notes:

[295] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Albumin at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point title	Change From Baseline in Albumin at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point description:

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10[296]	10		
Units: g/L				
median (inter-quartile range (Q1-Q3))				
Change at Week 3 (n = 10, 10)	-2.25 (-2.50 to -1.00)	-0.50 (-1.70 to 0.00)		
Change at Week 6 (n = 9, 9)	-1.00 (-3.00 to 0.00)	0.00 (-1.00 to 1.30)		
Change at Week 12 (n = 7, 7)	-2.00 (-4.00 to -1.50)	-0.70 (-1.00 to 1.50)		
Change at Week 18 (n = 8, 8)	-4.25 (-5.00 to -1.50)	0.00 (-1.60 to 0.50)		
Change at Week 24 (n = 5, 7)	-2.50 (-4.00 to -1.00)	-2.50 (-2.70 to 1.00)		
Change at Week 30 (n = 6, 6)	-2.50 (-4.00 to -2.00)	0.15 (-1.50 to 1.00)		
Change at Week 36 (n = 6, 8)	-2.00 (-3.00 to -2.00)	0.50 (-2.35 to 2.25)		
Change at Week 42 (n = 6, 7)	-1.25 (-4.00 to 0.00)	-0.70 (-1.00 to 2.00)		
Change at Week 48 (n = 6, 6)	-0.50 (-2.00 to 1.00)	0.50 (-4.70 to 1.00)		
Change at Extension Month 3 (n = 6, 5)	-2.50 (-3.00 to -1.00)	1.00 (-2.70 to 2.50)		
Change at Extension Month 6 (n = 3, 2)	-2.00 (-3.00 to -1.00)	-0.35 (-1.70 to 1.00)		
Change at Extension Month 9 (n = 0, 2)	99999 (99999 to 99999)	-1.35 (-3.70 to 1.00)		
Change at Extension Month 12 (n = 1, 1)	-1.00 (-1.00 to -1.00)	-2.70 (-2.70 to -2.70)		
Change at Extension Month 15 (n = 1, 1)	-1.00 (-1.00 to -1.00)	-11.70 (-11.70 to -11.70)		

Notes:

[296] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Platelets at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point title	Change From Baseline in Platelets at Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point description:

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 3, 6, 12, 18, 24, 30, 36, 42, and 48; and Extension Months 3, 6, 9, 12, and 15

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10[297]	9		
Units: 10^9/L				
median (inter-quartile range (Q1-Q3))				
Change at Week 3 (n = 10, 9)	-6.2 (-21.0 to -3.0)	-7.5 (-12.0 to 8.5)		
Change at Week 6 (n = 8, 6)	-12.0 (-28.8 to -2.3)	15.0 (1.0 to 26.5)		
Change at Week 12 (n = 6, 5)	-10.5 (-31.0 to 7.5)	-15.0 (-15.0 to -1.5)		
Change at Week 18 (n = 6, 7)	-15.0 (-21.9 to -8.5)	7.5 (-10.0 to 38.5)		
Change at Week 24 (n = 5, 6)	4.5 (-14.4 to 17.0)	-1.5 (-25.0 to 25.5)		
Change at Week 30 (n = 6, 5)	-11.4 (-23.5 to 15.0)	-5.5 (-9.0 to 6.5)		
Change at Week 36 (n = 6, 6)	-16.5 (-20.5 to -12.0)	9.8 (-6.5 to 39.5)		
Change at Week 42 (n = 6, 6)	-16.2 (-37.5 to -10.0)	9.0 (6.5 to 11.0)		
Change at Week 48 (n = 5, 5)	4.0 (-41.5 to 23.0)	-9.0 (-11.5 to 14.5)		
Change at Extension Month 3 (n = 6, 5)	-5.0 (-24.0 to 16.5)	-11.5 (-24.0 to -8.5)		
Change at Extension Month 6 (n = 3, 1)	48.5 (14.0 to 78.0)	-0.5 (-0.5 to -0.5)		
Change at Extension Month 9 (n = 0, 2)	99999 (99999 to 99999)	-4.5 (-5.5 to -3.5)		
Change at Extension Month 12 (n = 1, 1)	-2.0 (-2.0 to -2.0)	-3.5 (-3.5 to -3.5)		
Change at Extension Month 15 (n = 1, 1)	-9.0 (-9.0 to -9.0)	-22.5 (-22.5 to -22.5)		

Notes:

[297] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Bile Acids Concentration at Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Month 3

End point title	Change From Baseline in Total Bile Acids Concentration at Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Month 3

End point description:

Total bile acids (micromole [µM]) = total ursodeoxycholic acid (unconjugated, glyco-conjugate, tauro-conjugate) in µM + total chenodeoxycholic acid (unconjugated, glyco-conjugate, tauro-conjugate) in µM + total deoxycholic acid (unconjugated, glyco-conjugate, tauro-conjugate) in µM + total cholic acid (unconjugated, glyco-conjugate, tauroconjugate) in µM + total lithocholic acid (unconjugated, glyco-conjugate, tauro-conjugate) in µM.

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 6, 12, 18, 24, 30, 36, 48; and Extension Month 3

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7[298]	8		
Units: µM				
median (inter-quartile range (Q1-Q3))				
Change at Week 6 (n = 7, 8)	16.3 (-7.68 to 37.4)	8.09 (-15.9 to 37.1)		
Change at Week 12 (n = 6, 6)	0.863 (-21.0 to 88.4)	5.55 (-58.4 to 13.7)		
Change at Week 18 (n = 7, 7)	17.7 (-56.0 to 160)	12.8 (-169 to 36.0)		
Change at Week 24 (n = 4, 4)	3.29 (-76.6 to 30.6)	-3.14 (-14.5 to 21.3)		
Change at Week 30 (n = 4, 6)	26.0 (-56.0 to 98.5)	16.1 (-7.06 to 38.7)		
Change at Week 36 (n = 5, 8)	-15.2 (-79.4 to 10.0)	-1.54 (-22.9 to 24.6)		
Change at Week 48 (n = 4, 5)	63.2 (16.7 to 132)	0.876 (-4.07 to 19.5)		
Change at Extension Month 3 (n = 0, 1)	99999 (99999 to 99999)	-32.9 (-32.9 to -32.9)		

Notes:

[298] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Endogenous Bile Acids Concentration at Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Month 3

End point title	Change From Baseline in Total Endogenous Bile Acids Concentration at Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Month 3

End point description:

Total endogenous bile acids (µM) = total chenodeoxycholic acid (unconjugated, glyco-conjugate, tauro-conjugate) in µM + total deoxycholic acid (unconjugated, glyco-conjugate, tauro-conjugate) in µM + total cholic acid (unconjugated, glycoconjugate, tauro-conjugate) in µM + total lithocholic acid (unconjugated, glyco-conjugate, tauro-conjugate) in µM.

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Month 3

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7[299]	9		
Units: µM				
median (inter-quartile range (Q1-Q3))				
Change at Week 6 (n = 7, 9)	-4.98 (-6.88 to 36.2)	3.58 (-5.64 to 14.0)		
Change at Week 12 (n = 6, 6)	-3.97 (-13.3 to 63.9)	1.46 (-5.43 to 4.81)		
Change at Week 18 (n = 7, 7)	-5.00 (-20.2 to 51.0)	3.98 (-18.3 to 7.21)		
Change at Week 24 (n = 4, 6)	-6.76 (-18.5 to -1.25)	3.18 (-2.53 to 15.2)		
Change at Week 30 (n = 5, 6)	6.74 (-6.22 to 7.44)	1.47 (-3.87 to 13.6)		
Change at Week 36 (n = 6, 8)	-5.74 (-24.9 to -0.576)	-2.69 (-14.4 to 9.66)		
Change at Week 48 (n = 6, 6)	10.9 (6.32 to 19.8)	4.18 (-2.08 to 9.82)		
Change at Extension Month 3 (n = 0, 1)	99999 (99999 to 99999)	-9.57 (-9.57 to -9.57)		

Notes:

[299] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 7α-hydroxy-4-cholesten-3-one (C4) at Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Month 3

End point title	Change From Baseline in 7α-hydroxy-4-cholesten-3-one (C4) at Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Month 3

End point description:

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Month 3

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8[300]	9		
Units: ng/mL				
median (inter-quartile range (Q1-Q3))				
Change at Week 6 (n = 8, 9)	0.0990 (-0.0445 to 0.296)	0.0770 (-0.110 to 0.450)		
Change at Week 12 (n = 6, 7)	-0.0275 (-0.0690 to 0.156)	-0.289 (-1.31 to 0.0100)		
Change at Week 18 (n = 7, 8)	-0.0470 (-0.278 to 0.205)	-0.267 (-0.965 to 8.05)		
Change at Week 24 (n = 4, 6)	-0.00100 (-0.00700 to 0.692)	-0.141 (-1.67 to 1.07)		
Change at Week 30 (n = 5, 6)	0.0890 (0.0500 to 0.355)	-0.386 (-1.77 to 2.50)		
Change at Week 36 (n = 6, 8)	0.118 (-0.104 to 0.240)	-0.476 (-3.53 to 5.41)		
Change at Week 48 (n = 6, 6)	-0.170 (-0.491 to -0.0140)	-0.510 (-1.83 to 5.20)		
Change at Extension Month 3 (n = 0, 1)	99999 (99999 to 99999)	1.36 (1.36 to 1.36)		

Notes:

[300] - 99999 denotes data not available as there were no participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fibroblast Growth Factor-19 (FGF-19) Concentrations at Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Month 3

End point title	Change From Baseline in Fibroblast Growth Factor-19 (FGF-19) Concentrations at Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Month 3

End point description:

APD: Participants in the ITT population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 6, 12, 18, 24, 30, 36, and 48; and Extension Month 3

End point values	Placebo	Obeticholic Acid (OCA)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	9		
Units: picograms per milliliter (pg/mL)				
median (inter-quartile range (Q1-Q3))				
Change at Week 6 (n = 8, 9)	-50.7 (-142 to 33.0)	26.0 (4.50 to 101)		
Change at Week 12 (n = 6, 7)	-14.0 (-220 to 19.0)	119 (-25.6 to 174)		
Change at Week 18 (n = 7, 8)	-57.0 (-118 to 40.0)	136 (-28.3 to 298)		
Change at Week 24 (n = 4, 6)	-33.0 (-152 to 402)	16.6 (-24.0 to 219)		
Change at Week 30 (n = 5, 6)	-83.0 (-123 to 43.0)	142 (-45.0 to 168)		
Change at Week 36 (n = 6, 8)	26.0 (-34.0 to 102)	15.0 (-97.4 to 201)		
Change at Week 48 (n = 6, 6)	-28.5 (-161 to 84.5)	69.6 (8.00 to 145)		
Change at Extension Month 3 (n = 1, 1)	-117 (-117 to -117)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to approximately 3 years

Adverse event reporting additional description:

The Safety Population included all participants who received at least 1 dose of investigational product (OCA or placebo).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Obeticholic Acid (OCA)

Reporting group description:

Participants initiated treatment with OCA 5 mg tablets orally once weekly. At Week 12, if there were no safety concerns, the dose was up-titrated to OCA 5 mg twice weekly. Every 6 weeks thereafter, based on tolerability assessments, further up-titration of dose was considered. At each titration visit, the participants started the higher dose regimen no earlier than 2 days after the prior dose. The maximum dose titration was OCA 10 mg twice weekly at least 3 days apart. The minimum treatment duration was 48 Weeks. Participants, who had completed their 48 Week treatment, could continue the treatment until all randomized participants had completed their 48 Week treatment period and the database for that period was locked (total duration: approximately up to 3 years).

Reporting group title	Placebo

Reporting group description:

Participants received OCA matching placebo tablets orally once weekly or twice weekly for the duration of at least 48 Weeks. Participants, who had completed their 48 Week treatment, could continue the treatment until all randomized participants had completed their 48 Week treatment period and the database for that period was locked (total duration: approximately up to 3 years).

Serious adverse events	Obeticholic Acid (OCA)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 10 (70.00%)	9 / 12 (75.00%)	
number of deaths (all causes)	2	2	
number of deaths resulting from adverse events			
Vascular disorders			
Aortic aneurysm rupture			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac arrest			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Surgical and medical procedures			
Liver transplant			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hepatic encephalopathy			
subjects affected / exposed	0 / 10 (0.00%)	2 / 12 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)	2 / 12 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			

subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	3 / 10 (30.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrothorax			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (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	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Obeticholic Acid (OCA)	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	10 / 12 (83.33%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pituitary tumour benign			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Peripheral coldness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Haematoma			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 10 (20.00%)	1 / 12 (8.33%)	
occurrences (all)	3	1	
Chest discomfort			

subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Disease progression			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	1 / 10 (10.00%)	4 / 12 (33.33%)	
occurrences (all)	1	4	
Asthenia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	4	
Non-cardiac chest pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Breast pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	2 / 10 (20.00%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Haemoptysis			

subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Blood bilirubin increased			
subjects affected / exposed	1 / 10 (10.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Blood urea increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Cardiac murmur			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Tooth fracture			
subjects affected / exposed	1 / 10 (10.00%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Joint injury			
subjects affected / exposed	0 / 10 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Angina pectoris			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 10 (20.00%)	1 / 12 (8.33%)	
occurrences (all)	2	1	

Burning sensation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Balance disorder			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Encephalopathy			
subjects affected / exposed	1 / 10 (10.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Hypoaesthesia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Hepatic encephalopathy			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Neuralgia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Memory impairment			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 10 (30.00%)	1 / 12 (8.33%)	
occurrences (all)	3	1	
Iron deficiency anaemia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Ear and labyrinth disorders			

Ear pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Vitreous floaters			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	6 / 10 (60.00%)	4 / 12 (33.33%)	
occurrences (all)	6	4	
Abdominal distension			
subjects affected / exposed	2 / 10 (20.00%)	3 / 12 (25.00%)	
occurrences (all)	2	3	
Diarrhoea			
subjects affected / exposed	2 / 10 (20.00%)	1 / 12 (8.33%)	
occurrences (all)	3	2	
Nausea			
subjects affected / exposed	2 / 10 (20.00%)	2 / 12 (16.67%)	
occurrences (all)	3	3	
Vomiting			
subjects affected / exposed	2 / 10 (20.00%)	1 / 12 (8.33%)	
occurrences (all)	4	1	
Abdominal discomfort			
subjects affected / exposed	1 / 10 (10.00%)	1 / 12 (8.33%)	
occurrences (all)	3	1	
Dyspepsia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Frequent bowel movements			

subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Haematemesis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Haemorrhoids			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Melaena			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Abdominal pain lower			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	0 / 10 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Dry mouth			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastric antral vascular ectasia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastric polyps			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Irritable bowel syndrome			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Large intestine polyp			

subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Portal hypertensive gastropathy			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Varices oesophageal			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Abdominal Pain			
subjects affected / exposed	2 / 10 (20.00%)	1 / 12 (8.33%)	
occurrences (all)	3	1	
Hepatobiliary disorders			
Portal vein thrombosis			
subjects affected / exposed	2 / 10 (20.00%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 10 (30.00%)	2 / 12 (16.67%)	
occurrences (all)	4	4	
Skin mass			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Palmar erythema			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 10 (20.00%)	1 / 12 (8.33%)	
occurrences (all)	3	3	
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue			

disorders			
Pain in extremity			
subjects affected / exposed	2 / 10 (20.00%)	0 / 12 (0.00%)	
occurrences (all)	3	0	
Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)	2 / 12 (16.67%)	
occurrences (all)	2	3	
Limb mass			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Muscular weakness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Rhabdomyolysis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Muscle spasms			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Urinary tract infection			
subjects affected / exposed	3 / 10 (30.00%)	2 / 12 (16.67%)	
occurrences (all)	3	2	
Oesophageal candidiasis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Cytomegalovirus infection reactivation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			

subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Cellulitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Peritonitis bacterial			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Ear infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Fungal infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Skin infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hyperkalaemia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Hypokalaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	

Dehydration subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 May 2017	The changes in Version 2 were incorporated based on Food and Drug Administration (FDA) review of Version 1 of the protocol: • Background information was included to estimate the exposure difference between healthy subjects and subjects with moderate hepatic impairment to support the rationale for dose selection • Additional PK sampling times were added to adequately characterize the PK of OCA and its active metabolites at steady state in subjects with moderate and severe impairment when dosing weekly to biweekly • The period between screening and Day 1 was extended to at least 14 days to establish a baseline for serum biomarkers with at least two samples two weeks apart • The Week 3 contact Visit by email/telephone was changed to a Safety Visit to assess evidence of early hepatotoxicity • Guidelines were added to assess subjects for evidence of hepatotoxicity at each visit
04 January 2018	• The Introduction was revised to highlight the need for close monitoring specifically in subjects with clinical evidence of hepatic decompensation and other complications due to advanced cirrhosis. • Dosing regimens were updated to modify dosing to one regimen for subjects with moderate and severe hepatic impairment [e.g., same for child-pugh B and child-pugh C], not to exceed 10 mg twice weekly, to align with label dosing guidelines. Titration was then only based on tolerability and not CP score. • Reference to an option for open-label treatment was removed. An open-label extension was to be considered only after review of blinded safety and PK data from the double-blind treatment period. • Protocol was updated with discontinuation criteria for decompensation events and biochemical thresholds. A plan for monitoring and drug-induced liver injury algorithm was included to ensure careful monitoring and drug interruption/discontinuation. Analysis of decompensation events as adverse events of interest was added. Additionally, "Close Observation" per FDA Guidance for Industry on Drug Induced Liver Injury (DILI) was clearly defined in the protocol to ensure that subjects who experienced a potential DILI underwent a full evaluation. • Guidance was added that subjects should have been instructed to contact the site promptly upon awareness if they developed signs and symptoms of potential hepatic decompensation. • Guidance was added that the Investigator should have contacted the study Medical Monitor upon awareness when any signs and symptoms of hepatic decompensation were observed in any subject. • Guidance was added for monitoring amylase and lipase levels in subjects with suspected acute pancreatitis. • Gallbladder assessments were added at Screening or Day 1.
15 February 2019	• Updated clinical development data based on IB Version 18 (31 Jan 2019). • Exclusion criteria were updated to mitigate the inclusion of subjects who may have been pregnant or breastfeeding as an additional safety precaution or who had a known history of human immunodeficiency syndrome infection. • Exclusion criteria and prohibited medications sections were updated to prevent the concomitant use of fibrates and OCA. The primary objective of this study was to characterize the PK of OCA in subjects with PBC and mild to severe hepatic impairment. The drug-drug interactions of OCA with fibrates were not yet fully characterized in any population and were being restricted in this study as an additional safety precaution until data were available in a less advanced population.

19 May 2020	• Addendum was issued to multiple countries to describe the requirements and processes under which subjects who were unable to return to study sites during the COVID-19 pandemic may have completed protocol specified assessments and continued to receive investigational product until in-person site visits could resume.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported