



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 ($>8 \log_{10}$ 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 $-7 \log_{10}$ copies/mL change from baseline in the EDP-938 treatment arm compared to a $-2 \log_{10}$ 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 $\times \log_{10}$ copies/mL in the EDP-938 group vs. 232.5 (189.3) days $\times \log_{10}$ 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 $4.3 \log_{10}$ 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) | | | | |
| log ₁₀ TCID ₅₀ /mL - Day 1 | 4.3 | 5.7 | | |
| log ₁₀ TCID ₅₀ /mL - Day 4 | 3.6 | 0 | | |
| log ₁₀ TCID ₅₀ /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

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|--|---|
| 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

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|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 26.1 |

Reporting groups

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

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

| | | | |
|---|----------------|----------------|--|
| 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 | <p>Protocol Version 4.0:</p> <ol style="list-style-type: none">1. Changed age range of study population from 18 to 75 years to 16 to 75 years2. Changed Sponsor Medical Officer3. Changed protocol signatories4. Modified a secondary endpoint and added a new secondary endpoint5. In the pharmacokinetic (PK) secondary endpoint, added EDP-938 metabolite to list of analytes for PK analyses6. 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 imaging8. Specified time windows for HCTs8. Changed entry criteria for oxygen saturation from >92% on room air to >95% on room air9. 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 phototoxicity12. Clarified timing of RSV diagnosis13. Added body weight as an inclusion criterion.14. Changed contraceptive requirements15. Clarified type of treatment in exclusion criterion 716. Clarified wording in exclusion criterion 1117. Changed QTcF threshold in exclusion criterion 12 from >500 msec to >470 msec18. Modified exclusion criterion and prohibited medications to allow prophylactic azole antifungal therapies19. Added hypersensitivity to placebo or its excipients as an exclusion criterion and added a list of excipients.20. Added definition of end of the study21. Noted that the use of ribavirin for the treatment of RSV is allowed throughout the trial at the discretion of the Investigator22. Removed "preliminary" from description of results of Study EDP 938-00423. Added 150 mg tablet to drug product section. Deleted information about tablet count per bottle.24. Added PRA Pharmacovigilance Group to unblinded list25. Revised unblinding procedures.26. Added other regions for 24hour safety hotline |
| 07 March 2023 | <p>Protocol Version 8.0</p> <ol style="list-style-type: none">1. Updated title for sponsor signatory2. Added study stopping rules |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported