Clinical trial results:
A PROSPECTIVE, OPEN-LABEL, NON-COMPARATIVE STUDY TO ASSESS THE SAFETY, TOLERABILITY AND EFFICACY OF VORICONAZOLE FOR THE PRIMARY AND SALVAGE TREATMENT OF INVASIVE CANDIDIASIS, CANDIDEMIA, AND ESOPHAGEAL CANDIDIASIS IN PEDIATRIC SUBJECTS

Summary

EudraCT number	2009-012848-16
Trial protocol	DE HU SK CZ BG RO Outside EU/EEA
Global end of trial date	08 July 2013

Results information

Result version number	v1
This version publication date	23 May 2016
First version publication date	01 August 2015

Trial information

Trial identification

Sponsor protocol code	A1501085

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01092832
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 August 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 July 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of voriconazole for the treatment of invasive candidiasis, including candidemia, and esophageal candidiasis in pediatric subjects 2 to less than (<)18 years of age.

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 Conference on Harmonization (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	28 October 2010
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	Poland: 1
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Czech Republic: 7
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Mexico: 5
Country: Number of subjects enrolled	Philippines: 1
Country: Number of subjects enrolled	China: 2
Country: Number of subjects enrolled	Hong Kong: 3
Worldwide total number of subjects	22
EEA total number of subjects	11

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)	14
Adolescents (12-17 years)	8
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Total 22 subjects were treated from 11 centers across 8 countries. 21 subjects completed the study and 1 subject discontinued from the study, reason not specified.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Voriconazole: 2 to <12 years

Arm description:

Subjects aged 2 to <12 years with invasive candidiasis/candidemia (ICC) received a loading dose of voriconazole, every 12 hours (q12h) for the first 24 hours, followed by maintenance dose of voriconazole, q12h for a minimum of 5 days. Subjects with esophageal candidiasis (EC) received voriconazole, q12h for a minimum of 5 days. In both ICC and EC, once signs and symptoms of Candida infection had resolved and the subject was clinically stable, subjects were switched to oral (PO) therapy and received voriconazole, q12h. Voriconazole was administered for at least 7 days (subjects with EC) or 14 days (subjects with ICC) after last positive blood culture up to a maximum of 42 days of treatment.

Arm type	Experimental
Investigational medicinal product name	Voriconazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects with ICC received a loading dose of voriconazole 9 milligram per kilogram (mg/kg), intravenously (IV), q12h for the first 24 hours, followed by maintenance dosing of voriconazole 8 mg/kg, IV, q12h for a minimum of 5 days of IV therapy. Subjects with EC received voriconazole 4 mg/kg, IV, q12h for a minimum of 5 days of IV therapy.

Investigational medicinal product name	Voriconazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension, Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects in both ICC and EC, once signs and symptoms of Candida infection had resolved and was clinically stable received voriconazole (either oral suspension or tablets) 9 mg/kg, q12h (maximum dose of 350 mg).

Arm title	Voriconazole: 12 to <18 years

Arm description:

Subjects aged 12 to <18 years (excluding those aged 12-14 years weighing <50 kg) with ICC received a loading dose of voriconazole, q12h for the first 24 hours, followed by maintenance dose of voriconazole, q12h for a minimum of 7 days. Subjects with EC received voriconazole, q12h for a minimum of 5 days. In both ICC and EC, once signs and symptoms of Candida infection had resolved and the subject was clinically stable, subjects were switched to PO therapy and received voriconazole, q12h. Voriconazole was administered for at least 7 days (subjects with EC) or 14 days (subjects with ICC) after last positive blood culture up to a maximum of 42 days of treatment.

Arm type	Experimental

Investigational medicinal product name	Voriconazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects with ICC received a loading dose of voriconazole 6 mg/kg, IV, q12h for the first 24 hours, followed by maintenance dosing of voriconazole 4 mg/kg, IV, q12h for a minimum of 7 days of IV therapy. Subjects with EC received voriconazole 3 mg/kg, IV, q12h for a minimum of 5 days of IV therapy.

Investigational medicinal product name	Voriconazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension, Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects in both ICC and EC, once signs and symptoms of Candida infection had resolved and was clinically stable received voriconazole (either oral suspension or tablets) 200 mg, q12h.

Number of subjects in period 1	Voriconazole: 2 to <12 years	Voriconazole: 12 to <18 years
Started	14	8
Completed	13	8
Not completed	1	0
Not specified	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Voriconazole: 2 to <12 years

Reporting group description:

Subjects aged 2 to <12 years with invasive candidiasis/candidemia (ICC) received a loading dose of voriconazole, every 12 hours (q12h) for the first 24 hours, followed by maintenance dose of voriconazole, q12h for a minimum of 5 days. Subjects with esophageal candidiasis (EC) received voriconazole, q12h for a minimum of 5 days. In both ICC and EC, once signs and symptoms of Candida infection had resolved and the subject was clinically stable, subjects were switched to oral (PO) therapy and received voriconazole, q12h. Voriconazole was administered for at least 7 days (subjects with EC) or 14 days (subjects with ICC) after last positive blood culture up to a maximum of 42 days of treatment.

Reporting group title	Voriconazole: 12 to <18 years

Reporting group description:

Subjects aged 12 to <18 years (excluding those aged 12-14 years weighing <50 kg) with ICC received a loading dose of voriconazole, q12h for the first 24 hours, followed by maintenance dose of voriconazole, q12h for a minimum of 7 days. Subjects with EC received voriconazole, q12h for a minimum of 5 days. In both ICC and EC, once signs and symptoms of Candida infection had resolved and the subject was clinically stable, subjects were switched to PO therapy and received voriconazole, q12h. Voriconazole was administered for at least 7 days (subjects with EC) or 14 days (subjects with ICC) after last positive blood culture up to a maximum of 42 days of treatment.

Reporting group values	Voriconazole: 2 to <12 years	Voriconazole: 12 to <18 years	Total
Number of subjects	14	8	22
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	6.8	14.4	
standard deviation	± 2.9	± 1.7	-
Gender categorical Units: Subjects			
Female	8	6	14
Male	6	2	8

End points

End points reporting groups

Reporting group title	Voriconazole: 2 to <12 years

Reporting group description:

Subjects aged 2 to <12 years with invasive candidiasis/candidemia (ICC) received a loading dose of voriconazole, every 12 hours (q12h) for the first 24 hours, followed by maintenance dose of voriconazole, q12h for a minimum of 5 days. Subjects with esophageal candidiasis (EC) received voriconazole, q12h for a minimum of 5 days. In both ICC and EC, once signs and symptoms of Candida infection had resolved and the subject was clinically stable, subjects were switched to oral (PO) therapy and received voriconazole, q12h. Voriconazole was administered for at least 7 days (subjects with EC) or 14 days (subjects with ICC) after last positive blood culture up to a maximum of 42 days of treatment.

Reporting group title	Voriconazole: 12 to <18 years

Reporting group description:

Subjects aged 12 to <18 years (excluding those aged 12-14 years weighing <50 kg) with ICC received a loading dose of voriconazole, q12h for the first 24 hours, followed by maintenance dose of voriconazole, q12h for a minimum of 7 days. Subjects with EC received voriconazole, q12h for a minimum of 5 days. In both ICC and EC, once signs and symptoms of Candida infection had resolved and the subject was clinically stable, subjects were switched to PO therapy and received voriconazole, q12h. Voriconazole was administered for at least 7 days (subjects with EC) or 14 days (subjects with ICC) after last positive blood culture up to a maximum of 42 days of treatment.

Primary: Percentage of Subjects With Adverse Events - Overall Summary

End point title	Percentage of Subjects With Adverse Events - Overall Summary[1]

End point description:

Percentage of subjects with adverse events (AEs), serious adverse events (SAEs), severe AEs, who discontinued due to AEs, or who had dose reduced or temporarily discontinued due to AEs. Safety population.

End point type	Primary

End point timeframe:

Baseline up to 1 month follow-up

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: Because of the descriptive nature of this study, no formal statistical analysis was planned. Evaluation of the data consisted primarily of summary displays (i.e., descriptive statistics).

End point values	Voriconazole: 2 to <12 years	Voriconazole: 12 to <18 years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	8		
Units: percentage of subjects				
number (not applicable)				
With AEs	92.9	75		
With SAEs	14.3	12.5		
With severe AEs	28.6	37.5		
Discontinued due to AEs	14.3	25		
Dose reduced/temporary discontinuation due to AE	21.4	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With a Global Response of Success at End of Treatment (EOT)

End point title	Percentage of Subjects With a Global Response of Success at End of Treatment (EOT)

End point description:

Global response was determined programmatically based on investigator assessment of clinical and microbiological response. Global response of success was defined as clinical cure or improvement and microbiological eradication or presumed eradication. Exact 95 percent (%) confidence interval for binomial proportions using Clopper-Pearson method. Modified Intent-to-Treat (MITT) Population: all subjects who received at least 1 dose of study medication and who have confirmed ICC, EC or subjects with EC who do not have confirmation of EC by esophagoscopy, but who had at least confirmation of oropharyngeal candidiasis.

End point type	Secondary

End point timeframe:

EOT (upto Day 42)

End point values	Voriconazole: 2 to <12 years	Voriconazole: 12 to <18 years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: percentage of subjects				
number (confidence interval 95%)	88.9 (51.75 to 99.72)	62.5 (24.49 to 91.48)		

Statistical analyses

No statistical analyses for this end point

Secondary: All-Cause Mortality - Number of Subject Deaths

End point title	All-Cause Mortality - Number of Subject Deaths

End point description:

Safety population.

End point type	Secondary

End point timeframe:

Day 28 and 1 Month Follow-up

End point values	Voriconazole: 2 to <12 years	Voriconazole: 12 to <18 years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	8		
Units: subjects				
number (not applicable)				
Day 28	0	0		
1 Month Follow-up	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Death

End point title	Time to Death

End point description:

No subject died within the safety reporting period, therefore time to death was not applicable.

End point type	Secondary

End point timeframe:

Baseline up to 1 month follow-up

End point values	Voriconazole: 2 to <12 years	Voriconazole: 12 to <18 years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: months				
median (full range (min-max))	(to)	(to)		

Notes:

[2] - No subject died within the safety reporting period.

[3] - No subject died within the safety reporting period.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 28 days after last dose of study medication or the 1-month follow-up visit, whichever is later.

Adverse event reporting additional description:

The same event may appear as both an adverse event (AE) and a serious adverse event (SAE). However, what is presented are distinct events. An event may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Voriconazole: 2 to <12 years

Reporting group description:

Subjects aged 2 to <12 years with ICC received a loading dose of voriconazole 9 mg/kg, IV, q12h for the first 24 hours, followed by maintenance dosing of voriconazole 8 mg/kg, IV, q12h for a minimum of 5 days of IV therapy. Subjects with EC received voriconazole 4 mg/kg, IV, q12h for a minimum of 5 days of IV therapy. In both ICC and EC, once signs and symptoms of Candida infection had resolved and the subject was clinically stable, subjects were switched to PO therapy and received voriconazole 9 mg/kg, PO, q12h (maximum dose of 350 mg). Voriconazole was administered for at least 7 days (subjects with EC) or 14 days (subjects with ICC) after last positive blood culture up to a maximum of 42 days of treatment.

Reporting group title	Voriconazole 12 to <18 years

Reporting group description:

Subjects aged 12 to <18 years (excluding those aged 12-14 years weighing <50 kg) with ICC received a loading dose of voriconazole 6 mg/kg, IV, q12h for the first 24 hours, followed by maintenance dosing of voriconazole 4 mg/kg, IV, q12h for a minimum of 7 days of IV therapy. Subjects with EC received voriconazole 3 mg/kg, IV, q12h for a minimum of 5 days of IV therapy. In both ICC and EC, once signs and symptoms of Candida infection had resolved and the subject was clinically stable, subjects were switched to PO therapy and received voriconazole 200 mg, PO, q12h. Voriconazole was administered for at least 7 days (subjects with EC) or 14 days (subjects with ICC) after last positive blood culture up to a maximum of 42 days of treatment.

Serious adverse events	Voriconazole: 2 to <12 years	Voriconazole 12 to <18 years	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 14 (14.29%)	1 / 8 (12.50%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Pneumonia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic candidiasis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Voriconazole: 2 to <12 years	Voriconazole 12 to <18 years	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 14 (92.86%)	6 / 8 (75.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 14 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	4	0	
Phlebitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Venoocclusive disease			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Device occlusion			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Hypothermia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 8 (12.50%)	
occurrences (all)	3	2	
Pyrexia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 8 (12.50%)	
occurrences (all)	2	1	
Reproductive system and breast disorders			

Testicular mass			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
Bronchospasm			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Haemoptysis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Hydrothorax			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hypoventilation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
Pharyngeal erythema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Pneumothorax			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Respiratory disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Investigations			

Alanine aminotransferase abnormal				
subjects affected / exposed	3 / 14 (21.43%)	0 / 8 (0.00%)		
occurrences (all)	5	0		
Alanine aminotransferase increased				
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)		
occurrences (all)	3	0		
Aspartate aminotransferase abnormal				
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
Aspartate aminotransferase increased				
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)		
occurrences (all)	3	0		
Blood alkaline phosphatase abnormal				
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)		
occurrences (all)	2	0		
Blood triglycerides increased				
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
Drug level decreased				
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
Gamma-glutamyltransferase abnormal				
subjects affected / exposed	2 / 14 (14.29%)	0 / 8 (0.00%)		
occurrences (all)	3	0		
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
Haematocrit abnormal				
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)		
occurrences (all)	3	0		
Hepatic enzyme increased				
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)		
occurrences (all)	2	0		
Lymphocyte percentage abnormal				

subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Monocyte count abnormal			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Staphylococcus test positive			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Drug dose omission			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Incision site pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Incorrect drug administration rate			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Refractoriness to platelet transfusion			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
Transplant failure			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Underdose			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
Nervous system disorders			

Paraesthesia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	4	0	
Hypothrombinaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Leukocytosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Leukopenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
Neutropenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Platelet disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
Eye disorders			
Amaurosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Conjunctivitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Corneal opacity			

subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Eye pruritus			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Eyelid disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Photophobia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 8 (12.50%)	
occurrences (all)	3	2	
Retinal disorder			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Visual acuity reduced			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Ascites			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 14 (7.14%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Oesophagitis			
subjects affected / exposed	0 / 14 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	3	
Tongue ulceration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	

Vomiting			
subjects affected / exposed	1 / 14 (7.14%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Hepatobiliary disorders			
Gallbladder disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hepatosplenomegaly			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Jaundice			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Liver disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Dermatosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Purpura			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	3 / 14 (21.43%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
Scab			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			

Cystitis haemorrhagic			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Haematuria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Infections and infestations			
Anorectal cellulitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Bone abscess			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
Cellulitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Oral herpes			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Splenic candidiasis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 8 (12.50%)	
occurrences (all)	1	1	

Hyperkalaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hypermagnesaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Hypocalcaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hypochloraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Hypoglycaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	5	0	
Hyponatraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Hypophagia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Hypophosphataemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 8 (12.50%)	
occurrences (all)	3	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 November 2009	The primary reason for creation of this protocol amendment was to include additional visual safety assessments, as requested by the United States Food and Drug Administration (FDA). 1- Dilated fundoscopic examination at the EOT and at the 1-month follow-up visit. These assessments were in addition to the dilated fundoscopic examination already required at the time of Screening. 2- Confrontational and/or automated visual field test at the time of Screening and at the EOT in subjects 5 years of age and older. For subjects who were critically ill and/or clinically unstable at Baseline, visual field testing could be performed at a later time, when, in the investigator's judgment, the subject was clinically stable and able to perform the test adequately. 3- In subjects 3 years of age and younger, visual safety monitoring was limited to visual acuity and dilated fundoscopy. In children who were too young to perform the visual acuity test, fixation should have been assessed as to whether it is central, steady or maintained in each eye. 4- Assessment of vital signs, and signs and symptoms of Candida infection (including radiologic findings) every 3 days was no longer required in subjects who have been discharged from the hospital and are continuing to receive study drug treatment on an outpatient basis. 5- In subjects who experience a treatment-emergent cardiac arrhythmia that was felt to be, in the investigator's judgment, clinically significant, the investigator was to collect a standard 12-lead electro cardiaography (ECG) at the time of the event, or within 2 hours following the event, and send a duplicate of the ECG to the designated central ECG reader.
08 July 2010	Regarding the primary and salvage EC inclusion criteria: In addition to symptoms consistent with EC, subjects who could not undergo esophagoscopy due to neutropenia, thrombocytopenia, or HIV/advanced AIDS, were to have culture-proven oropharyngeal candidiasis in order to qualify for study entry.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was prematurely terminated due to slow enrollment. The study was not terminated due to safety issues or concerns. Interpretation of the data are limited due to the small sample size and descriptive design.

Notes: