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	31 March 2020

Results information

Result version number	v1
This version publication date	27 February 2021
First version publication date	27 February 2021

Trial information

Trial identification

Sponsor protocol code	APX001-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03604705
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amplyx Pharmaceuticals, Inc.
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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	18 December 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy and safety of APX001 for the treatment of adult non-neutropenic patients ≥18 years of age with candidemia that may include patients with suspected or confirmed resistance to standard of care (SOC) antifungal treatment.

Protection of trial subjects:

The study was conducted in full accordance with Food and Drug Administration Regulations, Institutional Review Board/Ethic Committee Regulations and International Council for Harmonisation Guidelines for Good Clinical Practices.

Written informed consent were obtained from all patients or their legal authorised representatives (when patients were unable to give consent and where permitted by local regulations) prior to any study-specific procedures being performed.

Patients were monitored for safety throughout the duration of the study. Safety assessments included vital signs, clinical laboratory assessments (serum chemistry, hematology, coagulation, and urinalysis), physical examinations (including neurological assessment), prior and concomitant medication reporting, and adverse event reporting.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 July 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	Israel: 10
Country: Number of subjects enrolled	United States: 3
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Belgium: 7
Worldwide total number of subjects	21
EEA total number of subjects	8

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:

Screening was triggered by the early identification of Candida spp. (or yeast) in blood drawn as SOC within a 96-hour window prior to first dose. Isolates of Candida spp. from the SOC culture must have been submitted to the mycology reference laboratory for confirmation of identification and susceptibility testing.

Period 1

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

Arms

Arm title	Modified Intent-to-Treat (MITT) Population

Arm description:

The number and percentage of patients with Treatment Success or Treatment Failure at the end of study drug treatment (EOST) in total for the Modified Intent-to-Treat (MITT).
The Intent-to-Treat (ITT) Population included all patients who received at least 1 dose of APX001 (21 patients (100%)).
The MITT Population included all patients who met ITT criteria and had a confirmed diagnosis of candidemia (blood culture positive for Candida spp.) within 96 hours of the start of treatment with APX001. The MITT Population contained 20 (95.2%) patients.

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

Dosage and administration details:

On Study Day 1 (or over the first 24 hours if started in the evening), a 1000 mg APX001 loading dose was administered over 3 hours by IV infusion BID.
On Study Days 2 and 3 of study drug, a 600 mg APX001 maintenance dose were administered over 3 hours by IV infusion QD.
On Study Day 4 and onward, an APX001 maintenance dose were administered as either:
• 600 mg APX001 IV infusion QD over 3 hours, or
• 700 mg PO QD

Number of subjects in period 1[1]	Modified Intent-to-Treat (MITT) Population
Started	20
Completed	20

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The Intent-to-Treat (ITT) Population included all patients who received at least 1 dose of APX001 (21 patients (100%)).

The Modified Intent-to-Treat (MITT) Population included all patients who met ITT criteria and had a confirmed diagnosis of candidemia (blood culture positive for Candida spp.) within 96 hours of the start of treatment with APX001. The MITT Population contained 20 (95.2%) patients.

Baseline characteristics

Reporting groups

Reporting group title	Treatment Period-MITT

Reporting group description:

Evaluation of APX001 for the first-line treatment for candidemia, including suspected or confirmed antifungal-resistant candidemia, in non-neutropenic patients ≥ 18 years of age who had at least 1 positive blood culture within the 96 hours prior to starting study drug.
Modified Intent-to-Treat (MITT) Population.
Treatment Success is defined as meeting all of the following criteria:
• Two consecutive blood cultures negative for Candida spp.
• Alive at EOST
• No concomitant use of any other systemic antifungal therapies through end of study treatment.

Reporting group values	Treatment Period-MITT	Total	
Number of subjects	20	20	
Age categorical			
Adult 16-64 years old and adult over 65 years.			
Units: Subjects			
Adults (18-64 years)	10	10	
From 65-84 years	10	10	
Gender categorical Units: Subjects			
Female	7	7	
Male	13	13	

End points

End points reporting groups

Reporting group title	Modified Intent-to-Treat (MITT) Population

Reporting group description:

The number and percentage of patients with Treatment Success or Treatment Failure at the end of study drug treatment (EOST) in total for the Modified Intent-to-Treat (MITT).
The Intent-to-Treat (ITT) Population included all patients who received at least 1 dose of APX001 (21 patients (100%)).
The MITT Population included all patients who met ITT criteria and had a confirmed diagnosis of candidemia (blood culture positive for Candida spp.) within 96 hours of the start of treatment with APX001. The MITT Population contained 20 (95.2%) patients.

Subject analysis set title	NEEDED for single arm trial statistical comparison
Subject analysis set type	Full analysis

Subject analysis set description:

Subject analysis set included only to permit selection as a comparison arm for statistical analysis.

Primary: Efficacy at EOST

End point title	Efficacy at EOST

End point description:

Treatment Success was defined as meeting all of the following criteria:
• 2 consecutive blood cultures negative for Candida spp.;
• Alive at EOST; and
• No concomitant use of any other systemic antifungal therapies through EOST.

Treatment Failure was defined as any case that did not meet the criteria for Treatment Success.

End point type	Primary

End point timeframe:

14 days after treatment initiation.

End point values	Modified Intent-to-Treat (MITT) Population	NEEDED for single arm trial statistical comparison		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	20	1		
Units: subject	20	1		

Statistical analyses

Statistical analysis title	Primary Efficacy Analysis

Statistical analysis description:

Treatment Success was defined as meeting all of the following criteria:
1) 2 consecutive blood cultures were negative for Candida spp.; 2) Alive at EOST; and 3) No concomitant use of any other systemic antifungal therapies through EOST.

Treatment Failure is defined as any case that does not meet the criteria for Treatment Success.

Comparison groups	Modified Intent-to-Treat (MITT) Population v NEEDED for single

	arm trial statistical comparison
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	treatment success
Point estimate	80
Confidence interval	
level	95 %
sides	2-sided
lower limit	56.3
upper limit	94.3

Notes:

[1] - The 95% 2-sided exact binomial confidence interval (CI).
The given number for 'Subjects in this analysis' is automatically calculated and states 21. This is incorrect and the number included in the analysis = 20 subjects.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Evaluation of adverse events at Screening, Baseline, during Study Drug Treatment, at end of study treatment, end of treatment (EOT), and 2 and 4 weeks after EOT, or Early Termination.

Adverse event reporting additional description:

All AEs for the Safety Population.
Safety Population included all patients who received at least 1 dose of APX001. The Safety Population contained 21 (100.0%) patients. In this study, the Enrolled Population and the Safety Population contained identical patients and were equivalent

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Safety Population

Reporting group description:

The Population included all patients who received at least 1 dose of APX001. The population contained 21 (100.0%) patients.

Serious adverse events	Safety Population		
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	5		
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 / 0		
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 / 1		
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 / 1		

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 / 1		
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 / 0		
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 / 0		
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 / 0		
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 / 1		
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacterial sepsis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Enterobacter sepsis			

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

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

Non-serious adverse events	Safety Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 21 (95.24%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Catheter site extravasation			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
General physical health deterioration			
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		

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		
Pneumonia aspiration			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Rales			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Rhonchi			
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		
Amylase increased			
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		
Electrocardiogram T wave abnormal			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Haemoglobin decreased			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Lipase increased			
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		
Leukocytosis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Thrombocytosis			
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			
Abdominal pain lower			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Colitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Colitis ischaemic			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Diarrhoea			

subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Dyspepsia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Fistula of small intestine			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Small intestinal obstruction			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Stress ulcer			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	3		
Vomiting			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	5		
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	1 / 21 (4.76%)		
occurrences (all)	2		
Cellulitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Device related infection			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Empyema			
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)	1		
Klebsiella bacteraemia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Pneumonia moraxella			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Postoperative wound infection			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Staphylococcal sepsis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Urinary tract infection enterococcal			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	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? Yes

Date	Amendment
06 April 2018	Clinical Study Protocol Amendment 1 (Version 2.0, dated 06 April 2018) was developed to: • Clarify that the patient population should be non-neutropenic and have invasive candidiasis; • Revise study design by shortening Study Drug Treatment Period from 42 days (6 weeks) to 14 days; • Revise study design by differentiating between EOST and an additional visit at EOT; • Revise secondary objectives to evaluate outcomes at these new timepoints (eg, EOST and EOT visits); • Clarify the acceptability of rapid diagnostic tests of blood samples for eligibility assessments; • Revise the definition of an inappropriate fungal infection source control within the exclusion criteria; • Expand the exclusion criteria to incorporate the "diagnosis of deep-seated Candida-related infections causing intraperitoneal candidiasis, septic arthritis, osteomyelitis, endocarditis, myocarditis, meningitis, or central nervous system infection or site of infection that would require antifungal treatment to exceed maximal duration of study drug (14 days)"; • Clarify the list of excluded concomitant medications to be efavirenz, nevirapine, phenobarbital, modafinil, nafcillin, St. John's Wort, and enzalutamide; • Allow further antifungal treatment (step-down therapy) with fluconazole (unless susceptibility results warranted alternative antifungal therapy) for up to a further 7 days if indicated, to adhere to the IDSA clinical practice guidelines for the treatment of candidiasis; • Specify a +2 day window to the 2-week follow-up visit after EOT; • Specify a +4 day window to the 4-week follow-up visit after EOT; • Change the window for study drug treatment visits from a minimum of ±2 days to a maximum of ±2 days; • Define bloodstream infection monitoring to be continued during Study Drug Treatment until 2 consecutive blood cultures were negative; • Add coagulation to the clinical laboratory parameters;
03 June 2019	Clinical Study Protocol Amendment 2 (Version 3.0, dated 03 June 2019) was developed to: • Update the age range of patients for 18 to 80 years of age (inclusive) to ≥18 years of age; • Clarify instructions for the timing of fundoscopic examinations; • Clarify that the DRC determined Treatment Success; • Clarify the timing for collection of vital signs; • Remove the need to have study drug PO doses administered within 30 minutes of removing from refrigeration; • Add a PK plasma sample to EOST; • Clarify the collection of blood cultures for determination of Candida spp. infection: 2 consecutive sets (1 aerobic and 1 anaerobic blood culture bottle per set) of blood cultures from 2 separate sites (1 from a CVC and 1 peripheral venipuncture, or 2 peripheral venipunctures, if a CVC was not applicable); • Update the instructions for submitting local laboratory blood culture isolates to the central mycology reference laboratory for confirmation of spp. identification and antifungal susceptibility testing; and • Clarify that only outpatients would record daily PO dosing in a diary.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported