Clinical trial results:
Post Marketing Surveillance Study to Observe the Safety and Efficacy of Voriconazole Intavenous Infusion

Summary

EudraCT number	2017-000197-11
Trial protocol	Outside EU/EEA
Global end of trial date	15 May 2012

Results information

Result version number	v1 (current)
This version publication date	08 June 2017
First version publication date	08 June 2017

Trial information

Trial identification

Sponsor protocol code	A1501067

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01073618
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, 110017
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 18007181021, 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	19 October 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 May 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to determine the efficacy and safety of Voriconazole, 200 mg intravenous infusion (IV).

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 trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 April 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Korea, Republic of: 692
Worldwide total number of subjects	692
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)	10
Children (2-11 years)	45
Adolescents (12-17 years)	42
Adults (18-64 years)	500
From 65 to 84 years	95

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 692 subjects were enrolled at multiple centers in Republic of Korea in this study. The study was conducted from 11-Apr-2006 to 19-Oct-2009.

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	Voriconazole

Arm description:

Subjects aged greater than (>) 12 years with invasive aspergillosis received Voriconazole intravenously at a loading dose of 6 milligrams per kilogram (mg/kg), every 12 hours for the first 24 hours, followed by the maintenance dose of 4 mg/kg intravenously, twice daily up to 2 weeks. Subjects aged >12 years with invasive candidemia received Voriconazole intravenously at a loading dose of 6 mg/kg intravenously, every 12 hours for the first 24 hours, followed by the maintenance dose of Voriconazole 3 to 4 mg/kg intravenously, twice daily up to 2 weeks.

Arm type	Experimental
Investigational medicinal product name	Voriconazole 6 mg/kg
Investigational medicinal product code	Voriconazole
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received loading dose of Voriconazole 6 mg/kg intravenously twice daily for the first 24 hours up to 2 weeks.

Investigational medicinal product name	Voriconazole 4 mg/kg
Investigational medicinal product code	Voriconazole
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received maintenance dose of Voriconazole 4 mg/kg intravenously twice daily up to 2 weeks.

Number of subjects in period 1	Voriconazole
Started	692
Completed	385
Not completed	307
Adverse Event	19
Death	208
Unspecified	80

Baseline characteristics

Reporting groups	
Reporting group title	Voriconazole

Reporting group description:

Subjects aged greater than (>) 12 years with invasive aspergillosis received Voriconazole intravenously at a loading dose of 6 milligrams per kilogram (mg/kg), every 12 hours for the first 24 hours, followed by the maintenance dose of 4 mg/kg intravenously, twice daily up to 2 weeks. Subjects aged >12 years with invasive candidemia received Voriconazole intravenously at a loading dose of 6 mg/kg intravenously, every 12 hours for the first 24 hours, followed by the maintenance dose of Voriconazole 3 to 4 mg/kg intravenously, twice daily up to 2 weeks.

Reporting group values	Voriconazole	Total	
Number of subjects	692	692	
Age Categorical Units: Subjects			
<18 years	97	97	
Between 18 and 44 years	218	218	
Between 45 and 64 years	282	282	
>=65 years	95	95	
Age continuous Units: years			
arithmetic mean	43.7		
standard deviation	± 19.7	-	
Gender, Male/Female Units: Subjects			
Female	275	275	
Male	417	417	

End points

End points reporting groups

Reporting group title	Voriconazole

Reporting group description:

Subjects aged greater than (>) 12 years with invasive aspergillosis received Voriconazole intravenously at a loading dose of 6 milligrams per kilogram (mg/kg), every 12 hours for the first 24 hours, followed by the maintenance dose of 4 mg/kg intravenously, twice daily up to 2 weeks. Subjects aged >12 years with invasive candidemia received Voriconazole intravenously at a loading dose of 6 mg/kg intravenously, every 12 hours for the first 24 hours, followed by the maintenance dose of Voriconazole 3 to 4 mg/kg intravenously, twice daily up to 2 weeks.

Primary: Percentage of Subjects With Categorical Clinical Response: Cure, Improvement, Failure, or Unevaluable

End point title	Percentage of Subjects With Categorical Clinical Response: Cure, Improvement, Failure, or Unevaluable[1]

End point description:

Clinical response was defined as: Cure = resolution of all baseline signs and symptoms of fungal infection(s); Improvement = lessening of baseline signs and symptoms or absence of one or more, but not all baseline findings; Failure = no improvement or deterioration of baseline condition; Unevaluable = Incomplete therapy (efficacy could not be evaluated or discontinuation was not followed up). Intent to treat (ITT) population included subjects who received study drug for the approved indication and had been evaluated for related parameters at least once.

End point type	Primary

End point timeframe:

Baseline (Day 1) up to 2 years

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 descriptive analysis was planned to be analyzed in this endpoint

End point values	Voriconazole			
Subject group type	Reporting group			
Number of subjects analysed	692			
Units: percentage of subjects				
number (not applicable)				
Cure	12.72			
Improvement	41.47			
Failure	17.92			
Unevaluable	27.89			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Cultivated Strain Mycological Response: Eradication, Persistence, Superinfection, or Not evaluable

End point title	Percentage of Subjects With Cultivated Strain Mycological Response: Eradication, Persistence, Superinfection, or Not evaluable

End point description:

Mycological response was defined as: Eradication = absence of signs and symptoms of fungal infection; Persistence = (no eradication) presence of fungal infection; Superinfection = existence of different strains from strains separated prior to study medication; Not evaluable = a follow-up mycological cultivation is not performed. ITT population included subjects who received study drug for the approved indication and had been evaluated for related parameters at least once. Here, 'N' (Number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1) up to 2 years

End point values	Voriconazole			
Subject group type	Reporting group			
Number of subjects analysed	159			
Units: percentage of subjects				
number (not applicable)				
Eradication	64.78			
Persistence	27.67			
Superinfection	3.77			
Not evaluable	3.77			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 28 days after last dose of study drug

Adverse event reporting additional description:

The same event may appear as both an AE and a 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	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Voriconazole

Reporting group description:

Subjects aged >12 years with invasive aspergillosis received Voriconazole intravenously at a loading dose of 6 mg/kg, every 12 hours for the first 24 hours, followed by the maintenance dose of 4 mg/kg intravenously, twice daily up to 2 weeks. Subjects aged >12 years with invasive candidemia received Voriconazole intravenously at a loading dose of 6 mg/kg intravenously, every 12 hours for the first 24 hours, followed by the maintenance dose of Voriconazole 3 to 4 mg/kg intravenously, twice daily up to 2 weeks.

Serious adverse events	Voriconazole		
Total subjects affected by serious adverse events			
subjects affected / exposed	239 / 692 (34.54%)		
number of deaths (all causes)	220		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 1		
Acute myeloid leukaemia			
subjects affected / exposed	7 / 692 (1.01%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 7		
Hypopharyngeal cancer			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

Leukaemia			
subjects affected / exposed	18 / 692 (2.60%)		
occurrences causally related to treatment / all	0 / 18		
deaths causally related to treatment / all	0 / 18		
Leukaemia recurrent			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Leukaemic infiltration			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm malignant			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Lymphoma			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Multiple myeloma			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour haemorrhage			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Rectal cancer			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Myelodysplastic syndrome			

subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 692 (0.43%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Shock			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Brain death			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Condition aggravated			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Disease progression			
subjects affected / exposed	14 / 692 (2.02%)		
occurrences causally related to treatment / all	3 / 14		
deaths causally related to treatment / all	3 / 14		
General physical health deterioration			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Multi-organ failure			
subjects affected / exposed	17 / 692 (2.46%)		
occurrences causally related to treatment / all	0 / 17		
deaths causally related to treatment / all	0 / 14		

Pyrexia				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Acute graft versus host disease in intestine				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Acute graft versus host disease in skin				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Graft versus host disease				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory distress syndrome				
subjects affected / exposed	12 / 692 (1.73%)			
occurrences causally related to treatment / all	1 / 12			
deaths causally related to treatment / all	1 / 9			
Acute respiratory failure				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Bronchopulmonary dysplasia				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Dyspnoea				

subjects affected / exposed	9 / 692 (1.30%)			
occurrences causally related to treatment / all	0 / 9			
deaths causally related to treatment / all	0 / 2			
Haemoptysis				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hydropneumothorax				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	9 / 692 (1.30%)			
occurrences causally related to treatment / all	0 / 9			
deaths causally related to treatment / all	0 / 4			
Pleural effusion				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 2			
Pneumothorax				
subjects affected / exposed	3 / 692 (0.43%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Pulmonary haemorrhage				
subjects affected / exposed	6 / 692 (0.87%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 4			
Pulmonary oedema				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory arrest				

subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Respiratory failure				
subjects affected / exposed	7 / 692 (1.01%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 7			
Pulmonary alveolar haemorrhage				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Acoustic stimulation tests				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood creatinine				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus test positive				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Liver function test abnormal				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oxygen saturation decreased				

subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transaminases increased			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Collapse of lung			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chemical peritonitis			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bradycardia			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

Cardiac arrest				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 2			
Cardiac failure				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Pericardial effusion				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Pericarditis				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Left ventricular dysfunction				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebral haemorrhage				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 2			
Cerebral infarction				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 1			
Convulsion				
subjects affected / exposed	8 / 692 (1.16%)			
occurrences causally related to treatment / all	2 / 8			
deaths causally related to treatment / all	2 / 2			
Haemorrhage intracranial				

subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Intracranial pressure increased				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Paraplegia				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mental impairment				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	3 / 692 (0.43%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 1			
Disseminated intravascular coagulation				
subjects affected / exposed	5 / 692 (0.72%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	1 / 2			
Febrile neutropenia				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	3 / 692 (0.43%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	1 / 3			
Thrombotic microangiopathy				

subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombotic thrombocytopenic purpura				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Gastrointestinal disorders				
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematochezia				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenic colitis				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis acute				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic failure				
subjects affected / exposed	3 / 692 (0.43%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 2			

Hepatic function abnormal			
subjects affected / exposed	4 / 692 (0.58%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Hepatorenal failure			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hepatosplenomegaly			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatotoxicity			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 1		
Hyperbilirubinaemia			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Liver disorder			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	3 / 692 (0.43%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	1 / 2		

Cystitis haemorrhagic			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nephropathy toxic			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Renal failure			
subjects affected / exposed	3 / 692 (0.43%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Renal failure acute			
subjects affected / exposed	9 / 692 (1.30%)		
occurrences causally related to treatment / all	2 / 9		
deaths causally related to treatment / all	2 / 4		
Renal failure chronic			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Renal impairment			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Euthyroid sick syndrome			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Aspergillosis			
subjects affected / exposed	6 / 692 (0.87%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 5		
Brain abscess			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cytomegalovirus infection			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Enterococcal sepsis			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Fungal infection			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 2		
Liver abscess			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningitis			

subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oral herpes				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	57 / 692 (8.24%)			
occurrences causally related to treatment / all	2 / 57			
deaths causally related to treatment / all	2 / 53			
Pneumonia fungal				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Pneumonia primary atypical				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Sepsis				
subjects affected / exposed	29 / 692 (4.19%)			
occurrences causally related to treatment / all	2 / 29			
deaths causally related to treatment / all	2 / 25			
Septic shock				
subjects affected / exposed	44 / 692 (6.36%)			
occurrences causally related to treatment / all	2 / 44			
deaths causally related to treatment / all	0 / 35			
Enterococcal infection				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Metabolism and nutrition disorders				
Acidosis				

subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Hypernatraemia			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolic acidosis			
subjects affected / exposed	3 / 692 (0.43%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	1 / 2		
Hyperkalaemia			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Voriconazole		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	94 / 692 (13.58%)		
Investigations			
Blood creatinine increased			
subjects affected / exposed	10 / 692 (1.45%)		
occurrences (all)	10		
Liver function test abnormal			
subjects affected / exposed	14 / 692 (2.02%)		
occurrences (all)	14		
Transaminases increased			
subjects affected / exposed	10 / 692 (1.45%)		
occurrences (all)	10		
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 692 (1.01%)		
occurrences (all)	7		

General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	 12 / 692 (1.73%) 12		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 9 / 692 (1.30%) 9 7 / 692 (1.01%) 7		
Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all)	 14 / 692 (2.02%) 14		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	 8 / 692 (1.16%) 8		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 7 / 692 (1.01%) 7		
Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all)	 10 / 692 (1.45%) 10		

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