Clinical trial results:
A Study of the Safety, Tolerability, and Pharmacokinetics of Intravenous (IV) and Powder for Oral Suspension Formulations of Posaconazole (POS) in Immunocompromised Pediatric Subjects with Neutropenia

Summary

EudraCT number	2014-002807-10
Trial protocol	DE NO SE DK CZ ES BE IT Outside EU/EEA
Global end of trial date	03 September 2018

Results information

Result version number	v2 (current)
This version publication date	08 May 2020
First version publication date	09 March 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	5592-097

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02452034
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000468-PIP02-12
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study aims to evaluate the pharmacokinetics (PK) of posaconazole (POS) administered intravenously (IV) or orally to immunocompromised pediatric participants.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 September 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Czech Republic: 19
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Germany: 27
Country: Number of subjects enrolled	Guatemala: 4
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Norway: 7
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	Thailand: 5
Country: Number of subjects enrolled	United States: 23
Worldwide total number of subjects	118
EEA total number of subjects	86

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)	73
Adolescents (12-17 years)	45
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:

Immunocompromised participants aged 2 to 17 years old, with neutropenia expected to last for at least 7 days following start of study treatment, were enrolled in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	3.5 mg/kg POS (2-7 years old)

Arm description:

Children 2 to less than 7 years of age received posaconazole (POS) at 3.5 mg/kg by intravenous (IV) solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by powder for oral suspension (PFS) for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Arm type	Experimental
Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	Noxafil
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Posaconazole at 3.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10.

Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	Noxafil
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Posaconazole at 3.5 mg/kg once daily by PFS for a minimum of 10 days

Arm title	3.5 mg/kg POS (7-17 years old)

Arm description:

Children 7 to 17 years of age received POS at 3.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Arm type	Experimental
Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	Noxafil
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Posaconazole at 3.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10.

Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	Noxafil
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Posaconazole at 3.5 mg/kg once daily by PFS for a minimum of 10 days

Arm title	4.5 mg/kg POS (2-7 years old)

Arm description:

Children 2 to less than 7 years of age received POS at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Arm type	Experimental
Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	Noxafil
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Posaconazole at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10.

Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	Noxafil
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Posaconazole at 4.5 mg/kg once daily by PFS for a minimum of 10 days

Arm title	4.5 mg/kg POS (7-17 years old)

Arm description:

Children 7 to 17 years of age received POS at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Arm type	Experimental
Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	Noxafil
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Posaconazole at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10.

Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	Noxafil
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Posaconazole at 4.5 mg/kg once daily by PFS for a minimum of 10 days

Arm title	6 mg/kg POS (2-7 years old)

Arm description:

Children 2 to less than 7 years of age received POS at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Arm type	Experimental
Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	Noxafil
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Posaconazole at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10.

Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	Noxafil
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Posaconazole at 6 mg/kg once daily by PFS for a minimum of 10 days

Arm title	6 mg/kg POS (7-17 years old)

Arm description:

Children 7 to 17 years of age received POS at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Arm type	Experimental
Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	Noxafil
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Posaconazole at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10.

Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	Noxafil
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Posaconazole at 6 mg/kg once daily by PFS for a minimum of 10 days

Number of subjects in period 1	3.5 mg/kg POS (2-7 years old)	3.5 mg/kg POS (7-17 years old)	4.5 mg/kg POS (2-7 years old)
Started	16	21	15
Treated	14	21	15
Completed	14	20	14
Not completed	2	1	1
Physician decision	-	1	1
Screen Failure	1	-	-
Adverse event, non-fatal	-	-	-
Death	-	-	-
Withdrawn by Parent/Guardian	1	-	-

Protocol deviation	-	-	-

Number of subjects in period 1	4.5 mg/kg POS (7-17 years old)	6 mg/kg POS (2-7 years old)	6 mg/kg POS (7-17 years old)
Started	17	20	29
Treated	16	20	29
Completed	16	19	26
Not completed	1	1	3
Physician decision	-	-	-
Screen Failure	1	-	-
Adverse event, non-fatal	-	-	1
Death	-	1	1
Withdrawn by Parent/Guardian	-	-	-
Protocol deviation	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	3.5 mg/kg POS (2-7 years old)
Reporting group description:	
Children 2 to less than 7 years of age received posaconazole (POS) at 3.5 mg/kg by intravenous (IV) solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by powder for oral suspension (PFS) for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.	
Reporting group title	3.5 mg/kg POS (7-17 years old)
Reporting group description:	
Children 7 to 17 years of age received POS at 3.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.	
Reporting group title	4.5 mg/kg POS (2-7 years old)
Reporting group description:	
Children 2 to less than 7 years of age received POS at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.	
Reporting group title	4.5 mg/kg POS (7-17 years old)
Reporting group description:	
Children 7 to 17 years of age received POS at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.	
Reporting group title	6 mg/kg POS (2-7 years old)
Reporting group description:	
Children 2 to less than 7 years of age received POS at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.	
Reporting group title	6 mg/kg POS (7-17 years old)
Reporting group description:	
Children 7 to 17 years of age received POS at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.	

Reporting group values	3.5 mg/kg POS (2-7 years old)	3.5 mg/kg POS (7-17 years old)	4.5 mg/kg POS (2-7 years old)
Number of subjects	16	21	15
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	16	4	15
Adolescents (12-17 years)	0	17	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0

Age Continuous			
Units: years			
arithmetic mean	3.9	13.9	4.1
standard deviation	± 1.5	± 2.1	± 1.4
Gender Categorical			
Units: Subjects			
Female	3	11	8
Male	13	10	7
Race			
Units: Subjects			
Asian	4	1	2
Black Or African American	0	0	0
Multiple	0	2	0
Native Hawaiian Or Other Pacific Islander	0	0	1
White	12	18	12
Ethnicity			
Units: Subjects			
Hispanic Or Latino	1	2	2
Not Hispanic Or Latino	15	19	12
Not Reported	0	0	1
Unknown	0	0	0

Reporting group values	4.5 mg/kg POS (7-17 years old)	6 mg/kg POS (2-7 years old)	6 mg/kg POS (7-17 years old)
Number of subjects	17	20	29
Age Categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	5	20	13
Adolescents (12-17 years)	12	0	16
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	12.5	3.9	12.0
standard deviation	± 2.7	± 1.6	± 3.5
Gender Categorical			
Units: Subjects			
Female	8	10	10
Male	9	10	19
Race			
Units: Subjects			
Asian	2	1	1
Black Or African American	0	1	2
Multiple	2	0	0

Native Hawaiian Or Other Pacific Islander	0	0	0
White	13	18	26
Ethnicity			
Units: Subjects			
Hispanic Or Latino	4	1	2
Not Hispanic Or Latino	12	18	27
Not Reported	1	0	0
Unknown	0	1	0

Reporting group values	Total		
Number of subjects	118		
Age Categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	73		
Adolescents (12-17 years)	45		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical			
Units: Subjects			
Female	50		
Male	68		
Race			
Units: Subjects			
Asian	11		
Black Or African American	3		
Multiple	4		
Native Hawaiian Or Other Pacific Islander	1		
White	99		
Ethnicity			
Units: Subjects			
Hispanic Or Latino	12		
Not Hispanic Or Latino	103		
Not Reported	2		
Unknown	1		

End points

End points reporting groups

Reporting group title	3.5 mg/kg POS (2-7 years old)

Reporting group description:

Children 2 to less than 7 years of age received posaconazole (POS) at 3.5 mg/kg by intravenous (IV) solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by powder for oral suspension (PFS) for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Reporting group title	3.5 mg/kg POS (7-17 years old)

Reporting group description:

Children 7 to 17 years of age received POS at 3.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Reporting group title	4.5 mg/kg POS (2-7 years old)

Reporting group description:

Children 2 to less than 7 years of age received POS at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Reporting group title	4.5 mg/kg POS (7-17 years old)

Reporting group description:

Children 7 to 17 years of age received POS at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Reporting group title	6 mg/kg POS (2-7 years old)

Reporting group description:

Children 2 to less than 7 years of age received POS at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Reporting group title	6 mg/kg POS (7-17 years old)

Reporting group description:

Children 7 to 17 years of age received POS at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Primary: Area under the plasma concentration versus time curve (AUC) from time 0 to 24 hours post-dose for POS

End point title	Area under the plasma concentration versus time curve (AUC) from time 0 to 24 hours post-dose for POS[1]

End point description:

Blood was collected from pre-dose up to 24 hours post-dose in order to determine the plasma AUC from time 0-24 hours post-dose (AUC0- 24hr) of posaconazole. A non-compartmental analysis of posaconazole plasma concentrations was performed. Results are reported for each treatment arm according to the formulation that participants received (IV or PFS). Participants receiving both formulations were counted once for each formulation. The population analyzed was all treated participants who received at least 7 days of POS dosing (IV and PFS), completed the full POS PK sampling, and met pre-specified acceptability criteria.

End point type	Primary

End point timeframe:

Any day from Day 7 to Day 10 of therapy for each formulation (up to 28 days) at pre-dose, within 15 minutes after end of infusion (up to 2 hours), and 4, 6, 8, 12, 24 hours post-infusion

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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	3.5 mg/kg POS (2-7 years old)	3.5 mg/kg POS (7-17 years old)	4.5 mg/kg POS (2-7 years old)	4.5 mg/kg POS (7-17 years old)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[2]	19[3]	14[4]	15[5]
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)				
IV	17800 (± 55.0)	27300 (± 49.7)	25600 (± 30.0)	29800 (± 42.9)
PFS	12200 (± 36.0)	20700 (± 33.8)	21600 (± 64.5)	28700 (± 33.7)

Notes:

[2] - IV n= 11; PFS n= 5

[3] - IV n= 19; PFS n= 10

[4] - IV n= 14; PFS n= 8

[5] - IV n= 15; PFS n= 8

End point values	6 mg/kg POS (2-7 years old)	6 mg/kg POS (7-17 years old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[6]	24[7]		
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)				
IV	31100 (± 48.9)	44200 (± 41.5)		
PFS	23000 (± 47.3)	25000 (± 184.3)		

Notes:

[6] - IV n= 17; PFS n= 7

[7] - IV n= 24; PFS n= 12

Statistical analyses

No statistical analyses for this end point

Primary: Maximum plasma concentration (Cmax) for POS

End point title	Maximum plasma concentration (Cmax) for POS[8]

End point description:

Blood was collected from pre-dose up to 24 hours post-dose in order to determine the plasma Cmax of posaconazole. A noncompartmental analysis of posaconazole plasma concentrations was performed. Results are reported for each treatment arm according to the formulation that participants received (IV or PFS). Participants receiving both formulations were counted once for each formulation. The population analyzed was all treated participants who received at least 7 days of POS dosing (IV and PFS), completed the full POS PK sampling, and met pre-specified acceptability criteria.

End point type	Primary

End point timeframe:

Any day from Day 7 to Day 10 of therapy for each formulation (up to 28 days) at pre-dose, within 15 minutes after end of infusion (up to 2 hours), and 4, 6, 8, 12, 24 hours post-infusion

Notes:

[8] - 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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	3.5 mg/kg POS (2-7 years old)	3.5 mg/kg POS (7-17 years old)	4.5 mg/kg POS (2-7 years old)	4.5 mg/kg POS (7-17 years old)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[9]	19[10]	14[11]	15[12]
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
IV	1590 (± 43.1)	2450 (± 72.7)	2320 (± 39.8)	2310 (± 40.3)
PFS	884 (± 44.4)	1340 (± 30.8)	1550 (± 40.8)	1670 (± 28.5)

Notes:

[9] - IV n=11; PFS n=5

[10] - IV n=19; PFS n=10

[11] - IV n=14; PFS n=8

[12] - IV n=15; PFS n=8

End point values	6 mg/kg POS (2-7 years old)	6 mg/kg POS (7-17 years old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[13]	24[14]		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
IV	3060 (± 54.1)	3340 (± 39.4)		
PFS	1510 (± 43.4)	1370 (± 178.5)		

Notes:

[13] - IV n=17; PFS n=7

[14] - IV n=24; PFS n=12

Statistical analyses

No statistical analyses for this end point

Primary: Minimum plasma concentration (Cmin) for POS

End point title	Minimum plasma concentration (Cmin) for POS[15]

End point description:

Blood was collected from pre-dose up to 24 hours post-dose in order to determine the plasma Cmin of posaconazole. A non-compartmental analysis of posaconazole plasma concentrations was performed. Results are reported for each treatment arm according to the formulation that participants received (IV or PFS). Participants receiving both formulations were counted once for each formulation. The population analyzed was all treated participants who received at least 7 days of POS dosing (IV and PFS), completed the full POS PK sampling, and met pre-specified acceptability criteria.

End point type	Primary

End point timeframe:

Any day from Day 7 to Day 10 of therapy for each formulation (up to 28 days) at pre-dose, within 15 minutes after end of infusion (up to 2 hours), and 4, 6, 8, 12, 24 hours post-infusion

Notes:

[15] - 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: Statistical comparisons between treatment groups were neither planned nor performed for

this primary endpoint.

End point values	3.5 mg/kg POS (2-7 years old)	3.5 mg/kg POS (7-17 years old)	4.5 mg/kg POS (2-7 years old)	4.5 mg/kg POS (7-17 years old)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[16]	19[17]	14[18]	15[19]
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
IV	400 (± 81.3)	670 (± 65.1)	501 (± 56.8)	737 (± 66.0)
PFS	254 (± 45.6)	579 (± 44.9)	476 (± 164.6)	790 (± 48.2)

Notes:

[16] - IV n=11; PFS n=5

[17] - IV n=19; PFS n=10

[18] - IV n=14; PFS n=8

[19] - IV n=15; PFS n=8

End point values	6 mg/kg POS (2-7 years old)	6 mg/kg POS (7-17 years old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[20]	24[21]		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
IV	626 (± 104.8)	1160 (± 60.4)		
PFS	542 (± 68.8)	713 (± 300.6)		

Notes:

[20] - IV n=17; PFS n=7

[21] - IV n=24; PFS n=12

Statistical analyses

No statistical analyses for this end point

Primary: Average steady-state plasma concentration (Cavg) for POS

End point title	Average steady-state plasma concentration (Cavg) for POS[22]

End point description:

Blood was collected from pre-dose up to 24 hours post-dose in order to determine the plasma Cavg of posaconazole. A non-compartmental analysis of posaconazole plasma concentrations was performed. Results are reported for each treatment arm according to the formulation that participants received (IV or PFS). Participants receiving both formulations were counted once for each formulation. The population analyzed was all treated participants who received at least 7 days of POS dosing (IV and PFS), completed the full POS PK sampling, and met pre-specified acceptability criteria.

End point type	Primary

End point timeframe:

Any day from Day 7 to Day 10 of therapy for each formulation (up to 28 days) at pre-dose, within 15 minutes after end of infusion (up to 2 hours), and 4, 6, 8, 12, 24 hours post-infusion

Notes:

[22] - 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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	3.5 mg/kg POS (2-7 years old)	3.5 mg/kg POS (7-17 years old)	4.5 mg/kg POS (2-7 years old)	4.5 mg/kg POS (7-17 years old)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[23]	19[24]	14[25]	15[26]
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
IV	743 (± 55.0)	1140 (± 49.7)	1070 (± 30.0)	1240 (± 42.9)
PFS	510 (± 36.0)	861 (± 33.8)	901 (± 64.5)	1200 (± 33.7)

Notes:

[23] - IV n=11; PFS n=5

[24] - IV n=19; PFS n=10

[25] - IV n=14; PFS n=8

[26] - IV n=15; PFS n=8

End point values	6 mg/kg POS (2-7 years old)	6 mg/kg POS (7-17 years old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[27]	24[28]		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
IV	1300 (± 48.9)	1840 (± 41.5)		
PFS	960 (± 47.3)	1040 (± 184.3)		

Notes:

[27] - IV n=17; PFS n=7

[28] - IV n=24; PFS n=12

Statistical analyses

No statistical analyses for this end point

Primary: Time of maximum plasma concentration (Tmax) for POS

End point title	Time of maximum plasma concentration (Tmax) for POS[29]

End point description:

Blood was collected from pre-dose up to 24 hours post-dose in order to determine the plasma Tmax of posaconazole. A non-compartmental analysis of posaconazole plasma concentrations was performed. Results are reported for each treatment arm according to the formulation that participants received (IV or PFS). Participants receiving both formulations were counted once for each formulation. The population analyzed was all treated participants who received at least 7 days of POS dosing (IV and PFS), completed the full POS PK sampling, and met pre-specified acceptability criteria.

End point type	Primary

End point timeframe:

Any day from Day 7 to Day 10 of therapy for each formulation (up to 28 days) at pre-dose, within 15 minutes after end of infusion (up to 2 hours), and 4, 6, 8, 12, 24 hours post-infusion

Notes:

[29] - 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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	3.5 mg/kg POS (2-7 years old)	3.5 mg/kg POS (7-17 years old)	4.5 mg/kg POS (2-7 years old)	4.5 mg/kg POS (7-17 years old)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[30]	19[31]	14[32]	15[33]
Units: Hours				
median (full range (min-max))				
IV	1.78 (1.67 to 5.53)	1.77 (0.00 to 3.50)	1.78 (1.42 to 5.90)	1.75 (1.52 to 1.80)
PFS	3.83 (1.92 to 4.25)	2.20 (1.92 to 6.03)	3.82 (1.88 to 5.92)	6.14 (1.98 to 7.98)

Notes:

[30] - IV n=11; PFS n=5

[31] - IV n=19; PFS n=10

[32] - IV n=14; PFS n=8

[33] - IV n=15; PFS n=8

End point values	6 mg/kg POS (2-7 years old)	6 mg/kg POS (7-17 years old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[34]	24[35]		
Units: Hours				
median (full range (min-max))				
IV	1.75 (1.57 to 1.83)	1.77 (1.33 to 6.00)		
PFS	4.00 (2.17 to 7.92)	2.78 (0.00 to 4.00)		

Notes:

[34] - IV n=17; PFS n=7

[35] - IV n=24; PFS n=12

Statistical analyses

No statistical analyses for this end point

Primary: Total body clearance (CL) for POS administered by IV

End point title	Total body clearance (CL) for POS administered by IV[36]

End point description:

Blood was collected from pre-dose up to 24 hours post-dose in order to determine the plasma CL of posaconazole administered by IV. A non-compartmental analysis of posaconazole plasma concentrations was performed. Results are reported for participants that received IV treatment. The population analyzed was all treated participants who received at least 7 days of POS IV solution therapy, completed the full POS PK sampling while on POS IV solution, and met pre-specified acceptability criteria.

End point type	Primary

End point timeframe:

Any day from Day 7 to Day 10 of therapy at pre-dose, within 15 minutes after end of infusion (up to 2 hours), and 4, 6, 8, 12, 24 hours post-infusion

Notes:

[36] - 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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	3.5 mg/kg POS (2-7 years old)	3.5 mg/kg POS (7-17 years old)	4.5 mg/kg POS (2-7 years old)	4.5 mg/kg POS (7-17 years old)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	19	14	15
Units: L/hr				
geometric mean (geometric coefficient of variation)	3.39 (± 52.8)	6.64 (± 38.6)	2.97 (± 36.2)	6.69 (± 37.3)

End point values	6 mg/kg POS (2-7 years old)	6 mg/kg POS (7-17 years old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	24		
Units: L/hr				
geometric mean (geometric coefficient of variation)	3.27 (± 49.3)	4.76 (± 55.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Apparent total body clearance (CL/F) for POS administered by PFS

End point title	Apparent total body clearance (CL/F) for POS administered by PFS[37]

End point description:

Blood was collected from pre-dose up to 24 hours post-dose in order to determine the plasma CL/F of posaconazole administered by PFS. A non-compartmental analysis of posaconazole plasma concentrations was performed. Results are reported for participants that received PFS treatment. The population analyzed was all treated participants who received at least 7 days of POS PFS therapy, completed the full POS PK sampling while on POS PFS, and met pre-specified acceptability criteria.

End point type	Primary

End point timeframe:

Any day from Day 7 to Day 10 of therapy (up to 28 days) at pre-dose, within 15 minutes after end of infusion (up to 2 hours), and 4, 6, 8, 12, 24 hours post-infusion

Notes:

[37] - 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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	3.5 mg/kg POS (2-7 years old)	3.5 mg/kg POS (7-17 years old)	4.5 mg/kg POS (2-7 years old)	4.5 mg/kg POS (7-17 years old)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	10	8	8
Units: L/hr				
geometric mean (geometric coefficient of variation)	4.97 (± 29.1)	7.67 (± 39.9)	3.49 (± 59.1)	7.84 (± 49.4)

End point values	6 mg/kg POS (2-7 years old)	6 mg/kg POS (7-17 years old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	12		
Units: L/hr				
geometric mean (geometric coefficient of variation)	4.60 (± 35.2)	8.39 (± 190.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with an Adverse Event (AE)

End point title	Number of participants with an Adverse Event (AE)

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product or protocol - specified procedure, whether or not considered related to the medicinal product or protocol - specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. The population analyzed was all participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

14 days after end of treatment (Up to 42 days)

End point values	3.5 mg/kg POS (2-7 years old)	3.5 mg/kg POS (7-17 years old)	4.5 mg/kg POS (2-7 years old)	4.5 mg/kg POS (7-17 years old)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	21	15	16
Units: Participants	13	21	15	16

End point values	6 mg/kg POS (2-7 years old)	6 mg/kg POS (7-17 years old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	29		
Units: Participants	19	29		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who discontinued treatment of study drug due to an Adverse Event (AE)

End point title	Number of participants who discontinued treatment of study drug due to an Adverse Event (AE)

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product or protocol - specified procedure, whether or not considered related to the medicinal product or protocol - specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. The population analyzed was all participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	3.5 mg/kg POS (2-7 years old)	3.5 mg/kg POS (7-17 years old)	4.5 mg/kg POS (2-7 years old)	4.5 mg/kg POS (7-17 years old)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	21	15	16
Units: Participants	3	3	0	2

End point values	6 mg/kg POS (2-7 years old)	6 mg/kg POS (7-17 years old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	29		
Units: Participants	4	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

14 days after end of treatment (up to day 42)

Adverse event reporting additional description:

All participants who received at least one dose of study drug. Participants were followed for survival up to 110 days; and deaths that occurred outside of the timeframe for adverse event reporting were recorded in the Disposition

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	3.5 mg/kg posaconazole (2-<7 years old)

Reporting group description:

Children 2 to less than 7 years of age received posaconazole (POS) at 3.5 mg/kg by intravenous (IV) solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by powder for oral suspension (PFS) for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Reporting group title	3.5 mg/kg posaconazole (7-17 years old)

Reporting group description:

Children 7 to 17 years of age received POS at 3.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Reporting group title	4.5 mg/kg posaconazole (2-<7 years old)

Reporting group description:

Children 2 to less than 7 years of age received posaconazole (POS) at 4.5 mg/kg by intravenous (IV) solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by powder for oral suspension (PFS) for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Reporting group title	4.5 mg/kg posaconazole (7-17 years old)

Reporting group description:

Children 7 to 17 years of age received POS at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Reporting group title	6.0 mg/kg posaconazole (2-<7 years old)

Reporting group description:

Children 2 to less than 7 years of age received posaconazole (POS) at 6 mg/kg by intravenous (IV) solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by powder for oral suspension (PFS) for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Reporting group title	6.0 mg/kg posaconazole (7-17 years old)

Reporting group description:

Children 7 to 17 years of age received POS at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

Serious adverse events	3.5 mg/kg posaconazole (2-<7 years old)	3.5 mg/kg posaconazole (7-17 years old)	4.5 mg/kg posaconazole (2-<7 years old)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 14 (21.43%)	8 / 21 (38.10%)	4 / 15 (26.67%)

number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Hypertension			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Thrombophlebitis superficial			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Venoocclusive disease			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 21 (9.52%)	0 / 15 (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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Engraftment syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transplant rejection			

subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Respiratory failure			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (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
Cardiomyopathy			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Presyncope			

subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Stomatitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Vomiting			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Hepatobiliary disorders			
Hepatic lesion			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venoocclusive liver disease			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Renal failure			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (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
Musculoskeletal and connective tissue disorders			
Chest wall haematoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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			
Adenovirus infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Enterobacter infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (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

Fungal infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Herpes zoster			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Pneumonia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal sepsis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Systemic mycosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection viral			

subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (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			
Hyponatraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (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

Serious adverse events	4.5 mg/kg posaconazole (7-17 years old)	6.0 mg/kg posaconazole (2-<7 years old)	6.0 mg/kg posaconazole (7-17 years old)
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 16 (31.25%)	3 / 20 (15.00%)	8 / 29 (27.59%)
number of deaths (all causes)	0	0	2
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis superficial			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (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
Venoocclusive disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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			
Drug hypersensitivity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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
Engraftment syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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
Transplant rejection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
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			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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
Hypoxia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (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 failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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

Cardiomyopathy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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			
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (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
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic lesion			

subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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
Venoocclusive liver disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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
Musculoskeletal and connective tissue disorders			
Chest wall haematoma			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (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			
Adenovirus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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
Cystitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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

Device related infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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
Fungal infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (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
Herpes zoster			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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
Parainfluenzae virus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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
Pneumonia viral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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
Streptococcal sepsis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (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
Systemic mycosis			

subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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
Urinary tract infection viral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (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

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

Non-serious adverse events	3.5 mg/kg posaconazole (2-<7 years old)	3.5 mg/kg posaconazole (7-17 years old)	4.5 mg/kg posaconazole (2-<7 years old)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 14 (92.86%)	20 / 21 (95.24%)	15 / 15 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	1 / 14 (7.14%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Haematoma			

subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hyperaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	5 / 14 (35.71%)	2 / 21 (9.52%)	2 / 15 (13.33%)
occurrences (all)	5	2	2
Hypotension			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pallor			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Phlebitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Venoocclusive disease			
subjects affected / exposed	2 / 14 (14.29%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
General disorders and administration site conditions			
Axillary pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Catheter site erythema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Catheter site haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Catheter site oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			

subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Catheter site swelling			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Face oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 14 (7.14%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
General physical health deterioration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Generalised oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Granuloma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Infusion site erythema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	3 / 14 (21.43%)	9 / 21 (42.86%)	5 / 15 (33.33%)
occurrences (all)	3	10	5
Oedema			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			

subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	8 / 14 (57.14%)	9 / 21 (42.86%)	6 / 15 (40.00%)
occurrences (all)	13	11	9
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Engraftment syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Graft versus host disease			
subjects affected / exposed	2 / 14 (14.29%)	2 / 21 (9.52%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Graft versus host disease in liver			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Graft versus host disease in skin			
subjects affected / exposed	0 / 14 (0.00%)	2 / 21 (9.52%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Immunodeficiency			

subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Immunodeficiency common variable			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Serum sickness			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Metrorrhagia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Perineal erythema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Perineal pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Scrotal oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Testicular oedema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal inflammation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal pruritus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	2 / 14 (14.29%)	0 / 21 (0.00%)	4 / 15 (26.67%)
occurrences (all)	2	0	4
Dysphonia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 14 (0.00%)	2 / 21 (9.52%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Epistaxis			
subjects affected / exposed	2 / 14 (14.29%)	1 / 21 (4.76%)	1 / 15 (6.67%)
occurrences (all)	4	1	1
Haemoptysis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 21 (9.52%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Increased viscosity of bronchial secretion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Lung infiltration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Pharyngeal inflammation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			

subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pleuritic pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tonsillar exudate			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Depressed mood			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Depression			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Irritability			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
BK polyomavirus test positive			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Bacterial test positive			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood albumin decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	1 / 14 (7.14%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Blood calcium decreased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			

subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Blood culture positive			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Blood immunoglobulin G decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood magnesium decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Blood potassium decreased			
subjects affected / exposed	1 / 14 (7.14%)	2 / 21 (9.52%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Blood potassium increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood uric acid decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Breath sounds abnormal			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0

C-reactive protein increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Cytomegalovirus test positive			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Drug level increased			
subjects affected / exposed	0 / 14 (0.00%)	2 / 21 (9.52%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Fibrin D dimer increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Fluid balance positive			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oxygen saturation decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Platelet count decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Pulmonary arterial pressure increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Red blood cells urine positive			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			

subjects affected / exposed	2 / 14 (14.29%)	1 / 21 (4.76%)	1 / 15 (6.67%)
occurrences (all)	2	1	1
Viral test positive			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Vitamin D decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Allergic transfusion reaction			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Buttock injury			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Eye contusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Head injury			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Infusion related reaction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Procedural pain			

subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Scratch			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Transfusion reaction			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pericardial effusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	1 / 14 (7.14%)	2 / 21 (9.52%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	1 / 14 (7.14%)	4 / 21 (19.05%)	0 / 15 (0.00%)
occurrences (all)	1	4	0
Hypoaesthesia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypotonia			

subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Intention tremor			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Myoclonus			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Opisthotonus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Anaemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 21 (4.76%)	1 / 15 (6.67%)
occurrences (all)	4	1	2
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	2 / 14 (14.29%)	3 / 21 (14.29%)	2 / 15 (13.33%)
occurrences (all)	2	3	2
Leukopenia			

subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 21 (9.52%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Pancytopenia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Splenomegaly			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 21 (9.52%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Ear and labyrinth disorders			
Ear haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Ear pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tinnitus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Dry eye			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Eye haemorrhage			

subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Eyelid oedema			
subjects affected / exposed	2 / 14 (14.29%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Periorbital oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Vision blurred			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	2 / 14 (14.29%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Abdominal pain			
subjects affected / exposed	2 / 14 (14.29%)	2 / 21 (9.52%)	2 / 15 (13.33%)
occurrences (all)	2	2	2

Abdominal pain upper			
subjects affected / exposed	1 / 14 (7.14%)	2 / 21 (9.52%)	2 / 15 (13.33%)
occurrences (all)	1	2	2
Anal fissure			
subjects affected / exposed	0 / 14 (0.00%)	2 / 21 (9.52%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Anal inflammation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Anorectal discomfort			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Anorectal disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Aphthous ulcer			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Colitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	3 / 14 (21.43%)	2 / 21 (9.52%)	2 / 15 (13.33%)
occurrences (all)	3	2	2
Diarrhoea			
subjects affected / exposed	5 / 14 (35.71%)	2 / 21 (9.52%)	5 / 15 (33.33%)
occurrences (all)	5	2	5
Dyspepsia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

Faeces hard			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Gingival bleeding			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Glossodynia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Haematemesis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Haematochezia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Lip pruritus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Loose tooth			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Mouth ulceration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 14 (7.14%)	4 / 21 (19.05%)	1 / 15 (6.67%)
occurrences (all)	1	5	1
Odynophagia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Oesophagitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oral disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oral mucosal blistering			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oral mucosal exfoliation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oral pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Scalloped tongue			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 14 (0.00%)	2 / 21 (9.52%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Subileus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Tongue haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tooth loss			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	4 / 14 (28.57%)	6 / 21 (28.57%)	2 / 15 (13.33%)
occurrences (all)	6	9	3
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Jaundice			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Blister			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Dermatitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dermatitis atopic			

subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dermatitis bullous			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Dermatitis diaper			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Drug eruption			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Erythema multiforme			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Macule			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Palmar erythema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Papule			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Petechiae			

subjects affected / exposed	1 / 14 (7.14%)	1 / 21 (4.76%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Pruritus			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Pruritus allergic			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	2 / 14 (14.29%)	4 / 21 (19.05%)	3 / 15 (20.00%)
occurrences (all)	3	4	4
Rash generalised			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin burning sensation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Skin exfoliation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Skin hyperpigmentation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	1 / 14 (7.14%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Skin mass			

subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Swelling face			
subjects affected / exposed	1 / 14 (7.14%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Urticaria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Cystitis haemorrhagic			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Glycosuria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Micturition urgency			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nephropathy toxic			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

Tubulointerstitial nephritis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Bone pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Joint range of motion decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Muscle tightness			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			

subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	2 / 14 (14.29%)	1 / 21 (4.76%)	1 / 15 (6.67%)
occurrences (all)	2	1	2
Pain in jaw			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Soft tissue swelling			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
BK virus infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Bacteraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Bacterial infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Clostridial infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Clostridium difficile colitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0

Clostridium difficile infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Corona virus infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cytomegalovirus infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	3
Device related infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Endocarditis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Enterobacter bacteraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Epstein-Barr virus infection			
subjects affected / exposed	1 / 14 (7.14%)	1 / 21 (4.76%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Escherichia sepsis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gingivitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Hepatitis E			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Human bocavirus infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Klebsiella bacteraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Klebsiella infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Localised infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Lung infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Mucosal infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Pneumonia parainfluenzae viral			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Proctitis herpes			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rhinovirus infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sepsis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Staphylococcal sepsis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Viraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Viral infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Viral upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 14 (14.29%)	4 / 21 (19.05%)	3 / 15 (20.00%)
occurrences (all)	2	4	3
Fluid intake reduced			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Fluid retention			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hypernatraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hypertriglyceridaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypochloraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Hypoglycaemia			

subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	3	0	1
Hypokalaemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Hypomagnesaemia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 21 (4.76%)	2 / 15 (13.33%)
occurrences (all)	2	1	3
Hyponatraemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Hypophagia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Hypophosphataemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Magnesium deficiency			
subjects affected / exposed	0 / 14 (0.00%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 21 (4.76%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Vitamin D deficiency			
subjects affected / exposed	1 / 14 (7.14%)	0 / 21 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	4.5 mg/kg posaconazole (7-17 years old)	6.0 mg/kg posaconazole (2-<7 years old)	6.0 mg/kg posaconazole (7-17 years old)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	19 / 20 (95.00%)	29 / 29 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Vascular disorders			

Capillary leak syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Flushing			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Hyperaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Hypertension			
subjects affected / exposed	1 / 16 (6.25%)	6 / 20 (30.00%)	4 / 29 (13.79%)
occurrences (all)	1	6	4
Hypotension			
subjects affected / exposed	2 / 16 (12.50%)	1 / 20 (5.00%)	2 / 29 (6.90%)
occurrences (all)	2	1	2
Pallor			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Venoocclusive disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Axillary pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Catheter site erythema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Catheter site haemorrhage			

subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Catheter site oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	2
Catheter site pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	2
Catheter site swelling			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Fatigue			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
General physical health deterioration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	3
Generalised oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Granuloma			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Infusion site erythema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	2
Mucosal inflammation			

subjects affected / exposed	4 / 16 (25.00%)	5 / 20 (25.00%)	6 / 29 (20.69%)
occurrences (all)	4	5	6
Oedema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	2 / 29 (6.90%)
occurrences (all)	0	1	2
Pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	10 / 16 (62.50%)	8 / 20 (40.00%)	8 / 29 (27.59%)
occurrences (all)	13	8	12
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 16 (0.00%)	2 / 20 (10.00%)	2 / 29 (6.90%)
occurrences (all)	0	2	3
Engraftment syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Graft versus host disease			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	2
Graft versus host disease in liver			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Graft versus host disease in skin			

subjects affected / exposed	1 / 16 (6.25%)	2 / 20 (10.00%)	1 / 29 (3.45%)
occurrences (all)	1	2	1
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 20 (10.00%)	0 / 29 (0.00%)
occurrences (all)	0	2	0
Immunodeficiency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Immunodeficiency common variable			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Serum sickness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Metrorrhagia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Perineal erythema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Perineal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Scrotal oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Testicular oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal inflammation			

subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pruritus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	3 / 29 (10.34%)
occurrences (all)	1	0	3
Dysphonia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Epistaxis			
subjects affected / exposed	5 / 16 (31.25%)	1 / 20 (5.00%)	3 / 29 (10.34%)
occurrences (all)	8	1	4
Haemoptysis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Hypoxia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	1 / 29 (3.45%)
occurrences (all)	1	1	1
Increased viscosity of bronchial secretion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Lung infiltration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Oropharyngeal pain			

subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	3 / 29 (10.34%)
occurrences (all)	0	0	3
Pharyngeal inflammation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Pleuritic pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Pulmonary oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Rales			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Tachypnoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Tonsillar exudate			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1

Anxiety			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Depressed mood			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Irritability			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	5 / 29 (17.24%)
occurrences (all)	0	1	5
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	5 / 29 (17.24%)
occurrences (all)	1	0	6
BK polyomavirus test positive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Bacterial test positive			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Blood albumin decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			

subjects affected / exposed	2 / 16 (12.50%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Blood calcium decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Blood culture positive			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Blood immunoglobulin G decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Blood magnesium decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Blood phosphorus decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Blood potassium increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Blood urea increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Blood uric acid decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0

Blood uric acid increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Breath sounds abnormal			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Cytomegalovirus test positive			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Drug level increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Fibrin D dimer increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Fluid balance positive			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Oxygen saturation decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	2
Platelet count decreased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	2 / 29 (6.90%)
occurrences (all)	2	1	2
Pulmonary arterial pressure increased			

subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Red blood cells urine positive			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Transaminases increased			
subjects affected / exposed	3 / 16 (18.75%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	3	0	0
Viral test positive			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Vitamin D decreased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Weight increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
White blood cell count decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Allergic transfusion reaction			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Buttock injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Eye contusion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Head injury			

subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	1	1	0
Procedural pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Scratch			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Transfusion reaction			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	1 / 29 (3.45%)
occurrences (all)	1	1	1
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Pericardial effusion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Sinus bradycardia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Headache			

subjects affected / exposed	5 / 16 (31.25%)	1 / 20 (5.00%)	5 / 29 (17.24%)
occurrences (all)	6	1	7
Hypoaesthesia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	2
Hypotonia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Intention tremor			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Myoclonus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Opisthotonus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	2 / 16 (12.50%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	3 / 16 (18.75%)	2 / 20 (10.00%)	2 / 29 (6.90%)
occurrences (all)	4	2	3
Disseminated intravascular coagulation			

subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Febrile neutropenia			
subjects affected / exposed	2 / 16 (12.50%)	7 / 20 (35.00%)	7 / 29 (24.14%)
occurrences (all)	2	7	8
Leukopenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Pancytopenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	2 / 16 (12.50%)	1 / 20 (5.00%)	2 / 29 (6.90%)
occurrences (all)	2	3	4
Ear and labyrinth disorders			
Ear haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Tinnitus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Vertigo			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Conjunctival haemorrhage			

subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Dry eye			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	2 / 29 (6.90%)
occurrences (all)	1	1	2
Eye haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Eye irritation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Eyelid oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Ocular hyperaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Periorbital oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Photophobia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	2
Visual impairment			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1

Abdominal distension			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	6 / 16 (37.50%)	2 / 20 (10.00%)	5 / 29 (17.24%)
occurrences (all)	8	2	7
Abdominal pain upper			
subjects affected / exposed	0 / 16 (0.00%)	2 / 20 (10.00%)	2 / 29 (6.90%)
occurrences (all)	0	2	2
Anal fissure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Anal inflammation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Anorectal discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Anorectal disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Aphthous ulcer			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Ascites			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Colitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	4 / 29 (13.79%)
occurrences (all)	1	0	4
Diarrhoea			
subjects affected / exposed	4 / 16 (25.00%)	5 / 20 (25.00%)	4 / 29 (13.79%)
occurrences (all)	4	6	5

Dyspepsia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Faeces hard			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Gingival pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Glossodynia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Haematemesis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Lip dry			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1

Lip pruritus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Loose tooth			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Mouth ulceration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	3 / 16 (18.75%)	2 / 20 (10.00%)	7 / 29 (24.14%)
occurrences (all)	5	2	9
Odynophagia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Oesophagitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Oral disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Oral mucosal blistering			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Oral mucosal exfoliation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Scalloped tongue			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0

Stomatitis			
subjects affected / exposed	1 / 16 (6.25%)	3 / 20 (15.00%)	6 / 29 (20.69%)
occurrences (all)	1	3	6
Subileus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Tongue haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Tooth loss			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	6 / 16 (37.50%)	6 / 20 (30.00%)	6 / 29 (20.69%)
occurrences (all)	8	8	13
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Hyperbilirubinaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Jaundice			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Blister			

subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Dermatitis atopic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Dermatitis bullous			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Dermatitis contact			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Dermatitis diaper			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Drug eruption			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	2
Dry skin			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	1 / 16 (6.25%)	3 / 20 (15.00%)	1 / 29 (3.45%)
occurrences (all)	1	4	1
Erythema multiforme			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	2	0
Macule			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Night sweats			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Palmar erythema			

subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Papule			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	2 / 16 (12.50%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	2	0	1
Pruritus			
subjects affected / exposed	5 / 16 (31.25%)	4 / 20 (20.00%)	7 / 29 (24.14%)
occurrences (all)	5	5	7
Pruritus allergic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	2 / 16 (12.50%)	4 / 20 (20.00%)	3 / 29 (10.34%)
occurrences (all)	2	6	3
Rash generalised			
subjects affected / exposed	0 / 16 (0.00%)	2 / 20 (10.00%)	0 / 29 (0.00%)
occurrences (all)	0	2	0
Rash macular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Rash pruritic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Skin burning sensation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			

subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Skin mass			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Skin ulcer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Cystitis haemorrhagic			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	1 / 29 (3.45%)
occurrences (all)	1	1	1
Dysuria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Glycosuria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1

Nephropathy toxic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Urinary retention			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	3 / 16 (18.75%)	1 / 20 (5.00%)	3 / 29 (10.34%)
occurrences (all)	4	1	3
Bone pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Joint range of motion decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Muscle tightness			

subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	3 / 29 (10.34%)
occurrences (all)	1	0	3
Pain in extremity			
subjects affected / exposed	3 / 16 (18.75%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	5	1	0
Pain in jaw			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Soft tissue swelling			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
BK virus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Bacteraemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Bacterial infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0

Clostridial infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Corona virus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Cytomegalovirus infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	2 / 29 (6.90%)
occurrences (all)	1	1	2
Device related infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Endocarditis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Enterobacter bacteraemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Epstein-Barr virus infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	2 / 29 (6.90%)
occurrences (all)	0	1	2

Escherichia sepsis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Gingivitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Hepatitis E			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Human bocavirus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	2
Klebsiella bacteraemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Klebsiella infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	2
Mucosal infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1

Paronychia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Pneumonia parainfluenzae viral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Proctitis herpes			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Rhinovirus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Sepsis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Staphylococcal infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Staphylococcal sepsis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0

Viraemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 16 (6.25%)	3 / 20 (15.00%)	4 / 29 (13.79%)
occurrences (all)	1	3	4
Fluid intake reduced			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Fluid retention			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	1	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Hypernatraemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 20 (10.00%)	2 / 29 (6.90%)
occurrences (all)	0	2	2
Hypocalcaemia			

subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Hypochloraemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	3 / 16 (18.75%)	3 / 20 (15.00%)	7 / 29 (24.14%)
occurrences (all)	3	3	8
Hypomagnesaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 20 (0.00%)	4 / 29 (13.79%)
occurrences (all)	1	0	5
Hyponatraemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Hypophagia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 16 (0.00%)	3 / 20 (15.00%)	1 / 29 (3.45%)
occurrences (all)	0	3	1
Magnesium deficiency			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Metabolic acidosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 20 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2015	Amendment 1: The primary reason for the amendment was to note a change in the suspension vehicle used to prepare the oral formulation of the study medication. In the initial protocol the oral formulation was called oral granules for suspension (OGS) and was to be suspended in water. In amendment 1 the suspension vehicle was changed to Oral-Blend and the name of the oral formulation was changed to powder for oral suspension (PFS).
15 May 2017	Amendment 2: The primary reason for this amendment was to add a third dose cohort of 6mg/kg. Based on interim analysis of the first 2 dose cohorts, the primary PK targets were not met in both age groups for both formulations (oral and IV). In addition the number of participants enrolled in a dedicated safety cohort was increased.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported