Clinical trial results:
Phase 1B Study of the Safety, Tolerance, and Pharmacokinetics of Oral Posaconazole in Immunocompromised Children With Neutropenia

Summary

EudraCT number	2007-004645-15
Trial protocol	IT DE NL GR Outside EU/EEA
Global end of trial date	01 April 2015

Results information

Result version number	v2 (current)
This version publication date	23 March 2016
First version publication date	29 January 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	MK-5592-032

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01716234
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Protocol Code: P03579

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., +1 800-672-6372, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., +1 800-672-6372, 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	01 April 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 April 2015
Global end of trial reached?	Yes
Global end of trial date	01 April 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this dose-escalation study was to evaluate the pharmacokinetics, safety, and tolerability of oral posaconazole (POS) in immunocompromised children with neutropenia or expected neutropenia.

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.

The following additional measures defined for this individual study were in place for the protection of trial subjects: 1) for any subject who meets institutional criteria to start standard empirical or pre-emptive antifungal therapy or who has a proven breakthrough fungal infection, posaconazole will be discontinued and pre-emptive or empirical therapy with standard of care will be initiated, 2) study drug will not be administered to the higher dosage group in a given age group until after safety data obtained in at least 6 completed subjects in the lower dosage group in a corresponding age group are reviewed independently by the external Data Monitoring Committee and the Sponsor, and 3) the subjects in the youngest age group (3 months to <2 years of age) will not be enrolled until all safety and pharmacokinetics data obtained from the two older age groups in the first two dosage levels are reviewed independently by the Sponsor and external Data Monitoring Committee.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 April 2008
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	Canada: 22
Country: Number of subjects enrolled	Greece: 9
Country: Number of subjects enrolled	Netherlands: 15
Country: Number of subjects enrolled	United States: 52
Country: Number of subjects enrolled	Germany: 44
Worldwide total number of subjects	142
EEA total number of subjects	68

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)	1
Children (2-11 years)	95
Adolescents (12-17 years)	46
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Within a given age group, escalation to the next higher dosage level will be permitted only after mutual agreement by the sponsor and the external Data Monitoring Committee.

Pre-assignment

Screening details:

The study enrolled immunocompromised children with neutropenia or expected neutropenia aged 3 months to <18 years. A total of 160 participants were screened, 142 were randomized / enrolled, and 136 were treated. An arm aged 3 months to <2 years planned to receive posaconazole 18 mg/kg/day TID was never initiated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	POS 12 BID 2 to <7 Years

Arm description:

Participants aged 2 to <7 years received posaconazole oral suspension 12 mg/kg/day divided into 2 doses (BID) until recovery from neutropenia or up to 28 days.

Arm type	Experimental
Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	MK-5592, SCH 56592, Noxafil®
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Posaconazole oral suspension 12 mg/kg/day divided into 2 doses (BID) (maximum 800 mg/day)

Arm title	POS 12 BID 7 to <18 Years

Arm description:

Participants aged 7 to <18 years received posaconazole oral suspension 12 mg/kg/day divided into 2 doses (BID) until recovery from neutropenia or up to 28 days.

Arm type	Experimental
Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	MK-5592, SCH 56592, Noxafil®
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Posaconazole oral suspension 12 mg/kg/day divided into 2 doses (BID) (maximum 800 mg/day)

Arm title	POS 18 BID 2 to <7 Years

Arm description:

Participants aged 2 to <7 years received posaconazole oral suspension 18 mg/kg/day divided into 2 doses (BID) until recovery from neutropenia or up to 28 days.

Arm type	Experimental

Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	MK-5592, SCH 56592, Noxafil®
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Posaconazole oral suspension 18 mg/kg/day divided into 2 doses (BID) (maximum 1200 mg/day)

Arm title	POS 18 BID 7 to <18 Years

Arm description:

Participants aged 7 to <18 years received posaconazole oral suspension 18 mg/kg/day divided into 2 doses (BID) until recovery from neutropenia or up to 28 days.

Arm type	Experimental
Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	MK-5592, SCH 56592, Noxafil®
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Posaconazole oral suspension 18 mg/kg/day divided into 2 doses (BID) (maximum 1200 mg/day)

Arm title	POS 18 TID 2 to <7 Years

Arm description:

Participants aged 2 to <7 years received posaconazole oral suspension 18 mg/kg/day divided into 3 doses (TID) until recovery from neutropenia or up to 28 days.

Arm type	Experimental
Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	MK-5592, SCH 56592, Noxafil®
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Posaconazole oral suspension 18 mg/kg/day divided into 3 doses (TID) (maximum 1200 mg/day)

Arm title	POS 18 TID 7 to <18 Years

Arm description:

Participants aged 7 to <18 years received posaconazole oral suspension 18 mg/kg/day divided into 3 doses (TID) until recovery from neutropenia or up to 28 days.

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Other name	MK-5592, SCH 56592, Noxafil®
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Posaconazole oral suspension 18 mg/kg/day divided into 3 doses (TID) (maximum 1200 mg/day)

Arm title	POS 12 TID 3 months to <2 Years

Arm description:

Participants aged 3 months to <2 years received posaconazole oral suspension 12 mg/kg/day divided into 3 doses (TID) until recovery from neutropenia or up to 28 days.

Arm type	Experimental

Investigational medicinal product name	Posaconazole
Investigational medicinal product code	
Other name	MK-5592, SCH 56592, Noxafil®
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Posaconazole oral suspension 12 mg/kg/day divided into 3 doses (TID) (maximum 800 mg/day)

Number of subjects in period 1	POS 12 BID 2 to <7 Years	POS 12 BID 7 to <18 Years	POS 18 BID 2 to <7 Years
Started	24	22	20
Treated	22	21	19
Completed	14	12	15
Not completed	10	10	5
Did not meet protocol eligibility	-	-	1
Consent withdrawn by subject	3	-	2
Adverse event, non-fatal	7	10	2
Protocol deviation	-	-	-
Lack of efficacy	-	-	-

Number of subjects in period 1	POS 18 BID 7 to <18 Years	POS 18 TID 2 to <7 Years	POS 18 TID 7 to <18 Years
Started	28	15	32
Treated	28	15	30
Completed	16	10	18
Not completed	12	5	14
Did not meet protocol eligibility	-	-	4
Consent withdrawn by subject	2	1	3
Adverse event, non-fatal	8	3	6
Protocol deviation	1	1	1
Lack of efficacy	1	-	-

Number of subjects in period 1	POS 12 TID 3 months to <2 Years
Started	1
Treated	1
Completed	1
Not completed	0
Did not meet protocol eligibility	-
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Protocol deviation	-
Lack of efficacy	-

Baseline characteristics

Reporting groups	
Reporting group title	POS 12 BID 2 to <7 Years
Reporting group description:	
Participants aged 2 to <7 years received posaconazole oral suspension 12 mg/kg/day divided into 2 doses (BID) until recovery from neutropenia or up to 28 days.	
Reporting group title	POS 12 BID 7 to <18 Years
Reporting group description:	
Participants aged 7 to <18 years received posaconazole oral suspension 12 mg/kg/day divided into 2 doses (BID) until recovery from neutropenia or up to 28 days.	
Reporting group title	POS 18 BID 2 to <7 Years
Reporting group description:	
Participants aged 2 to <7 years received posaconazole oral suspension 18 mg/kg/day divided into 2 doses (BID) until recovery from neutropenia or up to 28 days.	
Reporting group title	POS 18 BID 7 to <18 Years
Reporting group description:	
Participants aged 7 to <18 years received posaconazole oral suspension 18 mg/kg/day divided into 2 doses (BID) until recovery from neutropenia or up to 28 days.	
Reporting group title	POS 18 TID 2 to <7 Years
Reporting group description:	
Participants aged 2 to <7 years received posaconazole oral suspension 18 mg/kg/day divided into 3 doses (TID) until recovery from neutropenia or up to 28 days.	
Reporting group title	POS 18 TID 7 to <18 Years
Reporting group description:	
Participants aged 7 to <18 years received posaconazole oral suspension 18 mg/kg/day divided into 3 doses (TID) until recovery from neutropenia or up to 28 days.	
Reporting group title	POS 12 TID 3 months to <2 Years
Reporting group description:	
Participants aged 3 months to <2 years received posaconazole oral suspension 12 mg/kg/day divided into 3 doses (TID) until recovery from neutropenia or up to 28 days.	

Reporting group values	POS 12 BID 2 to <7 Years	POS 12 BID 7 to <18 Years	POS 18 BID 2 to <7 Years
Number of subjects	24	22	20
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	4	11.9	4.4
standard deviation	± 1.3	± 3.5	± 1.5
Gender Categorical Units: Subjects			
Female	10	12	8
Male	14	10	12

Reporting group values	POS 18 BID 7 to <18 Years	POS 18 TID 2 to <7 Years	POS 18 TID 7 to <18 Years
Number of subjects	28	15	32

Age Categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	12.2	4.1	13.1
standard deviation	± 3.2	± 1.3	± 3
Gender Categorical Units: Subjects			
Female	9	6	14
Male	19	9	18

Reporting group values	POS 12 TID 3 months to <2 Years	Total	
Number of subjects	1	142	
Age Categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	0.9		
standard deviation	± 0	-	
Gender Categorical Units: Subjects			
Female	0	59	
Male	1	83	

End points

End points reporting groups

Reporting group title	POS 12 BID 2 to <7 Years
Reporting group description:	
Participants aged 2 to <7 years received posaconazole oral suspension 12 mg/kg/day divided into 2 doses (BID) until recovery from neutropenia or up to 28 days.	
Reporting group title	POS 12 BID 7 to <18 Years
Reporting group description:	
Participants aged 7 to <18 years received posaconazole oral suspension 12 mg/kg/day divided into 2 doses (BID) until recovery from neutropenia or up to 28 days.	
Reporting group title	POS 18 BID 2 to <7 Years
Reporting group description:	
Participants aged 2 to <7 years received posaconazole oral suspension 18 mg/kg/day divided into 2 doses (BID) until recovery from neutropenia or up to 28 days.	
Reporting group title	POS 18 BID 7 to <18 Years
Reporting group description:	
Participants aged 7 to <18 years received posaconazole oral suspension 18 mg/kg/day divided into 2 doses (BID) until recovery from neutropenia or up to 28 days.	
Reporting group title	POS 18 TID 2 to <7 Years
Reporting group description:	
Participants aged 2 to <7 years received posaconazole oral suspension 18 mg/kg/day divided into 3 doses (TID) until recovery from neutropenia or up to 28 days.	
Reporting group title	POS 18 TID 7 to <18 Years
Reporting group description:	
Participants aged 7 to <18 years received posaconazole oral suspension 18 mg/kg/day divided into 3 doses (TID) until recovery from neutropenia or up to 28 days.	
Reporting group title	POS 12 TID 3 months to <2 Years
Reporting group description:	
Participants aged 3 months to <2 years received posaconazole oral suspension 12 mg/kg/day divided into 3 doses (TID) until recovery from neutropenia or up to 28 days.	

Primary: Average Concentration of Posaconazole (Cavg) on Day 1 (Single Dose)

End point title	Average Concentration of Posaconazole (Cavg) on Day 1 (Single Dose)[1]
End point description:	
Blood samples for determination of plasma posaconazole concentration were collected predose and approximately 3, 5, 8, and 12 hours after the first dose on Day 1. The 12-hour sample was not obtained for the TID dose groups. Day 1 pharmacokinetic samples were not collected for participants 3 months to <2 years of age weighing <6.5 kg. The pharmacokinetic evaluable population included all treated participants with evaluable samples applicable to the endpoint.	
End point type	Primary
End point timeframe:	
Up to 12 hours after the first dose (BID dose groups) or up to 8 hours after the first dose (TID dose (TID dose groups)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics were planned for Average Concentration of Posaconazole (Cavg) on Day 1 (Single Dose), including means and standard deviations.

End point values	POS 12 BID 2 to <7 Years	POS 12 BID 7 to <18 Years	POS 18 BID 2 to <7 Years	POS 18 BID 7 to <18 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	19	12	12
Units: ng/mL				
arithmetic mean (standard deviation)	122 (± 101)	107 (± 92.5)	112 (± 86.9)	113 (± 100)

End point values	POS 18 TID 2 to <7 Years	POS 18 TID 7 to <18 Years	POS 12 TID 3 months to <2 Years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	10	1	
Units: ng/mL				
arithmetic mean (standard deviation)	68.4 (± 40.4)	57.9 (± 30.2)	68.5 (± 0)	

Statistical analyses

No statistical analyses for this end point

Primary: Average Concentration of Posaconazole (Cavg) on Day 7 (Steady State)

End point title	Average Concentration of Posaconazole (Cavg) on Day 7 (Steady State)[2]

End point description:

Blood samples for determination of plasma posaconazole concentration were collected predose and approximately 3, 5, 8, and 12 hours after the first dose on Day 7 (steady state). The 12-hour sample was not obtained for the TID dose groups. The pharmacokinetic evaluable population included alltreated participants with evaluable samples applicable to the endpoint. The target Cavg range was 500to <2500 ng/mL.

End point type	Primary

End point timeframe:

Up to 12 hours after the first dose on Day 7 (BID dose groups) or up to 8 hours after the first dose on Day 7 (TID dose groups)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics were planned for Average Concentration of Posaconazole (Cavg) on Day 7 (Steady State), including means and standard deviations.

End point values	POS 12 BID 2 to <7 Years	POS 12 BID 7 to <18 Years	POS 18 BID 2 to <7 Years	POS 18 BID 7 to <18 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	14	12	12
Units: ng/mL				
arithmetic mean (standard deviation)	604 (± 779)	1050 (± 789)	485 (± 306)	1240 (± 1400)

End point values	POS 18 TID 2 to <7 Years	POS 18 TID 7 to <18 Years	POS 12 TID 3 months to <2 Years	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	10	1	
Units: ng/mL				
arithmetic mean (standard deviation)	620 (± 411)	1150 (± 750)	453 (± 0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with an Adverse Event

End point title	Number of Participants with an Adverse Event

End point description:

An adverse event is any untoward medical occurrence in a participant administered a pharmaceutical product, biologic (at any dose), or medical device, which does not necessarily have a causal relationship with the treatment. Adverse events may include the onset of new illness and the exacerbation of preexisting conditions. The population analyzed was all treated participants.

End point type	Secondary

End point timeframe:

Up to Day 58

End point values	POS 12 BID 2 to <7 Years	POS 12 BID 7 to <18 Years	POS 18 BID 2 to <7 Years	POS 18 BID 7 to <18 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	19	28
Units: Participants	21	21	16	26

End point values	POS 18 TID 2 to <7 Years	POS 18 TID 7 to <18 Years	POS 12 TID 3 months to <2 Years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	30	1	
Units: Participants	13	30	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with an Adverse Event Leading to Study Drug Discontinuation

End point title	Number of Participants with an Adverse Event Leading to Study Drug Discontinuation

End point description:

An adverse event is any untoward medical occurrence in a participant administered a pharmaceutical product, biologic (at any dose), or medical device, which does not necessarily have a causal relationship

with the treatment. Adverse events may include the onset of new illness and the exacerbation of preexisting conditions. The population analyzed was all treated participants.

End point type	Secondary

End point timeframe:

Up to Day 28

End point values	POS 12 BID 2 to <7 Years	POS 12 BID 7 to <18 Years	POS 18 BID 2 to <7 Years	POS 18 BID 7 to <18 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	19	28
Units: Participants	7	9	2	9

End point values	POS 18 TID 2 to <7 Years	POS 18 TID 7 to <18 Years	POS 12 TID 3 months to <2 Years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	30	1	
Units: Participants	3	6	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs: from Day 1 up to Day 39; SAEs: up to Day 58

Adverse event reporting additional description:

The population analyzed is all treated participants.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	POS 12 BID 2 to <7 yrs

Reporting group description:

Participants aged 2 to <7 years received posaconazole oral suspension 12 mg/kg/day divided into 2 doses (BID) until
recovery from neutropenia or up to 28 days.

Reporting group title	POS 12 BID 7 to <18 yrs

Reporting group description:

Participants aged 7 to <18 years received posaconazole oral suspension 12 mg/kg/day divided into 2 doses (BID) until
recovery from neutropenia or up to 28 days.

Reporting group title	POS 18 BID 2 to <7 yrs

Reporting group description:

Participants aged 2 to <7 years received posaconazole oral suspension 18 mg/kg/day divided into 2 doses (BID) until
recovery from neutropenia or up to 28 days.

Reporting group title	POS 18 BID 7 to <18 yrs

Reporting group description:

Participants aged 7 to <18 years received posaconazole oral suspension 18 mg/kg/day divided into 2 doses (BID) until
recovery from neutropenia or up to 28 days.

Reporting group title	POS 18 TID 2 to <7 yrs

Reporting group description:

Participants aged 2 to <7 years received posaconazole oral suspension 18 mg/kg/day divided into 3 doses (TID) until
recovery from neutropenia or up to 28 days.

Reporting group title	POS 18 TID 7 to <18 yrs

Reporting group description:

Participants aged 7 to <18 years received posaconazole oral suspension 18 mg/kg/day divided into 3 doses (TID) until
recovery from neutropenia or up to 28 days.

Reporting group title	POS 12 TID 3 months to <2 yrs

Reporting group description:

Participants aged 3 months to <2 years received posaconazole oral suspension 12 mg/kg/day divided into 3 doses (TID) until
recovery from neutropenia or up to 28 days.

Serious adverse events	POS 12 BID 2 to <7 yrs	POS 12 BID 7 to <18 yrs	POS 18 BID 2 to <7 yrs
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 22 (22.73%)	3 / 21 (14.29%)	1 / 19 (5.26%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Burkitt's Lymphoma Recurrent			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Hypothermia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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
Mucosal Inflammation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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
Multi-Organ Failure			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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
Pyrexia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (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
Immune system disorders			
Anaphylactic Reaction			

subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	0 / 19 (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
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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
Epistaxis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (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
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (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
Chemotherapeutic Drug Level Increased			

subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (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
Electrocardiogram T Wave Inversion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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
Transaminases Increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (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
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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			
Headache			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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
Seizure			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	0 / 19 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile Neutropenia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (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

Neutropenia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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
Thrombocytopenia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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 Haemorrhage			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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
Hepatic Vein Occlusion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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 Disease			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venoocclusive Liver Disease			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin Lesion			

subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Catheter Site Cellulitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (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
Pneumonia Klebsiella			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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
Puncture Site Infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (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
Sepsis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (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 Bacteraemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	POS 18 BID 7 to <18 yrs	POS 18 TID 2 to <7 yrs	POS 18 TID 7 to <18 yrs
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 28 (25.00%)	7 / 15 (46.67%)	11 / 30 (36.67%)
number of deaths (all causes)	1	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Burkitt's Lymphoma Recurrent			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	0 / 30 (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			
Hypothermia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal Inflammation			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	0 / 30 (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
Multi-Organ Failure			
subjects affected / exposed	1 / 28 (3.57%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Pyrexia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic Reaction			

subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (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
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
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	1 / 28 (3.57%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
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 Failure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (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
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (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
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (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
Chemotherapeutic Drug Level Increased			

subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (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
Electrocardiogram T Wave Inversion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases Increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (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			
Bradycardia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
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			
Headache			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (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			
Anaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile Neutropenia			
subjects affected / exposed	3 / 28 (10.71%)	5 / 15 (33.33%)	5 / 30 (16.67%)
occurrences causally related to treatment / all	0 / 3	0 / 7	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Neutropenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	0 / 30 (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
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic Haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (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
Hepatic Vein Occlusion			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	0 / 30 (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
Hepatobiliary Disease			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (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 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin Lesion			

subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
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	1 / 28 (3.57%)	0 / 15 (0.00%)	0 / 30 (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
Renal Failure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (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			
Catheter Site Cellulitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (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 Klebsiella			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	0 / 30 (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
Puncture Site Infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	0 / 30 (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
Streptococcal Bacteraemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (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

Serious adverse events	POS 12 TID 3 months to <2 yrs		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Burkitt's Lymphoma Recurrent			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Hypothermia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mucosal Inflammation			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Multi-Organ Failure			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic Reaction			

subjects affected / exposed	0 / 1 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Menorrhagia				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute Respiratory Distress Syndrome				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory Failure				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine Aminotransferase Increased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate Aminotransferase Increased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chemotherapeutic Drug Level Increased				

subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Electrocardiogram T Wave Inversion			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transaminases Increased			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile Neutropenia			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic Haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic Vein Occlusion			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary Disease			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Venoocclusive Liver Disease			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin Lesion			

subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal Failure			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Catheter Site Cellulitis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia Klebsiella			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Puncture Site Infection			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Streptococcal Bacteraemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	POS 12 BID 2 to <7 yrs	POS 12 BID 7 to <18 yrs	POS 18 BID 2 to <7 yrs
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 22 (95.45%)	20 / 21 (95.24%)	16 / 19 (84.21%)
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	4 / 22 (18.18%)	1 / 21 (4.76%)	1 / 19 (5.26%)
occurrences (all)	5	1	1
Hypotension			
subjects affected / exposed	1 / 22 (4.55%)	3 / 21 (14.29%)	0 / 19 (0.00%)
occurrences (all)	1	3	0
Pallor			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Venoocclusive Disease			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Central Venous Catheter Removal			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Central Venous Catheterisation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Catheter Site Erythema			
subjects affected / exposed	2 / 22 (9.09%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	2	1	0
Catheter Site Pruritus			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Chills			

subjects affected / exposed	1 / 22 (4.55%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Device Occlusion			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Local Swelling			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Mucosal Inflammation			
subjects affected / exposed	9 / 22 (40.91%)	3 / 21 (14.29%)	2 / 19 (10.53%)
occurrences (all)	9	3	5
Oedema			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Oedema Peripheral			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	3
Pyrexia			
subjects affected / exposed	13 / 22 (59.09%)	8 / 21 (38.10%)	3 / 19 (15.79%)
occurrences (all)	14	9	3
Vessel Puncture Site Pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Engraftment Syndrome			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Graft Versus Host Disease In Skin			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Reproductive system and breast disorders			
Genital Pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Genital Rash			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Genital Ulceration			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Penile Oedema			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pruritus Genital			
subjects affected / exposed	2 / 22 (9.09%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 22 (9.09%)	3 / 21 (14.29%)	3 / 19 (15.79%)
occurrences (all)	2	3	3
Epistaxis			
subjects affected / exposed	1 / 22 (4.55%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Hypoxia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Nasal Congestion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Oropharyngeal Pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
Pleural Effusion			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Tachypnoea			

subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal Behaviour			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Hallucination			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 22 (4.55%)	1 / 21 (4.76%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Biopsy Skin			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood Bilirubin Increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood Glucose Increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Electrocardiogram QT Prolonged			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Fluid Balance Positive			

subjects affected / exposed	1 / 22 (4.55%)	3 / 21 (14.29%)	0 / 19 (0.00%)
occurrences (all)	1	5	0
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
International Normalised Ratio Decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Lymphocyte Count Decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Neutrophil Count Decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Platelet Count Decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	11
Transaminases Increased			
subjects affected / exposed	2 / 22 (9.09%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	2	1	0
Weight Increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
White Blood Cell Count Decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	3
Injury, poisoning and procedural complications			
Allergic Transfusion Reaction			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Fall			

subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Infusion Related Reaction			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Procedural Headache			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Skin Abrasion			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Transfusion Reaction			
subjects affected / exposed	1 / 22 (4.55%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Congenital, familial and genetic disorders			
Antithrombin III Deficiency			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Sinus Tachycardia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	3 / 22 (13.64%)	2 / 21 (9.52%)	1 / 19 (5.26%)
occurrences (all)	3	2	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 22 (0.00%)	2 / 21 (9.52%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Dysgeusia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Headache			

subjects affected / exposed	1 / 22 (4.55%)	2 / 21 (9.52%)	1 / 19 (5.26%)
occurrences (all)	1	2	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 22 (18.18%)	2 / 21 (9.52%)	3 / 19 (15.79%)
occurrences (all)	6	3	6
Coagulopathy			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Febrile Neutropenia			
subjects affected / exposed	1 / 22 (4.55%)	4 / 21 (19.05%)	0 / 19 (0.00%)
occurrences (all)	1	4	0
Leukopenia			
subjects affected / exposed	5 / 22 (22.73%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	5	0	0
Lymphopenia			
subjects affected / exposed	2 / 22 (9.09%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Neutropenia			
subjects affected / exposed	3 / 22 (13.64%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	3	0	1
Thrombocytopenia			
subjects affected / exposed	8 / 22 (36.36%)	7 / 21 (33.33%)	3 / 19 (15.79%)
occurrences (all)	19	15	10
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	1 / 22 (4.55%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
Conjunctival Hyperaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dry Eye			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Eye Movement Disorder			

subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Eye Pruritus			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
Eye Swelling			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Eyelid Oedema			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Abdominal Pain			
subjects affected / exposed	7 / 22 (31.82%)	6 / 21 (28.57%)	1 / 19 (5.26%)
occurrences (all)	7	7	1
Abdominal Pain Upper			
subjects affected / exposed	2 / 22 (9.09%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
Ascites			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 22 (0.00%)	4 / 21 (19.05%)	1 / 19 (5.26%)
occurrences (all)	0	4	1
Diarrhoea			
subjects affected / exposed	5 / 22 (22.73%)	3 / 21 (14.29%)	3 / 19 (15.79%)
occurrences (all)	5	3	5
Dyspepsia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Enteritis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Frequent Bowel Movements			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gingival Pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Lip Dry			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Loose Tooth			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	5 / 22 (22.73%)	3 / 21 (14.29%)	2 / 19 (10.53%)
occurrences (all)	8	3	5
Oral Pain			
subjects affected / exposed	0 / 22 (0.00%)	2 / 21 (9.52%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Proctalgia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Proctitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	3 / 22 (13.64%)	0 / 21 (0.00%)	2 / 19 (10.53%)
occurrences (all)	4	0	2
Tongue Coated			
subjects affected / exposed	1 / 22 (4.55%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	1	1	0

Vomiting			
subjects affected / exposed	8 / 22 (36.36%)	3 / 21 (14.29%)	5 / 19 (26.32%)
occurrences (all)	13	5	6
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dermatitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	3
Dermatitis Diaper			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Ecchymosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	2 / 22 (9.09%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Petechiae			
subjects affected / exposed	2 / 22 (9.09%)	2 / 21 (9.52%)	2 / 19 (10.53%)
occurrences (all)	2	2	2
Pruritus			
subjects affected / exposed	3 / 22 (13.64%)	5 / 21 (23.81%)	1 / 19 (5.26%)
occurrences (all)	3	5	1
Rash			
subjects affected / exposed	4 / 22 (18.18%)	1 / 21 (4.76%)	2 / 19 (10.53%)
occurrences (all)	4	1	3
Red Man Syndrome			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Proteinuria			

subjects affected / exposed	1 / 22 (4.55%)	2 / 21 (9.52%)	0 / 19 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	1 / 22 (4.55%)	2 / 21 (9.52%)	1 / 19 (5.26%)
occurrences (all)	1	2	1
Bone Pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Pain In Extremity			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Infections and infestations			
Alpha Haemolytic Streptococcal Infection			
subjects affected / exposed	0 / 22 (0.00%)	2 / 21 (9.52%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Bacteraemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Clostridium Difficile Infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gingivitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pseudomonal Bacteraemia			

subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Respiratory Tract Infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	3
Sinusitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Streptococcal Infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Viraemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Viral Infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vulvitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Fluid Overload			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hyperalbuminaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Hypertriglyceridaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Hypoglycaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	2 / 22 (9.09%)	3 / 21 (14.29%)	1 / 19 (5.26%)
occurrences (all)	2	6	1
Hypomagnesaemia			
subjects affected / exposed	1 / 22 (4.55%)	4 / 21 (19.05%)	0 / 19 (0.00%)
occurrences (all)	1	4	0
Hyponatraemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	2 / 22 (9.09%)	2 / 21 (9.52%)	0 / 19 (0.00%)
occurrences (all)	2	2	0

Non-serious adverse events	POS 18 BID 7 to <18 yrs	POS 18 TID 2 to <7 yrs	POS 18 TID 7 to <18 yrs
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 28 (92.86%)	13 / 15 (86.67%)	28 / 30 (93.33%)
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	3 / 28 (10.71%)	2 / 15 (13.33%)	2 / 30 (6.67%)
occurrences (all)	3	3	2
Hypotension			

subjects affected / exposed	3 / 28 (10.71%)	2 / 15 (13.33%)	2 / 30 (6.67%)
occurrences (all)	3	2	2
Pallor			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Venoocclusive Disease			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Central Venous Catheter Removal			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Central Venous Catheterisation			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Catheter Site Erythema			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Catheter Site Pruritus			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Chills			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	3 / 30 (10.00%)
occurrences (all)	1	0	3
Device Occlusion			
subjects affected / exposed	2 / 28 (7.14%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	3	0	0
Fatigue			
subjects affected / exposed	3 / 28 (10.71%)	0 / 15 (0.00%)	6 / 30 (20.00%)
occurrences (all)	3	0	7
Local Swelling			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Mucosal Inflammation			

subjects affected / exposed	7 / 28 (25.00%)	1 / 15 (6.67%)	4 / 30 (13.33%)
occurrences (all)	7	1	4
Oedema			
subjects affected / exposed	2 / 28 (7.14%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences (all)	2	0	1
Oedema Peripheral			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Pyrexia			
subjects affected / exposed	8 / 28 (28.57%)	2 / 15 (13.33%)	6 / 30 (20.00%)
occurrences (all)	10	4	7
Vessel Puncture Site Pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Engraftment Syndrome			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Graft Versus Host Disease In Skin			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Genital Pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Genital Rash			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Genital Ulceration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Penile Oedema			

subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Pruritus Genital			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 28 (3.57%)	2 / 15 (13.33%)	2 / 30 (6.67%)
occurrences (all)	1	2	2
Epistaxis			
subjects affected / exposed	2 / 28 (7.14%)	1 / 15 (6.67%)	3 / 30 (10.00%)
occurrences (all)	3	1	4
Hypoxia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Nasal Congestion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal Pain			
subjects affected / exposed	2 / 28 (7.14%)	1 / 15 (6.67%)	4 / 30 (13.33%)
occurrences (all)	2	1	4
Pleural Effusion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	2 / 28 (7.14%)	1 / 15 (6.67%)	1 / 30 (3.33%)
occurrences (all)	2	1	1
Psychiatric disorders			
Abnormal Behaviour			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Agitation			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Hallucination			

subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	3 / 28 (10.71%)	2 / 15 (13.33%)	2 / 30 (6.67%)
occurrences (all)	3	5	2
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 28 (3.57%)	2 / 15 (13.33%)	1 / 30 (3.33%)
occurrences (all)	1	5	1
Biopsy Skin			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Blood Bilirubin Increased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	4	0
Blood Glucose Increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT Prolonged			
subjects affected / exposed	2 / 28 (7.14%)	1 / 15 (6.67%)	2 / 30 (6.67%)
occurrences (all)	2	1	3
Fluid Balance Positive			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
International Normalised Ratio Decreased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Lymphocyte Count Decreased			

subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	5
Neutrophil Count Decreased			
subjects affected / exposed	1 / 28 (3.57%)	1 / 15 (6.67%)	2 / 30 (6.67%)
occurrences (all)	1	3	4
Platelet Count Decreased			
subjects affected / exposed	1 / 28 (3.57%)	2 / 15 (13.33%)	4 / 30 (13.33%)
occurrences (all)	1	5	11
Transaminases Increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Weight Increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
White Blood Cell Count Decreased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	3 / 30 (10.00%)
occurrences (all)	0	3	4
Injury, poisoning and procedural complications			
Allergic Transfusion Reaction			
subjects affected / exposed	2 / 28 (7.14%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Contusion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	2
Fall			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Infusion Related Reaction			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Procedural Headache			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Skin Abrasion			

subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Transfusion Reaction			
subjects affected / exposed	2 / 28 (7.14%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Congenital, familial and genetic disorders			
Antithrombin III Deficiency			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Sinus Tachycardia			
subjects affected / exposed	0 / 28 (0.00%)	2 / 15 (13.33%)	1 / 30 (3.33%)
occurrences (all)	0	2	2
Tachycardia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 15 (6.67%)	3 / 30 (10.00%)
occurrences (all)	2	1	4
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	4 / 30 (13.33%)
occurrences (all)	1	0	4
Dysgeusia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	8 / 28 (28.57%)	1 / 15 (6.67%)	3 / 30 (10.00%)
occurrences (all)	10	1	3
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 28 (28.57%)	3 / 15 (20.00%)	6 / 30 (20.00%)
occurrences (all)	12	11	12
Coagulopathy			
subjects affected / exposed	2 / 28 (7.14%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0

Febrile Neutropenia			
subjects affected / exposed	4 / 28 (14.29%)	4 / 15 (26.67%)	5 / 30 (16.67%)
occurrences (all)	4	5	5
Leukopenia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 15 (6.67%)	2 / 30 (6.67%)
occurrences (all)	2	1	2
Thrombocytopenia			
subjects affected / exposed	6 / 28 (21.43%)	1 / 15 (6.67%)	5 / 30 (16.67%)
occurrences (all)	22	2	8
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Conjunctival Hyperaemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Dry Eye			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Eye Movement Disorder			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Eye Pruritus			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Eye Swelling			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Eyelid Oedema			

subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Photophobia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain			
subjects affected / exposed	2 / 28 (7.14%)	3 / 15 (20.00%)	4 / 30 (13.33%)
occurrences (all)	2	3	5
Abdominal Pain Upper			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	2 / 30 (6.67%)
occurrences (all)	1	0	2
Ascites			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Constipation			
subjects affected / exposed	1 / 28 (3.57%)	1 / 15 (6.67%)	4 / 30 (13.33%)
occurrences (all)	1	1	5
Diarrhoea			
subjects affected / exposed	7 / 28 (25.00%)	3 / 15 (20.00%)	5 / 30 (16.67%)
occurrences (all)	7	7	5
Dyspepsia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Enteritis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Frequent Bowel Movements			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Gingival Pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0

Lip Dry			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	3 / 30 (10.00%)
occurrences (all)	0	0	3
Loose Tooth			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	9 / 28 (32.14%)	3 / 15 (20.00%)	13 / 30 (43.33%)
occurrences (all)	9	3	21
Oral Pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	2
Proctalgia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Proctitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Retching			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	4 / 28 (14.29%)	5 / 15 (33.33%)	6 / 30 (20.00%)
occurrences (all)	5	9	8
Tongue Coated			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	11 / 28 (39.29%)	7 / 15 (46.67%)	9 / 30 (30.00%)
occurrences (all)	14	11	14
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Dermatitis			

subjects affected / exposed	1 / 28 (3.57%)	2 / 15 (13.33%)	0 / 30 (0.00%)
occurrences (all)	1	2	0
Dermatitis Diaper			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Erythema			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Petechiae			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Pruritus			
subjects affected / exposed	3 / 28 (10.71%)	2 / 15 (13.33%)	3 / 30 (10.00%)
occurrences (all)	5	5	3
Rash			
subjects affected / exposed	4 / 28 (14.29%)	2 / 15 (13.33%)	5 / 30 (16.67%)
occurrences (all)	5	2	5
Red Man Syndrome			
subjects affected / exposed	1 / 28 (3.57%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Bone Pain			

subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	2 / 30 (6.67%)
occurrences (all)	1	0	2
Pain In Extremity			
subjects affected / exposed	0 / 28 (0.00%)	2 / 15 (13.33%)	3 / 30 (10.00%)
occurrences (all)	0	2	4
Infections and infestations			
Alpha Haemolytic Streptococcal Infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Bacteraemia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 15 (6.67%)	1 / 30 (3.33%)
occurrences (all)	1	1	1
Cellulitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Clostridium Difficile Infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Gingivitis			
subjects affected / exposed	0 / 28 (0.00%)	2 / 15 (13.33%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Pseudomonal Bacteraemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Respiratory Tract Infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Rhinitis			

subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Streptococcal Infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Viraemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Viral Infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Vulvitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1 / 28 (3.57%)	3 / 15 (20.00%)	8 / 30 (26.67%)
occurrences (all)	1	3	9
Fluid Overload			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	2 / 30 (6.67%)
occurrences (all)	0	1	2
Hyperalbuminaemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Hyperglycaemia			
subjects affected / exposed	1 / 28 (3.57%)	2 / 15 (13.33%)	3 / 30 (10.00%)
occurrences (all)	1	4	3
Hypertriglyceridaemia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	1	2	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 28 (0.00%)	2 / 15 (13.33%)	1 / 30 (3.33%)
occurrences (all)	0	4	1

Hypocalcaemia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	1	3	0
Hypoglycaemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	1 / 28 (3.57%)	4 / 15 (26.67%)	2 / 30 (6.67%)
occurrences (all)	2	6	3
Hypomagnesaemia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	2 / 30 (6.67%)
occurrences (all)	2	0	3
Hyponatraemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Hypophosphataemia			
subjects affected / exposed	1 / 28 (3.57%)	2 / 15 (13.33%)	0 / 30 (0.00%)
occurrences (all)	1	3	0

Non-serious adverse events	POS 12 TID 3 months to <2 yrs		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Pallor			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Venoocclusive Disease			

subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Central Venous Catheter Removal			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Central Venous Catheterisation			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Catheter Site Erythema			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Catheter Site Pruritus			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Device Occlusion			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Local Swelling			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Mucosal Inflammation			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Oedema			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Oedema Peripheral			

subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Vessel Puncture Site Pain subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		
Immune system disorders Engraftment Syndrome subjects affected / exposed occurrences (all) Graft Versus Host Disease In Skin subjects affected / exposed occurrences (all)	 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		
Reproductive system and breast disorders Genital Pain subjects affected / exposed occurrences (all) Genital Rash subjects affected / exposed occurrences (all) Genital Ulceration subjects affected / exposed occurrences (all) Penile Oedema subjects affected / exposed occurrences (all) Pruritus Genital subjects affected / exposed occurrences (all)	 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypoxia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Nasal Congestion			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Oropharyngeal Pain			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Pleural Effusion			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Tachypnoea			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Abnormal Behaviour			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Agitation			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hallucination			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Investigations			

Alanine Aminotransferase Increased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Aspartate Aminotransferase Increased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Biopsy Skin				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Blood Bilirubin Increased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Blood Glucose Increased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Electrocardiogram QT Prolonged				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Fluid Balance Positive				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Gamma-Glutamyltransferase Increased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
International Normalised Ratio Decreased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Lymphocyte Count Decreased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Neutrophil Count Decreased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Platelet Count Decreased				

subjects affected / exposed occurrences (all) Transaminases Increased subjects affected / exposed occurrences (all) Weight Increased subjects affected / exposed occurrences (all) White Blood Cell Count Decreased subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		
Injury, poisoning and procedural complications Allergic Transfusion Reaction subjects affected / exposed occurrences (all) Contusion subjects affected / exposed occurrences (all) Fall subjects affected / exposed occurrences (all) Infusion Related Reaction subjects affected / exposed occurrences (all) Procedural Headache subjects affected / exposed occurrences (all) Skin Abrasion subjects affected / exposed occurrences (all) Transfusion Reaction subjects affected / exposed occurrences (all)	 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		
Congenital, familial and genetic disorders			

Antithrombin III Deficiency			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Sinus Tachycardia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Coagulopathy			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Febrile Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Leukopenia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Lymphopenia			

subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Eye disorders			
Conjunctival Hyperaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dry Eye			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Eye Movement Disorder			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Eye Pruritus			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Eye Swelling			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Eyelid Oedema			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Photophobia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			

Abdominal Distension				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Abdominal Pain				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Abdominal Pain Upper				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Ascites				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Constipation				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Diarrhoea				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Dyspepsia				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Enteritis				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Frequent Bowel Movements				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Gingival Pain				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Lip Dry				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Loose Tooth				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			

Nausea			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Oral Pain			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Proctalgia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Proctitis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Retching			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Tongue Coated			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dermatitis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dermatitis Diaper			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Ecchymosis			

subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all) Petechiae subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Red Man Syndrome subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) Proteinuria subjects affected / exposed occurrences (all)	 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		
Musculoskeletal and connective tissue disorders Back Pain subjects affected / exposed occurrences (all) Bone Pain subjects affected / exposed occurrences (all) Pain In Extremity subjects affected / exposed occurrences (all)	 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		
Infections and infestations			

Alpha Haemolytic Streptococcal Infection				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Bacteraemia				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Cellulitis				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Clostridium Difficile Infection				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Cystitis				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Gingivitis				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Infection				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Pseudomonal Bacteraemia				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Respiratory Tract Infection				
subjects affected / exposed	1 / 1 (100.00%)			
occurrences (all)	1			
Rhinitis				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Sinusitis				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Streptococcal Infection				

subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Viraemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Viral Infection			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Vulvitis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Fluid Overload			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hyperalbuminaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypertriglyceridaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		

Hypokalaemia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Hypophosphataemia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 January 2008	Protocol Amendment 1: this amendment documented a switch from central safety lab collection to local safety lab collection, which addressed concerns raised regarding the volume of blood collection.
17 November 2008	Protocol Amendment 2: This amendment made the following significant changes to the trial design: 1) clarification of the exclusion criteria related to the prohibited medications, 2) protocol has changed in order to reflect potential discontinuation in cases of any related Grade 3 or Grade 4 adverse events, 3) change in the prohibited medications section.
13 October 2010	Protocol Amendment 3: This amendment made the following significant change to the trial design: the following addition was made to the list of clinical situations applicable to inclusion criterion #3: Recipients of allogeneic hematopoietic stem cell transplantation during the pre-engraftment period (neutropenia period).
17 April 2013	Protocol Amendment 4: Several key changes were made based on a review of the available clinical pharmacokinetics and safety pediatric data from this ongoing study: 1) enrollment in Age Group 1 Dose Group 2 (7 to <18 years receiving 18 mg/kg/day divided BID) was stopped early, 2) the dosing schedule for Age Group 3 Dose Group 1 (3 months to <2 years) was changed to 12 mg/kg/day divided TID, 3) the dosing schedule for Age Group 3 Dose Group 2 was changed to 18 mg/kg/day divided TID, 4) for Age Group 3 (3 months to <7 years), Dose Group 3 was removed, and 5) an additional pharmacokinetic and safety analysis was added for all available TID data across age groups.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Study was terminated early (10 July 2015) based on preliminary analysis of pharmacokinetic data. Only 1 participant was enrolled in the POS 12 TID 3 months to <2 years group, limiting conclusions that may be drawn for pharmacokinetics or safety.

Notes: