Clinical trial results:
An Open-Label Study to Evaluate the Efficacy and Safety of APX001 in Non-Neutropenic Patients with Candidemia, with or without Invasive Candidiasis, Inclusive of Patients with Suspected Resistance to Standard of Care Antifungal Treatment.

Summary

EudraCT number	2017-003571-56
Trial protocol	DE BE ES
Global end of trial date	02 July 2020

Results information

Result version number	v2 (current)
This version publication date	06 June 2024
First version publication date	27 February 2021
Version creation reason	• New data added to full data set Sponsor details must be updated

Trial information

Trial identification

Sponsor protocol code	C4791009

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03604705
WHO universal trial number (UTN)	-
Other trial identifiers	APX001-201: Study id

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 +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	31 March 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy and safety of APX001 for the treatment of adult non-neutropenic subjects greater than or equal to (>=) 18 years of age with candidemia that had included subjects with suspected or confirmed resistance to standard of care (SOC) antifungal treatment.

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 Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 October 2018
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	United States: 21
Worldwide total number of subjects	21
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

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

From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 21 subjects were enrolled in this study.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	APX001 IV

Arm description:

Subjects were administered 1000 milligram (mg) APX001 loading dose BID (Twice daily) followed by a 600 mg APX001 maintenance dose QD (once daily) on Study Day 2 and Day 3. From Study Day 4 onwards, the APX001 maintenance dose was administered as either 600 mg APX001 IV infusion over 3 hours QD or may be switched to 700 mg PO (Orally) QD when the criteria for PO dosing were met.

Arm type	Experimental
Investigational medicinal product name	APX001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for injection, Dispersion for infusion, Powder for concentrate for dispersion for infusion, Dispersible tablet
Routes of administration	Intravenous use, Intraventricular use , Oral use

Dosage and administration details:

1000 mg APX001 loading dose was given by IV. Followed by 600 mg maintenance dose by IV route or 700 mg PO.

Number of subjects in period 1	APX001 IV
Started	21
Completed	16
Not completed	5
Physician decision	2
Adverse event, non-fatal	3

Baseline characteristics

Reporting groups	
Reporting group title	APX001 IV

Reporting group description:

Subjects were administered 1000 milligram (mg) APX001 loading dose BID (Twice daily) followed by a 600 mg APX001 maintenance dose QD (once daily) on Study Day 2 and Day 3. From Study Day 4 onwards, the APX001 maintenance dose was administered as either 600 mg APX001 IV infusion over 3 hours QD or may be switched to 700 mg PO (Orally) QD when the criteria for PO dosing were met.

Reporting group values	APX001 IV	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	62.9		
standard deviation	± 10.59	-	
Gender Categorical Units: Subjects			
Female	7	7	
Male	14	14	
Race Units: Subjects			
Black or African American	1	1	
White	20	20	
Ethnicity Units: Subjects			
Not Hispanic or Latino	18	18	
Not reported	3	3	

End points

End points reporting groups

Reporting group title	APX001 IV

Reporting group description:

Subjects were administered 1000 milligram (mg) APX001 loading dose BID (Twice daily) followed by a 600 mg APX001 maintenance dose QD (once daily) on Study Day 2 and Day 3. From Study Day 4 onwards, the APX001 maintenance dose was administered as either 600 mg APX001 IV infusion over 3 hours QD or may be switched to 700 mg PO (Orally) QD when the criteria for PO dosing were met.

Primary: Percentage of Subjects With Treatment Success at End of Study Treatment (EOST)

End point title	Percentage of Subjects With Treatment Success at End of Study Treatment (EOST)[1]

End point description:

Treatment success as determined by data review committee (DRC) was defined as meeting all of the following criteria: two consecutive blood cultures negative for Candida species; alive at EOST; no concomitant use of any other systemic antifungal therapies through EOST. 95% confidence intervals (CIs) were 2-sided exact binomial CIs. Modified intent-to treat (mITT) population included all subjects who received at least 1 dose of study drug; and had a confirmed diagnosis of candidemia (blood culture positive for Candida spp.) within 96 hours of the start of treatment with APX001.

End point type	Primary

End point timeframe:

Day 1 up to a maximum of Day 14

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 IV			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percentage of subjects				
number (confidence interval 95%)	80 (56.3 to 94.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Negative Blood Culture - Modified intent-to treat (MITT) Population

End point title	Time to First Negative Blood Culture - Modified intent-to treat (MITT) Population

End point description:

Time to first negative blood culture was defined as the number of days from first dose date of study drug to the date of first post-baseline negative blood culture + 1. Subjects without a negative blood culture at post-baseline visits were censored at the last assessment date. MITT population included all subjects who received at least 1 dose of study drug and had a confirmed diagnosis of candidemia within 96 hours of the start of treatment with APX001.

End point type	Secondary

End point timeframe:

Day 1 up to end of the study (up to 7 weeks)

End point values	APX001 IV			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Days				
median (confidence interval 95%)	2.0 (1.0 to 4.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Negative Blood Culture - Per-Protocol (PP) Population

End point title	Time to First Negative Blood Culture - Per-Protocol (PP) Population

End point description:

Time to first negative blood culture was defined as the number of days from first dose date of study drug to the date of first post-baseline negative blood culture + 1. Subjects without a negative blood culture at post-baseline visits were censored at the last assessment date. PP population included all subjects who received at least 1 dose of study drug, had a confirmed diagnosis of candidemia within 96 hours of the start of treatment with APX001; did not exceed prior antifungal treatment (per eligibility assessed by DRC); met the protocol's key inclusion and exclusion criteria, and had no major protocol violations.

End point type	Secondary

End point timeframe:

Day 1 up to end of the study (up to 7 weeks)

End point values	APX001 IV			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Days				
median (confidence interval 95%)	2.0 (1.0 to 4.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Eradication at End of Study Treatment and End of Treatment - PP Population

End point title	Percentage of Subjects With Eradication at End of Study Treatment and End of Treatment - PP Population

End point description:

Eradication was defined as a negative blood culture(s) for Candida species in the absence of additional antifungal therapy through EOST and EOT respectively. 95% CIs were 2-sided exact binomial CIs. PP population included all subjects who received at least 1 dose of study drug, had a confirmed diagnosis of candidemia within 96 hours of the start of treatment with APX001; did not exceed prior antifungal treatment (per eligibility assessed by DRC); met the protocol's key inclusion and exclusion criteria, and had no major protocol violations.

End point type	Secondary

End point timeframe:

EOST: Day 1 up to Day 14, EOT: Day 1 up to maximum of Day 21

End point values	APX001 IV			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percentage of subjects				
number (confidence interval 95%)				
EOST	80.0 (56.3 to 94.3)			
EOT	75.0 (50.9 to 91.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Eradication at End of Study Treatment and End of Antifungal Treatment- MITT Population

End point title	Percentage of Subjects With Eradication at End of Study Treatment and End of Antifungal Treatment- MITT Population

End point description:

Eradication was defined as a negative blood culture(s) for Candida species in the absence of concomitant antifungal therapy through EOST and EOT respectively. 95% confidence intervals (CIs) were 2-sided exact binomial CIs. MITT Population included all subjects who received at least 1 dose of study drug; had a confirmed diagnosis of candidemia within 96 hours of the start of treatment with APX001.

End point type	Secondary

End point timeframe:

EOST: Day 1 up to Day 14, EOT: Day 1 up to maximum of Day 21

End point values	APX001 IV			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percentage of subjects				
number (confidence interval 95%)				
EOST	80.0 (56.3 to 94.3)			
EOT	75.0 (50.9 to 91.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Recurrence at 2 and 4 Weeks After End of Treatment - PP Population

End point title	Percentage of Subjects With Recurrence at 2 and 4 Weeks After End of Treatment - PP Population

End point description:

Recurrence (mycological) was defined as a mycologically confirmed infection based on blood culture with the same baseline Candida species. during the 4 weeks after EOT. 95% CIs were 2-sided exact binomial. 99999 indicates 95% CI could not estimate because of less number of subjects with this event. PP population included all participants who received at least 1 dose of study drug, had a confirmed diagnosis of candidemia within 96 hours of the start of treatment with APX001; did not exceed prior antifungal treatment (per eligibility assessed by DRC) met the protocol's key inclusion and exclusion criteria, and had no major protocol violations.

End point type	Secondary

End point timeframe:

2 weeks and 4 weeks after EOT

End point values	APX001 IV			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percentage of Subjects				
number (confidence interval 95%)				
2 Weeks after EOT	5.0 (0.1 to 24.9)			
4 Weeks after EOT	0.0 (-99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Recurrence at 2 and 4 Weeks After End of Treatment -MITT Population

End point title	Percentage of Subjects With Recurrence at 2 and 4 Weeks After End of Treatment -MITT Population

End point description:

Recurrence (mycological) was defined as mycologically confirmed infection based on blood culture with the same baseline Candida species, during the 4 weeks after EOT. 95% CIs were 2-sided exact binomial CIs. 99999 indicates 95% CI could not estimate because of less number of subjects with this event. MITT population included all participants who received at least 1 dose of study drug; had a confirmed diagnosis of candidemia within 96 hours of the start of treatment with APX001.

End point type	Secondary

End point timeframe:

2 weeks and 4 weeks after EOT

End point values	APX001 IV			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percentage of subjects				
number (confidence interval 95%)				
2 Weeks	5.0 (0.1 to 24.9)			
4 Weeks	0.0 (-99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Treatment Success at End of Treatment and 2 and 4 Weeks After End of Treatment - MITT Population

End point title	Percentage of Subjects With Treatment Success at End of Treatment and 2 and 4 Weeks After End of Treatment - MITT Population

End point description:

Treatment success as determined by DRC was defined as meeting all of the following criteria: two consecutive blood cultures negative for Candida species; alive at EOST; no concomitant use of any other systemic antifungal therapies through EOST. 95% CIs were 2-sided exact binomial CIs. MITT population included all subjects who received at least 1 dose of study drug; had a confirmed diagnosis of candidemia within 96 hours of the start of treatment with APX001.

End point type	Secondary

End point timeframe:

EOT (Day 21), 2 weeks and 4 weeks after EOT

End point values	APX001 IV			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percentage of subjects				
number (confidence interval 95%)				
2 Weeks after EOT	60.0 (36.1 to 80.9)			
4 Weeks after EOT	55.0 (31.5 to 76.9)			
EOT	75.0 (50.9 to 91.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Treatment Success at End of Treatment and 2 and 4 Weeks After End of Treatment- PP Population

End point title	Percentage of Subjects With Treatment Success at End of Treatment and 2 and 4 Weeks After End of Treatment- PP Population

End point description:

Treatment success as determined by DRC was defined as meeting all of the following criteria: two consecutive blood cultures negative for Candida species; alive at EOST; no concomitant use of any other systemic antifungal therapies through EOST. 95% CIs were 2-sided exact binomial CIs. The PP population included all subjects who satisfied the following criteria: received at least 1 dose of study drug; had a confirmed diagnosis of candidemia within 96 hours of the start of treatment with APX001; did not exceed prior antifungal treatment (per eligibility assessed by DRC); met the protocol's key inclusion and exclusion criteria; had no major protocol violations.

End point type	Secondary

End point timeframe:

EOT (Day 21), 2 weeks and 4 weeks after EOT

End point values	APX001 IV			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percentage of Subjects				
number (confidence interval 95%)				
2 Weeks after EOT	60.0 (36.1 to 80.9)			
4 Weeks after EOT	55.0 (31.5 to 76.9)			
EOT	75.0 (50.9 to 91.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Alive or Dead at Study Day 30 - MITT Population

End point title	Number of Subjects Alive or Dead at Study Day 30 - MITT Population

End point description:

MITT population included all subjects who received at least 1 dose of study drug; had a confirmed diagnosis of candidemia within 96 hours of the start of treatment with APX001.

End point type	Secondary

End point timeframe:

At day 30

End point values	APX001 IV			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Count of Subjects				
Alive	17			
Dead	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Alive or Dead at Study Day 30 - PP Population

End point title	Number of Subjects Alive or Dead at Study Day 30 - PP Population

End point description:

PP Population included all subjects who satisfied the following criteria: received at least 1 dose of study drug; had a confirmed diagnosis of candidemia within 96 hours of the start of treatment with APX001; did not exceed prior antifungal treatment (per eligibility assessed by DRC); met the protocol's key inclusion and exclusion criteria; had no major protocol violations.

End point type	Secondary

End point timeframe:

At Day 30

End point values	APX001 IV			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Count of Subjects				
Alive	17			
Dead	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in administered medicinal product, event need not necessarily have a causal relationship with product treatment or usage. TEAEs were defined as adverse events that started on or after the administration of study drug. Safety population included all subjects who had received at least 1 dose of APX001.

End point type	Secondary

End point timeframe:

Day 1 up to a maximum of 7 weeks

End point values	APX001 IV			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Count of subjects	20			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study treatment on Day 1 up to 7 weeks

Adverse event reporting additional description:

Same event may appear as both non-SAE and SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and non-serious in another subjects, or one subject may have experienced both serious and non-serious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	APX001

Reporting group description: -

Serious adverse events	APX001		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 21 (42.86%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 5		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 5		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 5		
General disorders and administration site conditions			
Euthanasia			

subjects affected / exposed	1 / 21 (4.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 5			
General physical health deterioration				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 5			
Gastrointestinal disorders				
Gastrointestinal fistula				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 5			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 5			
Interstitial lung disease				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 5			
Infections and infestations				
Urinary tract infection bacterial				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 5			
Bacteraemia				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 5			
Bacterial sepsis				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 5			

Enterobacter sepsis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 5		
Necrotising fasciitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 5		
Sepsis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 5		
Septic shock			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 5		
Stenotrophomonas sepsis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 5		
Systemic candida			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 5		

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

Non-serious adverse events	APX001		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 21 (95.24%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
General disorders and administration			

site conditions			
Catheter site extravasation			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Non-cardiac chest pain			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Pain			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	5		
Asthenia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Hypercapnia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Increased bronchial secretion			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Lung infiltration			

subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Pleural effusion			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	4		
Rales			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Rhonchi			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Pneumonia aspiration			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Delirium			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Blood uric acid increased			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Electrocardiogram QT prolonged			

subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Electrocardiogram ST-T segment abnormal			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Haemoglobin decreased			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Stenotrophomonas test positive			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Transfusion reaction			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Neuropathy peripheral			

subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Peroneal nerve palsy			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Sciatica			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Eosinophilia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Thrombocytosis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Leukocytosis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		

Abdominal pain upper				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences (all)	1			
Abdominal pain lower				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences (all)	1			
Vomiting				
subjects affected / exposed	3 / 21 (14.29%)			
occurrences (all)	5			
Stress ulcer				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences (all)	2			
Small intestinal obstruction				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences (all)	1			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences (all)	1			
Fistula of small intestine				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences (all)	1			
Dyspepsia				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences (all)	1			
Diarrhoea				
subjects affected / exposed	3 / 21 (14.29%)			
occurrences (all)	3			
Constipation				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences (all)	1			
Colitis ischaemic				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences (all)	1			
Nausea				
subjects affected / exposed	2 / 21 (9.52%)			
occurrences (all)	2			

Hepatobiliary disorders			
Portal vein thrombosis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Hyperkeratosis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Skin lesion			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Skin mass			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Hydronephrosis			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Renal failure			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Synovitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Infections and infestations			

Bacteraemia subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 2			
Cellulitis subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1			
Device related infection subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1			
Empyema subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1			
Enterococcal bacteraemia subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1			
Escherichia bacteraemia subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1			
Klebsiella bacteraemia subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1			
Pneumonia moraxella subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1			
Postoperative wound infection subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1			
Staphylococcal sepsis subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1			
Urinary tract infection enterococcal subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1			
Metabolism and nutrition disorders Hyperkalaemia				

subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Hypernatraemia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Hyperproteinaemia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Metabolic alkalosis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported