Clinical trial results:
A Randomised, Phase 2a, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Pharmacokinetics and Antiviral Activity of Multiple Doses of Orally Administered EDP-938 Against Respiratory Syncytial Virus Infection in the Virus Challenge Model

Summary

EudraCT number	2018-001878-21
Trial protocol	GB
Global end of trial date	18 October 2019

Results information

Result version number	v2 (current)
This version publication date	02 June 2022
First version publication date	29 July 2021
Version creation reason	• Correction of full data set Updates made to the descriptions of 4 endpoints to align data presentation across registries.

Trial information

Trial identification

Sponsor protocol code	EDP 938-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03691623
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ENANTA Pharmaceuticals, Inc
Sponsor organisation address	500 Arsenal Street, Watertown, MA, United States,
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	18 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the antiviral activity of EDP-938 compared to placebo in healthy adult participants inoculated with respiratory syncytial virus-A (RSV-A) Memphis 37b.

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	15 October 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: 179
Worldwide total number of subjects	179
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	179
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 179 participants enrolled in the trial at one site in the United Kingdom from October 2018 to October 2019.

Pre-assignment

Screening details:

For Part 1, 115 participants were inoculated with respiratory syncytial virus-A (RSV-A) Memphis 37b of whom 114 were randomized and treated. For Part 2, 64 participants were inoculated with RSV-A Memphis 37b of whom 63 were randomized and treated. Only treated participants are included in the subject disposition and subsequent analyses.

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	Part 1: EDP-938 600 mg

Arm description:

Participants were administered EDP-938 oral suspension once daily (OD) at a dose of 600 mg, followed by a placebo dose 12 hours later (OD). Treatments were administered for a total of 10 doses over 5 days.

Arm type	Experimental
Investigational medicinal product name	EDP-938
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

EDP-938 was administered as a powder for oral suspension.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Placebo was administered as a powder for oral suspension.

Arm title	Part 1: EDP-938 500 mg then 300 mg

Arm description:

Participants were administered EDP-938 oral suspension as a single Loading Dose (LD) of 500 mg followed by a 300 mg dose twice daily (BD) every 12 hours for a total of 10 doses.

Arm type	Experimental
Investigational medicinal product name	EDP-938
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

EDP-938 was administered as a powder for oral suspension.

Arm title	Part 1: Placebo

Arm description:

Participants were administered a placebo dose twice a day (BD) every 12 hours for a total of 10 doses.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Placebo was administered as a powder for oral suspension.

Arm title	Part 2: EDP-938 600 mg then 300 mg

Arm description:

Participants were administered a single loading dose (LD) of 600 mg EDP-938, followed by a 300 mg EDP-938 dose once a day (OD), and with dosing for 5 days.

Arm type	Experimental
Investigational medicinal product name	EDP-938
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

EDP-938 was administered as a powder for oral suspension.

Arm title	Part 2: EDP-938 400 mg then 200 mg

Arm description:

Participants were administered a single loading dose (LD) of 400 mg EDP-938 followed by 200 mg EDP-938 at 12 hours, then 200 mg doses of EDP-938 twice daily (BD), and with dosing for 5 days.

Arm type	Experimental
Investigational medicinal product name	EDP-938
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

EDP-938 was administered as a powder for oral suspension.

Arm title	Part 2: Placebo

Arm description:

Participants were administered a placebo twice daily (BD) for 5 days, with dosing at 12 hour intervals.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Placebo was administered as a powder for oral suspension.

Number of subjects in period 1[1]	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 1: Placebo
Started	38	38	38
Received treatment	38	38	38
Completed	38	38	38

Number of subjects in period 1[1]	Part 2: EDP-938 600 mg then 300 mg	Part 2: EDP-938 400 mg then 200 mg	Part 2: Placebo
Started	21	21	21
Received treatment	21	21	21
Completed	21	21	21

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: For Part 1, 115 participants were inoculated with respiratory syncytial virus-A (RSV-A) Memphis 37b of whom 114 were randomized and treated. For Part 2, 64 participants were inoculated with RSV-A Memphis 37b of whom 63 were randomized and treated. Only treated participants are included in the subject disposition and subsequent analyses.

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: EDP-938 600 mg
Reporting group description:	
Participants were administered EDP-938 oral suspension once daily (OD) at a dose of 600 mg, followed by a placebo dose 12 hours later (OD). Treatments were administered for a total of 10 doses over 5 days.	
Reporting group title	Part 1: EDP-938 500 mg then 300 mg
Reporting group description:	
Participants were administered EDP-938 oral suspension as a single Loading Dose (LD) of 500 mg followed by a 300 mg dose twice daily (BD) every 12 hours for a total of 10 doses.	
Reporting group title	Part 1: Placebo
Reporting group description:	
Participants were administered a placebo dose twice a day (BD) every 12 hours for a total of 10 doses.	
Reporting group title	Part 2: EDP-938 600 mg then 300 mg
Reporting group description:	
Participants were administered a single loading dose (LD) of 600 mg EDP-938, followed by a 300 mg EDP-938 dose once a day (OD), and with dosing for 5 days.	
Reporting group title	Part 2: EDP-938 400 mg then 200 mg
Reporting group description:	
Participants were administered a single loading dose (LD) of 400 mg EDP-938 followed by 200 mg EDP-938 at 12 hours, then 200 mg doses of EDP-938 twice daily (BD), and with dosing for 5 days.	
Reporting group title	Part 2: Placebo
Reporting group description:	
Participants were administered a placebo twice daily (BD) for 5 days, with dosing at 12 hour intervals.	

Reporting group values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 1: Placebo
Number of subjects	38	38	38
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)	38	38	38
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	28.5	27.2	27.6
standard deviation	± 5.84	± 7.50	± 7.86
Gender categorical Units: Subjects			
Female	13	18	13
Male	25	20	25

Race Units: Subjects			
Asian	1	1	2
Black or African American	0	1	2
White	33	32	31
Other	4	4	3
Body Mass Index (BMI) Units: Kilograms per meter squared			
arithmetic mean	24.33	23.27	23.69
standard deviation	± 2.853	± 2.734	± 2.239

Reporting group values	Part 2: EDP-938 600 mg then 300 mg	Part 2: EDP-938 400 mg then 200 mg	Part 2: Placebo
Number of subjects	21	21	21
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)	21	21	21
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	23.4	24.4	23.1
standard deviation	± 3.22	± 5.83	± 5.54
Gender categorical Units: Subjects			
Female	10	11	9
Male	11	10	12
Race Units: Subjects			
Asian	1	1	0
Black or African American	0	1	0
White	18	17	19
Other	2	2	2
Body Mass Index (BMI) Units: Kilograms per meter squared			
arithmetic mean	23.70	23.66	23.72
standard deviation	± 3.399	± 2.641	± 2.436

Reporting group values	Total		
Number of subjects	177		
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)	177		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	74		
Male	103		
Race			
Units: Subjects			
Asian	6		
Black or African American	4		
White	150		
Other	17		
Body Mass Index (BMI)			
Units: Kilograms per meter squared			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Part 1: EDP-938 600 mg
Reporting group description:	
Participants were administered EDP-938 oral suspension once daily (OD) at a dose of 600 mg, followed by a placebo dose 12 hours later (OD). Treatments were administered for a total of 10 doses over 5 days.	
Reporting group title	Part 1: EDP-938 500 mg then 300 mg
Reporting group description:	
Participants were administered EDP-938 oral suspension as a single Loading Dose (LD) of 500 mg followed by a 300 mg dose twice daily (BD) every 12 hours for a total of 10 doses.	
Reporting group title	Part 1: Placebo
Reporting group description:	
Participants were administered a placebo dose twice a day (BD) every 12 hours for a total of 10 doses.	
Reporting group title	Part 2: EDP-938 600 mg then 300 mg
Reporting group description:	
Participants were administered a single loading dose (LD) of 600 mg EDP-938, followed by a 300 mg EDP-938 dose once a day (OD), and with dosing for 5 days.	
Reporting group title	Part 2: EDP-938 400 mg then 200 mg
Reporting group description:	
Participants were administered a single loading dose (LD) of 400 mg EDP-938 followed by 200 mg EDP-938 at 12 hours, then 200 mg doses of EDP-938 twice daily (BD), and with dosing for 5 days.	
Reporting group title	Part 2: Placebo
Reporting group description:	
Participants were administered a placebo twice daily (BD) for 5 days, with dosing at 12 hour intervals.	

Primary: Area Under the Curve (AUC) of Respiratory Syncytial Virus (RSV) Viral Load

End point title	Area Under the Curve (AUC) of Respiratory Syncytial Virus (RSV) Viral Load
End point description:	
Measured in nasal washes by quantitative reverse transcription polymerase chain reaction (RT-qPCR) in participants inoculated with respiratory syncytial virus-A (RSV-A) Memphis 37b.	
End point type	Primary
End point timeframe:	
Twice daily on Day 2 through Day 11 and once on Day 12	

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 1: Placebo	Part 2: EDP-938 600 mg then 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	31	30	15
Units: h*log10 copies/milliliter				
geometric mean (geometric coefficient of variation)	134.70 (± 85.1)	113.51 (± 99.9)	624.30 (± 51.7)	80.61 (± 112.1)

End point values	Part 2: EDP-938 400 mg then 200 mg	Part 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: h*log10 copies/milliliter				
geometric mean (geometric coefficient of variation)	160.81 (± 63.3)	808.28 (± 37.1)		

Statistical analyses

Statistical analysis title	Part 1: EDP-938 600mg vs Part 1: Placebo
Comparison groups	Part 1: EDP-938 600 mg v Part 1: Placebo
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-588.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-719.8
upper limit	-456.35

Statistical analysis title	Part 1:EDP-938 500mg then 300mg vs Part 1: Placebo
Comparison groups	Part 1: Placebo v Part 1: EDP-938 500 mg then 300 mg
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-564.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-689.23
upper limit	-440.02

Statistical analysis title	Part 2:EDP-938 600mg then 300mg vs Part 2: Placebo
Comparison groups	Part 2: EDP-938 600 mg then 300 mg v Part 2: Placebo
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-716.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-879.92
upper limit	-552.24

Statistical analysis title	Part 2:EDP-938 400mg then 200mg vs Part 2: Placebo
Comparison groups	Part 2: Placebo v Part 2: EDP-938 400 mg then 200 mg
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-736.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-916.36
upper limit	-556.11

Secondary: Area Under the Curve (AUC) of Total Symptom Score

End point title	Area Under the Curve (AUC) of Total Symptom Score

End point description:

Total symptom scores (from the 10-item symptom diary card) were used to calculate the AUC. Each individual symptom score was graded on a scale of 0-3, where Grade 0 is absence, Grade 1 is just noticeable, Grade 2 is bothersome but does not prevent participation in activities and Grade 3 is bothersome and interferes with activities:
• Runny nose
• Stuffy nose
• Sneezing
• Sore throat
• Earache
• Malaise (Tiredness)
• Cough
• Shortness of breath
• Headache
• Muscle/ joint ache/ stiffness

End point type	Secondary

End point timeframe:

Three times daily on Day 0 to Day 11, once on Day 12

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 1: Placebo	Part 2: EDP-938 600 mg then 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	31	30	15
Units: h*score				
geometric mean (geometric coefficient of variation)	61.18 (± 347.8)	37.36 (± 1640.1)	252.49 (± 243.9)	26.70 (± 730.2)

End point values	Part 2: EDP-938 400 mg then 200 mg	Part 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: h*score				
geometric mean (geometric coefficient of variation)	27.81 (± 436.8)	232.53 (± 530.9)		

Statistical analyses

Statistical analysis title	Part 1: EDP-938 600mg vs Part 1: Placebo
Comparison groups	Part 1: EDP-938 600 mg v Part 1: Placebo
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-355.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-506.12
upper limit	-205.69

Statistical analysis title	Part 1:EDP-938 500mg then 300mg vs Part 1: Placebo
Comparison groups	Part 1: Placebo v Part 1: EDP-938 500 mg then 300 mg

Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-326.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-469.68
upper limit	-183.6

Statistical analysis title	Part 2:EDP-938 600mg then 300mg vs Part 2: Placebo
Comparison groups	Part 2: EDP-938 600 mg then 300 mg v Part 2: Placebo
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-313.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-494.27
upper limit	-133.69

Statistical analysis title	Part 2:EDP-938 400mg then 200mg vs Part 2: Placebo
Comparison groups	Part 2: Placebo v Part 2: EDP-938 400 mg then 200 mg
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-312.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-508.05
upper limit	-117.4

Secondary: Peak Total Symptom Score

End point title	Peak Total Symptom Score

End point description:

Peak total symptom score was defined as the highest total symptom score between first dose of study drug and Day 12. Values presented are a sum of individual symptom scores. Total symptom scores at the time of the first dose of study drug can be before or after dosing.

Measured by the 10-item Diary Card. Each individual symptom score was graded on a scale of 0-3, where Grade 0 is absence, Grade 1 is just noticeable, Grade 2 is bothersome but does not prevent participation in activities and Grade 3 is bothersome and interferes with activities:
• Runny nose
• Stuffy nose
• Sneezing
• Sore throat
• Earache
• Malaise (Tiredness)
• Cough
• Shortness of breath
• Headache
• Muscle/ joint ache/ stiffness

End point type	Secondary

End point timeframe:

Day 2 to Day 12

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 1: Placebo	Part 2: EDP-938 600 mg then 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	31	30	15
Units: h*score				
geometric mean (geometric coefficient of variation)	2.3 (± 53.9)	1.9 (± 89.8)	4.9 (± 77.9)	1.6 (± 68.5)

End point values	Part 2: EDP-938 400 mg then 200 mg	Part 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: h*score				
geometric mean (geometric coefficient of variation)	1.8 (± 55.6)	4.2 (± 85.8)		

Statistical analyses

Statistical analysis title	Part 1: EDP-938 600mg vs Part 1: Placebo
Comparison groups	Part 1: EDP-938 600 mg v Part 1: Placebo

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.3
upper limit	-2

Statistical analysis title	Part 1:EDP-938 500mg then 300mg vs Part 1: Placebo
Comparison groups	Part 1: Placebo v Part 1: EDP-938 500 mg then 300 mg
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.5
upper limit	-2.4

Statistical analysis title	Part 2:EDP-938 600mg then 300mg vs Part 2: Placebo
Comparison groups	Part 2: EDP-938 600 mg then 300 mg v Part 2: Placebo
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	-1.2

Statistical analysis title	Part 2:EDP-938 400mg then 200mg vs Part 2: Placebo

Comparison groups	Part 2: Placebo v Part 2: EDP-938 400 mg then 200 mg
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	-0.9

Secondary: Total Symptom Score

End point title	Total Symptom Score

End point description:

Measured by the 10-item Diary Card. Each individual symptom score was graded on a scale of 0-3, where Grade 0 is absence, Grade 1 is just noticeable, Grade 2 is bothersome but does not prevent participation in activities and Grade 3 is bothersome and interferes with activities:
• Runny nose
• Stuffy nose
• Sneezing
• Sore throat
• Earache
• Malaise (Tiredness)
• Cough
• Shortness of breath
• Headache
• Muscle/ joint ache/ stiffness

End point type	Secondary

End point timeframe:

Day 2 to Day 12

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 1: Placebo	Part 2: EDP-938 600 mg then 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25[1]	31[2]	30[3]	15[4]
Units: Scores on a scale				
geometric mean (geometric coefficient of variation)				
Relative Day 2 Assessment 1	0.9 (± 97.5)	0.8 (± 155.4)	1.9 (± 117.0)	0.5 (± 140.8)
Relative Day 2 Assessment 2	0.8 (± 94.0)	0.7 (± 160.3)	2.4 (± 110.3)	0.4 (± 185.2)
Relative Day 2 Assessment 3	0.5 (± 117.0)	0.6 (± 184.4)	2.7 (± 94.9)	0.3 (± 196.2)
Relative Day 3 Assessment 1	0.4 (± 137.3)	0.7 (± 148.5)	2.6 (± 99.1)	0.4 (± 166.9)
Relative Day 3 Assessment 2	0.4 (± 144.3)	0.6 (± 175.2)	2.7 (± 90.5)	0.3 (± 207.0)
Relative Day 3 Assessment 3	0.3 (± 190.9)	0.6 (± 167.7)	2.5 (± 103.7)	0.2 (± 332.6)
Relative Day 4 Assessment 1	0.3 (± 177.1)	0.5 (± 154.9)	2.3 (± 103.8)	0.2 (± 343.9)
Relative Day 4 Assessment 2	0.3 (± 186.5)	0.6 (± 163.1)	1.8 (± 115.3)	0.1 (± 387.3)

Relative Day 4 Assessment 3	0.3 (± 263.0)	0.4 (± 163.5)	1.8 (± 103.1)	0.2 (± 280.3)
Relative Day 5 Assessment 1	0.2 (± 228.2)	0.5 (± 158.9)	1.6 (± 108.3)	0.2 (± 244.9)
Relative Day 5 Assessment 2	0.3 (± 191.3)	0.4 (± 177.1)	1.4 (± 109.2)	0.2 (± 314.0)
Relative Day 5 Assessment 3	0.1 (± 364.8)	0.4 (± 162.0)	1.3 (± 115.9)	0.1 (± 280.3)
Relative Day 6 Assessment 1	0.2 (± 300.9)	0.4 (± 186.9)	1.2 (± 106.0)	0.2 (± 314.0)
Relative Day 6 Assessment 2	0.2 (± 288.7)	0.4 (± 186.9)	1.0 (± 112.8)	0.1 (± 387.3)
Relative Day 6 Assessment 3	0.2 (± 280.9)	0.3 (± 184.6)	1.0 (± 100.5)	0.1 (± 387.3)
Relative Day 7 Assessment 1	0.2 (± 225.1)	0.2 (± 205.3)	0.7 (± 124.9)	0.1 (± 387.3)
Relative Day 7 Assessment 2	0.2 (± 196.2)	0.2 (± 162.0)	0.7 (± 115.7)	0.1 (± 346.4)
Relative Day 7 Assessment 3	0.2 (± 291.0)	0.2 (± 185.8)	0.9 (± 89.9)	0.1 (± 331.7)
Relative Day 8 Assessment 1	0.1 (± 291.0)	0.2 (± 199.9)	0.9 (± 94.9)	0.1 (± 331.7)
Relative Day 8 Assessment 2	0.1 (± 374.2)	0.1 (± 244.1)	0.9 (± 99.4)	0.2 (± 264.6)
Relative Day 8 Assessment 3	0.0 (± 999999)	0.4 (± 149.1)	0.6 (± 129.1)	0.0 (± 0.0)
Relative Day 9 Assessment 1	0.0 (± 999999)	0.0 (± 999999)	0.4 (± 140.5)	0.0 (± 999999)
Relative Day 9 Assessment 2	0.0 (± 999999)	0.0 (± 999999)	0.5 (± 91.3)	0.0 (± 999999)

Notes:

[1] - n values range from 3-25. 999999 = %CV not calculable as Geometric Mean = 0.0

[2] - n values range from 3-31. 999999 = %CV not calculable as Geometric Mean = 0.0

[3] - n values range from 5-30 (n=30, 29, 24, 23, 19, 17, 10, 5)

[4] - n values range from 4-15. 999999 = %CV not calculable as Geometric Mean = 0.0

End point values	Part 2: EDP-938 400 mg then 200 mg	Part 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[5]	12[6]		
Units: Scores on a scale				
geometric mean (geometric coefficient of variation)				
Relative Day 2 Assessment 1	0.3 (± 222.5)	3.0 (± 66.6)		
Relative Day 2 Assessment 2	0.5 (± 179.8)	2.9 (± 82.5)		
Relative Day 2 Assessment 3	0.2 (± 331.7)	2.6 (± 94.3)		
Relative Day 3 Assessment 1	0.2 (± 254.2)	2.2 (± 103.0)		
Relative Day 3 Assessment 2	0.3 (± 237.1)	2.3 (± 101.0)		
Relative Day 3 Assessment 3	0.3 (± 276.4)	2.2 (± 95.3)		
Relative Day 4 Assessment 1	0.2 (± 254.2)	1.9 (± 92.6)		
Relative Day 4 Assessment 2	0.1 (± 331.7)	1.7 (± 85.0)		
Relative Day 4 Assessment 3	0.1 (± 331.7)	1.8 (± 88.3)		
Relative Day 5 Assessment 1	0.2 (± 254.2)	1.6 (± 87.9)		
Relative Day 5 Assessment 2	0.2 (± 254.2)	1.4 (± 112.8)		
Relative Day 5 Assessment 3	0.1 (± 331.7)	1.4 (± 89.6)		
Relative Day 6 Assessment 1	0.2 (± 237.1)	1.5 (± 83.3)		
Relative Day 6 Assessment 2	0.3 (± 185.4)	1.2 (± 102.4)		
Relative Day 6 Assessment 3	0.1 (± 210.8)	1.1 (± 116.5)		
Relative Day 7 Assessment 1	0.1 (± 316.2)	0.8 (± 126.1)		
Relative Day 7 Assessment 2	0.1 (± 300.0)	0.9 (± 153.5)		
Relative Day 7 Assessment 3	0.0 (± 999999)	0.7 (± 179.2)		
Relative Day 8 Assessment 1	0.0 (± 999999)	0.5 (± 153.7)		
Relative Day 8 Assessment 2	0.0 (± 999999)	0.2 (± 170.8)		
Relative Day 8 Assessment 3	0.0 (± 999999)	0.2 (± 200.0)		
Relative Day 9 Assessment 1	0.0 (± 999999)	0.2 (± 200.0)		
Relative Day 9 Assessment 2	0.0 (± 999999)	0.4 (± 141.4)		

Notes:

[5] - n values range from 0-11. 999999 = %CV not calculable as Geometric Mean = 0.0

[6] - n values range from 2-12 (n=12, 11, 10, 7, 4, 2)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Peak Total Symptom Score

End point title	Time to Peak Total Symptom Score

End point description:

Time to peak total symptom score was defined as the time in days to the highest total symptom score between first dose of study drug and Day 12. Total symptom scores at the time of the first dose of study drug can be before or after dosing.

End point type	Secondary

End point timeframe:

Day 2 to Day 12

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 1: Placebo	Part 2: EDP-938 600 mg then 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	31	30	15
Units: Days				
geometric mean (geometric coefficient of variation)	1.18 (± 137.8)	1.76 (± 110.0)	2.15 (± 71.4)	1.45 (± 131.9)

End point values	Part 2: EDP-938 400 mg then 200 mg	Part 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: Days				
geometric mean (geometric coefficient of variation)	1.09 (± 136.4)	1.94 (± 80.5)		

Statistical analyses

Statistical analysis title	Part 1: EDP-938 600mg vs Part 1: Placebo
Comparison groups	Part 1: EDP-938 600 mg v Part 1: Placebo

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.199
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.09
upper limit	0.44

Statistical analysis title	Part 1:EDP-938 500mg then 300mg vs Part 1: Placebo
Comparison groups	Part 1: Placebo v Part 1: EDP-938 500 mg then 300 mg
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.714
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	1.43

Statistical analysis title	Part 2:EDP-938 600mg then 300mg vs Part 2: Placebo
Comparison groups	Part 2: EDP-938 600 mg then 300 mg v Part 2: Placebo
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.844
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.15
upper limit	1.77

Statistical analysis title	Part 2:EDP-938 400mg then 200mg vs Part 2: Placebo

Comparison groups	Part 2: Placebo v Part 2: EDP-938 400 mg then 200 mg
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.21
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.46
upper limit	0.79

Secondary: Time to Resolution from Peak Total Symptom Score

End point title	Time to Resolution from Peak Total Symptom Score

End point description:

Time to resolution from peak total symptom score was defined as the time in days from the highest total symptom score (between first dose of study drug and Day 12) until the start of the first 24-hour symptom-free period (after the highest total symptom score). Total symptom scores at the time of the first dose of study drug can be before or after dosing.

End point type	Secondary

End point timeframe:

Day 2 to Day 12

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 1: Placebo	Part 2: EDP-938 600 mg then 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	24	30	12
Units: Days				
geometric mean (geometric coefficient of variation)	2.49 (± 70.1)	2.83 (± 77.5)	3.30 (± 61.7)	2.19 (± 70.0)

End point values	Part 2: EDP-938 400 mg then 200 mg	Part 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: Days				
geometric mean (geometric coefficient of variation)	1.38 (± 116.5)	5.17 (± 383)		

Statistical analyses

Statistical analysis title	Part 1: EDP-938 600mg vs Part 1: Placebo
Comparison groups	Part 1: EDP-938 600 mg v Part 1: Placebo
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.145
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.37
upper limit	0.36

Statistical analysis title	Part 1:EDP-938 500mg then 300mg vs Part 1: Placebo
Comparison groups	Part 1: Placebo v Part 1: EDP-938 500 mg then 300 mg
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.352
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.03
upper limit	0.73

Statistical analysis title	Part 2:EDP-938 600mg then 300mg vs Part 2: Placebo
Comparison groups	Part 2: EDP-938 600 mg then 300 mg v Part 2: Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.55
upper limit	-1.15

Statistical analysis title	Part 2:EDP-938 400mg then 200mg vs Part 2: Placebo
Comparison groups	Part 2: Placebo v Part 2: EDP-938 400 mg then 200 mg
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.19
upper limit	-1.61

Secondary: Total Weight of Nasal Mucus Produced	
End point title	Total Weight of Nasal Mucus Produced
End point description: Measured via weighed paper tissues.	
End point type	Secondary
End point timeframe: Day 2 to Day 12	

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 1: Placebo	Part 2: EDP-938 600 mg then 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	31	30	15
Units: Weight (g)				
arithmetic mean (standard deviation)	12.965 (± 13.0314)	7.428 (± 11.1324)	33.416 (± 37.8072)	2.983 (± 4.4226)

End point values	Part 2: EDP-938 400 mg then 200 mg	Part 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: Weight (g)				
arithmetic mean (standard deviation)	4.716 (± 6.0015)	22.391 (± 20.6005)		

Statistical analyses

Statistical analysis title	Part 1: EDP-938 600mg vs Part 1: Placebo
Comparison groups	Part 1: EDP-938 600 mg v Part 1: Placebo
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-24.081
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.554
upper limit	-11.607

Statistical analysis title	Part 1:EDP-938 500mg then 300mg vs Part 1: Placebo
Comparison groups	Part 1: Placebo v Part 1: EDP-938 500 mg then 300 mg
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-25.954
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.695
upper limit	-14.213

Statistical analysis title	Part 2:EDP-938 600mg then 300mg vs Part 2: Placebo
Comparison groups	Part 2: EDP-938 600 mg then 300 mg v Part 2: Placebo

Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-18.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.176
upper limit	-9.083

Statistical analysis title	Part 2:EDP-938 400mg then 200mg vs Part 2: Placebo
Comparison groups	Part 2: Placebo v Part 2: EDP-938 400 mg then 200 mg
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-19.329
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.106
upper limit	-9.552

Secondary: Peak Viral Load	
End point title	Peak Viral Load
End point description:	
Peak viral load was defined as the highest quantitative reverse transcription polymerase chain reaction (RT-qPCR) viral load value between first dose of study drug and Day 12. Measured by nasal wash RT-qPCR.	
End point type	Secondary
End point timeframe:	
Day 2 to Day 12	

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 1: Placebo	Part 2: EDP-938 600 mg then 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	31	30	15
Units: log10 copies/mL				
arithmetic mean (standard deviation)	4.3552 (± 1.56334)	4.3111 (± 1.76974)	6.4727 (± 1.60659)	3.9718 (± 1.78873)

End point values	Part 2: EDP-938 400 mg then 200 mg	Part 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: log10 copies/mL				
arithmetic mean (standard deviation)	4.7727 (± 1.35014)	7.0973 (± 1.24388)		

Statistical analyses

Statistical analysis title	Part 1: EDP-938 600mg vs Part 1: Placebo
Comparison groups	Part 1: EDP-938 600 mg v Part 1: Placebo
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.1292
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8491
upper limit	-1.4093

Statistical analysis title	Part 1:EDP-938 500mg then 300mg vs Part 1: Placebo
Comparison groups	Part 1: Placebo v Part 1: EDP-938 500 mg then 300 mg
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.1129

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7938
upper limit	-1.4319

Statistical analysis title	Part 2:EDP-938 600mg then 300mg vs Part 2: Placebo
Comparison groups	Part 2: EDP-938 600 mg then 300 mg v Part 2: Placebo
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.2191
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1915
upper limit	-2.2467

Statistical analysis title	Part 2:EDP-938 400mg then 200mg vs Part 2: Placebo
Comparison groups	Part 2: Placebo v Part 2: EDP-938 400 mg then 200 mg
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.7831
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8522
upper limit	-1.714

Secondary: Time to Peak Viral Load

End point title	Time to Peak Viral Load

End point description:

Time to peak viral load was defined as the time to the highest quantitative reverse transcription polymerase chain reaction (RT-qPCR) viral load value between first dose of study drug and Day 12. Measured by nasal wash RT-qPCR.

End point type	Secondary

End point timeframe:
Day 2 to Day 12

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 1: Placebo	Part 2: EDP-938 600 mg then 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	31	30	15
Units: Days				
geometric mean (geometric coefficient of variation)	0.74 (± 75.6)	0.80 (± 130.2)	2.59 (± 48.5)	0.88 (± 181.3)

End point values	Part 2: EDP-938 400 mg then 200 mg	Part 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: Days				
geometric mean (geometric coefficient of variation)	0.79 (± 64.0)	3.43 (± 33.7)		

Statistical analyses

Statistical analysis title	Part 1: EDP-938 600mg vs Part 1: Placebo
Comparison groups	Part 1: EDP-938 600 mg v Part 1: Placebo
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.67
upper limit	-1.35

Statistical analysis title	Part 1:EDP-938 500mg then 300mg vs Part 1: Placebo
Comparison groups	Part 1: Placebo v Part 1: EDP-938 500 mg then 300 mg

Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-1.16

Statistical analysis title	Part 2:EDP-938 600mg then 300mg vs Part 2: Placebo
Comparison groups	Part 2: EDP-938 600 mg then 300 mg v Part 2: Placebo
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.43
upper limit	-0.54

Statistical analysis title	Part 2:EDP-938 400mg then 200mg vs Part 2: Placebo
Comparison groups	Part 2: Placebo v Part 2: EDP-938 400 mg then 200 mg
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	-0.82

Secondary: Time to Resolution from Peak Viral Load

End point title	Time to Resolution from Peak Viral Load

End point description:

Time to resolution from peak viral load was defined as the time from peak until first confirmed undetectable assessment between first dose of study drug and Day 12. Measured by by nasal wash quantitative reverse transcription polymerase chain reaction (RT-qPCR).

End point type	Secondary

End point timeframe:

Day 2 to Day 12

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 1: Placebo	Part 2: EDP-938 600 mg then 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	30	30	14
Units: Days				
geometric mean (geometric coefficient of variation)	2.03 (± 72.1)	2.02 (± 79.7)	4.03 (± 47.5)	1.67 (± 77.1)

End point values	Part 2: EDP-938 400 mg then 200 mg	Part 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: Days				
geometric mean (geometric coefficient of variation)	1.63 (± 43.7)	3.58 (± 45.6)		

Statistical analyses

Statistical analysis title	Part 1: EDP-938 600mg vs Part 1: Placebo
Comparison groups	Part 1: EDP-938 600 mg v Part 1: Placebo
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.04
upper limit	-1.17

Statistical analysis title	Part 1:EDP-938 500mg then 300mg vs Part 1: Placebo
Comparison groups	Part 1: Placebo v Part 1: EDP-938 500 mg then 300 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.89
upper limit	-1.11

Statistical analysis title	Part 2:EDP-938 600mg then 300mg vs Part 2: Placebo
Comparison groups	Part 2: EDP-938 600 mg then 300 mg v Part 2: Placebo
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.06
upper limit	-0.89

Statistical analysis title	Part 2:EDP-938 400mg then 200mg vs Part 2: Placebo
Comparison groups	Part 2: Placebo v Part 2: EDP-938 400 mg then 200 mg
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.64
upper limit	-1.29

Secondary: Time to Cessation of Virus Detection

End point title	Time to Cessation of Virus Detection

End point description:

Time to cessation of virus detection was measured by nasal wash quantitative reverse transcription polymerase chain reaction (RT-qPCR).

End point type	Secondary

End point timeframe:

Day 2 to Day 12

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 1: Placebo	Part 2: EDP-938 600 mg then 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	30	30[7]	14
Units: Days				
median (inter-quartile range (Q1-Q3))	3.5 (2.0 to 4.5)	3.2 (1.5 to 4.5)	8.5 (6.5 to 9.999999)	2.7 (1.5 to 4.0)

Notes:

[7] - 9.999999=upper quartile is non-estimable as there were too many censored values in the placebo group

End point values	Part 2: EDP-938 400 mg then 200 mg	Part 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: Days				
median (inter-quartile range (Q1-Q3))	2.5 (1.5 to 3.5)	8.5 (7.0 to 9.0)		

Statistical analyses

Statistical analysis title	Part 1: EDP-938 600mg vs Part 1: Placebo
Comparison groups	Part 1: EDP-938 600 mg v Part 1: Placebo
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank

Statistical analysis title	Part 1:EDP-938 500mg then 300mg vs Part 1: Placebo
Comparison groups	Part 1: Placebo v Part 1: EDP-938 500 mg then 300 mg

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank

Statistical analysis title	Part 2:EDP-938 600mg then 300mg vs Part 2: Placebo
Comparison groups	Part 2: EDP-938 600 mg then 300 mg v Part 2: Placebo
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Logrank

Statistical analysis title	Part 2:EDP-938 400mg then 200mg vs Part 2: Placebo
Comparison groups	Part 2: Placebo v Part 2: EDP-938 400 mg then 200 mg
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank

Secondary: Safety and Tolerability as Assessed by Number of Participants with Treatment-emergent Adverse Events (TEAEs)

End point title	Safety and Tolerability as Assessed by Number of Participants with Treatment-emergent Adverse Events (TEAEs)

End point description:

A TEAE was defined as any untoward medical occurrence in participants that happened after study drug administration. Any clinically significant physical examinations, vital signs, clinical laboratory tests (including biochemistry, hematology, coagulation [if required], cardiac enzymes and urine analysis), 12-lead electrocardiograms (ECGs) and spirometry results were recorded as AEs. AEs were assessed using the Common Terminology Criteria for Adverse Events (CTCAE); Version 5.0.

End point type	Secondary

End point timeframe:

Day 2 to Day 28

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 1: Placebo	Part 2: EDP-938 600 mg then 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	38	38	21
Units: Number of participants	20	21	21	8

End point values	Part 2: EDP-938 400 mg then 200 mg	Part 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: Number of participants	10	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of EDP-938 and its Metabolites

End point title	Maximum Plasma Concentration (Cmax) of EDP-938 and its Metabolites[8]

End point description:

The metabolites of EDP-938 that were assessed were EP-024636, EP-024594 and EP-024595.

End point type	Secondary

End point timeframe:

Day 2 to Day 6: Pre-dose; Day 2 and Day 6: 0.5, 1, 2, 3, 4, 5, 6, 8, 10 and 12 hours post-dose, and Day 7 only: 15, 24, 30, 36, 48, 60 and 72 hours post-dose

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Pharmacokinetic data is only presented for arms where participants received the investigational product (EDP-938), and not for placebo arms.

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 2: EDP-938 600 mg then 300 mg	Part 2: EDP-938 400 mg then 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	37	21	20
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
EDP-938 First Dose	1370 (± 49.7)	1151 (± 46.9)	1237.91 (± 33.2)	800.73 (± 44.9)
EDP-938 Last Dose	1740 (± 52.8)	1480 (± 33.4)	1010 (± 15.9)	901 (± 27.9)
EP-024636 First Dose	256 (± 39.3)	215 (± 41.3)	264 (± 42.0)	177 (± 48.2)
EP-024636 Last Dose	361 (± 34.8)	342 (± 27.8)	230 (± 23.0)	232 (± 32.0)
EP-024594 First Dose	96.3 (± 48.1)	76.8 (± 54.8)	102 (± 61.1)	72.3 (± 49.1)
EP-024594 Last Dose	203 (± 32.6)	240 (± 30.1)	130 (± 44.1)	168 (± 32.9)
EP-024595 First Dose	150 (± 63.2)	102 (± 79.6)	167 (± 81.1)	100 (± 72.1)
EP-024595 Last Dose	717 (± 45.6)	1000 (± 49.1)	499 (± 89.0)	692 (± 50.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Plasma Concentration (Tmax) of EDP-938 and its Metabolites

End point title	Time to Maximum Plasma Concentration (Tmax) of EDP-938 and its Metabolites[9]

End point description:

The metabolites of EDP-938 that were assessed were EP-024636, EP-024594 and EP-024595.

End point type	Secondary

End point timeframe:

Day 2 to Day 6: Pre-dose; Day 2 and Day 6: 0.5, 1, 2, 3, 4, 5, 6, 8, 10 and 12 hours post-dose, and Day 7 only: 15, 24, 30, 36, 48, 60 and 72 hours post-dose

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic data is only presented for arms where participants received the investigational product (EDP-938), and not for placebo arms.

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 2: EDP-938 600 mg then 300 mg	Part 2: EDP-938 400 mg then 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	37	21	20
Units: Hours				
median (full range (min-max))				
EDP-938 First Dose	4.56 (2.0 to 10.0)	5.00 (1.0 to 12.0)	5.80 (1.9 to 10.2)	6.07 (2.0 to 10.2)
EDP-938 Last Dose	4.52 (1.9 to 17.0)	4.10 (0.0 to 10.1)	4.98 (1.0 to 15.9)	4.04 (0.0 to 10.0)
EP-024636 First Dose	5.91 (2.9 to 23.5)	5.97 (2.0 to 12.0)	7.97 (3.1 to 11.9)	6.99 (2.0 to 11.8)
EP-024636 Last Dose	5.00 (2.8 to 15.0)	4.88 (0.5 to 8.0)	6.00 (3.0 to 17.0)	4.04 (0.0 to 8.3)
EP-024594 First Dose	10.07 (4.1 to 24.1)	10.23 (4.0 to 12.0)	11.83 (6.2 to 23.8)	10.14 (4.9 to 11.9)
EP-024594 Last Dose	8.07 (4.0 to 20.1)	4.98 (0.0 to 12.0)	8.00 (0.5 to 17.2)	5.03 (0.0 to 8.3)
EP-024595 First Dose	23.72 (8.0 to 24.1)	11.85 (8.0 to 12.2)	23.75 (11.8 to 24.0)	11.83 (5.8 to 12.0)
EP-024595 Last Dose	10.90 (3.0 to 22.0)	5.07 (0.4 to 12.0)	11.88 (2.8 to 22.3)	4.04 (0.0 to 9.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Phase Half-Life (t1/2) of EDP-938 and its Metabolites

End point title	Terminal Phase Half-Life (t1/2) of EDP-938 and its

End point description:

The metabolites of EDP-938 that were assessed were EP-024636, EP-024594 and EP-024595.

End point type	Secondary

End point timeframe:

Day 2 to Day 6: Pre-dose; Day 2 and Day 6: 0.5, 1, 2, 3, 4, 5, 6, 8, 10 and 12 hours post-dose, and

Day 7 only: 15, 24, 30, 36, 48, 60 and 72 hours post-dose

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic data is only presented for arms where participants received the investigational product (EDP-938), and not for placebo arms.

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 2: EDP-938 600 mg then 300 mg	Part 2: EDP-938 400 mg then 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	35	21	20
Units: Hours				
geometric mean (geometric coefficient of variation)				
EDP-938	14.5 (± 25.4)	13.8 (± 27.4)	14.5 (± 31.3)	13.7 (± 23.5)
EP-024636	14.5 (± 21.5)	13.4 (± 21.1)	14.4 (± 29.8)	13.5 (± 21.2)
EP-024594	17.8 (± 18.2)	16.2 (± 18.5)	17.5 (± 25.1)	15.4 (± 17.0)
EP-024595	28.5 (± 38.2)	25.5 (± 25.1)	22.7 (± 15.6)	23.0 (± 19.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Systemic Clearance (CLss/F) of EDP-938

End point title	Apparent Systemic Clearance (CLss/F) of EDP-938[11]

End point description:

CLss/F is presented instead of CL/F.

End point type	Secondary

End point timeframe:

Day 2 to Day 6: Pre-dose; Day 2 and Day 6: 0.5, 1, 2, 3, 4, 5, 6, 8, 10 and 12 hours post-dose, and Day 7 only: 15, 24, 30, 36, 48, 60 and 72 hours post-dose

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic data is only presented for arms where participants received the investigational product (EDP-938), and not for placebo arms.

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 2: EDP-938 600 mg then 300 mg	Part 2: EDP-938 400 mg then 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	35	21	20
Units: litres per hour				
geometric mean (geometric coefficient of variation)				
EDP-938	26.9 (± 44.8)	24.1 (± 28.4)	21.3 (± 17.6)	25.0 (± 23.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Phase Rate Constant Calculated by Linear Regression of the Terminal Loglinear Portion of the Concentration vs. Time Curve (λz) of EDP-938 and its Metabolites

End point title	Terminal Phase Rate Constant Calculated by Linear Regression of the Terminal Loglinear Portion of the Concentration vs. Time Curve (λz) of EDP-938 and its Metabolites[12]

End point description:

The metabolites of EDP-938 that were assessed were EP-024636, EP-024594 and EP-024595.

End point type	Secondary

End point timeframe:

Day 2 to Day 6: Pre-dose; Day 2 and Day 6: 0.5, 1, 2, 3, 4, 5, 6, 8, 10 and 12 hours post-dose, and Day 7 only: 15, 24, 30, 36, 48, 60 and 72 hours post-dose

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic data is only presented for arms where participants received the investigational product (EDP-938), and not for placebo arms.

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 2: EDP-938 600 mg then 300 mg	Part 2: EDP-938 400 mg then 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	35	21	20
Units: 1/hour				
geometric mean (geometric coefficient of variation)				
EDP-938	0.05 (± 1.2)	0.05 (± 1.6)	0.05 (± 1.5)	0.05 (± 1.2)
EP-024636	0.05 (± 1.1)	0.05 (± 1.2)	0.05 (± 1.3)	0.05 (± 1.1)
EP-024594	0.04 (± 0.7)	0.04 (± 0.8)	0.04 (± 1.0)	0.05 (± 0.8)
EP-024595	0.03 (± 1.3)	0.03 (± 0.9)	0.03 (± 0.5)	0.03 (± 0.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution at Steady State (Vss/F) of EDP-938

End point title	Volume of Distribution at Steady State (Vss/F) of EDP-938[13]

End point description:

Vss/F is presented instead of Vd/F.

End point type	Secondary

End point timeframe:

Day 2 to Day 6: Pre-dose; Day 2 and Day 6: 0.5, 1, 2, 3, 4, 5, 6, 8, 10 and 12 hours post-dose, and Day 7 only: 15, 24, 30, 36, 48, 60 and 72 hours post-dose

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic data is only presented for arms where participants received the investigational product (EDP-938), and not for placebo arms.

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 2: EDP-938 600 mg then 300 mg	Part 2: EDP-938 400 mg then 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	35	21	20
Units: litre(s)				
geometric mean (geometric coefficient of variation)				
EDP-938	560 (± 42.8)	476 (± 23.1)	442 (± 24.1)	491 (± 28.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration at 12 Hours (C12) of EDP-938 and its Metabolites

End point title	Plasma Concentration at 12 Hours (C12) of EDP-938 and its Metabolites[14]

End point description:

The metabolites of EDP-938 that were assessed were EP-024636, EP-024594 and EP-024595. Data were specifically collected for BID dosing groups at the specified times.

End point type	Secondary

End point timeframe:

Day 2, Day 6 and Day 7; 12 hours post-dose

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic data is only presented for arms where participants received the investigational product (EDP-938), and not for placebo arms.

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 2: EDP-938 600 mg then 300 mg	Part 2: EDP-938 400 mg then 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[15]	37	0[16]	20
Units: Nanograms per milliliter				
geometric mean (geometric coefficient of variation)				
EDP-938 First Dose	()	679.35 (± 34.5)	()	565.60 (± 39.5)
EDP-938 Last Dose	()	822 (± 35.2)	()	525 (± 30.0)
EP-024636 First Dose	()	168 (± 32.1)	()	149 (± 41.0)
EP-024636 Last Dose	()	228 (± 27.8)	()	153 (± 28.9)
EP-024594 First Dose	()	75.3 (± 54.4)	()	68.8 (± 50.8)
EP-024594 Last Dose	()	188 (± 27.4)	()	133 (± 31.7)
EP-024595 First Dose	()	100 (± 79.6)	()	99.3 (± 75.4)
EP-024595 Last Dose	()	705 (± 39.1)	()	515 (± 40.2)

Notes:

[15] - C12 is reported for twice daily (BD) dosing groups only.

[16] - C12 is reported for twice daily (BD) dosing groups only.

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration at 24 Hours (C24) of EDP-938 and its Metabolites

End point title	Plasma Concentration at 24 Hours (C24) of EDP-938 and its Metabolites[17]

End point description:

The metabolites of EDP-938 that were assessed were EP-024636, EP-024594 and EP-024595. Data were specifically collected for OD dosing groups at the specified times.

End point type	Secondary

End point timeframe:

Day 7; 24 hours post-dose

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic data is only presented for arms where participants received the investigational product (EDP-938), and not for placebo arms.

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 2: EDP-938 600 mg then 300 mg	Part 2: EDP-938 400 mg then 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	0[18]	21	0[19]
Units: Nanograms per milliliter				
geometric mean (geometric coefficient of variation)				
EDP-938 First Dose	404 (± 46.9)	()	453 (± 31.6)	()
EDP-938 Last Dose	491 (± 56.4)	()	287 (± 74.0)	()
EP-024636 First Dose	121 (± 43.5)	()	136 (± 30.5)	()
EP-024636 Last Dose	148 (± 44.4)	()	88.3 (± 64.8)	()
EP-024594 First Dose	78.8 (± 43.7)	()	87.8 (± 56.0)	()
EP-024594 Last Dose	127 (± 29.3)	()	74.5 (± 72.4)	()
EP-024595 First Dose	142 (± 57.5)	()	163 (± 79.4)	()
EP-024595 Last Dose	461 (± 41.6)	()	287 (± 93.8)	()

Notes:

[18] - C24 is reported for once daily (OD) dosing groups relative to last dose.

[19] - C24 is reported for once daily (OD) dosing groups relative to last dose.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Time Curve Time 0 to Time of Last Quantifiable Concentration (AUC0-last) of EDP-938 and its Metabolites

End point title	Area Under the Concentration Time Curve Time 0 to Time of Last Quantifiable Concentration (AUC0-last) of EDP-938 and its Metabolites[20]

End point description:

The metabolites of EDP-938 that were assessed were EP-024636, EP-024594 and EP-024595.

End point type	Secondary

End point timeframe:

Day 2 to Day 6: Pre-dose; Day 2 and Day 6: 0.5, 1, 2, 3, 4, 5, 6, 8, 10 and 12 hours post-dose, and Day 7 only: 15, 24, 30, 36, 48, 60 and 72 hours post-dose

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Pharmacokinetic data is only presented for arms where participants received the investigational product (EDP-938), and not for placebo arms.

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 2: EDP-938 600 mg then 300 mg	Part 2: EDP-938 400 mg then 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	37	21	20
Units: Nanogram hours per mililitre				
geometric mean (geometric coefficient of variation)				
EDP-938 First Dose	16730 (± 47.0)	7540 (± 45.8)	16420 (± 24.0)	5970 (± 40.5)
EDP-938 Last Dose	32000 (± 52.9)	27300 (± 40.8)	20500 (± 32.1)	17800 (± 29.0)
EP-024636 First Dose	3800 (± 42.9)	1490 (± 49.3)	4080 (± 36.2)	1300 (± 45.9)
EP-024636 Last Dose	8680 (± 42.9)	7690 (± 32.8)	5550 (± 24.1)	5180 (± 28.8)
EP-024594 First Dose	1610 (± 55.3)	512 (± 73.1)	1740 (± 64.2)	487 (± 51.5)
EP-024594 Last Dose	6880 (± 31.7)	7160 (± 27.5)	4320 (± 37.3)	4990 (± 31.6)
EP-024595 First Dose	2510 (± 72.1)	540 (± 95.6)	2420 (± 83.1)	541 (± 67.1)
EP-024595 Last Dose	29600 (± 40.5)	36900 (± 38.4)	19700 (± 77.1)	25800 (± 46.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve Over the Dosing Interval (AUC0-tau) of EDP-938 and its Metabolites

End point title	Area Under the Plasma Concentration-Time Curve Over the Dosing Interval (AUC0-tau) of EDP-938 and its Metabolites[21]

End point description:

The metabolites of EDP-938 that were assessed were EP-024636, EP-024594 and EP-024595.

End point type	Secondary

End point timeframe:

Day 2 to Day 6: Pre-dose; Day 2 and Day 6: 0.5, 1, 2, 3, 4, 5, 6, 8, 10 and 12 hours post-dose, and Day 7 only: 15, 24, 30, 36, 48, 60 and 72 hours post-dose

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Pharmacokinetic data is only presented for arms where participants received the investigational product (EDP-938), and not for placebo arms.

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 2: EDP-938 600 mg then 300 mg	Part 2: EDP-938 400 mg then 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	35	21	20
Units: Nanogram hours per mililitre				
geometric mean (geometric coefficient of variation)				
EDP-938	22300 (± 46.5)	12500 (± 29.7)	14100 (± 18.5)	8010 (± 24.9)

EP-024636	5770 (± 36.1)	3270 (± 25.2)	3640 (± 24.5)	2210 (± 30.8)
EP-024594	3830 (± 30.6)	2470 (± 26.1)	2410 (± 45.4)	1710 (± 33.8)
EP-024595	12100 (± 41.9)	8950 (± 36.7)	8350 (± 82.0)	6210 (± 44.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Correlation of Plasma Pharmacokinetic (PK) Area Under the Curve (AUC) and Viral Load AUC

End point title	Number of Participants with Correlation of Plasma Pharmacokinetic (PK) Area Under the Curve (AUC) and Viral Load AUC[22]

End point description:

The overall criteria to define correlation was based on identifying a PK AUC associated with a less favorable viral load AUC i.e. a low PK AUC and a high viral load AUC indicated a correlation.

End point type	Secondary

End point timeframe:

Day 2 to Day 18

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic data is only presented for arms where participants received the investigational product (EDP-938), and not for placebo arms.

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 2: EDP-938 600 mg then 300 mg	Part 2: EDP-938 400 mg then 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	38	21	21
Units: Number of participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Correlation of Plasma Pharmacokinetic (PK) Area Under the Curve (AUC) and Total Symptom Score (TSS) AUC

End point title	Number of Participants with Correlation of Plasma Pharmacokinetic (PK) Area Under the Curve (AUC) and Total Symptom Score (TSS) AUC[23]

End point description:

The overall criteria to define correlation was based on identifying a PK AUC associated with a less favorable TSS AUC, i.e. a low PK AUC and a high TSS AUC indicated a correlation.

End point type	Secondary

End point timeframe:

Day 2 to Day 18

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Pharmacokinetic data is only presented for arms where participants received the investigational product (EDP-938), and not for placebo arms.

End point values	Part 1: EDP-938 600 mg	Part 1: EDP-938 500 mg then 300 mg	Part 2: EDP-938 600 mg then 300 mg	Part 2: EDP-938 400 mg then 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	38	21	21
Units: Number of participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 2 to Day 28	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	Part 1: EDP-938 600mg
Reporting group description:	
Participants received EDP-938 oral suspension at 600 mg followed after 12 hours by a placebo dose on each of 5 days of dosing for a total of 10 doses.	
Reporting group title	Part 1: EDP-938 500mg then 300mg
Reporting group description:	
Participants received EDP-938 oral suspension as a single Loading Dose (LD) of 500 mg followed by 300 mg dose twice daily (BD) (every 12 hours) for a total of 10 doses.	
Reporting group title	Part 1: Placebo
Reporting group description:	
Participants received placebo dose twice a day (BD) (every 12 hours) for a total of 10 doses.	
Reporting group title	Part 2: EDP-938 600mg then 300mg
Reporting group description:	
Participants received a single Loading Dose (LD) of 600 mg EDP-938, followed by a 300 mg EDP-938 dose once a day (OD), and with dosing for 5 days. Participants also received placebo OD to mimic the twice daily (BD) dosing group.	
Reporting group title	Part 2: EDP-938 400mg then 200mg
Reporting group description:	
Participants received a single Loading Dose (LD) of 400 mg EDP-938 followed by 200 mg EDP-938 at 12 hours, then 200 mg doses of EDP-938 twice daily (BD), and with dosing for 5 days.	
Reporting group title	Part 2: Placebo
Reporting group description:	
Participants received placebo twice daily (BD) for 5 days, with dosing at 12 hours intervals.	

Serious adverse events	Part 1: EDP-938 600mg	Part 1: EDP-938 500mg then 300mg	Part 1: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Part 2: EDP-938 600mg then 300mg	Part 2: EDP-938 400mg then 200mg	Part 2: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from			

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

Non-serious adverse events	Part 1: EDP-938 600mg	Part 1: EDP-938 500mg then 300mg	Part 1: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 38 (52.63%)	21 / 38 (55.26%)	21 / 38 (55.26%)
General disorders and administration site conditions			
Catheter site related reaction			
subjects affected / exposed	1 / 38 (2.63%)	1 / 38 (2.63%)	2 / 38 (5.26%)
occurrences (all)	1	1	2
Chest discomfort			
subjects affected / exposed	1 / 38 (2.63%)	1 / 38 (2.63%)	1 / 38 (2.63%)
occurrences (all)	1	1	1
Pyrexia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Thirst			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Vessel puncture site haematoma			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences (all)	0	1	0
Vessel puncture site pain			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Feeling hot			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site paraesthesia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			

Hypersensitivity			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 38 (2.63%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences (all)	1	1	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences (all)	0	1	0
Throat irritation			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 38 (0.00%)	2 / 38 (5.26%)	2 / 38 (5.26%)
occurrences (all)	0	2	2
Forced expiratory volume decreased			
subjects affected / exposed	2 / 38 (5.26%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences (all)	3	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
FEV1/FVC ratio decreased			

subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Forced vital capacity decreased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Soft tissue injury			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 38 (10.53%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences (all)	4	0	1
Headache			
subjects affected / exposed	4 / 38 (10.53%)	1 / 38 (2.63%)	3 / 38 (7.89%)
occurrences (all)	5	2	3
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	2 / 38 (5.26%)
occurrences (all)	0	1	2
Hypoacusis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Eye disorders			
Blepharospasm			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Conjunctival haemorrhage			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences (all)	0	1	0
Ocular hyperaemia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	1 / 38 (2.63%)
occurrences (all)	0	1	2

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 38 (0.00%)	2 / 38 (5.26%)	1 / 38 (2.63%)
occurrences (all)	0	2	1
Diarrhoea			
subjects affected / exposed	3 / 38 (7.89%)	3 / 38 (7.89%)	0 / 38 (0.00%)
occurrences (all)	3	3	0
Dyspepsia			
subjects affected / exposed	1 / 38 (2.63%)	2 / 38 (5.26%)	0 / 38 (0.00%)
occurrences (all)	1	2	0
Haemorrhoids			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 38 (2.63%)	1 / 38 (2.63%)	3 / 38 (7.89%)
occurrences (all)	1	1	3
Vomiting			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
Abdominal discomfort			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Abdominal tenderness			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	2 / 38 (5.26%)
occurrences (all)	0	0	2
Rash papular			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences (all)	0	1	0
Skin irritation			

subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	2 / 38 (5.26%)
occurrences (all)	0	0	2
Dermatitis contact			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Skin mass			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
Muscle spasms			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	1 / 38 (2.63%)
occurrences (all)	0	1	2
Musculoskeletal chest pain			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
Musculoskeletal pain			

subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Angular cheilitis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
Herpes simplex			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 38 (5.26%)	2 / 38 (5.26%)	4 / 38 (10.53%)
occurrences (all)	2	2	4
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
Urinary tract infection			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Viral tonsillitis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	2 / 38 (5.26%)
occurrences (all)	1	0	2

Non-serious adverse events	Part 2: EDP-938 600mg then 300mg	Part 2: EDP-938 400mg then 200mg	Part 2: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 21 (38.10%)	10 / 21 (47.62%)	11 / 21 (52.38%)
General disorders and administration site conditions			
Catheter site related reaction			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0

Chest discomfort			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Thirst			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Feeling hot			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Vessel puncture site paraesthesia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 21 (0.00%)
occurrences (all)	0	1	0

Throat irritation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Forced expiratory volume decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
FEV1/FVC ratio decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Forced vital capacity decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Soft tissue injury			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 21 (0.00%)	2 / 21 (9.52%)	1 / 21 (4.76%)
occurrences (all)	0	2	1

Headache			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	2 / 21 (9.52%)
occurrences (all)	0	1	2
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Hypoacusis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Blepharospasm			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	1 / 21 (4.76%)	1 / 21 (4.76%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
Dyspepsia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 21 (4.76%)	3 / 21 (14.29%)	0 / 21 (0.00%)
occurrences (all)	1	3	0
Vomiting			

subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Abdominal discomfort			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Abdominal tenderness			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Rash papular			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Petechiae			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Skin mass			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Micturition urgency			

subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 21 (0.00%)	2 / 21 (9.52%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
Neck pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Angular cheilitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 21 (4.76%)	2 / 21 (9.52%)	1 / 21 (4.76%)
occurrences (all)	1	2	1
Viral upper respiratory tract infection			

subjects affected / exposed	0 / 21 (0.00%)	2 / 21 (9.52%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
Urinary tract infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Viral tonsillitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 September 2018	Amendment 1, dated 4 September 2018 (protocol version 2.0), revised the protocol in line with MHRA recommendations/requests included in the Response to Grounds for Non-Acceptance letter dated 24 August 2018: • Section 7.3: Inclusion criterion #4 updated to reduce BMI upper limit of 30 kg/m^2 • Section 7.3: Inclusion criterion #5 on contraception updated to align with contraceptive methods in the Clinical Trials Facilitation Group (GTFG) guidance. • Section 18.5.1: Stopping criteria for the study updated to provide definitive stopping criteria information and Table 18.1 This amendment also clarified PK blood sampling for Dose 9, 12-hours post dose sample, and dose 10, pre-dose. The SME abbreviation was also clarified (=Sponsor's Medical Expert).
30 October 2018	Amendment 2, dated 30 October 2018 (protocol version 3.0), included a change in the Principal Investigator (PI). The Study Personnel Contact List was updated with PI contact details. The 72 h PK plasma sample collection for participants who started dosing on the afternoon of Day 5 post viral challenge was clarified. This amendment also clarified the rescreening process for participants who were found ineligible based on review of eligibility criteria.
11 July 2019	Amendment 3, dated 11 July 2019 (protocol version 4.0), included a change in the Principal Investigator (PI). The Study Personnel Contact List was updated with PI contact details. This amendment confirmed the treatment groups for Part 2 in the light of the emerging data from Part 1. Due to the combination in dosing schedule (i.e., OD and BD), all participants were treated twice daily (similar to Part 1) in order to maintain the blind between treatment groups. The duration of dosing for Part 2 was clarified as a 5 days dosing regimen. The number of participants enrolled in each of the treatment groups for Part 2 was confirmed as n=21 participants per treatment group. The randomization ratio for Part 2 was clarified as a 1:1:1 ratio. The PK blood sampling schedule for Part 2 was clarified as was the adverse events reporting for 15% drop in spirometry.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported