Clinical trial results:
A Phase 2b, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Effects of EDP-938 in Hematopoietic Cell Transplant Recipients With Acute Respiratory Syncytial Virus Infection of the Upper Respiratory Tract

Summary

EudraCT number	2020-002213-18
Trial protocol	FR DE BE PL GR IT
Global end of trial date	29 June 2023

Results information

Result version number	v1 (current)
This version publication date	22 August 2024
First version publication date	22 August 2024

Trial information

Trial identification

Sponsor protocol code	EDP 938-103

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04633187
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 135874

Notes:

Sponsors

Sponsor organisation name	Enanta Pharmaceuticals, Inc.
Sponsor organisation address	500 Arsenal St., Watertown, United States, MA 02472
Public contact	Medical Monitor, Enanta Pharmaceuticals, Inc., +1 617607 0705, nadda@enanta.com
Scientific contact	Medical Monitor, Enanta Pharmaceuticals, Inc., +1 617607 0705, 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	08 May 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 June 2023
Global end of trial reached?	Yes
Global end of trial date	29 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of EDP-938 on the development of lower respiratory tract complication (LRTC) in hematopoietic cell transplant (HCT) participants with an acute respiratory syncytial virus (RSV) infection of the upper respiratory tract (URTI)

Protection of trial subjects:

The study was conducted in compliance with this protocol, the principles of E6 Good Clinical Practice: Consolidated Guidance (ICH-GCP), the Declaration of Helsinki, and all applicable local laws and regulations governing clinical studies. Each participant provided a signed and dated ICF before enrollment into the study.

Background therapy:

The most frequently reported concomitant medication drug class in the EDP-938 treatment group (>40% of participants) were antibacterials for systemic use, antivirals for systemic use, drugs for acid related disorders (5 participants [100%] each), immunosuppressants, analgesics, antianemic preparations (4 participants [80%] each), corticosteroids for systemic use and antimycotics for systemic use (3 participants [60%] each).

Evidence for comparator:

This study is placebo-controlled and placebo is used for comparator.

Actual start date of recruitment	01 November 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Brazil: 1
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	South Africa: 1
Country: Number of subjects enrolled	Türkiye: 1
Worldwide total number of subjects	9
EEA total number of subjects	5

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)	9
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 9 participants were randomly assigned to receive either EDP-938 or Placebo. 5 participants were randomized to the EDP-938 treatment group (1 to 150 mg, 1 to 400 mg, and 3 to 800 mg EDP-938) and 4 participants were randomized to the placebo treatment group. All randomized participants completed the treatment and follow-up.

Pre-assignment

Screening details:

190 participants were planned to be randomized. However, due to low enrollment, the study was terminated after 9 participants were randomized and completed treatment.

Pre-assignment period milestones

Number of subjects started	9
Number of subjects completed	9

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	EDP-938

Arm description:

Participants were randomly assigned (2:1 ratio) on Day 1 to receive EDP-938 administered orally once daily (QD) for a total of 21 days.

Arm type	Experimental
Investigational medicinal product name	EDP-938
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were randomly assigned (2:1 ratio) on Day 1 to receive EDP-938 administered orally once daily (QD) for a total of 21 days. The dose administered QD was to be either:
- 800 mg of EDP-938 (for participants not taking azole antifungals that were moderate or strong CYP3A4 inhibitors)
- 400 mg of EDP-938 (for participants taking azole antifungals that were moderate CYP3A4 inhibitors)
- 150 mg of EDP-938 (for participants taking azole antifungals that were strong CYP3A4 inhibitors)

Arm title	Placebo

Arm description:

Participants were randomly assigned (2:1 ratio) on Day 1 to receive Placebo administered orally once daily (QD) for a total of 21 days.

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:

Participants were randomly assigned (2:1 ratio) on Day 1 to receive Placebo administered orally once daily
(QD) for a total of 21 days. The dose administered QD was to be either:
- 800 mg of Placebo (for participants not taking azole antifungals that were moderate or strong CYP3A4 inhibitors)
- 400 mg of Placebo (for participants taking azole antifungals that were moderate CYP3A4 inhibitors)
- 150 mg of Placebo (for participants taking azole antifungals that were strong CYP3A4 inhibitors)

Number of subjects in period 1	EDP-938	Placebo
Started	5	4
Completed	5	4

Baseline characteristics

Reporting groups	
Reporting group title	EDP-938
Reporting group description:	
Participants were randomly assigned (2:1 ratio) on Day 1 to receive EDP-938 administered orally once daily (QD) for a total of 21 days.	
Reporting group title	Placebo
Reporting group description:	
Participants were randomly assigned (2:1 ratio) on Day 1 to receive Placebo administered orally once daily (QD) for a total of 21 days.	

Reporting group values	EDP-938	Placebo	Total
Number of subjects	5	4	9
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)	5	4	9
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	44.4	44.3	
standard deviation	± 15.98	± 15.99	-
Gender categorical			
Units: Subjects			
Female	2	2	4
Male	3	2	5

End points

End points reporting groups

Reporting group title	EDP-938
Reporting group description:	
Participants were randomly assigned (2:1 ratio) on Day 1 to receive EDP-938 administered orally once daily (QD) for a total of 21 days.	
Reporting group title	Placebo
Reporting group description:	
Participants were randomly assigned (2:1 ratio) on Day 1 to receive Placebo administered orally once daily (QD) for a total of 21 days.	
Subject analysis set title	ITT population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The Intent-to-Treat (ITT) population included all participants who received at least one dose of study drug. All participants in the ITT population were analyzed according to the treatment as randomized. The ITT population was used for the primary efficacy analysis and analysis of FLU-PRO data.	
Subject analysis set title	mITT by RT-qPCR population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The modified Intent-to-Treat by RT-qPCR (quantitative reverse transcription polymerase chain reaction) (mITT by RT-qPCR) population included all participants in the ITT population, excluding participants who had undetectable or missing RSV viral load by RT-qPCR at baseline. The mITT by RT-qPCR population was used for efficacy analysis of RSV viral load by RT-qPCR.	
Subject analysis set title	mITT by CBIA
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The modified Intent-to-Treat by cell-based infectivity assay (CBIA) (mITT by CBIA) population included all participants in the ITT population, excluding participants who had undetectable or missing RSV viral load by CBIA at baseline. The mITT by CBIA population was used for efficacy analysis of RSV viral load by CBIA.	
Subject analysis set title	SAF Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety (SAF) Population included all participants who received at least one dose of study drug. All participants in the safety population were analyzed according to the treatment actually received.	

Primary: Incidence of LRTC through Day 28 defined as determined by the Endpoint Adjudication Committee

End point title	Incidence of LRTC through Day 28 defined as determined by the Endpoint Adjudication Committee[1]
End point description:	
For the primary efficacy endpoint, the incidence of LRTC as determined by the Endpoint Adjudication Committee was 0% (0 of 5 participants) in the EDP-938-treatment group and 25% (1 of 4 participants) in the placebo treatment group. The single LRTC reported in the placebo group was categorized as an LRTC due to unknown etiology by the Endpoint Adjudication Committee.	
End point type	Primary
End point timeframe:	
Through Day 28	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics were performed.

End point values	EDP-938	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: percent				
number (not applicable)				
Incidence of LRTC as determined by the Endpoint Ad	0	25		

Statistical analyses

No statistical analyses for this end point

Secondary: RSV Viral Load by RT-qPCR AUC From Day 1 Through Day 49

End point title	RSV Viral Load by RT-qPCR AUC From Day 1 Through Day 49

End point description:

Six participants (3 in each treatment group) had detectable RSV by RT-qPCR at baseline and were included in the mITT by RT-qPCR analysis population. The placebo-treated participant with the adjudicated LRTC had high viral load (>8 log10 copies/mL) at all post-treatment timepoints. All other participants achieved RSV viral load at or below the limit of detection. RSV viral load showed a -7 log10 copies/mL change from baseline in the EDP-938 treatment arm compared to a -2 log10 copies/mL change in the placebo arm on Day 49.
In the mITT population, the mean (SD) RSV RNA viral load AUC was 109.9 (43.4) days × log10 copies/mL in the EDP-938 group vs. 232.5 (189.3) days × log10 copies/mL in the placebo group.

End point type	Secondary

End point timeframe:

From Day 1 through Day 49

End point values	EDP-938	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: number				
arithmetic mean (standard deviation)				
RSV Viral Load by RT-qPCR AUC from Day 1 - Day 49	109.904 (± 43.4419)	232.480 (± 189.2527)		

Statistical analyses

No statistical analyses for this end point

Secondary: RSV Viral Load by CBIA by Days 1, 4, 7, 11, 16, 21, 28, and 49

End point title	RSV Viral Load by CBIA by Days 1, 4, 7, 11, 16, 21, 28, and 49

End point description:

Two participants (1 in each treatment group) had detectable RSV by CBIA at baseline and were included in the mITT by CBIA analysis population. Given this limited sample size, detailed comparisons of the treatment groups were not performed. The RSV by CBIA assessments in these 2 individuals are provided below:
• The EDP-938 treated participant had RSV viral load measurements of 4.3 log10 TCID50/mL on Day 1,

3.6 log10 TCID50/mL on Day 4, and target not detected on Days 7, 11, 16, 21, 28, and 49.
• The placebo-treated participant had RSV viral load measurements of 5.7 log10 TCID50/mL on Day 1 and target not detected on Days 4, 7, 11, 16, 21, 28, and 49

End point type	Secondary

End point timeframe:

From Day 1 through Day 49

End point values	EDP-938	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	1		
Units: number				
number (not applicable)				
log10 TCID50/mL - Day 1	4.3	5.7		
log10 TCID50/mL - Day 4	3.6	0		
log10 TCID50/mL on Days 7, 11, 16, 21, 28 and 49	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: FLU-PRO questionnaire scores through Day 49

End point title	FLU-PRO questionnaire scores through Day 49

End point description:

The mean FLU-PRO total scores showed symptom improvement with a -1.2 decrease from baseline in the EDP-938 arm compared to a -0.6 decrease in the placebo arm on Day 49 in the ITT population. This mean change was based on 2 participants on each treatment group that had both baseline and Day 49 and FLU-PRO total scores. The detailed summary statistics of the FLU-PRO symptom scores on Days 1, 4, 7, 11, 16, 21, 28, and 49.

End point type	Secondary

End point timeframe:

Through Day 49

End point values	EDP-938	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: number				
arithmetic mean (standard deviation)				
Change from Baseline - Day 4	-0.333 (± 0.2954)	-0.156 (± 0.0442)		
Change from Baseline - Day 7	-0.177 (± 0.4161)	0.198 (± 0.6748)		
Change from Baseline - Day 11	-0.490 (± 0.3207)	-0.302 (± 0.1263)		
Change from Baseline - Day 16	-0.615 (± 0.3622)	-0.490 (± 0.0722)		

Change from Baseline - Day 21	-0.875 (± 0.5144)	-0.563 (± 0.1432)		
Change from Baseline - Day 28	-0.906 (± 0.5788)	-0.547 (± 0.1547)		
Change from Baseline - Day 49	-1.172 (± 0.1989)	-0.594 (± 0.1768)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The reported adverse events are collected since the start of the study till the follow-up period completeness.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	EDP-938
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	EDP-938	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)	0 / 4 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Mucosal infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	EDP-938	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	3 / 4 (75.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	2 / 5 (40.00%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	2 / 5 (40.00%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Productive cough			

subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Hallucination			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Cerebellar infarction			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Intensive care unit acquired weakness			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			

Anaemia of chronic disease			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Febrile neutropenia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Neutropenia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Middle ear inflammation			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	2 / 5 (40.00%)	1 / 4 (25.00%)	
occurrences (all)	2	1	
Stomatitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Swollen tongue			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	2 / 5 (40.00%)	1 / 4 (25.00%)	
occurrences (all)	2	1	
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			

Hyperhidrosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Rash maculo-papular			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Cytomegalovirus hepatitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Cytomegalovirus infection			

subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Cytomegalovirus infection reactivation			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Epstein-Barr virus infection reactivation			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Folliculitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Mucosal infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Sepsis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Calcium deficiency			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			
subjects affected / exposed	2 / 5 (40.00%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Hypervolaemia			

subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Hypocalcaemia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Hypokalaemia			
subjects affected / exposed	2 / 5 (40.00%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Hypomagnesaemia			
subjects affected / exposed	2 / 5 (40.00%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Hyponatraemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Vitamin C deficiency			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Vitamin D deficiency			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Zinc deficiency			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 August 2021	Protocol Version 4.0: 1. Changed age range of study population from 18 to 75 years to 16 to 75 years 2. Changed Sponsor Medical Officer 3. Changed protocol signatories 4. Modified a secondary endpoint and added a new secondary endpoint 5. In the pharmacokinetic (PK) secondary endpoint, added EDP-938 metabolite to list of analytes for PK analyses 6. Added dose modifications for subjects taking concomitant azole antifungal medications that are moderate or strong inhibitors of CYP3A4. 7. Changed chest X-ray to chest imaging 8. Specified time windows for HCTs 8. Changed entry criteria for oxygen saturation from >92% on room air to >95% on room air 9. Added text about treatment of HCT recipients with azole antifungals. 10. Added Study EDP 938-007 to list of EDP-938 clinical studies and added text about results of Studies 938-003 and 938-007. 11. Updated potential risk language to include information on phototoxicity 12. Clarified timing of RSV diagnosis 13. Added body weight as an inclusion criterion. 14. Changed contraceptive requirements 15. Clarified type of treatment in exclusion criterion 7 16. Clarified wording in exclusion criterion 11 17. Changed QTcF threshold in exclusion criterion 12 from >500 msec to >470 msec 18. Modified exclusion criterion and prohibited medications to allow prophylactic azole antifungal therapies 19. Added hypersensitivity to placebo or its excipients as an exclusion criterion and added a list of excipients. 20. Added definition of end of the study 21. Noted that the use of ribavirin for the treatment of RSV is allowed throughout the trial at the discretion of the Investigator 22. Removed “preliminary” from description of results of Study EDP 938-004 23. Added 150 mg tablet to drug product section. Deleted information about tablet count per bottle. 24. Added PRA Pharmacovigilance Group to unblinded list 25. Revised unblinding procedures. 26. Added other regions for 24hour safety hotline
07 March 2023	Protocol Version 8.0 1. Updated title for sponsor signatory 2. Added study stopping rules

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported