# Clinical trial results:
# A Phase 2, Open-Label Study to Evaluate the Safety and Efficacy of APX001 in the Treatment of Patients With Invasive Mold Infections Caused by Aspergillus Species or Rare Molds

## Summary

| | |
|---|---|
| EudraCT number | 2019-001386-33 |
| Trial protocol | BE |
| Global end of trial date | 09 May 2022 |

### Results information

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 14 April 2023 |
| First version publication date | 14 April 2023 |
| Summary attachment (see zip file) | null (apx001-107-synopsis.pdf) |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | C4791010 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04240886 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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 | 21 November 2022 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 09 May 2022 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the safety and efficacy of APX001 for the treatment of adult subjects aged 18 years and above with invasive mold infection (IMIs) caused by Aspergillus spp. or rare molds (e.g., Scedosporium spp., Fusarium spp., and Mucorales fungi), who have limited antifungal treatment options.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 04 January 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 | Belgium: 10 |
| Country: Number of subjects enrolled | Germany: 3 |
| Country: Number of subjects enrolled | Israel: 4 |
| Country: Number of subjects enrolled | United States: 4 |
| Worldwide total number of subjects | 21 |
| EEA total number of subjects | 13 |

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) | 11 |

| | |
|---|---|
| From 65 to 84 years | 10 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Study was planned to be conducted in two cohorts: Cohort A included subjects with invasive mold infections (IMA) and exploratory Cohort B planned to include subjects with invasive aspergillus, who had COVID-19 or Influenza A/B. Study was terminated early; no subjects were enrolled in Cohort B; hence data is not reported for Cohort B in any section.

### Period 1

| | |
|---|---|
| Period 1 title | Treatment Phase |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| **Arm title** | APX001 (Fosmanogepix): Cohort A |

Arm description:

Eligible subjects aged 18 years or older with invasive mold infections (IMI) and limited antifungal treatment options were included in this arm. On Day 1, subjects received APX001 1000 milligram (mg) as a loading dose over 3 hours by intravenous (IV) infusion twice daily (BID). On Days 2 and 3, subjects received APX001 600 mg as maintenance dose over 3 hours by IV infusion once daily (QD). From Day 4 till end of study treatment, for maintenance dose subjects received either APX001 600 mg IV infusion QD over 3 hours or switched to APX001 800 mg orally QD on investigator discretion. Total treatment duration was maximum of 42 days. Subjects had a follow-up visit at 4 weeks after last dose of study treatment and a follow-up telephone call was required on Day 84.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Fosmanogepix |
| Investigational medicinal product code | APX001 |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion, Solution for infusion, Tablet |
| Routes of administration | Intravenous use, Oral use |

Dosage and administration details:

Loading dose: 1000 mg APX001 administered by IV infusion BID on Day 1. Maintenance dose: 600 mg APX001 administered by IV infusion QD on Days 2 and 3. From Day 4 to end of study treatment, 600 mg APX001 administered by IV infusion QD or switched to oral administration of 800 mg APX001 QD.

| **Number of subjects in period 1** | APX001 (Fosmanogepix): Cohort A |
|---|---|
| Started | 21 |
| Completed | 11 |
| Not completed | 10 |
| Death | 4 |
| Discontinuation by Subject | 1 |
| Adverse event | 5 |

## Period 2

| | |
|---|---|
| Period 2 title | Follow-up Phase |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| **Arm title** | APX001 (Fosmanogepix): Cohort A |

Arm description:

Eligible subjects aged 18 years or older with invasive mold infections (IMI) and limited antifungal treatment options were included in this arm. On Day 1, subjects received APX001 1000 milligram (mg) as a loading dose over 3 hours by intravenous (IV) infusion twice daily (BID). On Days 2 and 3, subjects received APX001 600 mg as maintenance dose over 3 hours by IV infusion once daily (QD). From Day 4 till end of study treatment, for maintenance dose subjects received either APX001 600 mg IV infusion QD over 3 hours or switched to APX001 800 mg orally QD on investigator discretion. Total treatment duration was maximum of 42 days. Subjects had a follow-up visit at 4 weeks after last dose of study treatment and a follow-up telephone call was required on Day 84.

| | |
|---|---|
| Arm type | No intervention |

No investigational medicinal product assigned in this arm

| **Number of subjects in period 2** | APX001 (Fosmanogepix): Cohort A |
|---|---|
| Started | 11 |
| Completed | 13 |
| Not completed | 4 |
| Adverse event, serious fatal | 2 |
| Consent withdrawn by subject | 1 |
| Discontinuation by Subject | 1 |
| Joined | 6 |
| Continued to follow-up | 6 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | APX001 (Fosmanogepix): Cohort A |

Reporting group description:

Eligible subjects aged 18 years or older with invasive mold infections (IMI) and limited antifungal treatment options were included in this arm. On Day 1, subjects received APX001 1000 milligram (mg) as a loading dose over 3 hours by intravenous (IV) infusion twice daily (BID). On Days 2 and 3, subjects received APX001 600 mg as maintenance dose over 3 hours by IV infusion once daily (QD). From Day 4 till end of study treatment, for maintenance dose subjects received either APX001 600 mg IV infusion QD over 3 hours or switched to APX001 800 mg orally QD on investigator discretion. Total treatment duration was maximum of 42 days. Subjects had a follow-up visit at 4 weeks after last dose of study treatment and a follow-up telephone call was required on Day 84.

| Reporting group values | APX001 (Fosmanogepix): Cohort A | Total | |
|---|---|---|---|
| Number of subjects | 21 | 21 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 11 | 11 | |
| From 65-84 years | 10 | 10 | |
| 85 years and over | 0 | 0 | |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 62.38 | | |
| standard deviation | ± 11.71 | - | |
| Sex: Female, Male<br>Units: Subjects | | | |
| Female | 2 | 2 | |
| Male | 19 | 19 | |
| Race<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 0 | 0 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 0 | 0 | |
| White | 20 | 20 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 1 | 1 | |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 1 | 1 | |
| Not Hispanic or Latino | 19 | 19 | |

| | | | |
|---|---|---|---|
| Unknown or Not Reported | 1 | 1 | |

## End points

### End points reporting groups

| Reporting group title | APX001 (Fosmanogepix): Cohort A |
|---|---|

Reporting group description:

Eligible subjects aged 18 years or older with invasive mold infections (IMI) and limited antifungal treatment options were included in this arm. On Day 1, subjects received APX001 1000 milligram (mg) as a loading dose over 3 hours by intravenous (IV) infusion twice daily (BID). On Days 2 and 3, subjects received APX001 600 mg as maintenance dose over 3 hours by IV infusion once daily (QD). From Day 4 till end of study treatment, for maintenance dose subjects received either APX001 600 mg IV infusion QD over 3 hours or switched to APX001 800 mg orally QD on investigator discretion. Total treatment duration was maximum of 42 days. Subjects had a follow-up visit at 4 weeks after last dose of study treatment and a follow-up telephone call was required on Day 84.

| Reporting group title | APX001 (Fosmanogepix): Cohort A |
|---|---|

Reporting group description:

Eligible subjects aged 18 years or older with invasive mold infections (IMI) and limited antifungal treatment options were included in this arm. On Day 1, subjects received APX001 1000 milligram (mg) as a loading dose over 3 hours by intravenous (IV) infusion twice daily (BID). On Days 2 and 3, subjects received APX001 600 mg as maintenance dose over 3 hours by IV infusion once daily (QD). From Day 4 till end of study treatment, for maintenance dose subjects received either APX001 600 mg IV infusion QD over 3 hours or switched to APX001 800 mg orally QD on investigator discretion. Total treatment duration was maximum of 42 days. Subjects had a follow-up visit at 4 weeks after last dose of study treatment and a follow-up telephone call was required on Day 84.

### Primary: Percentage of Subjects who Died After the First Dose of Study Drug Through Day 42

| End point title | Percentage of Subjects who Died After the First Dose of Study Drug Through Day 42[1] |
|---|---|

End point description:

Percentage of subjects who died due to any cause after first dose in the study through Day 42 were reported in this endpoint. Endpoint was analysed in Modified Intent-to-Treat (mITT) population included all subjects who entered in the study, received at least 1 dose of study drug, and had a diagnosis of proven or probable IMI confirmed by the Data Review Committee (DRC).

| End point type | Primary |
|---|---|

End point timeframe:

After first dose on Day 1 through Day 42

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: For Cohort A, the 1-sided exact binomial test at the alpha = 0.1 level of significance was used and the 80% confidence interval was presented in the descriptive summary; hence, statistical analysis is not presented for this endpoint.

| End point values | APX001 (Fosmanogepix): Cohort A | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 20 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 80%) | 25.0 (12.7 to 41.5) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Global Response Based on Data Review Committee (DRC) Assessment at End of Study Drug Treatment (EOST)

| End point title | Percentage of Subjects With Global Response Based on Data Review Committee (DRC) Assessment at End of Study Drug Treatment (EOST) |
|---|---|

End point description:

Global response was classified as treatment success (complete or partial response [CR or PR]) or treatment failure (stable response [SR], progression of fungal disease [PD], or death) as determined by DRC. CR: resolution of all attributable symptoms and signs of disease and radiological (rad) abnormalities, and mycological (myco) evidence of eradication of disease. PR: improvement in attributable symptoms and signs of disease and rad abnormalities, and evidence of clearance of cultures or reduction of fungal burden. SR: minor or no improvement in fungal disease, but no evidence of progression, based on a composite of clinical, rad, and myco criteria, PD or death. PD: evidence of progressive fungal disease based on a composite of clinical, rad, and myco criteria. CR, PR and PD: survival within prespecified period of observation. Death: death during prespecified period of evaluation, regardless of attribution. End point analysed in mITT population.

| End point type | Secondary |
|---|---|

End point timeframe:

Any day from Day 1 up to maximum of Day 42

| **End point values** | APX001 (Fosmanogepix): Cohort A | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 20 | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| CR | 20.0 | | | |
| PR | 20.0 | | | |
| SR | 10.0 | | | |
| PD | 30.0 | | | |
| Death | 20.0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Treatment Success or Treatment Failure for Global Response Based on Data Review Committee (DRC) Assessment at End of Study Drug Treatment (EOST)

| End point title | Percentage of Subjects With Treatment Success or Treatment Failure for Global Response Based on Data Review Committee (DRC) Assessment at End of Study Drug Treatment (EOST) |
|---|---|

End point description:

Global response was classified as treatment success (CR or PR) or treatment failure (SR, PD or death) as determined by DRC. CR: resolution of all attributable symptoms and signs of disease and rad abnormalities and myco evidence of eradication of disease. PR: improvement in attributable symptoms and signs of disease and rad abnormalities and evidence of clearance of cultures or reduction of fungal

burden. SR: minor or no improvement in fungal disease but no evidence of progression based on a composite of clinical, rad and myco criteria, PD or death. PD: evidence of progressive fungal disease based on a composite of clinical, rad and myco criteria. CR, PR and PD: survival within prespecified period of observation. Death: death during prespecified period of evaluation, regardless of attribution. Percentage of subjects with treatment success (CR, PR), treatment failure (SR, PD, death) along with 2-sided exact binomial 80% confidence interval is presented. Analysed in mITT population.

| End point type | Secondary |
|---|---|

End point timeframe:

Any day from Day 1 up to maximum of Day 42

| **End point values** | APX001 (Fosmanogepix): Cohort A | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 20 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 80%) | | | | |
| Treatment success | 40.0 (24.9 to 56.7) | | | |
| Treatment failure | 60.0 (43.3 to 75.1) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Clinically Significant Abnormality in Laboratory Test Evaluations

| End point title | Number of Subjects With Clinically Significant Abnormality in Laboratory Test Evaluations |
|---|---|

End point description:

Clinical laboratory assessments included serum chemistry (bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, creatinine, creatine kinase), hematology (including hemoglobin, hematocrit, platelets, leukocytes, lymphocytes, neutrophils, basophils, eosinophils and monocytes), coagulation (including Prothrombin time [PT]/ International normalized ratio [INR]), and urinalysis. Number of subjects with clinically significant abnormality in any laboratory parameter as judged by investigator and reported as adverse events were presented. Safety population included all subjects who received at least 1 dose of study drug.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 up to maximum of 31 days of follow up post last dose of study treatment, where maximum treatment duration was 42 days (maximum up to 73 days)

| End point values | APX001 (Fosmanogepix): Cohort A | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: Subjects | 12 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Clinically Significant Abnormal Electrocardiogram (ECG) Findings

| End point title | Number of Subjects With Clinically Significant Abnormal Electrocardiogram (ECG) Findings |
|---|---|

End point description:

ECG parameters included PR interval, QRS interval, QT interval, QT interval corrected using the Fridericia's formula (QTcF), QT interval corrected using the Bazett's formula (QTcB), RR interval and heart rate. Number of subjects with clinically significant abnormal ECG findings as judged by investigator were presented. Safety population included all subjects who received at least 1 dose of study drug.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 up to maximum of 31 days of follow up post last dose of study treatment, where maximum treatment duration was 42 days (maximum up to 73 days)

| End point values | APX001 (Fosmanogepix): Cohort A | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: Subjects | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Clinically Significant Abnormality in Vital Signs

| End point title | Number of Subjects With Clinically Significant Abnormality in Vital Signs |
|---|---|

End point description:

Vital signs included body temperature, blood pressure, heart rate, respiratory rate, and oxygen saturation. Number of subjects with clinically significant abnormality in vital signs as judged by investigator were reported in this endpoint. Safety population included all subjects who received at least 1 dose of study drug.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 up to maximum of 31 days of follow up post last dose of study treatment, where maximum

treatment duration was 42 days (maximum up to 73 days)

| End point values | APX001 (Fosmanogepix): Cohort A | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: Subjects | 5 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Clinically Significant Change From Baseline in Physical and Neurological Examinations

| End point title | Number of Subjects With Clinically Significant Change From Baseline in Physical and Neurological Examinations |
|---|---|

End point description:

Physical examination included an assessment of general appearance, skin, eyes, heart, chest, abdomen, and a neurological examination. Components of the neurological examination included cranial nerve, sensory, and motor examination; reflex and gait testing; and coordination assessment. Clinically significant changes were judged by investigator. Safety population included all subjects who received at least 1 dose of study drug.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 up to maximum of 31 days of follow up post last dose of study treatment, where maximum treatment duration was 42 days (maximum up to 73 days)

| End point values | APX001 (Fosmanogepix): Cohort A | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: Subjects | 3 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Plasma Concentrations of Fosmanogepix

| End point title | Plasma Concentrations of Fosmanogepix |
|---|---|

End point description:

The Pharmacokinetic (PK) Population included all subjects who received any amount of study drug and had evaluable PK data. Here, "n" signifies subjects evaluable at specified time points. 99999 indicates geometric coefficient of variation could not be calculated as a single participant was analysed

| End point type | Secondary |
|---|---|

End point timeframe:

Days 1, 2, 3, 4, 7: Pre-dose and 3 hours post-dose; Days 6, 13, 14: 3 hours post-dose, Day 15: pre-dose

| **End point values** | APX001 (Fosmanogepix): Cohort A | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: nanogram per milliliter | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Day 1: Pre-dose; n=21 | 0.0 (± 0.0) | | | |
| Day 1: 3 hours post-dose; n=18 | 387.4 (± 289.6) | | | |
| Day 2: Pre-dose; n=7 | 20.4 (± 138.1) | | | |
| Day 2: 3 hours post-dose; n=20 | 406.4 (± 202.9) | | | |
| Day 3: Pre-dose; n=6 | 8.6 (± 184.1) | | | |
| Day 3: 3 hours post-dose; n=19 | 486.7 (± 154.6) | | | |
| Day 4: Pre-dose; n=2 | 2.9 (± 141.3) | | | |
| Day 4: 3 hours post-dose; n=2 | 85.2 (± 14743.4) | | | |
| Day 6: 3 hours post-dose; n=2 | 6.8 (± 1541.9) | | | |
| Day 7: Pre-dose; n=2 | 9.8 (± 716.5) | | | |
| Day 7: 3 hours post-dose; n=7 | 37.9 (± 382.3) | | | |
| Day 13: 3 hours post-dose; n=1 | 96.4 (± 99999) | | | |
| Day 14: 3 hours post-dose; n=4 | 706.8 (± 181.0) | | | |
| Day 15: Pre-dose; n=1 | 0.5 (± 99999) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

| End point title | Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) |
|---|---|

End point description:

An adverse event was any untoward medical occurrence in a subject who received study treatment without regard to possibility of causal relationship. TEAEs were events between first dose of study treatment and up to 4 weeks post last dose of study treatment that were absent before treatment or that worsened relative to pretreatment state. An SAE was any untoward medical occurrence that occurred, at any dose: resulted in death; required inpatient hospitalisation or prolongation of existing hospitalisation; was life-threatening; resulted in persistent or significant disability/ incapacity; was a congenital anomaly/birth defect and other important medical events. AEs included SAEs and all non-SAEs. Safety population included all subjects who received at least 1 dose of study drug.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 up to maximum of 31 days of follow up post last dose of study treatment, where maximum treatment duration was 42 days (maximum up to 73 days)

| **End point values** | APX001 (Fosmanogepix): Cohort A | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: Subjects | | | | |
| TEAEs | 21 | | | |
| SAEs | 13 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

For adverse events (SAEs and non-SAEs): Day 1 up to maximum of 31 days of follow up post last dose of study treatment, where maximum treatment duration was 42 days (maximum up to 73 days); for all-cause mortality: Throughout the study (Day 1 to Day 84)

Adverse event reporting additional description:

Same event may appear as AE and SAE, what is presented are distinct events. Event may be categorized as serious in 1 subject and as non-serious in another subject or 1 subject may have experienced both serious and non-serious event during study.

| | |
|---|---|
| Assessment type | Non-systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 25.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | APX001 (Fosmanogepix): Cohort A |

Reporting group description:

Eligible participants aged 18 years or older with IMI and limited antifungal treatment options were included in this arm. On Day 1, participants received APX001 1000 mg as a loading dose over 3 hours by IV infusion BID. On Days 2 and 3, participants received APX001 600 mg as maintenance dose over 3 hours by IV infusion QD. On Day 4 till end of study treatment, for maintenance dose participants received either APX001 600 mg IV infusion QD over 3 hours or participants on investigator discretion switched to APX001 800 mg orally QD. Total treatment duration was maximum of 42 days. Participants had a follow-up visit at 4 weeks (+ 4 days) after last dose of study drug and a follow-up telephone call was required on Day 84.

| **Serious adverse events** | APX001 (Fosmanogepix): Cohort A | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 21 (61.90%) | | |
| number of deaths (all causes) | 9 | | |
| number of deaths resulting from adverse events | | | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Ventricular tachycardia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Sudden death | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory failure | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| Renal and urinary disorders | | | |
| Renal impairment | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fungal infection | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Endocarditis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device related sepsis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Catheter site infection | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Stenotrophomonas bacteraemia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Sepsis | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic shock | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 2 %

| **Non-serious adverse events** | APX001 (Fosmanogepix): Cohort A | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 21 / 21 (100.00%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia refractory | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Vascular disorders | | | |
| Subclavian vein thrombosis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Hypotension | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 2 | | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Chills | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | | |
| occurrences (all) | 5 | | |
| Facial pain | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Fatigue | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences (all) | 3 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Inflammation | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Malaise | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 6 / 21 (28.57%) | | |
| occurrences (all) | 7 | | |
| Pyrexia | | | |
| subjects affected / exposed | 5 / 21 (23.81%) | | |
| occurrences (all) | 6 | | |
| Immune system disorders | | | |
| Graft versus host disease | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Graft versus host disease in gastrointestinal tract | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Graft versus host disease in skin | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Reproductive system and breast disorders | | | |
| Scrotal dermatitis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | | |
|---|---|---|---|---|
| Cough | | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | | |
| occurrences (all) | 3 | | | |
| Hyperventilation | | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | | |
| occurrences (all) | 1 | | | |
| Hypoxia | | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | | |
| occurrences (all) | 1 | | | |
| Lung infiltration | | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | | |
| occurrences (all) | 1 | | | |
| Lung opacity | | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | | |
| occurrences (all) | 1 | | | |
| Oropharyngeal pain | | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | | |
| occurrences (all) | 2 | | | |
| Pleural thickening | | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | | |
| occurrences (all) | 1 | | | |
| Productive cough | | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | | |
| occurrences (all) | 1 | | | |
| Pulmonary embolism | | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | | |
| occurrences (all) | 1 | | | |
| Rales | | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | | |
| occurrences (all) | 1 | | | |
| Dyspnoea | | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | | | |
| occurrences (all) | 4 | | | |
| Tachypnoea | | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | | |
| occurrences (all) | 1 | | | |

| | | | |
|---|---|---|---|
| Pleuritic pain<br>subjects affected / exposed<br>occurrences (all) | 2 / 21 (9.52%)<br>2 | | |
| Psychiatric disorders<br>Confusional state<br>subjects affected / exposed<br>occurrences (all)<br><br>Disorientation<br>subjects affected / exposed<br>occurrences (all)<br><br>Restlessness<br>subjects affected / exposed<br>occurrences (all)<br><br>Sleep disorder<br>subjects affected / exposed<br>occurrences (all) | <br>1 / 21 (4.76%)<br>1<br><br>1 / 21 (4.76%)<br>1<br><br>1 / 21 (4.76%)<br>1<br><br>1 / 21 (4.76%)<br>1 | | |
| Investigations<br>Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)<br><br>Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all)<br><br>Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all)<br><br>Blood calcium decreased<br>subjects affected / exposed<br>occurrences (all)<br><br>Blood creatinine decreased<br>subjects affected / exposed<br>occurrences (all)<br><br>Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)<br><br>Blood lactate dehydrogenase increased | <br><br>3 / 21 (14.29%)<br>3<br><br>3 / 21 (14.29%)<br>5<br><br>1 / 21 (4.76%)<br>1<br><br>1 / 21 (4.76%)<br>1<br><br>1 / 21 (4.76%)<br>1<br><br>1 / 21 (4.76%)<br>2 | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Blood sodium decreased | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Drug level fluctuating | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Immunosuppressant drug level decreased | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 5 | | |
| Spleen scan abnormal | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Weight increased | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | | |
| occurrences (all) | 4 | | |
| Injury, poisoning and procedural complications | | | |
| Wound haemorrhage | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Contusion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Febrile nonhaemolytic transfusion reaction | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Skin injury | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Toxicity to various agents | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Vascular access site occlusion | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Pericarditis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 2 | | |
| Tachycardia | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences (all) | 3 | | |
| Nervous system disorders | | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Dizziness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Headache | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | | |
| occurrences (all) | 4 | | |
| Presyncope | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Seizure | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Taste disorder | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Tremor | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 6 | | |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Eosinophilia | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences (all) | 4 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Pancytopenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 4 | | |
| Ear and labyrinth disorders | | | |
| Ear pain | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences (all) | 3 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | | |
| occurrences (all) | 4 | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Anal incontinence | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 10 / 21 (47.62%) | | |
| occurrences (all) | 11 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Mouth haemorrhage | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Nausea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 13 / 21 (61.90%) | | |
| occurrences (all) | 19 | | |
| Subileus | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 9 / 21 (42.86%) | | |
| occurrences (all) | 13 | | |
| Constipation | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Hepatobiliary disorders | | | |
| Jaundice | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Rash papular | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 2 | | |
| Rash | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Purpura | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Petechiae | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Night sweats | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Alopecia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Decubitus ulcer | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Skin lesion | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Skin hyperpigmentation | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Nocturia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Endocrine disorders | | | |
| Euthyroid sick syndrome | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Inappropriate antidiuretic hormone secretion | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---|---|---|
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Sarcopenia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Atypical pneumonia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Bacterial disease carrier | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Colonic abscess | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Enterococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Escherichia bacteraemia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 3 | | |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Moraxella infection | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Oral candidiasis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Rhinovirus infection | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 6 / 21 (28.57%) | | |
| occurrences (all) | 6 | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences (all) | 1 | | |

| | | | |
|---|---|---|---|
| Hypoalbuminaemia<br>subjects affected / exposed<br>occurrences (all) | 2 / 21 (9.52%)<br>2 | | |
| Hypocalcaemia<br>subjects affected / exposed<br>occurrences (all) | 3 / 21 (14.29%)<br>3 | | |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 21 (4.76%)<br>1 | | |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all) | 2 / 21 (9.52%)<br>2 | | |
| Hyponatraemia<br>subjects affected / exposed<br>occurrences (all) | 2 / 21 (9.52%)<br>2 | | |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all) | 4 / 21 (19.05%)<br>4 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 29 May 2020 | In addition to the Cohort A which represented the study population in the original protocol (Version 1.0), a parallel Cohort B was to be added to enroll up to 10 subjects with IMI who also had a lower respiratory tract infection due to SARS-CoV-2 or influenza A/B, so that the total planned number of subjects (approximately 50) in the study remained unchanged. |
| 29 September 2020 | The following additional exclusion criteria were added<br>Subjects on mechanical ventilation;<br>Subjects with severe renal impairment as determined by estimated glomerular filtration rate (eGFR) <30 milliliters per minute per 1.173 square meter (mL/min/1.173 m^2) calculated by chronic kidney disease epidemiology collaboration (CKD-EPI), including subjects on dialysis;<br>Subjects with a Karnofsky performance status <=30 at Screening |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---|---|---|
| 15 September 2020 | Enrollment pause for additional clinical data review by DSMB. | 23 September 2020 |

Notes:

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Total of 17 participants started follow-up; due to system limitation this is reported as 11 who completed treatment and started follow-up and 6 who did not complete treatment, indicated under 'Joined as continued to follow-up'.

Notes: