Clinical trial results:
A Phase 2 Dose Ranging, Randomized, Double Blind, Placebo-controlled Study Evaluating the Safety, Tolerability, Pharmacokinetics and Efficacy of EDP-305 in Subjects with Primary Biliary Cholangitis (PBC) with or without an Inadequate Response to Ursodeoxycholic Acid (UDCA)

Summary

EudraCT number	2017-003528-62
Trial protocol	DE GB BE ES AT NL
Global end of trial date	16 January 2020

Results information

Result version number	v1 (current)
This version publication date	07 February 2021
First version publication date	07 February 2021

Trial information

Trial identification

Sponsor protocol code	EDP 305-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03394924
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Enanta Pharmaceuticals, Inc.
Sponsor organisation address	500 Arsenal St., Watertown, United States, MA 02472
Public contact	Nathalie Adda, Enanta Pharmaceuticals, Inc., +1 6176070705, nadda@enanta.com
Scientific contact	Nathalie Adda, Enanta Pharmaceuticals, Inc., +1 6176070705, nadda@enanta.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	16 January 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the effect of EDP-305 on alkaline phosphatase (ALP) levels.

Protection of trial subjects:

This study was conducted in accordance with the protocol, the guideline for Good Clinical Practice E6(R2), the Declaration of Helsinki, and all applicable local laws and national regulations governing clinical studies.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 December 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 30
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Netherlands: 2
Worldwide total number of subjects	68
EEA total number of subjects	30

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)	51
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial included 68 participants from 43 sites in Australia, Canada, Europe and the United states from December 2017 to January 2020.

Pre-assignment

Screening details:

132 participants were screened, 64 of which were screen failures. The remaining 68 were enrolled and received trial treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	EDP-305 1 mg

Arm description:

Participants took EDP-305 1 mg as an oral tablet once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	EDP-305
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral tablet

Arm title	EDP-305 2.5 mg

Arm description:

Participants took EDP-305 2.5 mg as an oral tablet once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	EDP-305
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral tablet

Arm title	Placebo

Arm description:

Participants received an oral placebo matching EDP-305 once daily for 12 weeks.

Arm type	Experimental

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

Dosage and administration details:

Oral tablet

Number of subjects in period 1	EDP-305 1 mg	EDP-305 2.5 mg	Placebo
Started	31	28	9
Completed	28	22	9
Not completed	3	6	0
Did not meet all inclusion criteria	1	-	-
Consent withdrawn by subject	2	-	-
Adverse event, non-fatal	-	5	-
Lost to follow-up	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	EDP-305 1 mg
Reporting group description:	
Participants took EDP-305 1 mg as an oral tablet once daily for 12 weeks.	
Reporting group title	EDP-305 2.5 mg
Reporting group description:	
Participants took EDP-305 2.5 mg as an oral tablet once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received an oral placebo matching EDP-305 once daily for 12 weeks.	

Reporting group values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo
Number of subjects	31	28	9
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	57.4	54.9	56.9
standard deviation	± 8.61	± 10.92	± 8.49
Gender categorical Units: Subjects			
Female	31	27	9
Male	0	1	0
Race Units: Subjects			
White	28	27	9
All other races	3	1	0
Ethnicity Units: Subjects			
Hispanic or Latino	3	2	0
Not Hispanic or Latino	27	25	9
Not Reported	1	1	0
Unknown	0	0	0

Reporting group values	Total		
Number of subjects	68		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	67		
Male	1		
Race Units: Subjects			
White	64		
All other races	4		
Ethnicity Units: Subjects			
Hispanic or Latino	5		
Not Hispanic or Latino	61		
Not Reported	2		
Unknown	0		

End points

End points reporting groups

Reporting group title	EDP-305 1 mg
Reporting group description:	
Participants took EDP-305 1 mg as an oral tablet once daily for 12 weeks.	
Reporting group title	EDP-305 2.5 mg
Reporting group description:	
Participants took EDP-305 2.5 mg as an oral tablet once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received an oral placebo matching EDP-305 once daily for 12 weeks.	
Subject analysis set title	EDP-305 1 mg - Pharmacokinetic Substudy
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Blood samples for Pharmacokinetic (PK) analysis were collected from a subset of study sites.	
Subject analysis set title	EDP-305 2.5 mg - Pharmacokinetic Substudy
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Blood samples for Pharmacokinetic (PK) analysis were collected from a subset of study sites.	

Primary: Percentage of Participants with At Least a 20% Reduction in Alkaline Phosphatase (ALP) or Normalization of ALP at Week 12 Compared to Baseline

End point title	Percentage of Participants with At Least a 20% Reduction in Alkaline Phosphatase (ALP) or Normalization of ALP at Week 12 Compared to Baseline
End point description:	
End point type	Primary
End point timeframe:	
Baseline and Week 12	

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	28	9	
Units: Percentage of participants				
number (not applicable)	45.2	46.4	11.1	

Statistical analyses

Statistical analysis title	Primary Analysis for EDP-305 1 mg
Comparison groups	EDP-305 1 mg v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.106
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	52

Statistical analysis title	Primary Analysis for EDP-305 2.5 mg
Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.063
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	65.22

Secondary: Percentage of Participants With a Treatment-Emergent Adverse Event (TEAE) during On-Treatment Period

End point title	Percentage of Participants With a Treatment-Emergent Adverse Event (TEAE) during On-Treatment Period

End point description:

An adverse event (AE) was defined as any event, side effect, or untoward medical occurrence in a subject enrolled in a clinical trial whether or not it is considered to have a causal relationship to the study drug. A TEAE was an AE that first occurred or began previous to and worsened on or after the first dose date and before the last dose date +7 days.

End point type	Secondary

End point timeframe:

Up to approximately Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	28	9	
Units: Percentage of participants				
number (not applicable)	71.0	89.3	88.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Treatment-Emergent Serious Adverse Event (SAE) during On-Treatment Period

End point title	Percentage of Participants With a Treatment-Emergent Serious Adverse Event (SAE) during On-Treatment Period

End point description:

A SAE is any untoward medical occurrence at any dose that results in death, is a life-threatening event, requires inpatient hospitalization or prolonged hospitalization of an existing hospitalization, results in permanent or prolonged disability or incapacity, is a congenital anomaly or birth defect in the offspring of a study subjects, or is a medically important event.

End point type	Secondary

End point timeframe:

Up to approximately Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	28	9	
Units: Percentage of participants				
number (not applicable)	3.2	7.1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Stopped Study Treatment Due to a Treatment-Emergent Adverse Event (TEAE) during On-Treatment Period

End point title	Percentage of Participants Who Stopped Study Treatment Due to a Treatment-Emergent Adverse Event (TEAE) during On-Treatment Period

End point description:

An adverse event (AE) was defined as any event, side effect, or untoward medical occurrence in a subject enrolled in a clinical trial whether or not it is considered to have a causal relationship to the study drug. A TEAE was an AE that first occurred or began previous to and worsened on or after the first dose date and before the last dose date +7 days.

End point type	Secondary

End point timeframe:

Up to approximately Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	28	9	
Units: Percentage of participants				
number (not applicable)	3.2	17.9	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 12 in Total, Conjugated and Unconjugated Bilirubin

End point title	Change from Baseline to Week 12 in Total, Conjugated and Unconjugated Bilirubin

End point description:

The data presented below was measured using least square mean change from baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[1]	28[2]	9	
Units: µmol/L				
least squares mean (confidence interval 95%)				
Total	-0.04 (-0.93 to 0.86)	-0.31 (-1.35 to 0.74)	-0.50 (-2.13 to 1.12)	
Conjugated	-0.55 (-1.03 to -0.06)	-0.51 (-1.08 to 0.06)	0.13 (-0.75 to 1.00)	
Unconjugated	0.71 (-0.02 to 1.44)	0.22 (-0.61 to 1.06)	-0.50 (-1.81 to 0.81)	

Notes:

[1] - Analysed participants: 28

[2] - Analysed participants: 21

Statistical analyses

Statistical analysis title	Analysis for EDP-305 1 mg Total Bilirubin

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical

comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.616
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.39
upper limit	2.32

Statistical analysis title	Analysis for EDP-305 2.5 mg Total Bilirubin

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.844
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.78
upper limit	2.16

Statistical analysis title	Analysis for EDP-305 1 mg Conjugated Bilirubin

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.18
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.67
upper limit	0.32

Statistical analysis title	Analysis for EDP-305 2.5 mg Conjugated Bilirubin

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.239
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.71
upper limit	0.44

Statistical analysis title	Analysis for EDP-305 1 mg Unconjugated Bilirubin

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.116
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.31
upper limit	2.73

Statistical analysis title	Analysis for EDP-305 2.5 mg Unconjugated Bilirubin

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.36
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	2.28

Secondary: Change from Baseline to Week 12 in alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma glutamyl transferase (GGT)

End point title	Change from Baseline to Week 12 in alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma glutamyl transferase (GGT)

End point description:

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[3]	28[4]	9	
Units: U/L				
least squares mean (confidence interval 95%)				
ALT	-17.35 (-24.45 to -10.25)	-13.14 (-21.58 to -4.71)	8.20 (-4.61 to 21.02)	
AST	-12.08 (-17.49 to -6.68)	-11.51 (-17.91 to -5.10)	9.33 (-0.43 to 19.09)	
GGT	-95.91 (-114.12 to -77.70)	-124.55 (-146.00 to -103.11)	-9.42 (-42.19 to 23.35)	

Notes:

[3] - Analysed participants: 28

[4] - Analysed participants: 21

Statistical analyses

Statistical analysis title	Analysis for EDP-305 1 mg ALT

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-25.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.07
upper limit	-11.04

Statistical analysis title	Analysis for EDP-305 2.5 mg ALT

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-21.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.1
upper limit	-5.6

Statistical analysis title	Analysis for EDP-305 1 mg AST

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-21.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.48
upper limit	-10.35

Statistical analysis title	Analysis for EDP-305 2.5 mg AST

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-20.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.8
upper limit	-8.87

Statistical analysis title	Analysis for EDP-305 1 mg GGT

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-86.49

Confidence interval	
level	95 %
sides	2-sided
lower limit	-123.78
upper limit	-49.21

Statistical analysis title	Analysis for EDP-305 2.5 mg GGT

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-115.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-155.04
upper limit	-75.22

Secondary: Change from Baseline to Week 12 in Noninvasive Liver Fibrosis Markers: Enhanced Liver Fibrosis (ELF) panel and N-terminal Type III Collagen Propeptide (PRO C3)

End point title	Change from Baseline to Week 12 in Noninvasive Liver Fibrosis Markers: Enhanced Liver Fibrosis (ELF) panel and N-terminal Type III Collagen Propeptide (PRO C3)

End point description:

The ELF panel included hyaluronic acid (HA), procollagen III amino terminal peptide (PIIINP), and tissue inhibitor of metalloproteinase 1 (TIMP 1). This endpoint also presents PRO C3 results.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[5]	28[6]	9[7]	
Units: µg/L				
least squares mean (confidence interval 95%)				

HA	1.17 (-16.69 to 19.03)	-1.16 (-22.20 to 19.87)	27.83 (-4.20 to 59.86)	
PIIINP	-0.08 (-1.28 to 1.11)	-0.77 (-2.20 to 0.65)	3.01 (0.72 to 5.30)	
TIMP 1	-16.29 (-32.31 to -0.27)	-20.90 (-39.58 to -2.22)	25.66 (-3.64 to 54.97)	
PRO C3	-0.67 (-4.97 to 3.63)	2.33 (-2.31 to 6.96)	9.06 (2.16 to 15.95)	

Notes:

[5] - Analysed participants: 28 for HA, PIIINP and TIMP 1; 19 for PRO C3.

[6] - Analysed participants: 21 for HA, PIIINP and TIMP 1; 18 for PRO C3.

[7] - Analysed participants: 9 for HA, PIIINP and TIMP 1; 8 for PRO C3.

Statistical analyses

Statistical analysis title	Analysis for EDP-305 1 mg HA

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.148
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-26.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-63.1
upper limit	9.79

Statistical analysis title	Analysis for EDP-305 2.5 mg HA

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.142
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-28.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-68.02
upper limit	10.05

Statistical analysis title	Analysis for EDP-305 1 mg PIIINP
Statistical analysis description: Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table “Number of subjects analysed.” Actual number included in this statistical comparison is 37.	
Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-3.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.68
upper limit	-0.51

Statistical analysis title	Analysis for EDP-305 2.5 mg PIIINP
Statistical analysis description: Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table “Number of subjects analysed.” Actual number included in this statistical comparison is 30.	
Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-3.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	-0.97

Statistical analysis title	Analysis for EDP-305 1 mg TIMP 1
Statistical analysis description: Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table “Number of subjects analysed.” Actual number included in this statistical comparison is 37.	
Comparison groups	EDP-305 1 mg v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-41.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-75.47
upper limit	-8.44

Statistical analysis title	Analysis for EDP-305 2.5 mg TIMP 1

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-46.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-81.91
upper limit	-11.21

Statistical analysis title	Analysis for EDP-305 1 mg PRO C3

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 27.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-9.73

Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.7
upper limit	-1.75

Statistical analysis title	Analysis for EDP-305 2.5 mg PRO C3

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 26.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.125
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-6.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.41
upper limit	1.95

Secondary: Change from Baseline to Week 12 in Noninvasive Liver Fibrosis Markers: AST to Platelet Ratio Index (APRI) Score

End point title	Change from Baseline to Week 12 in Noninvasive Liver Fibrosis Markers: AST to Platelet Ratio Index (APRI) Score

End point description:

APRI was calculated as ([AST IU/L/AST ULN]/[Platelet count 1^09/L])×100. AST is aspartate aminotransferase. ALT is alanine aminotransferase. IU is International Units. ULN is Upper Limit of Normal range for test.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[8]	28[9]	9[10]	
Units: AST to Platelet Ratio Index				
least squares mean (confidence interval 95%)	-0.16 (-0.25 to 0.06)	-0.12 (-0.23 to 0.01)	0.22 (0.05 to 0.38)	

Notes:

[8] - Analysed participants: 24

[9] - Analysed participants: 20

[10] - Analysed participants: 8

Statistical analyses

Statistical analysis title	Analysis for EDP-305 1 mg APRI

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 32.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	-0.18

Statistical analysis title	Analysis for EDP-305 2.5 mg APRI

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 28.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	-0.13

Secondary: Change from Baseline to Week 12 in Noninvasive Liver Fibrosis Markers:

Fibrosis-4 (FIB-4) Score

End point title	Change from Baseline to Week 12 in Noninvasive Liver Fibrosis Markers: Fibrosis-4 (FIB-4) Score

End point description:

FIB-4 score was calculated as (Age [years]×AST [IU/L])/(Platelet count [10^9/L]×(sqrt ALT [IU/L])). AST is aspartate aminotransferase. ALT is alanine aminotransferase. IU is International Units. ULN is Upper Limit of Normal range for test.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[11]	28[12]	9[13]	
Units: Fibrosis 4 Index				
least squares mean (confidence interval 95%)	-0.14 (-0.29 to 0.01)	-0.05 (-0.22 to 0.11)	0.21 (-0.06 to 0.47)	

Notes:

[11] - Analysed participants: 24

[12] - Analysed participants: 20

[13] - Analysed participants: 8

Statistical analyses

Statistical analysis title	Analysis for EDP-305 1 mg FIB-4

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 32.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	-0.04

Statistical analysis title	Analysis for EDP-305 2.5 mg FIB-4

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 28.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.104
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	0.05

Secondary: Change from Baseline to Week 12 in Fibrinogen and C Reactive Protein (CRP) Levels

End point title	Change from Baseline to Week 12 in Fibrinogen and C Reactive Protein (CRP) Levels

End point description:

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[14]	28[15]	9[16]	
Units: mg/dL				
least squares mean (confidence interval 95%)				
Fibrinogen	16.28 (-5.39 to 37.95)	41.25 (15.56 to 66.93)	9.47 (-28.82 to 47.76)	
CRP	-0.57 (-1.62 to 0.49)	-2.69 (-3.89 to -1.50)	0.41 (-1.53 to 2.34)	

Notes:

[14] - Analysed participants: 28 for fibrinogen; 27 for CRP.

[15] - Analysed participants: 20 for fibrinogen; 21 for CRP.

[16] - Analysed participants: 9 for fibrinogen; 8 for CRP.

Statistical analyses

Statistical analysis title	Analysis for EDP-305 1 mg Fibrinogen

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table “Number of subjects analysed.” Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.757
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	6.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.17
upper limit	50.78

Statistical analysis title	Analysis for EDP-305 2.5 mg Fibrinogen

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 29.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.174
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	31.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.42
upper limit	77.97

Statistical analysis title	Analysis for EDP-305 1 mg CRP

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 35.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.378
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.98

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.18
upper limit	1.23

Statistical analysis title	Analysis for EDP-305 2.5 mg CRP

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 29.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.38
upper limit	-0.83

Secondary: Change from Baseline to Week 12 in Interleukin (IL) and Tumor Necrosis Factor (TNF) Levels

End point title	Change from Baseline to Week 12 in Interleukin (IL) and Tumor Necrosis Factor (TNF) Levels

End point description:

For IL, both IL6 and IL1β variants were analysed. For TNF, both TNF α and TNF β (also known as lymphotoxin alpha) variants were analyzed. Values of 99999 indicate that data could not be calculated.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[17]	28[18]	9[19]	
Units: ng/L				
least squares mean (confidence interval 95%)				
IL6	0.73 (-0.97 to 2.43)	-2.10 (-4.03 to -0.17)	0.39 (-2.57 to 3.34)	

IL1β	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
TNF α	-0.15 (-0.38 to 0.09)	-0.01 (-0.28 to 0.25)	0.39 (-0.03 to 0.81)	
TNF β	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Notes:

[17] - Analysed participants: 28 for TNF α and IL1β; 27 for IL6; 19 for TNF β.

[18] - Analysed participants: 21 for TNF α and IL1β; 21 for IL6; 18 for TNF β.

[19] - Analysed participants: 9 for TNF α, IL1β and IL6; 8 for TNF β.

Statistical analyses

Statistical analysis title	Analysis for EDP-305 1 mg IL6

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 36.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.841
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.07
upper limit	3.76

Statistical analysis title	Analysis for EDP-305 2.5 mg IL6

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.163
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-2.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.01
upper limit	1.04

Statistical analysis title	Analysis for EDP-305 1 mg TNF α
Statistical analysis description:	
Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.	
Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.02
upper limit	-0.05

Statistical analysis title	Analysis for EDP-305 2.5 mg TNF α
Statistical analysis description:	
Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.	
Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.11
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.09

Secondary: Change from Baseline to Week 12 in Haptoglobin and Alpha2 Macroglobulin Levels

End point title	Change from Baseline to Week 12 in Haptoglobin and Alpha2 Macroglobulin Levels

End point description:

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[20]	28[21]	9	
Units: g/L				
least squares mean (confidence interval 95%)				
Haptoglobin	-0.14 (-0.27 to -0.01)	-0.18 (-0.33 to -0.03)	-0.15 (-0.38 to 0.08)	
Alpha2 Macroglobulin	-0.02 (-0.09 to 0.05)	-0.00 (-0.08 to 0.08)	0.02 (-0.11 to 0.15)	

Notes:

[20] - Analysed participants: 28

[21] - Analysed participants: 21

Statistical analyses

Statistical analysis title	Analysis for EDP-305 1 mg Haptoglobin

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.944
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.27

Statistical analysis title	Analysis for EDP-305 2.5 mg Haptoglobin

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo

Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.83
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.24

Statistical analysis title	Analysis for EDP-305 1 mg Alpha2 Macroglobulin

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.546
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.1

Statistical analysis title	Analysis for EDP-305 2.5 mg Alpha2 Macroglobulin

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.785
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.13

Secondary: Change from Baseline to Week 12 in Triglycerides (TG), Total Cholesterol (TC), High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C)

End point title	Change from Baseline to Week 12 in Triglycerides (TG), Total Cholesterol (TC), High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C)

End point description:

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[22]	28[23]	9	
Units: mmol/L				
least squares mean (confidence interval 95%)				
TG	-0.13 (-0.25 to -0.00)	0.01 (-0.13 to 0.16)	0.05 (-0.17 to 0.27)	
TC	-0.47 (-0.80 to -0.14)	-0.46 (-0.85 to -0.08)	0.17 (-0.42 to 0.76)	
HDL-C	-0.16 (-0.31 to -0.02)	-0.46 (-0.62 to -0.30)	-0.24 (-0.49 to 0.01)	
LDL-C	-0.21 (-0.47 to 0.05)	-0.01 (-0.31 to 0.29)	0.29 (-0.19 to 0.76)	

Notes:

[22] - Analysed participants: 28

[23] - Analysed participants: 21

Statistical analyses

Statistical analysis title	Analysis for EDP-305 1 mg TG

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table “Number of subjects analysed.” Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.176
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	0.08

Statistical analysis title	Analysis for EDP-305 2.5 mg TG

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.783
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.23

Statistical analysis title	Analysis for EDP-305 1 mg TC

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.061
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.64

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.31
upper limit	0.03

Statistical analysis title	Analysis for EDP-305 2.5 mg TC

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.08
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.34
upper limit	0.08

Statistical analysis title	Analysis for EDP-305 1 mg HDL-C

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.584
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.37

Statistical analysis title	Analysis for EDP-305 2.5 mg HDL-C

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.148
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	0.08

Statistical analysis title	Analysis for EDP-305 1 mg LDL-C

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.074
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.04
upper limit	0.05

Statistical analysis title	Analysis for EDP-305 2.5 mg LDL-C

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo

Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.304
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.87
upper limit	0.28

Secondary: Change from Baseline to Week 12 in Domain and Total Scores on the 5D-Itch Scale

End point title	Change from Baseline to Week 12 in Domain and Total Scores on the 5D-Itch Scale

End point description:

The 5D-Itch scale is a multidimensional questionnaire completed by participants to quantify the magnitude of pruritus, assessed considering the past 2 weeks. Scale range is 1 to 5 covering five dimensions: duration (1=Less than 6 hrs/day to 5=All day), degree (1=Not present to 5=Unbearable), direction (1=Completely resolved to 5=Getting worse), disability (for Sleep rated as 1=Never affects sleep to 5=Delays falling asleep and frequently wakes me up at night; for Leisure/Social, Housework/Errands and Work/School rated as 1=Never affects activity to 5=Always affects activity), and distribution (assess if itching is present in 16 body locations, scored as 1=present at 0-2 locations to 5=present at 14-16 locations). Total scores (including highest disability score obtained from any of the daily activities) ranged between 5 and 25 where higher scores indicated more severe itching. Negative change scores indicate improvement from the baseline score.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[24]	28[25]	9[26]	
Units: Scores on a scale				
least squares mean (confidence interval 95%)				
Duration	0.01 (-0.27 to 0.29)	0.41 (0.11 to 0.71)	-0.24 (-0.73 to 0.25)	
Degree	0.00 (-0.25 to 0.26)	0.65 (0.37 to 0.93)	-0.53 (-0.96 to 0.10)	
Direction	-0.63 (-1.12 to -0.15)	0.36 (-0.17 to 0.90)	-0.65 (-1.46 to 0.16)	
Disability	-0.24 (-0.63 to 0.15)	0.85 (0.42 to 1.28)	-0.61 (-1.28 to 0.05)	
Distribution	0.07 (-0.32 to 0.45)	0.81 (0.38 to 1.24)	-0.42 (-1.08 to 0.24)	
Total	-0.95 (-2.29 to 0.39)	3.19 (1.74 to 4.64)	-3.16 (-5.50 to -0.82)	

Notes:

[24] - Analysed: 24 (Duration and Total); 25 (Direction); 26 (Degree, Disability and Distribution)

[25] - Analysed: 21

[26] - Analysed: 8 (Duration and Total); 9 (Direction, Degree, Disability and Distribution)

Statistical analyses

Statistical analysis title	Analysis for EDP-305 1 mg - Duration

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 32.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.378
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	0.82

Statistical analysis title	Analysis for EDP-305 2.5 mg - Duration

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 29.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	1.23

Statistical analysis title	Analysis for EDP-305 1 mg - Degree

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 35.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	1.03

Statistical analysis title	Analysis for EDP-305 2.5 mg - Degree

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.69

Statistical analysis title	Analysis for EDP-305 1 mg - Direction

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 34.

Comparison groups	EDP-305 1 mg v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.971
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	0.96

Statistical analysis title	Analysis for EDP-305 2.5 mg - Direction

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.042
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	1.99

Statistical analysis title	Analysis for EDP-305 1 mg - Disability

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 35.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.336
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.37

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	1.14

Statistical analysis title	Analysis for EDP-305 2.5 mg - Disability

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	1.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	2.26

Statistical analysis title	Analysis for EDP-305 1 mg - Distribution

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 35.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.214
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	1.25

Statistical analysis title	Analysis for EDP-305 2.5 mg - Distribution

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	2.02

Statistical analysis title	Analysis for EDP-305 1 mg - Total

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 32.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.103
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	2.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	4.9

Statistical analysis title	Analysis for EDP-305 2.5 mg - Total

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 29.

Comparison groups	EDP-305 2.5 mg v Placebo

Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	6.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.57
upper limit	9.13

Secondary: Change from Baseline to Week 12 in Visual Analog Score (VAS) for Itching

End point title	Change from Baseline to Week 12 in Visual Analog Score (VAS) for Itching

End point description:

An itch VAS (0-100mm) was used to record the intensity of the event. Participants drew a line on a scale corresponding to the maximum intensity of itch. Lines drawn towards the right of the line indicated greater itching and higher scores indicated more severe itching. Negative change scores indicate that participants' scores decreased from the baseline score.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[27]	28[28]	9	
Units: Scores on a scale				
least squares mean (confidence interval 95%)	0.55 (-8.35 to 9.44)	13.64 (4.00 to 23.29)	-11.93 (-27.05 to 3.18)	

Notes:

[27] - Analysed participants: 26

[28] - Analysed participants: 22

Statistical analyses

Statistical analysis title	Analysis for EDP-305 1 mg VAS Scale

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 35.

Comparison groups	EDP-305 1 mg v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.16
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	12.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.09
upper limit	30.06

Statistical analysis title	Analysis for EDP-305 2.5 mg VAS Scale

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 31.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	25.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.67
upper limit	43.48

Secondary: Change from Baseline to Week 12 in Domain Scores on the Primary Biliary Cholangitis-40 (PBC-40) Quality of Life (QoL) Assessment

End point title	Change from Baseline to Week 12 in Domain Scores on the Primary Biliary Cholangitis-40 (PBC-40) Quality of Life (QoL) Assessment

End point description:

The PBC-40 is a survey measuring health related quality of life in participants with PBC. The 40 questions from the PBC-40 questionnaire are scored from 1-5, with 5 representing the highest impact and 1 the lowest impact of PBC on the quality of life. Six domains were computed from the 40 questions: symptoms (score range 7-35), itch (0-15), fatigue (11-55), cognition (6-30), social (8-50) and emotional (1-15). Higher scores indicate worse quality of life and negative change scores indicate improvement from the baseline score.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[29]	28[30]	9	
Units: Scores on a scale				
least squares mean (confidence interval 95%)				
Symptoms	-0.21 (-1.47 to 1.06)	-1.46 (-2.93 to 0.00)	-0.06 (-2.30 to 2.18)	
Itch	0.18 (-0.72 to 1.09)	1.74 (0.69 to 2.78)	-1.73 (-3.33 to -0.13)	
Fatigue	-0.36 (-2.58 to 1.86)	-0.22 (-2.79 to 2.34)	0.10 (-3.82 to 4.01)	
Cognition	-0.21 (-1.46 to 1.04)	0.82 (-0.63 to 2.27)	-0.48 (-2.66 to 1.71)	
Social	-0.38 (-2.22 to 1.46)	0.96 (-1.17 to 3.08)	1.73 (-1.52 to 4.99)	
Emotional	-0.77 (-1.54 to 0.01)	0.23 (-0.68 to 1.13)	-0.15 (-1.52 to 1.22)	

Notes:

[29] - Analysed participants: 28

[30] - Analysed participants: 21

Statistical analyses

Statistical analysis title	Analysis for EDP-305 1 mg Symptoms

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.908
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.72
upper limit	2.43

Statistical analysis title	Analysis for EDP-305 2.5 mg Symptoms

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.298
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.09
upper limit	1.27

Statistical analysis title	Analysis for EDP-305 1 mg Itch

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.042
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	1.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	3.76

Statistical analysis title	Analysis for EDP-305 2.5 mg Itch

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	3.47

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.55
upper limit	5.38

Statistical analysis title	Analysis for EDP-305 1 mg Fatigue

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.839
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.96
upper limit	4.04

Statistical analysis title	Analysis for EDP-305 2.5 mg Fatigue

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.891
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	4.36

Statistical analysis title	Analysis for EDP-305 1 mg Cognition

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.834
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.25
upper limit	2.77

Statistical analysis title	Analysis for EDP-305 2.5 mg Cognition

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.327
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.33
upper limit	3.92

Statistical analysis title	Analysis for EDP-305 1 mg Social

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.262
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-2.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.86
upper limit	1.62

Statistical analysis title	Analysis for EDP-305 2.5 mg Social

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.69
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.68
upper limit	3.12

Statistical analysis title	Analysis for EDP-305 1 mg Emotional

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 37.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.433
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.62

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.19
upper limit	0.95

Statistical analysis title	Analysis for EDP-305 2.5 mg Emotional

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.653
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.28
upper limit	2.03

Secondary: Maximum Plasma Concentration (Cmax) of EDP-305 and its Metabolites

End point title	Maximum Plasma Concentration (Cmax) of EDP-305 and its Metabolites

End point description:

Metabolites of EDP-305 are EP-022571, EP-022572, and EP-022679.

End point type	Secondary

End point timeframe:

Day 1 and Week 12: Pre-dose and 2, 6 and 8 hours post-dose

End point values	EDP-305 1 mg - Pharmacokinetic Substudy	EDP-305 2.5 mg - Pharmacokinetic Substudy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5[31]	6[32]		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
EDP-305 Day 1	15.4 (± 44.30)	27.9 (± 54.19)		
EDP-305 Week 12	10.8 (± 67.77)	50.4 (± 53.20)		
EP-022571 Day 1	0.5 (± 44.58)	0.6 (± 61.81)		

EP-022571 Week 12	0.2 (± 59.57)	1.3 (± 160.28)		
EP-022572 Day 1	0.5 (± 41.69)	0.8 (± 38.27)		
EP-022572 Week 12	0.2 (± 41.74)	1.6 (± 138.55)		
EP-022679 Day 1	0.8 (± 113.24)	1.7 (± 115.17)		
EP-022679 Week 12	0.6 (± 147.81)	10.9 (± 352.53)		

Notes:

[31] - Analysed participants: 5 at Day 1 and 4 at Week 12.

[32] - Analysed participants: 5 at Day 1 and 4 at Week 12.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Plasma Concentration (Tmax) of EDP-305 and its Metabolites

End point title	Time to Maximum Plasma Concentration (Tmax) of EDP-305 and its Metabolites

End point description:

Metabolites of EDP-305 are EP-022571, EP-022572, and EP-022679.

End point type	Secondary

End point timeframe:

Day 1 and Week 12: Pre-dose and 2, 6 and 8 hours post-dose

End point values	EDP-305 1 mg - Pharmacokinetic Substudy	EDP-305 2.5 mg - Pharmacokinetic Substudy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5[33]	6[34]		
Units: hours				
median (full range (min-max))				
EDP-305 Day 1	6.00 (2.02 to 6.03)	6.02 (2.00 to 8.00)		
EDP-305 Week 12	7.01 (6.00 to 8.02)	6.01 (2.05 to 8.02)		
EP-022571 Day 1	2.0 (2.0 to 6.0)	6.0 (2.0 to 6.1)		
EP-022571 Week 12	6.0 (2.0 to 6.0)	4.0 (2.0 to 6.1)		
EP-022572 Day 1	2.0 (2.0 to 8.0)	6.0 (2.0 to 6.1)		
EP-022572 Week 12	6.0 (6.0 to 8.0)	4.0 (2.0 to 6.0)		
EP-022679 Day 1	6.0 (6.0 to 8.0)	6.1 (2.0 to 8.0)		
EP-022679 Week 12	6.0 (6.0 to 8.0)	6.0 (6.0 to 8.0)		

Notes:

[33] - Analysed participants: 5 at Day 1 and 4 at Week 12.

[34] - Analysed participants: 5 at Day 1 and 4 at Week 12.

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of EDP-305 and its Metabolites

End point title	Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of EDP-305 and its Metabolites

End point description:

Metabolites of EDP-305 are EP-022571, EP-022572, and EP-022679.

End point type	Secondary

End point timeframe:

Day 1 and Week 12: Pre-dose and 2, 6 and 8 hours post-dose

End point values	EDP-305 1 mg - Pharmacokinetic Substudy	EDP-305 2.5 mg - Pharmacokinetic Substudy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5[35]	6[36]		
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
EDP-305 Day 1	85.5 (± 51.57)	95.3 (± 141.72)		
EDP-305 Week 12	67.6 (± 75.47)	316.2 (± 42.34)		
EP-022571 Day 1	2.3 (± 37.32)	2.0 (± 132.47)		
EP-022571 Week 12	0.9 (± 78.75)	7.3 (± 154.62)		
EP-022572 Day 1	2.5 (± 32.37)	2.9 (± 96.70)		
EP-022572 Week 12	1.2 (± 53.12)	10.1 (± 148.55)		
EP-022679 Day 1	3.7 (± 109.30)	5.0 (± 305.62)		
EP-022679 Week 12	3.0 (± 203.04)	57.0 (± 343.47)		

Notes:

[35] - Analysed participants: 5 at Day 1 and 4 at Week 12.

[36] - Analysed participants: 5 at Day 1 and 4 at Week 12.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change from Baseline to Week 12 in Fibroblast Growth Factor 19 (FGF19), 7α-OH-4-cholesten-3-one (C4) and Bile Acid (BA) Concentrations

End point title	Percentage Change from Baseline to Week 12 in Fibroblast Growth Factor 19 (FGF19), 7α-OH-4-cholesten-3-one (C4) and Bile Acid (BA) Concentrations

End point description:

FGF19 was measured in plasma. BA was measured in serum. C4 was measured in serum.

End point type	Secondary

End point timeframe:

Day 1 and Week 12: Pre-dose and 2, 6 and 8 hours post-dose.

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[37]	28[38]	9[39]	
Units: Percentage change from baseline				
arithmetic mean (standard deviation)				
FGF19	28.10 (± 94.526)	46.90 (± 76.667)	39.83 (± 100.579)	
C4	-18.066 (± 114.9959)	-61.960 (± 42.8603)	39.839 (± 163.6265)	
BA	-21.79 (± 74.581)	-15.79 (± 112.934)	3.17 (± 48.656)	

Notes:

[37] - Analysed participants: 26 for FGF19 and C4; 23 for BA.

[38] - Analysed participants: 20 for FGF19 and C4; 14 for BA.

[39] - Analysed participants: 7

Statistical analyses

Statistical analysis title	Analysis for EDP-305 1 mg FGF19

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 33.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.971
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-71.51
upper limit	74.18

Statistical analysis title	Analysis for EDP-305 2.5 mg FGF19

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 27.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.882
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	5.54

Confidence interval	
level	95 %
sides	2-sided
lower limit	-68.86
upper limit	79.95

Statistical analysis title	Analysis for EDP-305 1 mg C4

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 33.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.242
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-51.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-139.27
upper limit	35.96

Statistical analysis title	Analysis for EDP-305 2.5 mg C4

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 27.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.042
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-94.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-184.85
upper limit	-3.75

Statistical analysis title	Analysis for EDP-305 1 mg BA

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 30.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.52
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-24.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-101.03
upper limit	51.89

Statistical analysis title	Analysis for EDP-305 2.5 mg BA

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 21.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.672
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-17.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-103.07
upper limit	67.16

Secondary: Percentage Change from Baseline to Week 12 in AUC0-8 and AUC2-8 of Fibroblast Growth Factor 19 (FGF19), 7α-OH-4-cholesten-3-one (C4) and Bile Acid (BA)

End point title	Percentage Change from Baseline to Week 12 in AUC0-8 and AUC2-8 of Fibroblast Growth Factor 19 (FGF19), 7α-OH-4-cholesten-3-one (C4) and Bile Acid (BA)

End point description:

AUC0-8 is area under the biomarker concentration-time curve from time zero to 8 hours. AUC2-8 is area under the biomarker concentration-time curve from 2 hours to 8 hours. FGF19 was measured in plasma. BA was measured in serum. C4 was measured in serum. Values of 99999 indicate that data could not be calculated.

End point type	Secondary

End point timeframe:

Day 1 and Week 12: Pre-dose and 2, 6 and 8 hours post-dose

End point values	EDP-305 1 mg	EDP-305 2.5 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[40]	28[41]	9[42]	
Units: Percentage change from baseline				
arithmetic mean (standard deviation)				
FGF19 AUC0-8	24.9 (± 68.90)	25.0 (± 71.72)	-25.9 (± 99999)	
FGF19 AUC 2-8	7.8 (± 86.25)	18.9 (± 66.35)	-25.3 (± 99999)	
C4 AUC0-8	3.7 (± 51.74)	100.0 (± 0.0)	138.2 (± 99999)	
C4 AUC2-8	-9.2 (± 66.30)	-100.0 (± 0.0)	122.5 (± 99999)	
BA AUC0-8	-20.7 (± 74.80)	-51.5 (± 41.06)	-26.1 (± 99999)	
BA AUC2-8	-33.6 (± 76.26)	-42.8 (± 56.77)	-24.4 (± 99999)	

Notes:

[40] - Analysed participants: 4 for AUC0-8 FGF19, C4 and BA; 5 for AUC2-8 FGF19, C4 and BA.

[41] - Analysed participants: 2 for AUC0-8 and AUC0-8 FGF19, and BA; 1 for AUC0-8 and AUC2-8 C4.

[42] - Analysed participants: 1

Statistical analyses

Statistical analysis title	Analysis for EDP-305 1 mg FGF19 AUC0-8

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 5.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.611
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	44.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-205.97
upper limit	295.06

Statistical analysis title	Analysis for EDP-305 2.5 mg FGF19 AUC0-8

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on

overall summary table “Number of subjects analysed.” Actual number included in this statistical comparison is 3.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.819
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-29.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-411.28
upper limit	351.31

Statistical analysis title	Analysis for EDP-305 1 mg FGF19 AUC2-8

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table “Number of subjects analysed.” Actual number included in this statistical comparison is 6.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.818
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	24.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-251.92
upper limit	300.74

Statistical analysis title	Analysis for EDP-305 2.5 mg FGF19 AUC2-8

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table “Number of subjects analysed.” Actual number included in this statistical comparison is 3.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.948
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-10.53

Confidence interval	
level	95 %
sides	2-sided
lower limit	-435.33
upper limit	414.27

Statistical analysis title	Analysis for EDP-305 1 mg C4 AUC0-8

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 5.

Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.412
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-91.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-475.92
upper limit	292.51

Statistical analysis title	Analysis for EDP-305 2.5 mg C4 AUC0-8

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 2.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.094
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-250.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-605.33
upper limit	104.98

Statistical analysis title	Analysis for EDP-305 1 mg C4 AUC2-8

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 6.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.266
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-83.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-279.15
upper limit	111.75

Statistical analysis title	Analysis for EDP-305 2.5 mg C4 AUC2-8

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 2.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-238.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-470.22
upper limit	-6.15

Statistical analysis title	Analysis for EDP-305 1 mg BA AUC0-8

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 5.

Comparison groups	EDP-305 1 mg v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.694
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	28.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-180.2
upper limit	237.02

Statistical analysis title	Analysis for EDP-305 2.5 mg BA AUC0-8

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 3.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.615
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-39.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-264.32
upper limit	185.32

Statistical analysis title	Analysis for EDP-305 1 mg BA AUC2-8

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 6.

Comparison groups	EDP-305 1 mg v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.974
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	2.93

Confidence interval	
level	95 %
sides	2-sided
lower limit	-229.6
upper limit	235.46

Statistical analysis title	Analysis for EDP-305 2.5 mg BA AUC2-8

Statistical analysis description:

Number of subjects included in analysis presented is automatically calculated by the system based on overall summary table "Number of subjects analysed." Actual number included in this statistical comparison is 3.

Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.793
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-26.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-283.24
upper limit	231.15

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 16 Weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1
Reporting groups	
Reporting group title	EDP-305 1 mg
Reporting group description: -	
Reporting group title	EDP-305 2.5 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	EDP-305 1 mg	EDP-305 2.5 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 31 (3.23%)	2 / 28 (7.14%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 31 (0.00%)	1 / 28 (3.57%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 31 (0.00%)	1 / 28 (3.57%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 28 (3.57%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	0 / 31 (0.00%)	1 / 28 (3.57%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 31 (0.00%)	1 / 28 (3.57%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Escherichia urinary tract infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 28 (3.57%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	1 / 31 (3.23%)	0 / 28 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	EDP-305 1 mg	EDP-305 2.5 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 31 (74.19%)	24 / 28 (85.71%)	8 / 9 (88.89%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 31 (6.45%)	0 / 28 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Contusion			
subjects affected / exposed	0 / 31 (0.00%)	0 / 28 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 31 (9.68%)	5 / 28 (17.86%)	3 / 9 (33.33%)
occurrences (all)	3	8	3
Paraesthesia			

subjects affected / exposed	1 / 31 (3.23%)	0 / 28 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Amnesia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 28 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Hyperaesthesia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 28 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 31 (6.45%)	1 / 28 (3.57%)	1 / 9 (11.11%)
occurrences (all)	2	1	1
Influenza like illness			
subjects affected / exposed	0 / 31 (0.00%)	2 / 28 (7.14%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Swelling			
subjects affected / exposed	0 / 31 (0.00%)	0 / 28 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 31 (0.00%)	0 / 28 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	4 / 31 (12.90%)	1 / 28 (3.57%)	0 / 9 (0.00%)
occurrences (all)	5	1	0
Diarrhoea			
subjects affected / exposed	1 / 31 (3.23%)	3 / 28 (10.71%)	0 / 9 (0.00%)
occurrences (all)	1	3	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 31 (3.23%)	3 / 28 (10.71%)	0 / 9 (0.00%)
occurrences (all)	1	6	0
Nausea			
subjects affected / exposed	2 / 31 (6.45%)	3 / 28 (10.71%)	1 / 9 (11.11%)
occurrences (all)	2	3	1
Abdominal distension			

subjects affected / exposed	2 / 31 (6.45%)	1 / 28 (3.57%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Dry mouth			
subjects affected / exposed	0 / 31 (0.00%)	1 / 28 (3.57%)	2 / 9 (22.22%)
occurrences (all)	0	1	2
Dyspepsia			
subjects affected / exposed	0 / 31 (0.00%)	2 / 28 (7.14%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Toothache			
subjects affected / exposed	0 / 31 (0.00%)	1 / 28 (3.57%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Vomiting			
subjects affected / exposed	2 / 31 (6.45%)	0 / 28 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 28 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 31 (0.00%)	1 / 28 (3.57%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Oropharyngeal pain			
subjects affected / exposed	0 / 31 (0.00%)	2 / 28 (7.14%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Epistaxis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 28 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Sinus congestion			
subjects affected / exposed	0 / 31 (0.00%)	0 / 28 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	11 / 31 (35.48%)	16 / 28 (57.14%)	3 / 9 (33.33%)
occurrences (all)	27	59	7
Pruritus generalised			

subjects affected / exposed	5 / 31 (16.13%)	9 / 28 (32.14%)	0 / 9 (0.00%)
occurrences (all)	5	13	0
Alopecia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 28 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 31 (0.00%)	3 / 28 (10.71%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Anxiety			
subjects affected / exposed	2 / 31 (6.45%)	0 / 28 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 28 (3.57%)	2 / 9 (22.22%)
occurrences (all)	0	1	2
Arthralgia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 28 (3.57%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Bursitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 28 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 28 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 31 (6.45%)	2 / 28 (7.14%)	0 / 9 (0.00%)
occurrences (all)	2	2	0
Nasopharyngitis			
subjects affected / exposed	1 / 31 (3.23%)	2 / 28 (7.14%)	1 / 9 (11.11%)
occurrences (all)	1	2	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 31 (9.68%)	0 / 28 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Sinusitis			

subjects affected / exposed	0 / 31 (0.00%)	1 / 28 (3.57%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Bronchitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 28 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Cytomegalovirus infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 28 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 31 (3.23%)	2 / 28 (7.14%)	0 / 9 (0.00%)
occurrences (all)	1	2	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 April 2018	• Various changes in the inclusion and exclusion criteria to better define the target subject population. • Additional details were included for the management of liver enzymes: the original protocol was incomplete as it did not address close observation of subjects for whom repeat assessment showed persistent elevations of transaminases, but who did not meet drug discontinuation criteria. For these subjects, the "close observation" guidelines were to be followed as noted in the FDA Guidance for Industry – Drug-Induced Liver Injury: Premarketing Clinical Evaluation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported