Clinical trial results:
A Phase 2 Dose Ranging, Randomized, Double Blind, and Placebo-controlled Study Evaluating the Safety, Tolerability, Pharmacokinetics and Efficacy of EDP-305 in Subjects with Non-Alcoholic Steatohepatitis (NASH)

Summary

EudraCT number	2017-004365-27
Trial protocol	FR GB
Global end of trial date	10 July 2019

Results information

Result version number	v1 (current)
This version publication date	10 June 2021
First version publication date	10 June 2021

Trial information

Trial identification

Sponsor protocol code	EDP-305-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03421431
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	Maria Gawryl, Enanta Pharmaceuticals, Inc., mgawryl@enanta.com
Scientific contact	Maria Gawryl, Enanta Pharmaceuticals, Inc., mgawryl@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	30 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 July 2019
Global end of trial reached?	Yes
Global end of trial date	10 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the study were to:
- Evaluate change in alanine aminotransferase (ALT) levels
- Evaluate the safety and tolerability of EDP-305

The secondary objectives of the study were to:
- Evaluate the effect of EDP-305 on liver fat
- Evaluate the effect of EDP-305 on fibrosis (liver stiffness)
- Evaluate the effect of EDP-305 on noninvasive liver fibrosis markers
- Evaluate the effects of EDP-305 on lipids
- Evaluate the effects of EDP-305 on glucose metabolism
- Evaluate the effects of EDP-305 on inflammatory markers
- Evaluate the PK of EDP-305 and its metabolites in plasma
- Evaluate the effect of EDP-305 on body weight
- Evaluate the effect of EDP-305 on waist-to-hip (WTH) ratio
- Evaluate the Pharmacodynamic (PD) of EDP-305

Protection of trial subjects:

This study was conducted in accordance with current applicable regulations, international council on Harmonisation (ICH) guidelines and local legal requirements. It complies with the ethical principles described in the 18th World Medical Assembly (Helsinki 1964) and amendments of the 29th (Tokyo 1975), 35th (Venice 1983), the 41st (Hong Kong 1989) and the 48th (South Africa 1996) World Medical Assemblies, Declaration of Helsinki.

From a safety perspective, appropriate study restrictions based on the mechanism of action of EDP-305 (i.e., farnesoid X receptor agonistic effect) were implemented including screening procedures and exclusion criteria to mitigate and minimise the risks and to ensure the safety of subjects. Each subject signed an informed consent form (ICF) containing appropriate study and study drug information and was provided a copy of the ICF.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 January 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	United States: 120

Worldwide total number of subjects	134
EEA total number of subjects	4

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)	122
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Out of 134 randomised subjects, 2 subjects (1 subject each in the EDP-305 2.5 mg and placebo groups) were randomised but not dosed because the subjects withdrew and were not included in the Safety and Efficacy Populations.

Pre-assignment period milestones

Number of subjects started	134
Intermediate milestone: Number of subjects	Number of subjects randomised: 134
Number of subjects completed	132

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Randomised but not dosed: 2

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	Placebo

Arm description:

A total of 24 subjects received at least one dose of placebo out of 25 randomised subjects, 1 subject withdrew the consent before dosing on Day 1 and was not dosed in the study followed by excluded from the Safety and Efficacy Populations.

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

Dosage and administration details:

A matching placebo tablet (EDP-305 1 mg or 2.5 mg) was administered orally once daily in the morning after fasting overnight for a minimum of 8 hours for 12 weeks. The matching placebo contained all the excipients present in the EDP-305 drug product tablets with the exception of the active drug.

Arm title	EDP-305 1 mg

Arm description:

All the 55 randomised subjects received at least one dose of EDP-305 1 mg and were included in the Safety and Efficacy Populations.

Arm type	Experimental

Investigational medicinal product name	EDP-305 1 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

EDP-305 1 mg tablet was administered orally once daily in the morning after fasting overnight for a minimum of 8 hours for 12 weeks.

Arm title	EDP-305 2.5 mg

Arm description:

A total of 53 subjects received at least one dose of EDP-305 2.5 mg out of 54 randomised subjects, 1 subject withdrew the consent before dosing on Day 1 and was not dosed in the study followed by excluded from the Safety and Efficacy Populations.

Arm type	Experimental
Investigational medicinal product name	EDP-305 2.5 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

EDP-305 2.5 mg tablet was administered orally once daily in the morning after fasting overnight for a minimum of 8 hours for 12 weeks.

Number of subjects in period 1[1]	Placebo	EDP-305 1 mg	EDP-305 2.5 mg
Started	24	55	53
Completed	18	49	39
Not completed	6	6	14
Stopping rules	-	1	-
Consent withdrawn by subject	3	2	1
Adverse event, non-fatal	2	1	12
Lost to follow-up	1	1	1
Protocol deviation	-	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Number of subjects included all the randomised subjects who received at least one dose of the study treatment (n = 132 [same for both Safety and Efficacy Populations]).
Out of 134 randomised subjects, 2 subjects (1 subject each in the EDP-305 2.5 mg and placebo groups) discontinued the study due to withdrawal of consent before dosing (on Day 1) and were excluded from the Safety and Efficacy Populations.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
A total of 24 subjects received at least one dose of placebo out of 25 randomised subjects, 1 subject withdrew the consent before dosing on Day 1 and was not dosed in the study followed by excluded from the Safety and Efficacy Populations.	
Reporting group title	EDP-305 1 mg
Reporting group description:	
All the 55 randomised subjects received at least one dose of EDP-305 1 mg and were included in the Safety and Efficacy Populations.	
Reporting group title	EDP-305 2.5 mg
Reporting group description:	
A total of 53 subjects received at least one dose of EDP-305 2.5 mg out of 54 randomised subjects, 1 subject withdrew the consent before dosing on Day 1 and was not dosed in the study followed by excluded from the Safety and Efficacy Populations.	

Reporting group values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg
Number of subjects	24	55	53
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	22	52	46
From 65-84 years	2	3	7
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	11	29	29
Male	13	26	24
Race Units: Subjects			
American Indian or Alaska Native	1	0	0
Asian	1	7	3
Black or African American	2	1	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	17	42	47
Not reported	2	2	1
Other	0	0	1
Mexican	1	1	1
Not specified	0	2	0

Reporting group values	Total		

Number of subjects	132		
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)	120		
From 65-84 years	12		
85 years and over	0		
Gender categorical Units: Subjects			
Female	69		
Male	63		
Race Units: Subjects			
American Indian or Alaska Native	1		
Asian	11		
Black or African American	3		
Native Hawaiian or Other Pacific Islander	0		
White	106		
Not reported	5		
Other	1		
Mexican	3		
Not specified	2		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
A total of 24 subjects received at least one dose of placebo out of 25 randomised subjects, 1 subject withdrew the consent before dosing on Day 1 and was not dosed in the study followed by excluded from the Safety and Efficacy Populations.	
Reporting group title	EDP-305 1 mg
Reporting group description:	
All the 55 randomised subjects received at least one dose of EDP-305 1 mg and were included in the Safety and Efficacy Populations.	
Reporting group title	EDP-305 2.5 mg
Reporting group description:	
A total of 53 subjects received at least one dose of EDP-305 2.5 mg out of 54 randomised subjects, 1 subject withdrew the consent before dosing on Day 1 and was not dosed in the study followed by excluded from the Safety and Efficacy Populations.	
Subject analysis set title	EDP-305 1 mg (PK Population)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The Pharmacokinetic (PK) Population included all subjects who received active study drug (EDP-305) and had any measurable plasma concentration of study drug at any timepoint.	
Subject analysis set title	EDP-305 2.5 mg (PK Population)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The PK Population included all subjects who received active study drug (EDP-305) and had any measurable plasma concentration of study drug at any timepoint.	

Primary: Mean Change From Baseline (Average) in ALT at Week 12

End point title	Mean Change From Baseline (Average) in ALT at Week 12
End point description:	
Blood samples were collected at specific timepoints for the laboratory evaluation to assess the ALT level. Baseline refers to the average of the screening and the Day 1 values; if either the screening or Day 1 values were missing, the non-missing value was used. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.	
End point type	Primary
End point timeframe:	
Baseline and Week 12	

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	48	38	
Units: unit(s)/litre				
arithmetic mean (standard deviation)	-13.85 (± 18.151)	-23.76 (± 28.135)	-26.14 (± 33.328)	

Statistical analyses

Statistical analysis title	Placebo versus (v) EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0495
Method	ANCOVA
Parameter estimate	Least Squares (LS) mean difference
Point estimate	12.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.029
upper limit	24.891

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3039
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	6.257
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.754
upper limit	18.268

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.213
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	6.203
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.615
upper limit	16.021

Secondary: Mean Change From Baseline in Percentage of Fat in the Liver as Assessed by Magnetic Resonance Imaging - Proton Density Fat Fraction (MRI-PDFF) at Week 12

End point title	Mean Change From Baseline in Percentage of Fat in the Liver as Assessed by Magnetic Resonance Imaging - Proton Density Fat Fraction (MRI-PDFF) at Week 12

End point description:

The liver fat percentage was assessed by MRI-PDFF, which is an established method that enables the quantification of fat content in the liver; the value of liver fat is expressed in percentage and ranges from 0 to 100% with higher values representing higher liver fat level. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	51	49	
Units: percentage of fat				
arithmetic mean (standard deviation)	-2.842 (± 4.4687)	-3.759 (± 5.1600)	-6.428 (± 7.2586)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0009
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	4.717
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.98
upper limit	7.455

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

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4946
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.934
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.766
upper limit	3.635

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0005
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	3.783
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.708
upper limit	5.858

Secondary: Mean Change From Baseline in Aspartate Aminotransferase to Platelet Ratio Index (APRI) at Week 12

End point title	Mean Change From Baseline in Aspartate Aminotransferase to Platelet Ratio Index (APRI) at Week 12

End point description:

Blood samples were collected at specific timepoints for the laboratory evaluation to assess the aspartate aminotransferase (AST) level and platelet count. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. The APRI score (AST to platelet ratio index) is an index comprised of biochemical values and is used to determine the degree of hepatic fibrosis. APRI is calculated from the level of AST measured in a blood test (international units per litre [IU/L]) and platelet count (10^9/L) according to the following formula:
APRI = ([AST value in IU/L / upper limit of the normal range of AST] / [platelet count in 10^9/L]) × 100.
In general, APRI scores range from 0 to >2.0, where scores <0.5 indicate no significant fibrosis, scores >1.5 indicate significant fibrosis, and scores >2.0 have been shown to be best correlated with the presence of cirrhosis. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	44	35	
Units: ratio				
arithmetic mean (standard deviation)	-0.180 (± 0.3462)	-0.107 (± 0.3396)	-0.194 (± 0.3533)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2756
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.076
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.062
upper limit	0.214

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9686
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.003
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.136
upper limit	0.131

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg

Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1406
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.079
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.026
upper limit	0.184

Secondary: Mean Change From Baseline in Triglycerides (TG) at Week 12

End point title	Mean Change From Baseline in Triglycerides (TG) at Week 12
End point description:	
Blood samples were collected at specific timepoints for the laboratory evaluation to assess the TG level. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.	
End point type	Secondary
End point timeframe:	
Baseline and Week 12	

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	48	38	
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	-0.151 (± 0.8529)	-0.366 (± 1.5858)	0.129 (± 1.1088)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.613
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.125

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.613
upper limit	0.363

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8366
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.049
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.521
upper limit	0.423

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7015
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.076
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.466
upper limit	0.315

Secondary: Mean Change From Baseline in Total Cholesterol at Week 12

End point title	Mean Change From Baseline in Total Cholesterol at Week 12

End point description:

Blood samples were collected at specific timepoints for the laboratory evaluation to assess the total cholesterol level. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:
Baseline and Week 12

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	49	38	
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	-0.175 (± 0.6879)	0.046 (± 0.6697)	-0.003 (± 1.0046)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3875
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.186
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.613
upper limit	0.24

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2331
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.248
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.657
upper limit	0.162

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7164
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.061
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.272
upper limit	0.395

Secondary: Mean Change From Baseline in High-Density Lipoprotein Cholesterol (HDL-C) at Week 12

End point title	Mean Change From Baseline in High-Density Lipoprotein Cholesterol (HDL-C) at Week 12

End point description:

Blood samples were collected at specific timepoints for the laboratory evaluation to assess the HDL-C level. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	49	38	
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	0.008 (± 0.1279)	-0.058 (± 0.1670)	-0.210 (± 0.2708)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	0.311

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.348
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.046
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.051
upper limit	0.143

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.164
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.085
upper limit	0.243

Secondary: Mean Change From Baseline in Low-Density Lipoprotein Cholesterol

(LDL-C) at Week 12	
End point title	Mean Change From Baseline in Low-Density Lipoprotein Cholesterol (LDL-C) at Week 12
End point description:	
Blood samples were collected at specific timepoints for the laboratory evaluation to assess the LDL-C level. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.	
End point type	Secondary
End point timeframe:	
Baseline and Week 12	

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	44	37	
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	-0.112 (± 0.6431)	0.129 (± 0.5099)	0.151 (± 0.8157)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0897
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.299
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.645
upper limit	0.047

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1411
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.251

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.586
upper limit	0.085

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.733
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.048
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.326
upper limit	0.23

Secondary: Mean Change From Baseline in Adiponectin at Week 12

End point title	Mean Change From Baseline in Adiponectin at Week 12

End point description:

Blood samples were collected at specific timepoints for the laboratory evaluation to assess the adiponectin level. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	48	38	
Units: nanogram(s)/millilitre				
arithmetic mean (standard deviation)	319.16 (± 689.387)	17.94 (± 828.494)	522.00 (± 2649.701)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9143
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	51.873
Confidence interval	
level	95 %
sides	2-sided
lower limit	-901.574
upper limit	1005.32

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3718
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	404.168
Confidence interval	
level	95 %
sides	2-sided
lower limit	-489.519
upper limit	1297.854

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3466
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-352.295
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1091.308
upper limit	386.719

Secondary: Mean Change From Baseline in Apolipoproteins A1 (ApoA-1) at Week 12	
End point title	Mean Change From Baseline in Apolipoproteins A1 (ApoA-1) at Week 12
End point description:	
Blood samples were collected at specific timepoints for the laboratory evaluation to assess the ApoA-1 level. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.	
End point type	Secondary
End point timeframe:	
Baseline and Week 12	

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	49	38	
Units: x 10^9/litre				
arithmetic mean (standard deviation)	-0.074 (± 0.1514)	-0.107 (± 0.1671)	-0.226 (± 0.2197)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.173
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.081
upper limit	0.264

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

Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5685
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.025
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.062
upper limit	0.113

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.147
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.075
upper limit	0.219

Secondary: Mean Change From Baseline in Apolipoproteins B (ApoB) at Week 12

End point title	Mean Change From Baseline in Apolipoproteins B (ApoB) at Week 12

End point description:

Blood samples were collected at specific timepoints for the laboratory evaluation to assess the ApoB level. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	49	38	
Units: x 10^9/litre				
arithmetic mean (standard deviation)	-0.028 (± 0.1687)	0.040 (± 0.1781)	0.099 (± 0.2898)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0282
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.133
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.252
upper limit	-0.015

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2412
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.068
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.182
upper limit	0.046

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg

Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1649
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.066
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.158
upper limit	0.027

Secondary: Mean Change From Baseline in Apolipoproteins C3 (ApoC3) at Week 12

End point title	Mean Change From Baseline in Apolipoproteins C3 (ApoC3) at Week 12

End point description:

Blood samples were collected at specific timepoints for the laboratory evaluation to assess the ApoC3 level. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	49	38	
Units: x 10^9/litre				
arithmetic mean (standard deviation)	-0.0094 (± 0.04388)	-0.0167 (± 0.03918)	-0.0122 (± 0.05721)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4357
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.009

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.014
upper limit	0.032

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8989
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.001
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.021
upper limit	0.023

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.412
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.008
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.011
upper limit	0.026

Secondary: Mean Change From Baseline in Fasting Blood Glucose at Week 12

End point title	Mean Change From Baseline in Fasting Blood Glucose at Week 12

End point description:

Blood samples were collected at specific timepoints for the laboratory evaluation to assess the fasting glucose level. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:
Baseline and Week 12

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	48	38	
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	-0.11 (± 2.130)	0.48 (± 1.847)	1.68 (± 3.396)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0134
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-1.731
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.095
upper limit	-0.368

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6263
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.327
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.656
upper limit	1.001

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0115
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-1.404
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.487
upper limit	-0.322

Secondary: Mean Change From Baseline in Fasting Insulin at Week 12

End point title	Mean Change From Baseline in Fasting Insulin at Week 12

End point description:

Blood samples were collected at specific timepoints for the laboratory evaluation to assess the fasting insulin. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	47	38	
Units: micro international unit(s)/millilitre				
arithmetic mean (standard deviation)	-0.688 (± 9.2808)	2.528 (± 14.6947)	-5.635 (± 52.7637)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4608
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-3.723
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.7
upper limit	6.253

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6238
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-2.377
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.962
upper limit	7.207

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7367
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-1.346
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.268
upper limit	6.576

Secondary: Mean Change From Baseline in Homeostasis Model Assessment (HOMA)

Index for Nondiabetic Subjects at Week 12

End point title	Mean Change From Baseline in Homeostasis Model Assessment (HOMA) Index for Nondiabetic Subjects at Week 12

End point description:

Blood samples were collected at specific timepoints for the laboratory evaluation; from the results of fasting glucose and insulin, an insulin resistance (IR) was estimated for the nondiabetic subjects using the HOMA-IR computer algorithm. A higher HOMA-IR indicates a higher degree of insulin resistance. Subjects who were not considered as having type 2 diabetes mellitus (T2DM) were identified as nondiabetic. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	11	13	
Units: units on a scale				
arithmetic mean (standard deviation)	0.587 (± 2.0088)	0.192 (± 2.7180)	-6.474 (± 24.9369)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8302
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.407
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.287
upper limit	3.474

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

Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5053
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.192
upper limit	2.632

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.476
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.873
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.62
upper limit	3.366

Secondary: Mean Change From Baseline in HOMA Index for Diabetic Subjects at Week 12

End point title	Mean Change From Baseline in HOMA Index for Diabetic Subjects at Week 12

End point description:

Blood samples were collected at specific timepoints for the laboratory evaluation; from the results of fasting glucose and insulin, an insulin resistance (IR) was estimated for the nondiabetic subjects using the HOMA-IR computer algorithm. A higher HOMA-IR indicates a higher degree of insulin resistance. Subjects who were considered as having T2DM were identified as diabetic. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	35	25	
Units: units on a scale				
arithmetic mean (standard deviation)	-0.493 (± 6.2624)	2.088 (± 6.6114)	5.059 (± 15.0113)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0639
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-5.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.171
upper limit	0.351

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4884
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-2.064
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.971
upper limit	3.843

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1532
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-3.846
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.156
upper limit	1.464

Secondary: Mean Change From Baseline in Glycated Haemoglobin (HbA1c) in Subjects With T2DM at Week 12

End point title	Mean Change From Baseline in Glycated Haemoglobin (HbA1c) in Subjects With T2DM at Week 12

End point description:

Blood samples were collected at specific timepoints for the laboratory evaluation to assess the HbA1c. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	38	25	
Units: percent				
arithmetic mean (standard deviation)	0.31 (± 0.685)	0.21 (± 0.776)	0.76 (± 0.963)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0811
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.46

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.978
upper limit	0.058

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6312
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.117
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.367
upper limit	0.601

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0099
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.577
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.011
upper limit	-0.143

Secondary: Maximum Plasma Concentration (Cmax) of EDP-305 on Day 1 and Week 12

End point title	Maximum Plasma Concentration (Cmax) of EDP-305 on Day 1 and Week 12

End point description:

The Cmax is the maximum observed plasma concentration, which was measured for EDP-305 on Day 1 and Week 12 for the samples collected according to the intensive sampling scheme for the subjects in the PK Population.

End point type	Secondary

End point timeframe:

Day 1 and Week 12

End point values	EDP-305 1 mg (PK Population)	EDP-305 2.5 mg (PK Population)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[1]	52[2]		
Units: nanogram(s)/millilitre				
geometric mean (geometric coefficient of variation)				
Day 1	11.1 (± 105)	25.1 (± 101)		
Week 12	15.9 (± 105)	41.1 (± 101)		

Notes:

[1] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 17

[2] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 13

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Plasma Concentration (Tmax) of EDP-305 on Day 1 and at Week 12

End point title	Time to Reach Maximum Plasma Concentration (Tmax) of EDP-305 on Day 1 and at Week 12

End point description:

The Tmax was measured for EDP-305 on Day 1 and at Week 12 for the samples collected according to the intensive sampling scheme for the subjects in the PK Population.

End point type	Secondary

End point timeframe:

Day 1 and Week 12

End point values	EDP-305 1 mg (PK Population)	EDP-305 2.5 mg (PK Population)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[3]	52[4]		
Units: hour				
median (full range (min-max))				
Day 1	6.00 (2.00 to 8.07)	6.00 (2.00 to 8.25)		
Week 12	6.00 (0.00 to 8.02)	6.00 (0.00 to 8.18)		

Notes:

[3] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 17

[4] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 13

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve (AUC) From Time Zero to the Time of the Last Quantifiable Concentration (AUC[Last]) of EDP-305 on Day 1 and at Week 12

End point title	Area Under the Plasma Concentration-Time Curve (AUC) From Time Zero to the Time of the Last Quantifiable Concentration (AUC[Last]) of EDP-305 on Day 1 and at Week 12

End point description:

AUC(last) is defined as the area under the plasma concentration-time curve from time zero to time the last quantifiable concentration, computed using the linear up/log down trapezoidal rule. AUC(last) was computed for EDP-305 on Day 1 and Week 12 for the samples collected according to the intensive sampling scheme for the subjects in the PK Population.

End point type	Secondary

End point timeframe:

Day 1 and at Week 12

End point values	EDP-305 1 mg (PK Population)	EDP-305 2.5 mg (PK Population)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[5]	52[6]		
Units: hour*nanogram/millilitre (h*ng/mL)				
geometric mean (geometric coefficient of variation)				
Day 1	53.6 (± 101)	129 (± 100)		
Week 12	87.2 (± 101)	264 (± 100)		

Notes:

[5] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 17

[6] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 12

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of EP-022571 on Day 1 and at Week 12

End point title	Cmax of EP-022571 on Day 1 and at Week 12

End point description:

The Cmax is the maximum observed plasma concentration, which was measured for EP-022571 (a metabolite of EDP-305) on Day 1 and Week 12 for the samples collected according to the intensive sampling scheme for the subjects in the PK Population.

End point type	Secondary

End point timeframe:

Day 1 and Week 12

End point values	EDP-305 1 mg (PK Population)	EDP-305 2.5 mg (PK Population)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[7]	52[8]		
Units: nanogram(s)/millilitre				
geometric mean (geometric coefficient of variation)				
Day 1	0.324 (± 983)	0.833 (± 177)		
Week 12	0.296 (± 1549)	0.787 (± 233)		

Notes:

[7] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 17
[8] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 13

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax of EP-022571 on Day 1 and at Week 12

End point title	Tmax of EP-022571 on Day 1 and at Week 12

End point description:

The Tmax was measured for EP-022571 (a metabolite of EDP-305) on Day 1 and at Week 12 for the samples collected according to the intensive sampling scheme for the subjects in the PK Population.

End point type	Secondary

End point timeframe:

Day 1 and Week 12

End point values	EDP-305 1 mg (PK Population)	EDP-305 2.5 mg (PK Population)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[9]	52[10]		
Units: hour				
median (full range (min-max))				
Day 1	6.00 (2.00 to 8.00)	6.00 (1.93 to 8.25)		
Week 12	6.00 (0.00 to 8.00)	6.00 (0.00 to 6.15)		

Notes:

[9] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 17
[10] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 13

Statistical analyses

No statistical analyses for this end point

Secondary: AUC(Last) of EP-022571 on Day 1 and at Week 12

End point title	AUC(Last) of EP-022571 on Day 1 and at Week 12

End point description:

AUC(last) is defined as the area under the plasma concentration-time curve from time zero to time the last quantifiable concentration, computed using the linear up/log down trapezoidal rule. AUC(last) was computed for EP-022571 (a metabolite of EDP-305) on Day 1 and Week 12 for the samples collected according to the intensive sampling scheme for the subjects in the PK Population.

End point type	Secondary

End point timeframe:

Day 1 and at Week 12

End point values	EDP-305 1 mg (PK Population)	EDP-305 2.5 mg (PK Population)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[11]	52[12]		
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1	1.48 (± 174)	3.77 (± 112)		
Week 12	1.41 (± 187.01)	3.81 (± 121.18)		

Notes:

[11] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 17
[12] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 12

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of EP-022572 on Day 1 and at Week 12

End point title	Cmax of EP-022572 on Day 1 and at Week 12

End point description:

The Cmax is the maximum observed plasma concentration, which was measured for EP-022572 (a metabolite of EDP-305) on Day 1 and Week 12 for the samples collected according to the intensive sampling scheme for the subjects in the PK Population.

End point type	Secondary

End point timeframe:

Day 1 and Week 12

End point values	EDP-305 1 mg (PK Population)	EDP-305 2.5 mg (PK Population)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[13]	52[14]		
Units: nanogram(s)/millilitre				
geometric mean (geometric coefficient of variation)				
Day 1	0.234 (± 1942)	0.571 (± 212)		
Week 12	0.214 (± 2863)	0.556 (± 212)		

Notes:

[13] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 17
[14] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 13

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax of EP-022572 on Day 1 and at Week 12

End point title	Tmax of EP-022572 on Day 1 and at Week 12

End point description:

The Tmax was measured for EP-022572 (a metabolite of EDP-305) on Day 1 and at Week 12 for the samples collected according to the intensive sampling scheme for the subjects in the PK Population.

End point type	Secondary

End point timeframe:

Day 1 and Week 12

End point values	EDP-305 1 mg (PK Population)	EDP-305 2.5 mg (PK Population)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[15]	52[16]		
Units: hour				
median (full range (min-max))				
Day 1	6.00 (2.00 to 8.07)	6.00 (2.00 to 8.00)		
Week 12	6.00 (0.00 to 8.00)	2.05 (0.00 to 8.18)		

Notes:

[15] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 17
[16] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 13

Statistical analyses

No statistical analyses for this end point

Secondary: AUC(Last) of EP-022572 on Day 1 and at Week 12

End point title	AUC(Last) of EP-022572 on Day 1 and at Week 12

End point description:

AUC(last) is defined as the area under the plasma concentration-time curve from time zero to time the

last quantifiable concentration, computed using the linear up/log down trapezoidal rule. AUC(last) was computed for EP-022572 (a metabolite of EDP-305) on Day 1 and Week 12 for the samples collected according to the intensive sampling scheme for the subjects in the PK Population.

End point type	Secondary

End point timeframe:

Day 1 and Week 12

End point values	EDP-305 1 mg (PK Population)	EDP-305 2.5 mg (PK Population)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[17]	52[18]		
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1	1.06 (± 220)	2.92 (± 114)		
Week 12	1.13 (± 212)	3.19 (± 116)		

Notes:

[17] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 17
[18] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 12

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of EP-022679 on Day 1 and at Week 12

End point title	Cmax of EP-022679 on Day 1 and at Week 12

End point description:

The Cmax is the maximum observed plasma concentration, which was measured for EP-022679 (a metabolite of EDP-305) on Day 1 and Week 12 for the samples collected according to the intensive sampling scheme for the subjects in the PK Population.

End point type	Secondary

End point timeframe:

Day 1 and Week 12

End point values	EDP-305 1 mg (PK Population)	EDP-305 2.5 mg (PK Population)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[19]	52[20]		
Units: nanogram(s)/millilitre				
geometric mean (geometric coefficient of variation)				
Day 1	0.574 (± 321)	1.28 (± 167)		
Week 12	1.41 (± 117)	3.85 (± 122)		

Notes:

[19] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 17

[20] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 13

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax of EP-022679 on Day 1 and at Week 12

End point title	Tmax of EP-022679 on Day 1 and at Week 12

End point description:

The Tmax was measured for EP-022679 (a metabolite of EDP-305) on Day 1 and at Week 12 for the samples collected according to the intensive sampling scheme for the subjects in the PK Population.

End point type	Secondary

End point timeframe:

Day 1 and Week 12

End point values	EDP-305 1 mg (PK Population)	EDP-305 2.5 mg (PK Population)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[21]	52[22]		
Units: hour				
median (full range (min-max))				
Day 1	8.00 (5.88 to 8.00)	8.00 (6.00 to 8.25)		
Week 12	6.03 (0.00 to 8.00)	6.00 (0.00 to 8.18)		

Notes:

[21] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 17
[22] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 13

Statistical analyses

No statistical analyses for this end point

Secondary: AUC(Last) of EP-022679 on Day 1 and at Week 12

End point title	AUC(Last) of EP-022679 on Day 1 and at Week 12

End point description:

AUC(last) is defined as the area under the plasma concentration-time curve from time zero to time the last quantifiable concentration, computed using the linear up/log down trapezoidal rule. AUC(last) was computed for EP-022679 (a metabolite of EDP-305) on Day 1 and Week 12 for the samples collected according to the intensive sampling scheme for the subjects in the PK Population.

End point type	Secondary

End point timeframe:

Day 1 and Week 12

End point values	EDP-305 1 mg (PK Population)	EDP-305 2.5 mg (PK Population)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[23]	52[24]		
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1	2.32 (± 137.54)	5.09 (± 117)		
Week 12	7.14 (± 113)	22.5 (± 104)		

Notes:

[23] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 17
[24] - Number of subjects analysed for Day 1 = 19
Number of subjects analysed for Week 12 = 12

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Body Weight at Week 12

End point title	Mean Change From Baseline in Body Weight at Week 12

End point description:

Body weight was measured at specific timepoints for the subjects. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	49	38	
Units: kilogram(s)				
arithmetic mean (standard deviation)	-0.877 (± 2.8100)	-1.440 (± 2.7984)	-2.114 (± 3.2829)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.112
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	1.356
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.322
upper limit	3.034

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4229
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.647
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.947
upper limit	2.24

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2764
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.577
upper limit	1.996

Secondary: Mean Change From Baseline in WTH Ratio at Week 12

End point title	Mean Change From Baseline in WTH Ratio at Week 12

End point description:

The WTH ratio is calculated as the ratio of waist to hip circumference, which was measured at specific timepoints. Baseline refers to the last non-missing value collected prior to the first dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	49	38	
Units: ratio				
arithmetic mean (standard deviation)	0.013 (± 0.0729)	-0.007 (± 0.0477)	0.014 (± 0.0509)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	EDP-305 2.5 mg v Placebo
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5606
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.008
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.037

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1002
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.023

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.004
upper limit	0.05

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2002
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.014
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.036
upper limit	0.008

Secondary: Mean Change From Baseline in Fibroblast Growth Factor 19 (FGF19) by Nominal Timepoint (Intensive PD Samples) at Week 12

End point title	Mean Change From Baseline in Fibroblast Growth Factor 19 (FGF19) by Nominal Timepoint (Intensive PD Samples) at Week 12

End point description:

Blood samples were collected according to the intensive sampling scheme at specific timepoints to assess the PD marker: FGF19. Baseline refers to the last non-missing pre-dose value collected prior to the most recent dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12 (8 hours post-dose)

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	18	14	
Units: nanogram(s)/litre				
arithmetic mean (standard deviation)	159.98 (± 165.245)	410.00 (± 260.223)	607.12 (± 891.553)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7014
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-178.787
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1098.454
upper limit	740.88

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.907
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	52.307
Confidence interval	
level	95 %
sides	2-sided
lower limit	-830.934
upper limit	935.547

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.536
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-231.094
Confidence interval	
level	95 %
sides	2-sided
lower limit	-967.273
upper limit	505.086

Secondary: Mean Change From Baseline in FGF19 by Bin Timepoint (Sparse PD Samples) at Week 12

End point title	Mean Change From Baseline in FGF19 by Bin Timepoint (Sparse PD Samples) at Week 12

End point description:

Blood samples were collected according to the sparse sampling scheme at specific timepoints to assess the PD marker: FGF19. Baseline refers to the last non-missing pre-dose value collected prior to the most recent dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12 (pre-dose)

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	23	17	
Units: nanogram(s)/litre				
arithmetic mean (standard deviation)	33.51 (± 155.744)	46.04 (± 88.662)	813.29 (± 3200.567)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2985
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-753.153
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2183.92
upper limit	677.614

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

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8413
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	139.107
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1236.689
upper limit	1514.902

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1168
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-892.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2011.705
upper limit	227.186

Secondary: Mean Change From Baseline in 7a-Hydroxy-4-Cholestene-3-One (C4) by Nominal Timepoint (Intensive PD Samples) at Week 12

End point title	Mean Change From Baseline in 7a-Hydroxy-4-Cholestene-3-One (C4) by Nominal Timepoint (Intensive PD Samples) at Week 12

End point description:

Blood samples were collected according to the intensive sampling scheme at specific timepoints to assess the PD marker: C4. Baseline refers to the last non-missing pre-dose value collected prior to the most recent dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12 (8 hours post-dose)

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	17	14	
Units: nanogram(s)/millilitre				
arithmetic mean (standard deviation)	-9.484 (± 20.6295)	-36.783 (± 24.6560)	-40.567 (± 20.9260)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	33.491
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.984
upper limit	48.998

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	30.814
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.802
upper limit	45.825

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg

Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6757
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	2.677
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.946
upper limit	15.3

Secondary: Mean Change From Baseline in C4 by Bin Timepoint (Sparse PD Samples) at Week 12

End point title	Mean Change From Baseline in C4 by Bin Timepoint (Sparse PD Samples) at Week 12

End point description:

Blood samples were collected according to the sparse sampling scheme at specific timepoints to assess the PD marker: C4. Baseline refers to the last non-missing pre-dose value collected prior to the most recent dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12 (pre-dose)

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	25	18	
Units: nanogram(s)/millilitre				
arithmetic mean (standard deviation)	-5.242 (± 30.5321)	-13.500 (± 26.2458)	-23.773 (± 20.7045)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0134
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	21.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.533
upper limit	38.067

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4686
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	5.847
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.116
upper limit	21.811

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0181
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	15.453
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.699
upper limit	28.206

Secondary: Mean Change From Baseline in Bile Acid (BA) by Nominal Timepoint (Intensive PD Samples) at Week 12

End point title	Mean Change From Baseline in Bile Acid (BA) by Nominal Timepoint (Intensive PD Samples) at Week 12

End point description:

Blood samples were collected according to the intensive sampling scheme at specific timepoints to assess the PD marker: BA. Baseline refers to the last non-missing pre-dose value collected prior to the most recent dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary
End point timeframe:	
Baseline and Week 12 (8 hours post-dose)	

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	18	14	
Units: micromole(s)/litre				
arithmetic mean (standard deviation)	4.47 (± 3.668)	2.16 (± 5.507)	0.14 (± 3.125)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	Placebo v EDP-305 2.5 mg
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0557
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	4.324
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.108
upper limit	8.756

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2867
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	2.305
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.955
upper limit	6.566

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2437
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.2437
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.39
upper limit	5.429

Secondary: Mean Change From Baseline in BA by Bin Timepoint (Sparse PD Samples) at Week 12

End point title	Mean Change From Baseline in BA by Bin Timepoint (Sparse PD Samples) at Week 12

End point description:

Blood samples were collected according to the sparse sampling scheme at specific timepoints to assess the PD marker: BA. Baseline refers to the last non-missing pre-dose value collected prior to the most recent dose of study treatment. Mean change was defined as the mean value at Week 12 minus the mean value at baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12 (pre-dose)

End point values	Placebo	EDP-305 1 mg	EDP-305 2.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	25	17	
Units: micromole(s)/litre				
arithmetic mean (standard deviation)	0.77 (± 5.789)	-0.11 (± 2.783)	0.74 (± 4.091)	

Statistical analyses

Statistical analysis title	Placebo v EDP-305 2.5 mg
Comparison groups	EDP-305 2.5 mg v Placebo

Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9913
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.019
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.491
upper limit	3.53

Statistical analysis title	Placebo v EDP-305 1 mg
Comparison groups	Placebo v EDP-305 1 mg
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.553
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.995
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.323
upper limit	4.314

Statistical analysis title	EDP-305 1 mg v EDP-305 2.5 mg
Comparison groups	EDP-305 1 mg v EDP-305 2.5 mg
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4729
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.976
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.665
upper limit	1.713

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were reported from the date of signing the consent form to the date of completion of the subject's end of the study visit (Week 16). Ongoing AEs were followed beyond the end of the study visit at the discretion of the investigator.

Adverse event reporting additional description:

Treatment-emergent adverse events were summarised for the Safety Population, which included all the randomised subjects who received at least one dose of the study treatment.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Out of 25 randomised subjects, 1 subject in the placebo group was not dosed due to consent withdrawal by the subject and was not included in Safety Population. Hence, AE details are presented for 24 subjects (Safety Population).

Reporting group title	EDP-305 1 mg

Reporting group description:

All the 55 randomised subjects in the EDP-305 1 mg were dosed and were included in the Safety Population.

Reporting group title	EDP-305 2.5 mg

Reporting group description:

Out of 54 randomised subjects, 1 subject in the EDP-305 2.5 mg group was not dosed due to consent withdrawal by the subject and was not included in Safety Population. Hence, AE details are presented for 53 subjects (Safety Population).

Serious adverse events	Placebo	EDP-305 1 mg	EDP-305 2.5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	1 / 55 (1.82%)	0 / 53 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 24 (4.17%)	0 / 55 (0.00%)	0 / 53 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 24 (0.00%)	1 / 55 (1.82%)	0 / 53 (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

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

Non-serious adverse events	Placebo	EDP-305 1 mg	EDP-305 2.5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 24 (33.33%)	17 / 55 (30.91%)	32 / 53 (60.38%)
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 24 (8.33%)	2 / 55 (3.64%)	2 / 53 (3.77%)
occurrences (all)	2	2	2
Dizziness			
subjects affected / exposed	1 / 24 (4.17%)	3 / 55 (5.45%)	1 / 53 (1.89%)
occurrences (all)	1	3	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 24 (8.33%)	2 / 55 (3.64%)	2 / 53 (3.77%)
occurrences (all)	2	2	2
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 24 (4.17%)	3 / 55 (5.45%)	2 / 53 (3.77%)
occurrences (all)	1	3	2
Diarrhoea			
subjects affected / exposed	0 / 24 (0.00%)	2 / 55 (3.64%)	3 / 53 (5.66%)
occurrences (all)	0	2	3
Vomiting			
subjects affected / exposed	2 / 24 (8.33%)	1 / 55 (1.82%)	1 / 53 (1.89%)
occurrences (all)	2	1	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 24 (0.00%)	1 / 55 (1.82%)	3 / 53 (5.66%)
occurrences (all)	0	1	3
Skin and subcutaneous tissue disorders			

Pruritus generalised			
subjects affected / exposed	1 / 24 (4.17%)	5 / 55 (9.09%)	25 / 53 (47.17%)
occurrences (all)	1	6	32
Rash			
subjects affected / exposed	0 / 24 (0.00%)	1 / 55 (1.82%)	4 / 53 (7.55%)
occurrences (all)	0	1	7
Pruritus			
subjects affected / exposed	1 / 24 (4.17%)	0 / 55 (0.00%)	3 / 53 (5.66%)
occurrences (all)	1	0	3
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 24 (0.00%)	3 / 55 (5.45%)	1 / 53 (1.89%)
occurrences (all)	0	3	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 24 (0.00%)	3 / 55 (5.45%)	1 / 53 (1.89%)
occurrences (all)	0	3	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported