Clinical trial results:
An open-label, intravenous to oral switch, multiple dose, multi-centre study to investigate the pharmacokinetics, safety and tolerability of Voriconazole in hospitalized children aged 2 to <12 years who require treatment for the prevention of systemic fungal infection

Summary

EudraCT number	2014-004184-21
Trial protocol	Outside EU/EEA
Global end of trial date	30 June 2004

Results information

Result version number	v1 (current)
This version publication date	13 June 2016
First version publication date	29 July 2015

Trial information

Trial identification

Sponsor protocol code	A1501037

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00174473
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	ClinicalTrials.gov Call Center, Pfizer Inc. , 001 8007181021, ClinicalTrials.govCallCenter@pfizer.com
Scientific contact	ClinicalTrials.gov Call Center, Pfizer Inc. , 001 8007181021, ClinicalTrials.govCallCenter@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000191-PIP01-08
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes
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	29 October 2004
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 June 2004
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the pharmacokinetics of voriconazole following intravenous to oral switch in children aged 2 to less than (<) 12 years.

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	11 June 2003
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	United States: 32
Country: Number of subjects enrolled	United Kingdom: 6
Worldwide total number of subjects	48
EEA total number of subjects	16

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)	48
Adolescents (12-17 years)	0

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:

The study was conducted in 3 countries and total 48 subjects were assigned to receive treatment. The study was started on 11 June 2003 and completed on 30 June 2004.

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?	No
Arm title	Cohort I: Voriconazole 4mg/kg Intravenous

Arm description:

Voriconazole 4 milligram per kilogram (mg/kg) intravenous infusion administered over 80 minutes every 12 hours up to and including Day 4 in pharmacokinetic period of cohort I.

Arm type	Experimental
Investigational medicinal product name	Voriconazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Voriconazole 4 mg/kg intravenous infusion administered at a rate of 3 mg/kg per hour (mg/kg/hr) over 80 minutes every 12 hours. The 12-hour dosing intervals may vary up to ± 30min.

Arm title	Cohort I: Voriconazole 6mg/kg Intravenous

Arm description:

Voriconazole 6mg/kg intravenous infusion administered over 120 minutes in the morning, and again 12 hours later on Day 1. Voriconazole 6 mg/kg intravenous infusion administered over the time period of 120 minutes at 12-hour intervals starting from Day 5 to Day 8 in pharmacokinetic period of cohort I. Subjects, if unable to take oral dose, continued to receive 6 mg/kg intravenous infusion, but could switch, if able, any morning between Days 10 and 20.

Arm type	Experimental
Investigational medicinal product name	Voriconazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Voriconazole 6 mg/kg intravenous infusion administered at a rate of 3 mg/kg/hr over 120 minutes every 12 hours. The 12-hour dosing intervals
may vary up to ±30min.

Arm title	Cohort I: Voriconazole 4mg/kg Oral Suspension

Arm description:

Voriconazole oral suspension 4 mg/kg twice daily at 12-hour intervals was given either one hour before or one hour after meals starting from Day 9 up to Day 12 in the pharmacokinetic period of cohort I.

Arm type	Experimental

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

Dosage and administration details:

Voriconazole oral suspension 4 mg/kg at 12 hour intervals was administered at least one hour before or one hour following a meal.

Arm title	Cohort I: Voriconazole non–pharmacokinetic period

Arm description:

Subjects who continued to receive voriconazole after the pharmacokinetic period from Day 12 up to Day 30 as per clinician's discretion due to
medical need such as persistent neutropenia (absolute neutrophil count [ANC <500/microliter [mcL]) were included in the non-pharmacokinetic period of cohort 1 and were assessed for safety.

Arm type	Experimental
Investigational medicinal product name	Voriconazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Voriconazole oral suspension 4 mg/kg at 12 hour intervals was administered at least one hour before or one hour following a meal on the discretion of medical need.

Investigational medicinal product name	Voriconazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Voriconazole 6 mg/kg intravenous infusion administered at a rate of 3 mg/kg/hr over 120 minutes every 12 hours. The 12-hour dosing intervals
may vary up to ±30min.

Arm title	Cohort II: Voriconazole 6mg/kg Intravenous

Arm description:

Voriconazole 6mg/kg intravenous infusion administered over 120 minutes in the morning, and again 12 hours later up to and including Day 4 in pharmacokinetic period of cohort II.

Arm type	Experimental
Investigational medicinal product name	Voriconazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Voriconazole 6 mg/kg intravenous infusion administered at a rate of 3 mg/kg/hr over 120 minutes every 12 hours. The 12-hour dosing intervals
may vary up to ±30min.

Arm title	Cohort II: Voriconazole 8mg/kg Intravenous

Arm description:

Voriconazole 8 mg/kg intravenous infusion administered at 12-hour intervals over 160 minutes starting from Day 5 up to Day 8 in pharmacokinetic period of cohort II. Subjects if unable to take oral dose, continued to receive 8 mg/kg intravenous infusion up to Day 12.

Arm type	Experimental

Investigational medicinal product name	Voriconazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Voriconazole 8 mg/kg intravenous infusion administered at a rate of 3 mg/kg/hr over 120 minutes every 12 hours. The 12-hour dosing intervals
may vary up to ±30min.

Arm title	Cohort II: Voriconazole 6mg/kg Oral Suspension

Arm description:

Voriconazole oral suspension 6 mg/kg twice daily at 12-hour intervals was given either one hour before or one hour after meals starting from Day 9 up to Day 12 in the pharmacokinetic period of cohort II. Subjects, if unable to take oral dose, continued to receive 8 mg/kg intravenous infusion, but could switch, if able, any morning between Days 10 and 20.

Arm type	Experimental
Investigational medicinal product name	Voriconazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Voriconazole oral suspension 6 mg/kg at 12 hour intervals was administered at least one hour before or one hour following a meal.

Arm title	Cohort II: Voriconazole non–pharmacokinectic period

Arm description:

Subjects who continued to receive voriconazole after the pharmacokinetic period from Day 12 up to Day 30 as per clinician’s discretion due to
medical need such as persistent neutropenia (ANC < 500/mcL) were included in the non-pharmacokinetic period of cohort II and were assessed for safety.

Arm type	Experimental
Investigational medicinal product name	Voriconazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Voriconazole 6 mg/kg intravenous infusion administered at a rate of 3 mg/kg/hr over 160 minutes every 12 ours. The 12-hour dosing intervals
may vary up to ± 30min.

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

Dosage and administration details:

Voriconazole oral suspension 6 mg/kg at 12 hour interval was administered at least one hour before or one hour following a meal on the discretion
of medical need.

Number of subjects in period 1	Cohort I: Voriconazole 4mg/kg Intravenous	Cohort I: Voriconazole 6mg/kg Intravenous	Cohort I: Voriconazole 4mg/kg Oral Suspension
Started	24	23	22
Completed	23	21	22
Not completed	1	2	0
Consent withdrawn by subject	1	1	-
Adverse Event	-	1	-
Unspecified	-	-	-

Number of subjects in period 1	Cohort I: Voriconazole non–pharmacokinetic period	Cohort II: Voriconazole 6mg/kg Intravenous	Cohort II: Voriconazole 8mg/kg Intravenous
Started	19	24	22
Completed	18	22	21
Not completed	1	2	1
Consent withdrawn by subject	-	2	-
Adverse Event	1	-	1
Unspecified	-	-	-

Number of subjects in period 1	Cohort II: Voriconazole 6mg/kg Oral Suspension	Cohort II: Voriconazole non–pharmacokinectic period
Started	20	12
Completed	18	11
Not completed	2	1
Consent withdrawn by subject	1	-
Adverse Event	1	-
Unspecified	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	48	48	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	5.8		
standard deviation	± 3	-	
Gender categorical Units: Subjects			
Female	19	19	
Male	29	29	

End points

End points reporting groups

Reporting group title	Cohort I: Voriconazole 4mg/kg Intravenous
Reporting group description:	
Voriconazole 4 milligram per kilogram (mg/kg) intravenous infusion administered over 80 minutes every 12 hours up to and including Day 4 in pharmacokinetic period of cohort I.	
Reporting group title	Cohort I: Voriconazole 6mg/kg Intravenous
Reporting group description:	
Voriconazole 6mg/kg intravenous infusion administered over 120 minutes in the morning, and again 12 hours later on Day 1. Voriconazole 6 mg/kg intravenous infusion administered over the time period of 120 minutes at 12-hour intervals starting from Day 5 to Day 8 in pharmacokinetic period of cohort I. Subjects, if unable to take oral dose, continued to receive 6 mg/kg intravenous infusion, but could switch, if able, any morning between Days 10 and 20.	
Reporting group title	Cohort I: Voriconazole 4mg/kg Oral Suspension
Reporting group description:	
Voriconazole oral suspension 4 mg/kg twice daily at 12-hour intervals was given either one hour before or one hour after meals starting from Day 9 up to Day 12 in the pharmacokinetic period of cohort I.	
Reporting group title	Cohort I: Voriconazole non–pharmacokinetic period
Reporting group description:	
Subjects who continued to receive voriconazole after the pharmacokinetic period from Day 12 up to Day 30 as per clinician’s discretion due to medical need such as persistent neutropenia (absolute neutrophil count [ANC <500/microliter [mcL]) were included in the non-pharmacokinetic period of cohort 1 and were assessed for safety.	
Reporting group title	Cohort II: Voriconazole 6mg/kg Intravenous
Reporting group description:	
Voriconazole 6mg/kg intravenous infusion administered over 120 minutes in the morning, and again 12 hours later up to and including Day 4 in pharmacokinetic period of cohort II.	
Reporting group title	Cohort II: Voriconazole 8mg/kg Intravenous
Reporting group description:	
Voriconazole 8 mg/kg intravenous infusion administered at 12-hour intervals over 160 minutes starting from Day 5 up to Day 8 in pharmacokinetic period of cohort II. Subjects if unable to take oral dose, continued to receive 8 mg/kg intravenous infusion up to Day 12.	
Reporting group title	Cohort II: Voriconazole 6mg/kg Oral Suspension
Reporting group description:	
Voriconazole oral suspension 6 mg/kg twice daily at 12-hour intervals was given either one hour before or one hour after meals starting from Day 9 up to Day 12 in the pharmacokinetic period of cohort II. Subjects, if unable to take oral dose, continued to receive 8 mg/kg intravenous infusion, but could switch, if able, any morning between Days 10 and 20.	
Reporting group title	Cohort II: Voriconazole non–pharmacokinectic period
Reporting group description:	
Subjects who continued to receive voriconazole after the pharmacokinetic period from Day 12 up to Day 30 as per clinician’s discretion due to medical need such as persistent neutropenia (ANC < 500/mcL) were included in the non-pharmacokinetic period of cohort II and were assessed for safety.	
Subject analysis set title	Voriconazole: Cohort I
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects received voriconazole 6mg/kg infusion on Day 1, followed by 4 mg/kg infusion every 12 hour from Day 2 to 4, then 6 mg/kg infusion from Day 5 to 8. Subjects either received 4mg/kg oral suspension every 12 hour or 6mg/kg intravenous (if unable to take oral suspension) from Day 9 up to Day 12 during the pharmacokinetic period.	
Subject analysis set title	Voriconazole: Cohort II
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects received voriconazole 6mg/kg infusion on every 12 hour up to Day 4, then 8 mg/kg infusion	

from Day 5 to 8. Subjects either received 6 mg/kg oral suspension every 12 hour or 8 mg/kg intravenous (if unable to take oral suspension) from Day 9 up to Day 12 during the pharmacokinetic period.

Primary: Area Under the Curve from Time Zero to End of Dosing Interval (AUCtau)

End point title	Area Under the Curve from Time Zero to End of Dosing Interval (AUCtau)[1][2]

End point description:

AUCtau was calculated by the linear trapezoidal method. Pharmacokinetic population included those subjects who had complete dosing for at least 1 dosing phase of the cohort and had at least 1 pharmacokinetic parameter derived on Day 4 of that dosing phase.

End point type	Primary

End point timeframe:

2 minute pre-infusion end (on Day 1, 4, 8, 12), 2, 4, 6, 8, 12 hour post-infusion start on Day 4, 8 for intravenous dosing; pre-dose, 0.5,1, 2, 4, 6, 8, 12 hour post-dose on Day 12 for oral dosing

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 data was planned to be reported for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to report only pharmacokinetic data.

End point values	Cohort I: Voriconazole 4mg/kg Intravenous	Cohort I: Voriconazole 6mg/kg Intravenous	Cohort I: Voriconazole 4mg/kg Oral Suspension	Cohort II: Voriconazole 6mg/kg Intravenous
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22[3]	21[4]	19[5]	19[6]
Units: nanogram*hour per milliliter (ng*hr/mL)				
geometric mean (standard deviation)	11826.5 (± 11354.1)	22914.2 (± 45327.14)	5183.8 (± 5036.65)	17248.7 (± 19636.41)

Notes:

[3] - Subjects who were evaluable for this measure.

[4] - Subjects who were evaluable for this measure.

[5] - Subjects who were evaluable for this measure.

[6] - Subjects who were evaluable for this measure.

End point values	Cohort II: Voriconazole 8mg/kg Intravenous	Cohort II: Voriconazole 6mg/kg Oral Suspension		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[7]	18[8]		
Units: nanogram*hour per milliliter (ng*hr/mL)				
geometric mean (standard deviation)	29776.4 (± 34089.15)	8373.4 (± 9225.43)		

Notes:

[7] - Subjects who were evaluable for this measure.

[8] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax)

End point title	Maximum Observed Plasma Concentration (Cmax)[9][10]

End point description:

Maximum Observed Plasma Concentration (Cmax) calculated by the recorded plasma concentration-time data. Pharmacokinetic population
included those subjects who had complete dosing for at least 1 dosing phase of the cohort and had at least 1 pharmacokinetic parameter
derived on Day 4 of that dosing phase.

End point type	Primary

End point timeframe:

2 minute pre-infusion end (on Day 1, 4, 8, 12), 2, 4, 6, 8, 12 hour post-infusion start on Day 4, 8 for intravenous dosing; pre-dose, 0.5,1, 2, 4, 6, 8, 12 hour post-dose on Day 12 for oral dosing

Notes:

[9] - 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 data was planned to be reported for this endpoint.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to report only pharmacokinetic data.

End point values	Cohort I: Voriconazole 4mg/kg Intravenous	Cohort I: Voriconazole 6mg/kg Intravenous	Cohort I: Voriconazole 4mg/kg Oral Suspension	Cohort II: Voriconazole 6mg/kg Intravenous
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23[11]	21[12]	21[13]	20[14]
Units: ng/mL				
geometric mean (standard deviation)	3212.4 (± 2546.68)	4352.6 (± 6027.41)	1177.8 (± 1123.67)	4286.1 (± 4758.73)

Notes:

[11] - Subjects who were evaluable for this measure.

[12] - Subjects who were evaluable for this measure.

[13] - Subjects who were evaluable for this measure.

[14] - Subjects who were evaluable for this measure.

End point values	Cohort II: Voriconazole 8mg/kg Intravenous	Cohort II: Voriconazole 6mg/kg Oral Suspension		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[15]	19[16]		
Units: ng/mL				
geometric mean (standard deviation)	5767.3 (± 10683.32)	1760.7 (± 1271.65)		

Notes:

[15] - Subjects who were evaluable for this measure.

[16] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Maximum Observed Plasma Concentration (Tmax)

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax)[17][18]

End point description:

Time to Reach Maximum Observed Plasma Concentration (Tmax) calculated by the recorded plasma concentration-time data. Pharmacokinetic population included those subjects who had complete dosing for at least 1 dosing phase of the cohortand had at least 1 pharmacokinetic parameter derived on Day 4 of that dosing phase.

End point type	Primary

End point timeframe:

2 minute pre-infusion end (on Day 1, 4, 8, 12), 2, 4, 6, 8, 12 hour post-infusion start on Day 4, 8 for intravenous dosing; pre-dose, 0.5,1, 2, 4, 6, 8, 12 hour post-dose on Day 12 for oral dosing

Notes:

[17] - 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 data was planned to be reported for this endpoint.

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to report only pharmacokinetic data.

End point values	Cohort I: Voriconazole 4mg/kg Intravenous	Cohort I: Voriconazole 6mg/kg Intravenous	Cohort I: Voriconazole 4mg/kg Oral Suspension	Cohort II: Voriconazole 6mg/kg Intravenous
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23[19]	21[20]	21[21]	20[22]
Units: hr				
arithmetic mean (standard deviation)	1.361 (± 0.2017)	1.97 (± 0)	1.429 (± 1.7485)	2.072 (± 0.4539)

Notes:

[19] - Subjects who were evaluable for this measure.

[20] - Subjects who were evaluable for this measure.

[21] - Subjects who were evaluable for this measure.

[22] - Subjects who were evaluable for this measure.

End point values	Cohort II: Voriconazole 8mg/kg Intravenous	Cohort II: Voriconazole 6mg/kg Oral Suspension		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[23]	19[24]		
Units: hr				
arithmetic mean (standard deviation)	2.836 (± 0.5019)	1.342 (± 1.2478)		

Notes:

[23] - Subjects who were evaluable for this measure.

[24] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Primary: Bioavailability (F)

End point title	Bioavailability (F)[25]

End point description:

Bioavailability is a measurement of the rate and extent to which a drug reaches the systemic circulation. Bioavailability was calculated as ratio of (AUC oral dosing*intravenous dose)/(AUC intravenous dosing*oral dose). Evaluable subjects for the pharmacokinetic bioavailability were those who had

AUCtau data from both the intravenous and oral phases of the study.

End point type	Primary

End point timeframe:

2 minute pre-infusion end (on Day 1, 4, 8, 12), 2, 4, 6, 8, 12 hour post-infusion start on Day 4, 8 for intravenous dosing; pre-dose, 0.5,1, 2, 4, 6, 8, 12 hour post-dose on Day 12 for oral dosing

Notes:

[25] - 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 data was planned to be reported for this endpoint.

End point values	Voriconazole: Cohort I	Voriconazole: Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19[26]	15[27]		
Units: ratio				
arithmetic mean (standard deviation)	0.66 (± 0.6368)	0.651 (± 0.4581)		

Notes:

[26] - Subjects who were evaluable for this measure.

[27] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects with Treatment Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

An AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. An SAE was an AE resulting in any
of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening
experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent are events between first dose of study drug and up to 30 days after last dose that were absent before treatment or that worsened relative to pretreatment state. All subjects who received study treatment were included in safety population. AEs included both SAEs and non-SAEs.

End point type	Secondary

End point timeframe:

Baseline up to 30 Days after the last dose of study drug

End point values	Cohort I: Voriconazole 4mg/kg Intravenous	Cohort I: Voriconazole 6mg/kg Intravenous	Cohort I: Voriconazole 4mg/kg Oral Suspension	Cohort I: Voriconazole non–pharmacokinetic period
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	23	22	19
Units: Subjects				
AEs	22	21	21	17
SAEs	0	2	2	2

End point values	Cohort II: Voriconazole 6mg/kg Intravenous	Cohort II: Voriconazole 8mg/kg Intravenous	Cohort II: Voriconazole 6mg/kg Oral Suspension	Cohort II: Voriconazole non–pharmacokinectic period
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	22	20	12
Units: Subjects				
AEs	19	22	20	12
SAEs	0	4	3	4

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs: Baseline up to 7 Days after last dose of study drug. SAEs: Baseline up to 30 Days after the 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	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Cohort I: Voriconazole 4mg/kg Intravenous

Reporting group description:

Voriconazole 4mg/kg intravenous infusion administered over 80 minutes every 12 hours up to and including Day 4 in pharmacokinetic period of cohort I.

Reporting group title	Cohort I: Voriconazole 6mg/kg Intravenous

Reporting group description:

Voriconazole 6mg/kg intravenous infusion administered over 120 minutes in the morning, and again 12 hours later on Day 1. Voriconazole 6mg/kg intravenous infusion administered over the time period of 120 minutes at 12-hour intervals starting from Day 5 to Day 8 in pharmacokinetic period of cohort I. Subjects, if unable to take oral dose, continued to receive 6mg/kg intravenous infusion, but could switch, if able, any morning between Days 10 and 20.

Reporting group title	Cohort I: Voriconazole 4mg/kg Oral Suspension

Reporting group description:

Voriconazole oral suspension 4mg/kg twice daily at 12-hour intervals was given either one hour before or one hour after meals starting from Day 9 up to Day 12 in the pharmacokinetic period of cohort I.

Reporting group title	Cohort I: Voriconazole non-pharmacokinetic period

Reporting group description:

Subjects who continued to receive voriconazole after the pharmacokinetic period from Day 12 up to Day 30 as per clinician’s discretion due to medical need such as persistent neutropenia (ANC<500/mcL) were included in the non-pharmacokinetic period of cohort II and were assessed for safety.

Reporting group title	Cohort II: Voriconazole 6mg/kg Intravenous

Reporting group description:

Voriconazole 6mg/kg intravenous infusion administered over 120 minutes in the morning, and again 12 hours later up to and including Day 4 in pharmacokinetic period of cohort II.

Reporting group title	Cohort II: Voriconazole 8mg/kg Intravenous

Reporting group description:

Voriconazole 8mg/kg intravenous infusion administered at 12-hour intervals over 160 minutes starting from Day 5 up to Day 8 in pharmacokinetic period of cohort II. Subjects if unable to take oral dose, continued to receive 8mg/kg intravenous infusion up to Day 12.

Reporting group title	Cohort II: Voriconazole 6mg/kg Oral Suspension

Reporting group description:

Voriconazole oral suspension 6mg/kg twice daily at 12-hour intervals was given either one hour before or one hour after meals starting from Day 9 up to Day 12 in the pharmacokinetic period of cohort II. Subjects, if unable to take oral dose, continued to receive 8mg/kg intravenous infusion, but could switch, if able, any morning between Days 10 and 20.

Reporting group title	Cohort II: Voriconazole non-pharmacokinetic period

Reporting group description:

Subjects who continued to receive voriconazole after the pharmacokinetic period from Day 12 up to Day 30 as per clinician’s discretion due to medical need such as persistent neutropenia (absolute neutrophil count [ANC<500/mcL]) were included in the non-pharmacokinetic period of cohort 1 and were assessed for safety.

Serious adverse events	Cohort I: Voriconazole 4mg/kg Intravenous	Cohort I: Voriconazole 6mg/kg Intravenous	Cohort I: Voriconazole 4mg/kg Oral Suspension
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	2 / 23 (8.70%)	2 / 22 (9.09%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Tonic convulsion			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Bone marrow transplant rejection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft versus host disease in skin			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Escherichia bacteraemia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis adenovirus			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	0 / 24 (0.00%)	2 / 23 (8.70%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort I: Voriconazole non-pharmacokinetic period	Cohort II: Voriconazole 6mg/kg Intravenous	Cohort II: Voriconazole 8mg/kg Intravenous
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 19 (10.53%)	0 / 24 (0.00%)	4 / 22 (18.18%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Tonic convulsion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Bone marrow transplant rejection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft versus host disease in skin			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Escherichia bacteraemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis adenovirus			

subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort II: Voriconazole 6mg/kg Oral Suspension	Cohort II: Voriconazole non-pharmacokinetic period	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)	4 / 12 (33.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Tonic convulsion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Bone marrow transplant rejection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft versus host disease in skin			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Escherichia bacteraemia			

subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis adenovirus			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort I: Voriconazole 4mg/kg Intravenous	Cohort I: Voriconazole 6mg/kg Intravenous	Cohort I: Voriconazole 4mg/kg Oral Suspension
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 24 (91.67%)	21 / 23 (91.30%)	21 / 22 (95.45%)
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Haemorrhage			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Hypertension			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Hypotension			

subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Venoocclusive disease			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Catheter site inflammation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Catheter site pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Device occlusion			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	2 / 22 (9.09%)
occurrences (all)	1	1	2
Generalised oedema			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Infusion site pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Mucosal inflammation			
subjects affected / exposed	7 / 24 (29.17%)	12 / 23 (52.17%)	9 / 22 (40.91%)
occurrences (all)	7	12	9
Mucosal pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Oedema			

subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Performance status decreased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Pyrexia			
subjects affected / exposed	4 / 24 (16.67%)	5 / 23 (21.74%)	2 / 22 (9.09%)
occurrences (all)	4	6	4
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Graft versus host disease			
subjects affected / exposed	0 / 24 (0.00%)	3 / 23 (13.04%)	5 / 22 (22.73%)
occurrences (all)	0	3	5
Graft versus host disease in skin			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Serum sickness			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Genital erythema			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Perineal erythema			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Atelectasis			

subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Dyspnoea			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Laryngospasm			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Pleural effusion			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Pulmonary oedema			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Respiratory distress			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 24 (0.00%)	2 / 23 (8.70%)	3 / 22 (13.64%)
occurrences (all)	0	2	3
Tachypnoea			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Psychiatric disorders			

Agitation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Confusional state			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 24 (0.00%)	2 / 23 (8.70%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Nightmare			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Bacterial test positive			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Blood magnesium decreased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Blood phosphorus decreased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Blood potassium decreased			

subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Blood pressure increased			
subjects affected / exposed	2 / 24 (8.33%)	2 / 23 (8.70%)	2 / 22 (9.09%)
occurrences (all)	2	2	2
Blood urea increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Cytomegalovirus test positive			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Drug level increased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 24 (4.17%)	2 / 23 (8.70%)	2 / 22 (9.09%)
occurrences (all)	1	2	2
Hepatic enzyme increased			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Immunosuppressant drug level decreased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Immunosuppressant drug level increased			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Liver function test abnormal			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Oxygen saturation decreased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Transaminases increased			

subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Waist circumference increased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Incision site pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Incorrect dose administered			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Skin abrasion			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Tongue injury			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Toxicity to various agents			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Cardiac disorders			
Bradyarrhythmia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Pericardial effusion			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Nervous system disorders			

Benign intracranial hypertension			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Convulsion			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 24 (4.17%)	3 / 23 (13.04%)	3 / 22 (13.64%)
occurrences (all)	1	4	3
Hemiparesis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Sedation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Blood and lymphatic system disorders			
Bone marrow failure			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Coagulopathy			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Febrile neutropenia			

subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Granulocytopenia			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Neutropenia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Pancytopenia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Dry eye			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Eye haemorrhage			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Eye pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Eye swelling			
subjects affected / exposed	0 / 24 (0.00%)	2 / 23 (8.70%)	2 / 22 (9.09%)
occurrences (all)	0	2	2
Ocular icterus			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			

subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Vision blurred			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Abdominal tenderness			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Anal fissure			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Chapped lips			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Cheilitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 24 (0.00%)	2 / 23 (8.70%)	2 / 22 (9.09%)
occurrences (all)	0	2	2
Diarrhoea			
subjects affected / exposed	2 / 24 (8.33%)	5 / 23 (21.74%)	3 / 22 (13.64%)
occurrences (all)	2	5	3
Enteritis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0

Gingival bleeding			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Haematochezia			
subjects affected / exposed	0 / 24 (0.00%)	2 / 23 (8.70%)	1 / 22 (4.55%)
occurrences (all)	0	2	1
Ileus			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	4 / 24 (16.67%)	3 / 23 (13.04%)	2 / 22 (9.09%)
occurrences (all)	4	3	2
Neutropenic colitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Oral disorder			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Proctalgia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Rectal fissure			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Vomiting			
subjects affected / exposed	3 / 24 (12.50%)	3 / 23 (13.04%)	2 / 22 (9.09%)
occurrences (all)	4	4	3
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Jaundice			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 24 (8.33%)	3 / 23 (13.04%)	3 / 22 (13.64%)
occurrences (all)	2	3	3
Dermatitis diaper			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Erythema			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Ingrowing nail			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Pruritus			
subjects affected / exposed	4 / 24 (16.67%)	5 / 23 (21.74%)	1 / 22 (4.55%)
occurrences (all)	7	5	1
Rash			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Rash erythematous			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Rash macular			

subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Rash maculo-papular			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Haematuria			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthropathy			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Compartment syndrome			

subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	1 / 24 (4.17%)	2 / 23 (8.70%)	2 / 22 (9.09%)
occurrences (all)	1	2	2
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Bacterial sepsis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Candida infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	3 / 22 (13.64%)
occurrences (all)	1	1	3
Cytomegalovirus infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Enterococcal infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis adenovirus			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Human polyomavirus infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Staphylococcal bacteraemia			
subjects affected / exposed	2 / 24 (8.33%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Viral rash			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
Electrolyte imbalance			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Fluid retention			
subjects affected / exposed	1 / 24 (4.17%)	2 / 23 (8.70%)	1 / 22 (4.55%)
occurrences (all)	1	2	1
Hyperglycaemia			

subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Hypomagnesaemia			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Hyponatraemia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Cohort I: Voriconazole non-pharmacokinetic period	Cohort II: Voriconazole 6mg/kg Intravenous	Cohort II: Voriconazole 8mg/kg Intravenous
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 19 (89.47%)	19 / 24 (79.17%)	22 / 22 (100.00%)
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Haemorrhage			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	3 / 19 (15.79%)	4 / 24 (16.67%)	7 / 22 (31.82%)
occurrences (all)	3	4	7
Hypotension			

subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Venoocclusive disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Catheter site inflammation			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Catheter site pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Device occlusion			
subjects affected / exposed	3 / 19 (15.79%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Generalised oedema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Infusion site pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	4 / 19 (21.05%)	3 / 24 (12.50%)	7 / 22 (31.82%)
occurrences (all)	4	4	7
Mucosal pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Oedema			

subjects affected / exposed	1 / 19 (5.26%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Oedema peripheral			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Performance status decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	3 / 19 (15.79%)	2 / 24 (8.33%)	5 / 22 (22.73%)
occurrences (all)	4	3	8
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Graft versus host disease			
subjects affected / exposed	5 / 19 (26.32%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	5	0	1
Graft versus host disease in skin			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Serum sickness			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Genital erythema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Perineal erythema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	2
Atelectasis			

subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	1 / 19 (5.26%)	1 / 24 (4.17%)	3 / 22 (13.64%)
occurrences (all)	1	1	3
Dyspnoea			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	3 / 22 (13.64%)
occurrences (all)	0	1	4
Laryngospasm			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Pulmonary oedema			
subjects affected / exposed	1 / 19 (5.26%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Respiratory distress			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	2 / 19 (10.53%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Tachypnoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Agitation			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nightmare			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 19 (5.26%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Bacterial test positive			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood magnesium decreased			
subjects affected / exposed	2 / 19 (10.53%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	2	0	1
Blood phosphorus decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood potassium decreased			

subjects affected / exposed	1 / 19 (5.26%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Blood pressure increased			
subjects affected / exposed	2 / 19 (10.53%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Blood urea increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Cytomegalovirus test positive			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Drug level increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 19 (10.53%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	2	1	1
Hepatic enzyme increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Immunosuppressant drug level decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Immunosuppressant drug level increased			
subjects affected / exposed	1 / 19 (5.26%)	2 / 24 (8.33%)	2 / 22 (9.09%)
occurrences (all)	1	2	2
Liver function test abnormal			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Oxygen saturation decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			

subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Waist circumference increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Incision site pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Incorrect dose administered			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Tongue injury			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Toxicity to various agents			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bradyarrhythmia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Pericardial effusion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Nervous system disorders			

Benign intracranial hypertension			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Convulsion			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 19 (5.26%)	2 / 24 (8.33%)	0 / 22 (0.00%)
occurrences (all)	1	2	0
Hemiparesis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Lethargy			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Neuralgia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Sedation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Bone marrow failure			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Coagulopathy			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			

subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	2	0	1
Granulocytopenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Pancytopenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Eye haemorrhage			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Eye swelling			
subjects affected / exposed	1 / 19 (5.26%)	1 / 24 (4.17%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Ocular icterus			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			

subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	2
Abdominal tenderness			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Anal fissure			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Chapped lips			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Cheilitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	2 / 19 (10.53%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	2 / 19 (10.53%)	2 / 24 (8.33%)	3 / 22 (13.64%)
occurrences (all)	2	2	3
Enteritis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0

Gingival bleeding			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Ileus			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	3 / 19 (15.79%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	3	1	1
Neutropenic colitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Oral disorder			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Rectal fissure			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Toothache			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0

Vomiting			
subjects affected / exposed	1 / 19 (5.26%)	2 / 24 (8.33%)	3 / 22 (13.64%)
occurrences (all)	1	2	6
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Jaundice			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 19 (15.79%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Dermatitis diaper			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Petechiae			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Pruritus			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Rash			
subjects affected / exposed	4 / 19 (21.05%)	6 / 24 (25.00%)	8 / 22 (36.36%)
occurrences (all)	4	6	9
Rash erythematous			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Rash macular			

subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Rash pruritic			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Renal failure			
subjects affected / exposed	2 / 19 (10.53%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	2	1	1
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthropathy			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Bone pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Compartment syndrome			

subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	3 / 19 (15.79%)	1 / 24 (4.17%)	1 / 22 (4.55%)
occurrences (all)	4	1	1
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Bacterial sepsis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Candida infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	2 / 19 (10.53%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Cytomegalovirus infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Enterococcal infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis adenovirus			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Human polyomavirus infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Viral rash			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Electrolyte imbalance			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Fluid retention			
subjects affected / exposed	1 / 19 (5.26%)	3 / 24 (12.50%)	4 / 22 (18.18%)
occurrences (all)	1	3	4
Hyperglycaemia			

subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Hypomagnesaemia			
subjects affected / exposed	1 / 19 (5.26%)	2 / 24 (8.33%)	2 / 22 (9.09%)
occurrences (all)	1	2	2
Hyponatraemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 19 (0.00%)	0 / 24 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort II: Voriconazole 6mg/kg Oral Suspension	Cohort II: Voriconazole non-pharmacokinetic period	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)	12 / 12 (100.00%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	8 / 20 (40.00%)	5 / 12 (41.67%)	
occurrences (all)	9	5	
Hypotension			

subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Venoocclusive disease			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Catheter site inflammation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Catheter site pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Chest pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Chills			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Device occlusion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Generalised oedema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Infusion site pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Mucosal inflammation			
subjects affected / exposed	4 / 20 (20.00%)	2 / 12 (16.67%)	
occurrences (all)	4	2	
Mucosal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Oedema			

subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Oedema peripheral			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Performance status decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	1 / 20 (5.00%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Graft versus host disease			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Graft versus host disease in skin			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Serum sickness			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Genital erythema			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Perineal erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Atelectasis			

subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Dyspnoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Laryngospasm			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Nasal congestion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pleural effusion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Pulmonary oedema			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Respiratory distress			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Tachypnoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			

Agitation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Confusional state			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hallucination			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Nightmare			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Bacterial test positive			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	3	
Blood bilirubin increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Blood magnesium decreased			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Blood phosphorus decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Blood potassium decreased			

subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Blood pressure increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Blood urea increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Cytomegalovirus test positive			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Drug level increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Immunosuppressant drug level decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Immunosuppressant drug level increased			
subjects affected / exposed	2 / 20 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Liver function test abnormal			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Oxygen saturation decreased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Transaminases increased			

subjects affected / exposed	2 / 20 (10.00%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Waist circumference increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Incision site pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Incorrect dose administered			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Skin abrasion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Tongue injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Toxicity to various agents			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Bradyarrhythmia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pericardial effusion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			

Benign intracranial hypertension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Convulsion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hemiparesis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Lethargy			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Neuralgia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Sedation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Somnolence			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Bone marrow failure			
subjects affected / exposed	2 / 20 (10.00%)	2 / 12 (16.67%)	
occurrences (all)	2	2	
Coagulopathy			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Febrile neutropenia			

subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Granulocytopenia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Neutropenia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pancytopenia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Dry eye			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Eye haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Eye pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Eye swelling			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Ocular icterus			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Periorbital oedema			

subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Photophobia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Vision blurred			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Abdominal tenderness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Anal fissure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Chapped lips			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Cheilitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	1 / 20 (5.00%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Enteritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	

Gingival bleeding			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Haematochezia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Ileus			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Mouth ulceration			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Neutropenic colitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Oral disorder			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Proctalgia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Rectal fissure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	

Vomiting			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Jaundice			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Dermatitis diaper			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Ingrowing nail			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Petechiae			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	5 / 20 (25.00%)	2 / 12 (16.67%)	
occurrences (all)	5	2	
Rash erythematous			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Rash macular			

subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Rash maculo-papular			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Rash pruritic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Urticaria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Haematuria			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Renal failure			
subjects affected / exposed	2 / 20 (10.00%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Arthropathy			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	2 / 20 (10.00%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Bone pain			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Compartment syndrome			

subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	2 / 20 (10.00%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Bacterial sepsis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Bronchitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Candida infection			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Conjunctivitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Cytomegalovirus infection			
subjects affected / exposed	2 / 20 (10.00%)	2 / 12 (16.67%)	
occurrences (all)	2	2	
Enterococcal infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastroenteritis adenovirus			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Gastroenteritis viral			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	

Human polyomavirus infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Paronychia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pneumonia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Rhinitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Viral infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Viral rash			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Electrolyte imbalance			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Fluid retention			
subjects affected / exposed	4 / 20 (20.00%)	2 / 12 (16.67%)	
occurrences (all)	4	2	
Hyperglycaemia			

subjects affected / exposed	2 / 20 (10.00%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Hyperkalaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hypokalaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Hypomagnesaemia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Hyponatraemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 20 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 April 2003	If Voriconazole treatment was stopped between Days 12 to Day 30 a physical examination and safety laboratory tests and a serum pregnancy test (for females with child bearing potential only) were to be performed on the last Day of dosing. If abnormalities were observed in any of the laboratory tests, those tests was to be repeated every 5-7 Days until they return to the normal, or until a reason for the abnormality was determined.
08 June 2004	Any serious adverse event or death was to be reported immediately independent of the circumstances or suspected cause if it occurred or came to the attention of the investigator at any time during the study through the one month follow-up visit required by the protocol or 30 Days after the last administration of study drug, whichever came later. Any serious adverse event occurring at any other time after completion of the study promptly reported if a causal relationship to study drug was suspected. The only exception to these reporting requirements were serious adverse events that occurred during a prerandomization/washout run-in period, during which either placebo alone was administered, or no active study drug or no protocol-specified background drug was administered.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported