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	v2 (current)
This version publication date	06 June 2024
First version publication date	14 April 2023
Version creation reason	• New data added to full data set Sponsor details must be updated. An incorrect study results synopsis has been removed.

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	Basilea Pharmaceutica International Ltd, Allschwil
Sponsor organisation address	Hegenheimermattweg 167b, Allschwil, Switzerland, 4123
Public contact	Marc Engelhardt, Basilea Pharmaceutica International Ltd, Allschwil, +41 +41 79 701 0551, marc.engelhardt@basilea.com
Scientific contact	Marc Engelhardt, Basilea Pharmaceutica International Ltd, Allschwil, +41 79 701 0551, marc.engelhardt@basilea.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 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 Units: Years			
arithmetic mean	62.38		
standard deviation	± 11.71	-	
Sex: Female, Male Units: Subjects			
Female	2	2	
Male	19	19	
Race 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 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: Only a descriptive analysis is possible for this single-arm study.

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

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 subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Psychiatric disorders Confusional state subjects affected / exposed occurrences (all) Disorientation subjects affected / exposed occurrences (all) Restlessness subjects affected / exposed occurrences (all) Sleep disorder subjects affected / exposed occurrences (all)	 1 / 21 (4.76%) 1 1 / 21 (4.76%) 1 1 / 21 (4.76%) 1 1 / 21 (4.76%) 1		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) Blood bilirubin increased subjects affected / exposed occurrences (all) Blood calcium decreased subjects affected / exposed occurrences (all) Blood creatinine decreased subjects affected / exposed occurrences (all) Blood creatinine increased subjects affected / exposed occurrences (all) Blood lactate dehydrogenase increased	 3 / 21 (14.29%) 3 3 / 21 (14.29%) 5 1 / 21 (4.76%) 1 1 / 21 (4.76%) 1 1 / 21 (4.76%) 1 1 / 21 (4.76%) 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 subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Hypocalcaemia subjects affected / exposed occurrences (all)	3 / 21 (14.29%) 3		
Hypokalaemia subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Hypomagnesaemia subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Hyponatraemia subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Hypophosphataemia subjects affected / exposed occurrences (all)	4 / 21 (19.05%) 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 Subjects on mechanical ventilation; 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; 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: